Efficacy and safety of simultaneous vaccination with two modified live virus vaccines against porcine reproductive and respiratory syndrome virus types 1 and 2 in pigs

The objective of the study was to compare responses of pigs vaccinated with a PRRS MLV vaccine against PRRSV-1 or PRRSV-2 with the responses of pigs vaccinated simultaneously with both vaccines. Furthermore, the efficacy of the two PRRSV MLV vaccination strategies was assessed following challenge. The experimental design included four groups of 4-weeks old SPF-pigs. On day 0 (DPV0), groups 1–3 (N = 18 per group) were vaccinated with modified live virus vaccines (MLV) containing PRRSV-1 virus (VAC-T1), PRRSV-2 virus (VAC-T2) or both (VAC-T1T2). One group was left unvaccinated (N = 12). On DPV 62, the pigs from groups 1–4 were mingled in new groups and challenged (DPC 0) with PRRSV-1, subtype 1, PRRSV-1, subtype 2 or PRRSV-2. On DPC 13/14 all pigs were necropsied. Samples were collected after vaccination and challenge. PRRSV was detected in all vaccinated pigs and the majority of the pigs were positive until DPV 28, but few of the pigs were still viremic 62 days after vaccination. Virus was detected in nasal swabs until DPV 7–14. No overt clinical signs were observed after challenge. PRRSV-2 vaccination resulted in a clear reduction in viral load in serum after PRRSV-2 challenge, whereas there was limited effect on the viral load in serum following challenge with the PRRSV-1 strains. Vaccination against PRRSV-1 had less impact on viremia following challenge. The protective effects of simultaneous vaccination with PRRSV Type 1 and 2 MLV vaccines and single PRRS MLV vaccination were comparable. None of the vaccines decreased the viral load in the lungs at necropsy. In conclusion, simultaneous vaccination with MLV vaccines containing PRRSV-1 and PRRSV-2 elicited responses comparable to single vaccination and the commercial PRRSV vaccines protected only partially against challenge with heterologous strains. Thus, simultaneous administration of the two vaccines is an option in herds with both PRRSV types.

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Authors: Kristensen, C. S. (Ekstern), Kvisgaard, L. K. (Intern), Pawlowski, M. (Intern), Holmgaard Carlsen, S. (Ekstern), Hjulsager, C. K. (Intern), Heegaard, P. M. H. (Intern), Bøtner, A. (Intern), Stadejek, T. (Ekstern), Haugegaard, S. (Ekstern), Larsen, L. (Intern)
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Design, development and experimental trial of a tailored cytotoxic T-cell vaccine against Porcine Reproductive and Respiratory Syndrome Virus-2

Porcine reproductive and respiratory syndrome virus (PRRSV) is one of the most important threats against the global swine production industry. The virus infects alveolar macrophages that leads to respiratory distress, fever, pneumonia and gives way to secondary respiratory pathogens. Infection of sows in late gestation can lead to late term abortion, early farrowing and birth of litters mixed with living, stillborn and mummified fetuses. Two species of PRRSV exist that are closely related in evolution and disease: PRRSV-1 and PRRSV-2. PRRSV has a positive sense RNA genome of about 15 kb and exhibits a high mutation rate that has led to a high degree of diversity within each species. Highly pathogenic strains evolve occasionally with large impact on animal health and production economy. Since its discovery in the late 1980s, massive efforts have been put in the development of an effective vaccine. Inspite of this, the most effective commercial vaccines available are only partly capable of protecting against a heterologous challenge. Furthermore, these vaccines are based on modified live virus that at more than one occasion have mutated back to a virulent form and have thus promoted rather than prevented viral spread. PRRSV exhibits a wide range of immunoevasive mechanisms that manipulate multiple branches of the porcine immune system. However, evidence exist that a cell-mediated immune (CMI) response is capable of clearing the virus from the organism, although this response is somewhat delayed. In the present PhD thesis, I describe the development of an innovative vaccine for the induction of a cytotoxic T lymphocyte response against PRRSV-2.

A major part of the project outline was to design a vaccine that would protect beyond genetic drift, why focus has been on identifying and selecting conserved epitopes specific for swine leukocyte antigen class I (SLA-I). Briefly, all naturally occurring 9- and 10-mer peptides derived from 104 highly curated PRRSV-2 whole genome sequences were analyzed for their predicted binding capacities against five SLA-I alleles. Two methods for epitope prediction was applied (NetMHCpan and Position Scanning Combinatorial peptide library). The outputs of the two methods were combined and the top 2% best candidates were analyzed using the PopCover algorithm, serving to prioritize the candidates according to conservation and SLA allele coverage. Based on this, 53 peptides were purchased for in vitro verification. This was done using the assays Peptide Affinity Assay and Scintillation Proximity Assay for the determination of peptide-SLA (pSLA) binding affinity and stability, respectively. From these analyses it was decided to proceed with three of the five SLAIs in combination with a total of 33 peptides/epitopes. A Classical swine fever virus (CSFV)-based virus replicon particle (VRP) was selected as vaccine platform. This VRP has the same tropism as CSFV and can thus infect dendritic cells that are the major inducers of a CMI response. On basis of this template VRP, 10 vaccine VRPs were designed for the expression of an inserted polypeptide with subsequent degradation via an uncleavable ubiquitining, thereby leading the epitopes into the MHC-I presentation pathway. One VRP was designed as a negative control and encoded an unrelated epitope, while the remaining nine encoded polypeptides of different combinations of the 33 PRRSV-2 epitopes. Infectivity of the VRPs and the induced polypeptide expression and degradation was verified using flow cytometry. 718 pigs of matching SLA profiles were vaccinated three times over a 10-week period with the control VRP (N=7) or the PRRSV-VRPs (N=11). After this, all pigs were inoculated with a Danish PRRSV-2 field strain and were euthanized after an additional four weeks. Seroconversion for both VRP and PRRSV was confirmed for all pigs. The induction of a CMI response was monitored using interferon-γ (IFN-γ) enzyme-linked immunospot (ELISPOT) assay pre challenge, but did unfortunately not provide any useful data. The setup was improved and post challenge ELISPOT provided evidence of a VRP-induced CMI. Viral load was measured post challenge in serum, but did not indicate any effects of vaccination. Viral load in lungs did however indicate an effect that was significant in one part of the lungs. Conclusively, the present study provides proof-of-concept that a peptide-specific CMI can be induced by vaccination with VRPs encoding conserved epitopes, along with indications of a protective effect on viral load in lungs. However, several improvements must be made to the concept before it can be subjected to field trials.

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Organisations: National Veterinary Institute, Virology, Adaptive Immunology, Department of Bio and Health Informatics, Genomic Epidemiology
Authors: Welner, S. (Intern), Larsen, L. E. (Intern), Jungersen, G. (Intern), Lund, O. (Intern)
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Relations
Projects:
Design, development and experimental trial of a tailored cytotoxic T-cell vaccine against Porcine Reproductive and Respiratory Syndrome Virus-2
Evolutionary analysis of whole-genome sequences confirms inter-farm transmission of Aleutian mink disease virus

Aleutian mink disease virus (AMDV) is a frequently encountered pathogen associated with mink farming. Previous phylogenetic analyses of AMDV have been based on shorter and more conserved parts of the genome, e.g. the partial NS1 gene. Such fragments are suitable for detection but are less useful for elucidating transmission pathways while sequencing entire viral genomes provides additional informative sites and often results in better-resolved phylogenies. We explore how whole-genome sequencing can benefit investigations of AMDV transmission by reconstructing the relationships between AMDV field samples from a Danish outbreak. We show that whole-genome phylogenies are much better resolved than those based on the partial NS1 gene sequences extracted from the same alignment. Well-resolved phylogenies contain more information about the underlying transmission trees and are useful for understanding the spread of a pathogen. In the main case investigated here, the transmission path suggested by the tree structure was supported by epidemiological data. The use of molecular clock models further improved tree resolution and provided time estimates for the viral ancestors consistent with the proposed direction of spread. It was however impossible to infer transmission pathways from the partial NS1 gene tree, since all samples from the case farms branched out from a single internal node. A sliding window analysis showed that there were no shorter genomic regions providing the same phylogenetic resolution as the entire genome. Altogether, these results suggest that phylogenetic analyses based on whole-genome sequencing taking into account sampling dates and epidemiological data is a promising set of tools for clarifying AMDV transmission.

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Organisations: Molecular Evolution, Department of Biotechnology and Biomedicine, Department of Bio and Health Informatics, Disease Intelligence and Molecular Evolution, National Veterinary Institute, Virology, Kopenhagen Fur
Authors: Hagberg, E. E. (Intern), Pedersen, A. G. (Intern), Larsen, L. E. (Intern), Krarup, A. (Ekstern)
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Web of Science (2008): Indexed yes
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Forskellige virusstammer var årsag til udbrud af plasmacytose i danske mink (Neovison vison) i 2015

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Genetic and biological characterization of a Porcine Reproductive and Respiratory Syndrome Virus 2 (PRRSV-2) causing significant clinical disease in the field
Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) is the cause of severe reproductive and respiratory disease in swine worldwide. In Denmark, both PRRSV-1 and PRRSV-2 are circulating and approximately 35% of pig herds are seropositive for PRRSV. In November 2010, a pig herd in the Northern part of Denmark experienced an infection with PRRSV-2 with clinical signs that were much more severe than normally reported from current Danish PRRSV-2 affected herds. Due to the clinical observations of reproductive failure in sows and high mortality in piglets, it was speculated that a new, more pathogenic or vaccine evading PRRSV strain had emerged in Denmark. The overall aim
of the present study was to perform a genetic and biological characterization of the virus isolated from the diseased herd. Complete genome sequencing of isolates from this herd revealed that although the case strain had some unique genetic features including a deduced 3 amino acid deletion, it was in overall very similar to the other PRRS-2 viruses circulating in Denmark. In an experimental trial in growing pigs, no overt clinical signs or pathology were observed following intranasal inoculation with the new virus isolate. Virus shedding, acute phase protein responses and serological responses were comparable to those seen after experimental challenge with a Danish PRRSV-2 reference strain isolated in 1997. Vaccination with a commercial modified live PRRSV-2 vaccine had a clear reducing effect on virus shedding, magnitude, and duration of viremia and viral load in the lungs. Overall, the results indicate that the severe disease observed in the field was contributed by additional factors in combination with the PRRS virus infection.
Global phylogenetic analysis of contemporary aleutian mink disease viruses (AMDV)

Aleutian mink disease has major economic consequences on the mink farming industry worldwide, as it causes a disease that affects both the fur quality and the health and welfare of the mink. The virus causing this disease is a single-stranded DNA virus of the genus Amdoparvovirus belonging to the family of Paroviridae. In Denmark, infection with AMDV has largely been restricted to a region in the northern part of the country since 2001, affecting only 5% of the total Danish mink farms. However, in 2015 outbreaks of AMDV were diagnosed in all parts of the country. Initial analyses revealed that the outbreaks were caused by two different strains of AMDV that were significantly different from the circulating Danish strains. To track the source of these outbreaks, a major investigation of global AMDV strains was initiated. Samples from 13 different countries were collected and partial NS1 gene was sequenced and subjected to phylogenetic analyses. The analyses revealed that AMDV exhibited substantial genetic diversity. No clear country-wise clustering was evident, but exchange of viruses between countries was revealed. One of the Danish outbreaks was caused by a strain of AMDV that closely resembled a strain originating from Sweden. In contrast, we did not identify any potential source for the other and more widespread outbreak strain. To the authors' knowledge, this is the first major global phylogenetic study of contemporary AMDV partial NS1 sequences. The study proved that partial NS1 sequencing can be used to distinguish
virus strains belonging to major clusters. The partial NS1 sequencing can therefore be a helpful tool in combination with epidemiological data, in relation to outbreak tracking. However detailed information on farm to farm transmission requires full genome sequencing.

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Scopus rating (2009): SJR 0.986 SNIP 0.754
Scopus rating (2008): SJR 0.618 SNIP 0.537
Web of Science (2008): Indexed yes
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**Identification of cross-reacting T-cell epitopes in structural and non-structural proteins of swine and pandemic H1N1 influenza A virus strains in pigs**

Heterologous protection against swine influenza viruses (SwIVs) of different lineages is an important concern for the pig industry. Cross-protection between 'avian-like' H1N1 and 2009 pandemic H1N1 lineages has been observed previously, indicating the involvement of cross-reacting T-cells. Here, reverse vaccinology was applied to identify cross-reacting MHC
class I T-cell epitopes from two different SwIV H1 lineages in pigs. In silico prediction followed by in vitro and in vivo testing was used to identify SLA-1*0702 T-cell epitopes in heterologous SwIV-infected pigs. Following viral infection, tetramer specific T-cell populations were identified. The majority of the identified T-cell epitopes were conserved between the examined lineages, suggesting that targeting cross-reactive T-cell epitopes could be used to improve vaccines against SwIV in SLA-1*0702-positive pigs.

**General information**

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Organisations: National Veterinary Institute, Virology, Adaptive Immunology, Universitat Autonoma de Barcelona, Centro de Investigación en Sanidad Animal
Authors: Baratelli, M. (Ekstern), Pedersen, L. E. (Intern), Trebbien, R. (Intern), Larsen, L. E. (Intern), Jungersen, G. (Intern), Blanco, E. (Ekstern), Nielsen, J. (Intern), Montoya, M. (Ekstern)
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ISI indexed (2013): ISI indexed yes
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Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.636 SNIP 1.068
Web of Science (2008): Indexed yes
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Leaching of viruses and other microorganisms naturally occurring in pig slurry to tile drains on a well-structured loamy field in Denmark

The amount of animal manure used in modern agriculture is increasing due to the increase in global animal production. Pig slurry is known to contain zoonotic bacteria such as E. coli, Salmonella spp. and Campylobacter spp., and viruses such as hepatitis E virus and group A rotavirus. Coliform bacteria, present in manure, have previously been shown to leach into tile drains. This poses a potential threat to aquatic environments and may also influence the quality of drinking water. As knowledge is especially scarce about the fate of viruses when applied to fields in natural settings, this project sets out to investigate the leaching potential of six different microorganisms: E. coli and Enterococcus spp. (detected by colony assay), somatic coliphages (using plaque assays), and hepatitis E virus, porcine circovirus type 2, and group A rotavirus (by real-time polymerase chain reaction). All six microorganisms leached through the soil entering the tile drains situated at 1-m depth the first day following pig slurry application. The leaching pattern of group A rotavirus differed substantially from the pattern for somatic coliphages, which are otherwise used as indicators for virus contamination. Furthermore, group A rotavirus was detected in monitoring wells at 3.5-m depth up to 2 months after pig slurry application. The detection of viral genomic material in drainage water and shallow groundwater signifies a potential hazard to human health that needs to be investigated further, as water reservoirs used for recreational use and drinking water are potentially contaminated with zoonotic pathogens.

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Organisations: National Veterinary Institute, Virology, Bacteriology & Parasitology, National Food Institute, Research Group for Microbial Food Safety, University of Copenhagen, Geological Survey of Denmark and Greenland, Aarhus University
Authors: Krog, J. S. (Intern), Forslund, A. (Intern), Larsen, L. E. (Intern), Dalsgaard, A. (Ekstern), Kjaer, J. (Ekstern), Olsen, P. (Ekstern), Schultz, A. C. (Intern)
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BFI (2015): BFI-level 1
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Lungebetændelse hos mink med ansamlinger af mononukleære inflammationsceller

General information
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Organisations: National Veterinary Institute, Pathology, Virology, Diagnostic & Development
Authors: Hansen, M. S. (Intern), Krog, J. S. (Intern), Hjulsager, C. K. (Intern), Chriél, M. (Intern), Larsen, L. E. (Intern), Kokotovic, B. (Intern)
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Molecular diagnostics of aleutian mink disease virus: applied use of next generation sequencing and phylogenetics

Aleutian Mink Disease virus (AMDV) is a parvovirus causing Aleutian Mink Disease (AMD), often referred to as plasmacytosis. It is a systemic infection affecting mink of all ages, and is globally the most important pathogen impacting mink farming. In Denmark AMDV has since 1999 been monitored by a national control program, which is based on serological screening of all animals and encourages infected farms to stamp out. Historically there has been no consensus about which genomic region of the virus to analyse e.g. in relation to surveillance, and most previous studies in this regard, have been based either on partial or entire genes, or on pure epidemiological data. Thus, when initiating this project, little was known about AMDV’s total genomic diversity and how the virus was spread between farms.

Recent advances in the field of molecular diagnostics have made high throughput tools such as next generation sequencing cheaper and more easily available. Whole genome sequencing and advanced phylogenetic analyses have successfully been applied to describe the molecular evolution and transmission patterns for viruses such as Foot and Mouth Disease Virus (FMDV), Ebola, and avian influenza virus, however not previously for AMDV. The overall aim with this thesis was to investigate if next generation sequencing and phylogenetic analyses of full length isolates could improve our understanding of the total genomic diversity and evolution of AMDV. Additionally, we wanted to evaluate if this knowledge could contribute to the elucidation of AMDV transmission between farms and improve molecular diagnostics. During the first phase of this project a method for performing whole genome sequencing of AMDV was developed. This protocol enabled the sequencing of a large number of in vivo infectious AMDV isolates and provided the necessary dataset to act as foundation for the remaining analyses in the thesis. The first original paper (Manuscript 1) describes this protocol.

Manuscript 2 is a proof-of-concept study which demonstrated the advantage of using the whole genome sequence approach, compared to the in Denmark traditionally used partial NS1 gene sequencing, for the elucidation of transmission pathways between farms. The study was performed on samples from a small local AMDV outbreak, and clearly illustrated that the phylogenies based on partial NS1 gene sequencing were uninformative and could not be used for determining transmission pathways, even in the light of supporting epidemiological data. The whole-genome approach on the other hand, confirmed the epidemiological hypothesis about the direction of spread.

In Manuscript 3, the methodologies from Manuscript 1 and 2 were applied to generate the to-date most comprehensive phylogenetic and genetic analysis of full-length AMDV isolates, composed of more than 200 field strains. The study shed light on the diversity and evolutionary behaviour of two distinct AMDV strains, in addition to providing the first robust evolutionary rate-estimates. Altogether, the work presented in this thesis provides a contribution to the molecular diagnostics of AMDV, enables us better to understand the virus’ evolutionary behaviour in the context of mink farming, and is anticipated to be of value for more accurately tracing back in time the emergence of future outbreaks.

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Organisations: Department of Bio and Health Informatics, Disease Intelligence and Molecular Evolution, Department of Biotechnology and Biomedicine, National Veterinary Institute, Virology, Copenhagen Diagnostics
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No evidence of enteric viral involvement in the new neonatal porcine diarrhoea syndrome in Danish pigs
The aim of this study was to investigate whether the syndrome New Neonatal Porcine Diarrhoea Syndrome (NNPDS) is associated with a viral aetiology. Four well-managed herds experiencing neonatal diarrhoea and suspected to be affected by NNPDS were included in a case-control set up. A total of 989 piglets were clinically examined on a daily basis. Samples from diarrhoeic and non-diarrhoeic piglets at the age of three to seven days were selected for extensive virological examination using specific real time polymerase chain reactions (qPCRs) and general virus detection methods. A total of 91.7% of the animals tested positive by reverse transcription qPCR (RT-qPCR) for porcine kobuvirus 1 (PKV-1)
while 9% and 3% were found to be positive for rotavirus A and porcine teschovirus (PTV), respectively. The overall prevalence of porcine astrovirus (PAstV) was 75% with 69.8% of the PAstV positive pigs infected with PAstV type 3. No animals tested positive for rotavirus C, coronavirus (TGEV, PEDV and PRCV), sapovirus, enterovirus, parechovirus, saffoldivirus, cosavirus, klassevirus or porcine circovirus type 2 (PCV2). Microarray analyses performed on a total of 18 animals were all negative, as were eight animals examined by Transmission Electron Microscopy (TEM). Using Next Generation de novo sequencing (de novo NGS) on pools of samples from case animals within all herds, PKV-1 was detected in four herds and rotavirus A, rotavirus C and PTV were detected in one herd each. Our detailed analyses of piglets from NNPDS-affected herds demonstrated that viruses did not pose a significant contribution to NNPDS. However, further investigations are needed to investigate if a systemic virus infection plays a role in the pathogenesis of NNPDS.
Outbreak tracking of Aleutian mink disease virus (AMDV) using partial NS1 gene sequencing

Aleutian Mink Disease (AMD) is an infectious disease of mink (Neovison vison) and globally a major cause of economic losses in mink farming. The disease is caused by Aleutian Mink Disease Virus (AMDV) that belongs to the genus Amdoparvovirus within the Parvoviridae family. Several strains have been described with varying virulence and the severity of infection also depends on the host's genotype and immune status. Clinical signs include respiratory distress in kits and unthriftiness and low quality of the pelts. The infection can also be subclinical. Systematic control of AMDV in Danish mink farms was voluntarily initiated in 1976. Over recent decades the disease was mainly restricted to the very northern part of the country (Northern Jutland), with only sporadic outbreaks outside this region. Most of the viruses from this region have remained very closely related at the nucleotide level for decades. However, in 2015, several outbreaks of AMDV occurred at mink farms throughout Denmark, and the sources of these outbreaks were not known. Partial NS1 gene sequencing, phylogenetic analyses data were utilized along with epidemiological to determine the origin of the outbreaks. The phylogenetic analyses of partial NS1 gene sequences revealed that the outbreaks were caused by two different clusters of viruses that were clearly different from the strains found in Northern Jutland. These clusters had restricted geographical distribution, and the variation within the clusters was remarkably low. The outbreaks on Zealand were epidemiologically linked and a close sequence match was found to two virus sequences from Sweden. The other cluster of outbreaks restricted to Jutland and Funen were linked to three feed producers (FP) but secondary transmissions between farms in the same geographical area could not be excluded. This study confirmed that partial NS1 sequencing can be used in outbreak tracking to determine major viral clusters of AMDV. Using this method, two new distinct AMDV clusters with low intra-cluster sequence diversity were identified, and epidemiological data helped to reveal possible ways of viral introduction into the affected herds.
nogle fuglearter dør hurtigt efter, de har fået H5N8 HPAI i udbrud, og dermed ikke kan flyve over størreafstande, mens smittebærere, muligvis fordi der kun er testet et meget begrænset antal fugle og fuglearter. Det er muligt at i det mindste fundet HPAI i én eneste prøve. Overvågningen har ikke afsløret, hvorvidt der indgår vilde fuglearter som raske H5N8 HPAI i 65 fugle (35%). I samme periode blev indsamlet prøver fra 678 levende vilde fugle, hvoraf der ikke blev indsamlingen af prøver fra levende vildefugle. I 4. kvartal blev over 186 dødfundne fugle testet, hvoraf der blev påvist virus, enten flere AI virus og/eller både AI og PMV virus. For 2016 var det muligt at sammenligne et udbrud af HPAI med blev der isoleret PMV fra 10 pools. Ligesom de foregående år viste mange pools sig at indeholde en blanding af flere tilstedeværelsen af aviærparamyxovirus (PMV), men ved dyrkning i æg for at isolere AI virus fra AI PCR positive pools, fugle i den danske overvågning gennem årene. De poolede prøver fra den aktive overvågning blev ikke specifikt testet for repræsentere tidligere påviste subtyper. Subtyperne H3N8, H4N6 og H6N2 er de subtyper, der oftest er påvist i vilde (n=2), H3N8 (n=3), H4N6 (n=1), H6N2(n=3), H6N? (n=1) og H12N5 (n=1). Alle isolaterne var fra svømmeænder, og subtypning af AI virusisolaterne fra den aktive overvågning i vilde fugle blev der fundet virus medfølgende subtyper: H2N3 tidligere år. AI virus kunne dyrkes fra 11 (22%) af de PCR positive pools, hvilket er på niveau med tidligere år. Ved subtypning af AI virusisolaterne fra den aktive overvågning i vilde fugle blev der fundet virus medfølgende subtyper: H2N3 (n=2), H3N8 (n=3), H4N6 (n=1), H6N2(n=3), H6N? (n=1) og H12N5 (n=1). Alle isolaterne var fra svømmeænder, og repræsenterer tidligere påviste subtyper. Subtyperne H3N8, H4N6 og H6N2 er de subtyper, der oftest er påvist i vilde fugle i den danske overvågning gennem årene. De poolede prøver fra den aktive overvågning blev ikke specifikt testet for tilstedeværelsen af aviærparamyxovirus (PMV), men ved dyrkning i æg for at isolere AI virus fra AI PCR positive pools, blev der isoleret PMV fra 10 pools. Ligesom de foregående år viste mange pools sig at indeholde en blanding af flere enten flere AI virus og/eller både AI og PMV virus. For 2016 var det muligt at sammenligne et udbrud af HPAI med indsamlingen af prøver fra levende vildefugle. I 4. kvartal blev over 186 dødfundne fugle testet, hvoraf der blev påvist H5N8 HPAI i 65 fugle (35%). I samme periode blev indsamlet prøver fra 678 levende vilde fugle, hvoraf der ikke blev fundet HPAI i én eneste prøve. Overvågningen har ikke afsløret, hvorvidt der indgår vilde fugleurer som raske smittebærere,muligvis fordi der kun er testet et meget begrænset antal fugle og fugleurer. Det er muligt at i det mindste nogle fugleurer dør hurtigt efter, de har fået H5N8 HPAI i udbrud, og dermed ikke kan flyve over størreafstande, mens

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**Overvågning af influenza A virus i svin - Slutrapport 2016**

The study from Eastern European countries proved that porcine reproductive and respiratory syndrome virus Type 1 (PRRSV-1) harbours high genetic diversity and that genetically divergent subtypes 2-4 circulate in this area. In the present study, we compared the pathogenicity of two different PRRSV-1 subtype 2 strains and a strain representing PRRSV-1 subtype 1. Four groups of 8-week-old specific pathogen free pigs were either infected with subtype 2 strain ILI6, subtype 2 strain or BOR59, subtype 1 strain 18794, or mock inoculated. The most pronounced clinical signs were observed in pigs infected with BOR59. Pigs from both subtype 2 strain infected groups exhibited significantly elevated mean body temperatures on DPI 2 compared to the other two groups, the difference remaining significant up to DPI 13 for the BOR59 infected pigs. The pigs in the latter group also displayed significantly highest levels of early viremia together with the most rapid APP response. Overall, the results indicated that BOR59 strain can be considered a highly pathogenic strain, similarly to subtype 3 strains Lena and SU1-bel, while the virulence of the other subtype 2 strain ILI6 was intermediate between BOR59 and subtype 1 strain.
Prediction and in vitro verification of potential CTL epitopes conserved among PRRSV-2 strains

Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) is the causative agent of one of the most important porcine diseases with a high impact on animal health, welfare, and production economy. PRRSV exhibits a multitude of immunoevasive strategies that, in combination with a very high mutation rate, has hampered the development of safe and broadly protective vaccines. Aiming at a vaccine inducing an effective cytotoxic T cell response, a bioinformatics approach was taken to identify conserved PRRSV-derived peptides predicted to react broadly with common swine leukocyte antigen (SLA) class I alleles. Briefly, all possible 9- and 10-mer peptides were generated from 104 complete PRRSV type 2 genomes of confirmed high quality, and peptides with high binding affinity to five common SLAs were identified combining the NetMHCpan and positional scanning combinatorial peptide libraries binding predictions. Predicted binders were prioritized according to genomic conservation and SLA coverage using the PopCover algorithm. From this, 53 peptides were acquired for further analysis. Binding affinity and stability of a subset of 101 peptide-SLA combinations were validated in vitro for 4 of the 5 SLAs. Eventually, 23% of the predicted peptide-SLA combinations showed to form complexes with a dissociation half-life ≥30 min. Additionally, combining the two prediction methods proved to be more robust across alleles than either method used alone in terms of predicted-to-observed correlations. In summary, our approach represents a finely tuned epitope prediction pipeline providing a rationally selected ensemble of peptides for future in vivo experiments with pigs expressing the included SLAs.
Rotavirus type A associated diarrhoea in neonatal piglets: importance and biodymanics

Background. Rotavirus A (RVA) is a well-known cause of diarrhoea in piglets, but the infection dynamics and clinical impact are not fully elucidated. The aim was to determine the significance of infection with RVA in relation to neonatal diarrhoea. Material/Methods. Two commercial swine herds with neonatal diarrhoea and a positive RVA diagnosis were included. Five litters from each of two herds and a total of 132 piglets were sampled. The animals were subjected to a daily clinical examination and faeces were collected daily from all piglets. The piglets were weighed at beginning and at the end of study. The outbreak day was defined as the day where >25% of the litter showed clinical diarrhoea, and for all litters this was either the 4th or 5th day of life. On outbreak day, fecal samples from all piglets in the litter were analyzed for RVA.
together with samples collected two days prior to outbreak day from 54 of the 132 piglets. The analyses were made by a RVA specific RT-qPCR. Virulent E. coli was ruled out by PCR as differential diagnosis in all litters by testing a pooled sample on the outbreak day. Results/Discussion. In total, 43%(57/132) of the piglets had clinical diarrhoea and 66%(87/132) were positive for RVA on the outbreak day. For comparison, 89%(51/57) of the diarrheic piglets and 48%(36/75) of the non-diarrheic piglets were positive for RVA which was significantly different (P<0.001). Piglets that tested negative for RVA had a higher weight gain over the 4-day period (mean 363g vs. 278g,P<0.05) despite that the positive piglets had a significantly higher birthweight (mean 1,45kg vs. 1,27kg,P<0.05). Furthermore, 63%(34/54) of the piglets developed diarrhoea within 24 hours after a positive RVA diagnosis. The results confirmed that RVA has a significant impact on incidence of diarrhoea and weight gain also in E. coli negative litters.

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Rotavirus Type A associated Diarrhoea in Neonatal Piglets: Importance and Biodynamics

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Authors: Rasmussen, M. (Ekstern), Moeller, C. (Ekstern), Hjulsager, C. K. (Intern), Kongsted, H. (Ekstern), Hansen, C. (Ekstern), Larsen, L. E. (Intern)
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Subtyping of swine influenza viruses using a high-throughput real time PCR platform
Introduction. Swine influenza is a respiratory disease caused by multiple subtypes of influenza A virus (IAV). The genome of IAV consists of 8 segments and subtype classification is based on the surface glycoproteins hemagglutinin (HA) and neuraminidase (NA). In Denmark, the influenza screening test and subsequent subtyping is performed by real time RT-PCR (RT-qPCR) but several assays are needed to cover the wide range of circulating subtypes which is expensive, resource and time demanding. To mitigate these restrictions the high-throughput qPCR platform BioMark (Fluidigm) has been explored. The BioMark platform uses less sample and reagent volume compared to standard qPCR platforms and allows for up to 9,216 parallel reactions on one chip. Materials and methods. A total of 14 PCR assays specific for the different subtypes of HA and NA genes relevant for swine influenza and 6 assays specific for the internal genes of IAV were validated and optimised to run under identical reaction conditions and assembled on a dynamic array chip (Fluidigm). Results. The sensitivity and specificity of the chip was assessed by testing cell culture isolates and field samples with known subtypes (based on sequencing). The results revealed that the performance of the dynamic chip was similar to conventional real time analysis. Discussion and conclusion. Application of the chip for subtyping of swine influenza has resulted in a significant reduction in time, cost and working hours. Thereby, it is possible to offer diagnostic services with reduced price and turnover time which will facilitate choice of vaccines and by that lead to reduction of antibiotic used.

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**Triple-reassortant influenza A virus with H3 of human seasonal origin, NA of swine origin, and internal A(H1N1) pandemic 2009 genes is established in Danish pigs**

This report describes a triple-reassortant influenza A virus with a HA that resembles H3 of human seasonal influenza from 2004 to 2005, N2 from influenza A virus already established in swine, and the internal gene cassette from A(H1N1)pdm09 has spread in Danish pig herds. The virus has been detected in several Danish pig herds during the last 2-3 years and may possess a challenge for human as well as animal health.
A fast and robust method for whole genome sequencing of the Aleutian Mink Disease Virus (AMDV) genome

Aleutian Mink Disease Virus (AMDV) is a frequently encountered pathogen associated with commercial mink breeding. AMDV infection leads to increased mortality and compromised animal health and welfare. Currently little is known about the molecular evolution of the virus, and the few existing studies have focused on limited regions of the viral genome. This paper describes a robust, reliable, and fast protocol for amplification of the full AMDV genome using long-range PCR. The method was used to generate next generation sequencing data for the non-virulent cell-culture adapted AMDV-G strain as well as for the virulent AMDV-Utah strain. Comparisons at nucleotide- and amino acid level showed that, in agreement with existing literature, the highest variability between the two virus strains was found in the left open reading frame, which encodes the non-structural (NS1–3) genes. This paper also reports a number of differences that potentially can be linked to virulence and host range. To the authors' knowledge, this is the first study to apply next generation sequencing on the entire AMDV genome. The results from the study will facilitate the development of new diagnostic tools and can form the basis for more detailed molecular epidemiological analyses of the virus.

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Aptasensor development for detection of virus in water

Contamination of water by waterborne viruses causes serious health issues worldwide. The current virus detection methods are expensive and time-consuming and require access to well-equipped laboratories. This thesis describes the development of an impedimetric all-polymer aptasensor for detection of three types of waterborne viruses: norovirus, rotavirus and hepatitis A virus. The development of the aptasensor involved sample preparation for aptamer selection of rotavirus and hepatitis A virus, an iterative design process of the aptasensor, investigation of the surface immobilisation of aptamers and finally an impedimetric electrical characterisation of the sensor.

The sample preparation of the rotavirus was based on purification and biotinylation of the virus to meet the requirements of the aptamer selection process. The selection process, performed by an external collaborator, was based on streptavidin coated magnetic bead separation, hence the needed biotinylation. It was found that the BPH linker gave the highest yield when the biotinylated rotavirus were immobilised onto the beads.

The design of the viral aptasensor was determined by an iterative design process. The final chip design was based on a SD card design with an injection moulded PC substrate and lid. The electrodes were screen-printed PEDOT:PSS. The surface immobilisation of aptamers through UV cross-linking onto different polymer substrates was tested. As the success of this step is crucial for the aptasensor specificity and performances, the surface immobilisation was thoroughly investigated. The aptamer UV cross-linking onto PEDOT:PSS was promising. Furthermore, some passive absorption of the aptamers onto the PEDOT:PSS was found.

The impedimetric electrical characterisation of the aptasensor chip was done with different media salinity and different pH values. The impedimetric measurements of the different media salinity showed the expected behaviour with the greatest change present in the region representing the solution resistance. The pH measurements did not show any significant change of the impedance, hence the chip was stable in the measured pH range, which corresponds to the expected pH range of water samples. The stability of the aptasensor chip was tested over a 2 week period in continuous flow. It was found that the electrodes were not damaged or degraded during the time period, as a constant impedance signal was measured.

A solid foundation for the further development of the aptasensor for viral detection has been established and from this a new cheap and simple viral detection method can emerge.

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Organisations: Department of Micro- and Nanotechnology, Polymer Microsystems for Medical Diagnostics, National Veterinary Institute, Virology, Nano Bio Integrated Systems
Engineering a CTL-Tailored Replicon RNA Vaccine against PRRSV

The development of vaccines against porcine reproductive and respiratory syndrome virus (PRRSV) has been hampered by the high mutation rate and the multiple immunoevasive strategies of the virus. With the overall aim of designing a broad coverage vaccine that induces an effective CTL response against PRRSV, we have used a bioinformatics approach to identify common PRRSV type 2 epitopes predicted to react broadly with predominant swine MHC (SLA) alleles.

All possible 9- and 10-mer peptides derived from 104 wild-type strains were analyzed in silico for their predicted binding affinity to 3 common SLA class I alleles and ranked according to genomic conservation and SLA binding coverage. Of the 53 top-ranked peptides, 33 were verified in vitro as high affinity binders. Polyepitope gene cassettes of these peptides, flanked by an upstream ubiquitin sequence and a downstream FLAG tag, were cloned into a classical swine fever virus (CSFV)-derived replicon vector. Virus replicon particles (VRP) were rescued by transfection of a complementing cell line with replicon RNA. Polyepitope expression and subsequent proteasomal degradation was confirmed indirectly by increased FLAG-tagged protein detection in the presence of a proteasome inhibitor.

Finally, a vaccination-challenge experiment using 18 SLA-matched pigs is currently being conducted until July 2016 in which a test group and a control group are being vaccinated twice with VRPs expressing PRRSV epitopes and non-sense control epitopes, respectively, before challenged with live wild type PRRSV. The induced epitope specific cell-mediated immune responses are being monitored by ELISPOT, flow cytometry and cytotoxicity assays, and the degree of protection against infection will be characterized by qPCR and antibody analysis. The results will be available for IVIS.

This study exemplifies how bioinformatics epitope prediction, recombinant SLA molecules and RNA virus replicon design can be used to engineer a replicating non-propagating vaccine tailored to deliver conserved and immunogenic CTL epitopes.

First characterization of avian influenza viruses from Greenland 2014

In late February 2014, unusually high numbers of wild birds, thick-billed murre (Uria lomvia), were found dead at the coast of South Greenland. To investigate the cause of death, 45 birds were submitted for laboratory examinations in Denmark. Avian influenza viruses (AIVs) with subtypes H11N2 and low pathogenic (LP) H5N1 were detected in some of the birds. Characterization of the viruses by full-genome sequencing revealed that all the gene segments belonged to the North American lineage of AIVs.

The seemingly sparse and mixed subtype occurrence of LP AIVs in these birds, in addition to an emaciated appearance of birds, suggests that the murre die-off was not due to infection with AIV, but could be the mere cause of sparse food availability or stormy weather. Here we present the first characterization of AIVs isolated in Greenland, and our results
support the idea that wild birds in Greenland may be involved in the movement of AIV between North America and Europe.

**General information**

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  - Scopus rating (2010): SJR 0.939 SNIP 1.117
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Forbedret diagnostik af mink enteritis virus (MEV)

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Forbedret diagnostik af mink enteritis virus (MEV)

Immunity raised by recent European subtype 1 PRRSV strains allows better replication of East European subtype 3 PRRSV strain Lena than that raised by an older strain

Stable spatial distribution of porcine reproductive and respiratory syndrome (PRRSV)-1 subtypes in Europe is accompanied by a strong population immunity induced by local PRRSV strains. In the present study, it was examined if the immunity induced by three West European subtype 1 PRRSV strains (2007 isolate 07V063 and 2013 isolates 13V091 and 13V117) offers protection against the highly virulent East European subtype 3 PRRSV strain Lena. The number of fever days was greater (p < 0.05) in the control group (7.6 ± 1.7 days) compared to the immune groups (07V063-immune: 4.0 ± 1.2 days, 13V091-immune: 4.6 ± 1.1 days, 13V117-immune: 4.0 ± 2.9 days). In all groups, protection was characterized by reduction (p < 0.05) of AUC values of nasal shedding (control: 14.6, 07V063-immune: 3.4, 13V091-immune: 8.9, 13V117-immune: 8.0) and viremia (control: 28.1, 07V063-immune: 5.4, 13V091-immune: 9.0, 13V117-immune: 8.3). Reduction of respiratory disease, nasal shedding (mean AUC and mean peak values) and viremia (mean AUC and mean peak values) was more pronounced in 07V063-immune (p < 0.05) than in 13V091-immune and 13V117-immune animals. Inoculation with subtype 1 PRRSV strains caused priming of the Lena-specific virus neutralization antibody response. Upon challenge with Lena, we observed a very strong serological booster effect for neutralizing antibodies against strains used for the first inoculation. Our results indicate that inoculation with subtype 1 PRRSV strains can partially protect against antigenically divergent subtype 3 strains. The lower protection level elicited by recently isolated subtype 1 PRRSV strains may impair the outcome of the spatial expansion of subtype 3 strains from East Europe to West Europe.

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Improving productivity in growing pigs by combining specific and non-specific monitoring

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Main Research Area: Technical/natural sciences
Electronic versions:
Book of abstracts
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016
Introduction of replacement gilts to PRRS-positive sow herds

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, SEGES Pig Research Center
Authors: Hoelstad, B. E. (Intern), Larsen, L. E. (Intern), Hjulsager, C. K. (Intern), Kristensen, C. (Ekstern)
Pages: 568-568
Publication date: 2016

Host publication information
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Main Research Area: Technical/natural sciences
Conference: 24th International Pig Veterinary Society (IPVS) Congress, Dublin, Ireland, 07/06/2016 - 07/06/2016
Electronic versions:
Book of abstracts
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Introduktion af polte i PRRSV-besætning: Notat nr. 1609
I dette veterinære speciale blev det vist, at polte, der var vaccineret mod PRRS-virus (PRRSV), ikke udskilte virus ved første løbning. Studiet fandt en tendens til en sammenhæng mellem brug af karantæne og det, at poltene var beskyttet af antistoffer mod PRRSV.

Studiet inkluderede 69 besætninger positive for PRRSV. Der blev taget 5 blodprøver fra løbeklare polte i hver besætning, og et spørgeskema vedrørende polterækkerstrategi, vaccinationsstrategi m.m. blev udfyldt.

Blodprøverne blev analyseret for PRRSV ved RT-qPCR, ELISA og IPT.

Studiet viste, at poltene fra de deltagende besætninger ikke havde PRRSV i blodet (var viræmiske) ved første løbning, og at der var en lille del, som ikke havde dannet antistoffer mod PRRSV trods vaccination. Sidstnævnte kunne tyde på et svigt i vaccinationsproceduren i besætningerne. Desuden var det meget få besætninger, der reelt havde en optimal karantæne. En optimal karantæne blev defineret som en stald, der ikke delte luftrom med øvrige staldafsnit, havde separat indgang og kørte alt ind/alt ud. På trods af at poltene ikke var viræmiske ved løbning, fører studiet ikke til ændringer i anbefalingerne vedrørende introduktion af polte i PRRS-positive besætninger.

Anbefalingerne er derfor stadig at immunisere poltene og så sætte dem i karantæne i minimum 8 uger og allerhelst 12.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology
Number of pages: 4
Publication date: 2016

Publication information
Publisher: Videncenter for Svineproduktion
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
Notat_1609.pdf
Links:
http://vsp.lf.dk/Publikationer/Kilder/Notater/2016/1609.aspx
Source: PublicationPreSubmission
Source-ID: 127552069
Publication: Commissioned › Report – Annual report year: 2016

Oral fluid samples for the monitoring of PRRSV status and dynamics

General information
Outbreaks of Aleutian mink disease in farmed mink (Neovison vison) in Denmark: molecular characterization by partial NS1 gene sequencing

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Danvet K/S, Boehringer Ingelheim AH
Authors: Holmgren, S. (Ekstern), Kvisgaard, L. K. (Intern), Bak, H. (Ekstern), Larsen, L. E. (Intern)
Pages: 578-578
Publication date: 2016

Host publication information
Title of host publication: 24th International Pig Veterinary Society Congress - abstracts book
Place of publication: Dublin, Ireland
Publisher: Royal Dublin Society
Article number: PO-PW1-087
Main Research Area: Technical/natural sciences
Conference: 24th International Pig Veterinary Society (IPVS) Congress, Dublin, Ireland, 07/06/2016 - 07/06/2016
Electronic versions:
Book of abstracts
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Overførsel af Aleutian Mink Disease Virus med lopper

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Department of Systems Biology, Center for Biological Sequence Analysis, Molecular Evolution, Department of Bio and Health Informatics, Kopenhagen Fur
Pages: 85-87
Publication date: 2016

Host publication information
Title of host publication: Proceedings of the XIth International Scientific Congress in Fur Animal Production
Place of publication: Helsinki, Finland
Publisher: Libris
Series: Scientifur
Volume: 40
Number: 3/4
ISSN: 2445-6292
Main Research Area: Technical/natural sciences
Electronic versions:
IFASA2016_Vol.40_1_.pdf

Links:
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Overførsel af Aleutian Mink Disease Virus med lopper

General information
State: Published
Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Section for Virology, KSL Consulting ApS, Kopenhagen Diagnostics, Aalborg University
Authors: Hartby, C. M. (Intern), Hammer Jensen, T. (Ekstern), Søholt Larsen, K. (Ekstern), Hansen, M. S. (Intern), Chriél, M. (Intern), Larsen, L. E. (Intern), Struve, T. (Ekstern), Hjulsager, C. K. (Intern)
Pages: 91-94
Publication date: 2016

Host publication information
Title of host publication: Faglig årsberetning 2015 : Kopenhagen Fur
Place of publication: Aarhus N
Publisher: Kopenhagen Fur
Main Research Area: Technical/natural sciences
Electronic versions:
Overvågning af aviær influenza i vilde fugle i Danmark 2015

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, University of Copenhagen
Authors: Hjulsager, C. K. (Intern), Krog, J. S. (Intern), Madsen, J. J. (Ekstern), Thorup, K. (Ekstern), Larsen, L. E. (Intern)
Number of pages: 33
Publication date: 2016

Publication information
Place of publication: Frederiksberg C
Publisher: Veterinærinstituttet, Danmarks Tekniske Universitet
Original language: Danish
Main Research Area: Technical/natural sciences
Source: FindIt
Source-ID: 2305680084
Publication: Research › Report – Annual report year: 2016

Overvågning af influenza A virus i svine - Slutrapport 2015

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology
Authors: Krog, J. S. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 29
Publication date: 2016

Publication information
Place of publication: Frederiksberg C
Publisher: DTU Veterinærinstituttet
Original language: Danish
Main Research Area: Technical/natural sciences
Electronic versions: Afrapportering_SIV_overv_gning_2015_nn_.pdf
Source: PublicationPreSubmission
Source-ID: 127962091
Publication: Research › Report – Annual report year: 2016

Pooling of faecal samples for quantitative virus diagnostics by real-time PCR

General information
State: Published
Organisations: National Veterinary Institute, Virology, Section for Virology
Authors: Hartby, C. M. (Intern), Andersen, M. R. (Intern), Kvisgaard, L. K. (Intern), Chriél, M. (Intern), Larsen, L. E. (Intern), Hjulsager, C. K. (Intern)
Pages: 27-30
Publication date: 2016

Host publication information
Title of host publication: Proceedings of the XIth International Scientific Congress in Fur Animal Production
Place of publication: Helsinki, Finland
Publisher: Libris
Editors: Mäki-Tanila, A., Valaja, J., Mononen, J., Sironen, T., Vapalahti, O.
Series: Scientifur
Volume: 40
Number: 3/4
ISSN: 2445-6292
Rapid detection and subtyping of European swine influenza viruses in porcine clinical samples by haemagglutinin- and neuraminidase-specific tetra- and triplex real-time RT-PCRs

Background
A diversifying pool of mammalian-adapted influenza A viruses (IAV) with largely unknown zoonotic potential is maintained in domestic swine populations worldwide. The most recent human influenza pandemic in 2009 was caused by a virus with genes originating from IAV isolated from swine. Swine influenza viruses (SIV) are widespread in European domestic pig populations and evolve dynamically. Knowledge regarding occurrence, spread and evolution of potentially zoonotic SIV in Europe is poorly understood.

Objectives
Efficient SIV surveillance programmes depend on sensitive and specific diagnostic methods which allow for cost-effective large-scale analysis.

Methods
New SIV haemagglutinin (HA) and neuraminidase (NA) subtype- and lineage-specific multiplex real-time RT-PCRs (RT-qPCR) have been developed and validated with reference virus isolates and clinical samples.

Results
A diagnostic algorithm is proposed for the combined detection in clinical samples and subtyping of SIV strains currently circulating in Europe that is based on a generic, M-gene-specific influenza A virus RT-qPCR. In a second step, positive samples are examined by tetraplex HA- and triplex NA-specific RT-qPCRs to differentiate the porcine subtypes H1, H3, N1 and N2. Within the HA subtype H1, lineages “av” (European avian-derived), “hu” (European human-derived) and “pdm” (human pandemic A/H1N1, 2009) are distinguished by RT-qPCRs, and within the NA subtype N1, lineage “pdm” is differentiated. An RT-PCR amplicon Sanger sequencing method of small fragments of the HA and NA genes is also proposed to safeguard against failure of multiplex RT-qPCR subtyping.

Conclusions
These new multiplex RT-qPCR assays provide adequate tools for sustained SIV monitoring programmes in Europe.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Friedrich-Loeffler-Institute, University Paris-Est Anses, Animal and Plant Health Agency, Istituto Zooprofilattico Sperimentale della Lombardia e dell’Emilia
Authors: Henritzi, D. (Ekstern), Zhao, N. (Ekstern), Starick, E. (Ekstern), Simon, G. (Ekstern), Krog, J. S. (Intern), Larsen, L. E. (Intern), Reid, S. M. (Ekstern), Brown, I. H. (Ekstern), Chiapponi, C. (Ekstern), Foni, E. (Ekstern), Wacheck, S. (Ekstern), Schmid, P. (Ekstern), Beer, M. (Ekstern), Hoffmann, B. (Ekstern), Harder, T. C. (Ekstern)
Number of pages: 14
Pages: 504-517
Publication date: 2016
Main Research Area: Technical/natural sciences
Significantly increased numbers of foetuses positive for porcine parvovirus (PPV) in Denmark in 2015 coincided with a shift in genotype

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, SEGES Pig Research Center
Authors: Krog, J. S. (Intern), Hjulsager, C. K. (Intern), Haugegaard, S. (Ekstern), Larsen, L. E. (Intern)
Pages: 452-452
Publication date: 2016

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Place of publication: Dublin, Ireland
Publisher: Royal Dublin Society
Article number: PO-PF3-156
Main Research Area: Technical/natural sciences
Conference: 24th International Pig Veterinary Society (IPVS) Congress, Dublin, Ireland, 07/06/2016 - 07/06/2016
Electronic versions:
Book of abstracts
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Simultaneous vaccination with PRRS MLV against both PRRSV type 1 and type 2: PRRSV in lungs following challenge

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, SEGES Pig Research Center, Technical University of Denmark, Warsawa University
Authors: Kristensen, C. S. (Ekstern), Kvisgaard, L. K. (Intern), Haugegaard, S. (Ekstern), Pawlowski, M. (Ekstern), Carlsen, S. H. (Ekstern), Stadejek, T. (Ekstern), Larsen, L. E. (Intern)
Pages: 577-577
Publication date: 2016

Host publication information
Title of host publication: 24th International Pig Veterinary Society Congress - abstracts book
Place of publication: Dublin, Ireland
Publisher: Royal Dublin Society
Article number: PO-PW1-089
Main Research Area: Technical/natural sciences
Conference: 24th International Pig Veterinary Society (IPVS) Congress, Dublin, Ireland, 07/06/2016 - 07/06/2016
Electronic versions:
Book of abstracts
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2016

Subtypning af influenza på danske minkfarmer i 2014

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology
Authors: Hjulsager, C. K. (Intern), Krog, J. S. (Intern), Chriélf, M. (Intern), Larsen, G. (Intern), Larsen, L. E. (Intern)
The global antigenic diversity of swine influenza A viruses

Swine influenza presents a substantial disease burden for pig populations worldwide and poses a potential pandemic threat to humans. There is considerable diversity in both H1 and H3 influenza viruses circulating in swine due to the frequent introductions of viruses from humans and birds coupled with geographic segregation of global swine populations. Much of this diversity is characterized genetically but the antigenic diversity of these viruses is poorly understood. Critically, the antigenic diversity shapes the risk profile of swine influenza viruses in terms of their epizootic and pandemic potential. Here, using the most comprehensive set of swine influenza virus antigenic data compiled to date, we quantify the antigenic diversity of swine influenza viruses on a multi-continental scale. The substantial antigenic diversity of recently circulating viruses in different parts of the world adds complexity to the risk profiles for the movement of swine and the potential for swine-derived infections in humans.
The Non-structural Protein 5 and Matrix Protein Are Antigenic Targets of T Cell Immunity to Genotype 1 Porcine Reproductive and Respiratory Syndrome Viruses

The porcine reproductive and respiratory syndrome virus (PRRSV) is the cause of one of the most economically important diseases affecting swine worldwide. Efforts to develop a next-generation vaccine have largely focused on envelope glycoproteins to target virus-neutralizing antibody responses. However, these approaches have failed to demonstrate the necessary efficacy to progress toward market. T cells are crucial to the control of many viruses through cytolysis and cytokine secretion. Since control of PRRSV infection is not dependent on the development of neutralizing antibodies, it has been proposed that T cell-mediated immunity plays a key role. Therefore, we hypothesized that conserved T cell antigens represent prime candidates for the development a novel PRRSV vaccine. Antigens were identified by screening a proteome-wide synthetic peptide library with T cells from cohorts of pigs rendered immune by experimental infections with a closely related (subtype 1) or divergent (subtype 3) PRRSV-1 strain. Dominant T cell IFN-gamma responses were directed against the non-structural protein 5 (NSP5), and to a lesser extent, the matrix (M) protein. The majority of NSP5-specific CD8 T cells and M-specific CD4 T cells expressed a putative effector memory phenotype and were polyfunctional as assessed by coexpression of TNF-alpha and mobilization of the cytotoxic degranulation marker CD107a. Both antigens were generally well conserved among strains of both PRRSV genotypes. Thus, M and NSP5 represent attractive vaccine candidate T cell antigens, which should be evaluated further in the context of PRRSV vaccine development.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Animal and Plant Health Agency, University of Veterinary Medicine, University of Surrey, University College London
Authors: Mokhtar, H. (Ekstern), Pedrera, M. (Ekstern), Frossard, J. (Ekstern), Biffar, L. (Ekstern), Hammer, S. E. (Ekstern), Kvisgaard, L. K. (Intern), Larsen, L. E. (Intern), Stewart, G. R. (Ekstern), Somavarapu, S. (Ekstern), Steinbach, F. (Ekstern), Graham, S. P. (Ekstern)
Number of pages: 14
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Frontiers in Immunology
Volume: 7
Article number: 40
ISSN (Print): 1664-3224
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Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 5.37 SJR 2.963 SNIP 1.483
Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 2.818 SNIP 1.29 CiteScore 5.09
Web of Science (2015): Indexed yes
Scopus rating (2014): SJR 2.382 SNIP 1.056 CiteScore 4.24
Web of Science (2014): Indexed yes
Scopus rating (2013): SJR 1.842 SNIP 0.837 CiteScore 3.55
ISI indexed (2013): ISI indexed no
Scopus rating (2012): SJR 0.785 SNIP 0.193 CiteScore 1.38
ISI indexed (2012): ISI indexed no
Scopus rating (2011): SJR 0.121
Web of Science (2011): Indexed yes
Original language: English
IMMUNOLOGY, EXPERIMENTAL CHALLENGE, LYMPHOCYTE SUBSETS, CLINICAL-DISEASE, SYNDROME PRRS, IFN-GAMMA, PIGS, VACCINE, RESPONSES, SWINE, IDENTIFICATION, porcine reproductive and respiratory syndrome virus, T cell, IFN-gamma, antigen identification, phenotype and function, vaccine, IFN-y
Electronic versions:
fimmu_07_00040.pdf
DOIs:
10.3389/fimmu.2016.00040
Source: FindIt
Source-ID: 2292311895
Publication: Research - peer-review > Journal article – Annual report year: 2016
Application of qPCR assays for diagnosing causes of viral mink diarrhea. Preliminary results

Gastrointestinal (GI) disorders is the main cause for submitting mink (Neovison vison) carcasses for post-mortem examination at the National Veterinary Institute in Denmark and has been described as the predominant cause of disease and mortality in the Danish mink production (Rattenborg et al. 1999). Diarrhea in mink can be caused by infectious agents (virus, bacteria and parasites) and food-related/multifactorial conditions. Known enteric viral infections are mink enteritis virus (MEV) and mink astrovirus. Coronaviruses and caliciviruses have also been implicated as potential causes or contributors to diarrhea in mink. Rotavirus is poorly described in mink, but has previously been demonstrated in feces from mink pups with and without clinical signs (Jorgensen et al. 1996). The pathogenicity of these viruses could be related to viral load, virulence and the age of the mink. Therefore, there is a need for a quantitative diagnostic approach. We have developed new or adapted previously published real-time PCR/RT-PCR assays for MEV, astrovirus, rota- and coronavirus diagnostics.

The technical test validation was initially carried out on archived diarrhea samples from diagnosed positive animals and on normal and diarrhea samples from a case-control study. In order to further validate the applicability of the assays, a testing scheme for normal and affected farms was set up and initiated in June 2015. This protocol will allow optimization of test characteristics (sensitivity, specificity and predictive value) and assessment of the validity of using pooled samples in order to reduce test costs.
Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) causes one of the most important diseases in all swine producing countries. The infection has a high impact on animal welfare, food safety and production economics. PRRSV possesses multiple immunoevasive strategies, from suppression of the host cell antiviral machinery, to the deceptive induction of a non-neutralizing antibody response through decoy antigen presentation. This, combined with a very high mutation rate, has hampered the development of safe and effective vaccines.

With the overall aim to design a vaccine that induces an effective CTL response against PRRSV, we have taken a bioinformatics approach to identify common PRRSV epitopes predicted to react broadly with predominant swine MHC (SLA) alleles. First, the genomic integrity and sequencing method was examined for 334 available complete PRRSV type 2 genomes leaving 104 strains of high quality. For each strain, a library of all possible 9- and 10-mer peptides was generated considering the known ribosomal frame shift sites and sites for post translational cleavage.

All peptides were in silico analyzed for binding affinity to either of five common SLA class I alleles. A quantitative rank score was generated for each peptide by combining two algorithms based on the NetMHCpan neural network and lab determined SLA binding affinity of each amino acid at any position in the peptide, respectively. Peptides with a rank score above a predefined threshold were further analyzed by the PopCover algorithm, providing a final list of 54 epitopes prioritized according to maximum coverage of PRRSV strains and SLA alleles.

This bioinformatics approach provides a rational strategy for selecting peptides for a CTL-activating vaccine with broad coverage of both virus and swine diversity. The immunogenicity of the selected peptides is in the process of being verified in vivo.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Center for Biological sequence analysis, Department of Systems Biology, Center for Biological Sequence Analysis, Immunological Bioinformatics, Section for Immunology and Vaccinology
Publication date: 2015
Event: Abstract from Keystone Symposia on Molecular and Cellular Biology: Accelerating life science discovery, Keystone, United States
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 103565755
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Characterization of the PRRSV strain circulating in a PRRSV type 1 positive herd before, during and after vaccination with a PRRSV type 1 vaccine
Danske PPV-stammer har ændret sig genetisk
I 2015 er der set en markant stigning i antallet af positive fund af porcin parvovirus (PPV) i indsendelser til undersøgelse af svineaborter (Tabel 1).
PPV forekommer udbredt i svinebesætninger og kan forårsage reproduktionsproblemer. Disse kan imidlertid kontrolleres med vacciner, der dog ikke forhinder infektion og virusudskillelse fra soerne, men beskytter mod reproduktionsproblemerne.
PPV-viruspartiklerne er meget modstandsdygtige overfor nedbrydelse i omgivelserne, så da virus formodentlig findes i de fleste besatninger, er det vigtigt med effektiv vaccination af alle avlsdyr for at beskytte mod PPV-relaterede reproduktionsproblemer.
Tidligere studier har vist, at europæiske PPV-virus, inklusive de danske, kan inddeles i to grupper (genotyper) baseret på forskelle i deres gensekvenser. For at undersøge de danske PPV-virus fra 2015 nærmere, har vi bestemt DNAsekvensen af hele virusgenomet fra fire af de positive indsendelser fra 2015.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology
Authors: Hjulsager, C. K. (Intern), Krog, J. S. (Intern), Larsen, L. E. (Intern)
Pages: 47-47
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Dansk Veterinaertidsskrift
Issue number: 15
ISSN (Print): 0106-6854
Ratings:
BFI (2017): BFI-level 1
BFI (2016): BFI-level 1
BFI (2015): BFI-level 1
BFI (2014): BFI-level 1
BFI (2013): BFI-level 1
ISI indexed (2013): ISI indexed no
BFI (2012): BFI-level 1
ISI indexed (2012): ISI indexed no
BFI (2011): BFI-level 1
ISI indexed (2011): ISI indexed no
BFI (2010): BFI-level 1
BFI (2009): BFI-level 1
BFI (2008): BFI-level 1
Original language: Danish
Electronic versions:
16021_2_.pdf
Source: PublicationPreSubmission
Source-ID: 118964661
Publication: Research - peer-review › Journal article – Annual report year: 2015
Detection of American lineage low pathogenic avian influenza viruses in Uria lomvia in Greenland

In early March 2014, unusual high numbers of wild bird Thick-billed Murre (Uria lomvia), order Charadriiformes, were found dead at the coast of South Greenland. To investigate the cause of death, 45 birds were submitted for diagnosis at the National Veterinary Institute, Technical University of Denmark. Five birds were randomly selected for diagnostic investigation and samples were taken from the cadavers (pooled oropharyngeal swabs, cloacal swabs, lung/trachea/heart tissues and liver/spleen/kidney tissues, and separate preparation of stomach from a single bird). Avian influenza virus (AIV) with subtype H11N2 was detected in all pools by RT-PCR. Virus was isolated from embryonated chicken-eggs by allantoic inoculation from all pools except the liver/spleen/kidney pool. Full-genome sequencing of AIV isolate revealed American lineage origin of genes. The remaining 40 birds were subsequently screened for AIV in oropharyngeal and cloacal swab specimens from each bird by RT-PCR. American lineage H11N2 AIV was detected in both oropharyngeal and cloacal swabs from one bird, and American lineage low pathogenic AIV with subtype H5N1 was detected in the cloacal swab from another bird. The sparse and mixed subtype occurrence of AIV together with an emaciated appearance of the birds, suggests that the Murre die-off may not have been caused by infection with AIV, but that the birds could have died from starvation. However, here we present the first characterization of AIVs from Greenland and our results supports the idea that wild birds in Greenland could be involved in the movement of AIV between North America and Europe.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology
Authors: Hjulsager, C. K. (Intern), Hartby, C. M. (Intern), Krog, J. S. (Intern), Holm, E. (Intern), Larsen, L. E. (Intern)
Publication date: 2015
Event: Abstract from 9th International Symposium on Avian Influenza, Athens, Georgia, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
AI_lomvier_til_ORBIT.pdf

Bibliographical note
Source: PublicationPreSubmission
Source-ID: 112051286
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Detection of PRRSV in air sampled inside and outside PRRSV-positive herds in Denmark

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Technical University of Denmark, Svinevet Pig Practise, Boehringer Ingelheim Danmark A/S
Authors: Priebe, A. (Ekstern), Kvisgaard, L. K. (Intern), Rathkjen, P. H. (Ekstern), Hjulsager, C. K. (Intern), Havn, K. (Ekstern), Larsen, L. E. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from International Porcine Reproductive And Respiratory Syndrome Congress, Ghent, Belgium.
Main Research Area: Technical/natural sciences
Electronic versions:
abstract1_pribe_final.pdf
Source: PublicationPreSubmission
Source-ID: 119056081
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Development of a real-time RT-PCR assay that detects a broad range of Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) Type 1 subtypes

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Parco Technologico Padano
Authors: Kvisgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Botti, S. (Ekstern), Larsen, L. E. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from International Porcine Reproductive And Respiratory Syndrome Congress, Ghent, Belgium.
Main Research Area: Technical/natural sciences
Electronic versions:
Development_of_a_real_time_RT_PCR_assay_final.pdf
Different clinical, virological, serological and tissue tropism outcomes of two new and one old Belgian type 1 subtype 1 porcine reproductive and respiratory virus (PRRSV) isolates

In this study, the pathogenic behavior of PRRSV 13V091 and 13V117, isolated in 2013 from two different Belgian farms with enzootic respiratory problems shortly after weaning in the nursery, were compared with the Belgian strain 07V063 isolated in 2007. Full-length genome sequencing was performed to identify their origin. Twelve weeks-old pigs were inoculated intranasally (IN) with 13V091, 13V117 or 07V063 (9 pigs/group). At 10 days post inoculation (dpi), 4 animals from each group were euthanized and tissues were collected for pathology, virological and serological analysis. 13V091 infection resulted in the highest respiratory disease scores and longest period of fever. Gross lung lesions were more pronounced for 13V091 (13%), than for 13V117 (7%) and 07V063 (11%). The nasal shedding and viremia was also most extensive with 13V091. The 13V091 group showed the highest virus replication in conchae, tonsils and retropharyngeal lymph nodes. 13V117 infection resulted in the lowest virus replication in lymphoid tissues. 13V091 showed higher numbers of sialoadhesin-infected cells/mm(2) in conchae, tonsils and spleen than 13V117 and 07V063. Neutralizing antibody response with 07V063 was stronger than with 13V091 and 13V117. It can be concluded that (i) 13V091 is a highly pathogenic type 1 subtype 1 PRRSV strain that replicates better than 07V063 and 13V117 and has a strong tropism for sialoadhesin-cells and (ii) despite the close genetic relationship between 13V117 and 07V063, 13V117 has an increased nasal replication and shedding, but a decreased replication in lymphoid tissues compared to 07V063.

General information

State: Published
Organisations: National Veterinary Institute, Section for Virology, Ghent University
Authors: Frydas, I. S. (Ekstern), Trus, I. (Ekstern), Kvisgaard, L. K. (Intern), Bonckaert, C. (Ekstern), Reddy, V. R. A. P. (Ekstern), Li, Y. (Ekstern), Larsen, L. E. (Intern), Nauwynck, H. J. (Ekstern)
Number of pages: 17
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Main Research Area: Technical/natural sciences

Publication information

Journal: Veterinary Research
Volume: 46
Article number: 37
ISSN (Print): 0928-4249
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BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): SJR 1.281 SNIP 1.142
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.342 SNIP 1.006 CiteScore 2.66
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.189 SNIP 1.197 CiteScore 2.46
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.353 SNIP 1.457 CiteScore 3.13
ISI indexed (2013): ISI indexed yes
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BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.254 SNIP 1.279 CiteScore 2.97
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.593 SNIP 1.645 CiteScore 3.85
ISI indexed (2011): ISI indexed yes
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Fugleinfluensvirus H10N7 spredte sig blandt danske sæler i 2014

General information
State: Published
Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Section for Virology
Authors: Hjulsager, C. K. (Intern), Krog, J. S. (Intern), Hansen, M. S. (Intern), Chriél, M. (Intern), Larsen, L. E. (Intern)
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BFI (2012): BFI-level 1
ISI indexed (2012): ISI indexed no
BFI (2011): BFI-level 1
ISI indexed (2011): ISI indexed no
BFI (2010): BFI-level 1
High-throughput Gene Expression Analysis In Pigs As Model For Respiratory Infections

Influenza A virus infections have great impact on human health and welfare and significant resources are linked to influenza epidemics due to excess hospitalizations and lost productivity. Up to 15% of the human population is affected when Influenza spreads around the world in seasonal epidemics (WHO).

Animal models are essential in understanding the mechanisms involved in human infectious disease and for the development of effective prevention and treatment strategies. It is increasingly realized that large animal models like the pig are exceptionally human like and serve as an excellent model for disease and inflammation. Pigs are fully susceptible to human influenza, and have been demonstrated to be involved in influenza evolution and ecology. Pigs share many similarities with humans regarding lung physiology and innate immune cell infiltration of the respiratory system and thus seem to be an obvious large animal model for respiratory infections. This study aimed at providing a better understanding of the involvement of circulating non-coding RNA and innate immune factors in porcine blood leukocytes during influenza virus infection. By employing the pig as a model we were able to perform highly controlled experimental infections and to study changes of symptoms, viral titer, and expression of microRNAs/mRNAs as the influenza infection progresses in time, generating information that would be difficult to obtain from human patients.

The Gram-negative bacterium Actinobacillus pleuropneumoniae causes pneumonia in pigs, a disease which is associated with high morbidity and mortality, as well as impaired animal welfare. The rapidly evolving pneumonia is characterized by large areas of lung necrosis resulting from the combined effect of tissue damage caused by the bacteria, and a strong proinflammatory immune response. To obtain in-depth understanding of this infection, concurrent gene expression of host and pathogen in lung samples collected from pigs experimentally infected with A. pleuropneumoniae was studied. We applied high-throughput RT-qPCR for the simultaneous analysis of host and pathogen gene expression. This parallel analysis was done in lung tissue samples as well as in the immediate surroundings of infection loci after laser capture microdissection. Regulation of gene expression of several immune factors was observed in agreement with protein levels of these factors in lung tissue, infection status and histopathological findings.

Influenza A(H10N7) Virus in Dead Harbor Seals, Denmark

Since April 2014, an outbreak of influenza in harbor seals has been ongoing in northern Europe. In Denmark during June-August, 152 harbor seals on the island of Anholt were found dead from severe pneumonia. We detected influenza A(H10N7) virus in 2 of 4 seals examined.
Influenza A virus H10N7 detected in dead harbor seals (Phoca vitulina) at several locations in Denmark 2014.

Influenza A virus (IAV) affects a wide range of species, though waterfowl is regarded the natural host for most IAV subtypes. Avian influenza (AI) viruses replicate in the intestinal tract of birds and are mainly transmitted by the fecal-oral route. Pinnipeds share the same shoreline habitats as many waterfowl species and are therefore potentially exposed to AIV. Outbreaks of AI in seals have been described in North America and Asia but prior to 2014 never in Europe. In 2014 massive deaths of harbor seals (Phoca vitulina) were reported in Northern Europe. In Denmark, harbor seals were initially found dead on the Danish island Anholt in Kattegat, which is the sea surrounded by Denmark, Norway and Sweden. Between June and August, 152 harbor seals were found dead. Four seals were submitted to the National Veterinary Institute in Denmark and diagnosed with severe pneumonia. Influenza A virus of the subtype H10N7 was detected in two out of four seals. Subsequently IAV was detected in dead harbor seals at several locations in Denmark. The IAV outbreak appeared to move with time to the west through the Limfjord to the North Sea and further down south along the west coast of Jutland to the Wadden Sea. Outbreaks were subsequently reported from Germany and The Netherlands. The aim of this study was to characterize the viruses detected at the several locations by molecular and phylogenetic analysis. All viruses were subtyped as H10N7 with genes of avian origin. The HA and NA genes of the viruses were highly similar to H10N7 IAV detected in harbor seals in Sweden in the spring of 2014 and in Germany in the autumn of 2014, suggesting that the same strain of virus had spread from Sweden to Denmark and further on to Germany.

MicroRNA regulation of TLRs in a post-influenza animal model

Introduction

Substantial morbidity and mortality is caused by secondary bacterial infections occurring in individuals after influenza A virus (IAV) infection. Results from studies in mice suggest that this may in part be due to a lack of responsiveness to Toll-like receptor (TLR) ligands in the post-IAV infected individual. Using the pig as an animal model, we have identified microRNAs (miRNAs) that are differentially expressed in lung tissue two weeks after challenge compared to uninfected controls, i.e. well after the infection has cleared. The role for differential expression of miRNA at this late time point remains unclear. We therefore seek to examine the potential involvement of miRNAs in the translational regulation of TLRs and associated proteins, thus contributing to the lowered responsiveness to bacterial TLR ligands at this late time point, making the individual vulnerable to secondary infections.

Methods and outcome

Pigs were experimentally challenged with a Danish reassortant IAV strain (A/sw/Denmark/12687/03(H1N2)). Lung tissue was harvested 14 days after challenge, as well as from uninfected control animals. Using RNAseq and high-throughput RT-qPCR, we quantified the expression of relevant miRNAs (e.g. miR-335 and miR-146a-5p) and mRNA levels of relevant
miRNA targets. Transcriptional analysis at the site of infection reveals a set of miRNAs to be regulated one week after the pigs had cleared the IAV infection (i.e. two weeks after challenge). This set included miRNAs experimentally validated or in silico predicted to bind to and regulate transcripts of TLRs and relevant co-factors and transcription factors (online tools). The antiviral immune response elicited by IAV infection thus includes late miRNA regulation, which in turn may be at the expense of host responsiveness to bacterial TLR ligands.

General information
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Organisations: National Veterinary Institute, Section for Immunology and Vaccinology, Section for Virology, IDT-Biologika GmbH
Authors: Brogaard, L. (Intern), Heegaard, P. M. H. (Intern), Larsen, L. E. (Intern), Dürwald, R. (Ekstern), Schlegel, M. (Ekstern), Skovgaard, K. (Intern)
Number of pages: 1
Publication date: 2015
Main Research Area: Technical/natural sciences
Electronic versions:
Abstract_TOLL2015_Louise_Brogaard_1.pdf

Bibliographical note
Poster presentation
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Source-ID: 118949835
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Molecular characterization of AI viruses from poultry and wild bird surveillance in Denmark
Infection with avian influenza virus (AIV) in poultry may cause devastating disease although the same virus may not cause disease in wild birds. Since AI viruses can be exchanged between poultry and wild birds, surveillance in wild birds provides important knowledge for control of disease in poultry. AIV’s from the Danish wild bird active surveillance were characterized, focusing on viruses from 2012, and from outbreaks of AI in poultry in Denmark. The matrix (M) gene from more than 50 viruses of different subtypes and the hemagglutinin (HA) gene from more than 30 subtype H5 low pathogenic viruses were sequenced and compared by alignment and phylogenetic analyses. The aim was to evaluate: the origin of viruses from outbreaks of AI in Danish poultry, the design of active surveillance in Denmark, and the suitability of the molecular diagnostic RT-PCR tests employed. All M-genes from Danish viruses grouped phylogenetically with Eurasian lineage viruses. Grouping among Danish sequences was not correlated to place or to the time of sampling within the same year, although there was a tendency to grouping according to the year of sampling. Similar results were observed for H5 sequences. M and H5/H7 gene sequences from poultry showed a high degree of similarity to Danish wild bird sequences, suggesting exchange of viruses between geographically close wild birds and poultry. Significant drift was observed in both M and H5 gene sequences that are important for adequate molecular diagnostics, thus highlighting the importance of continuous surveillance and molecular characterization of AI viruses.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, University of Copenhagen
Authors: Larsen, L. E. (Intern), Krog, J. S. (Intern), Madsen, J. J. (Ekstern), Thorup, K. (Ekstern), Hjulsager, C. K. (Intern)
Publication date: 2015
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Main Research Area: Technical/natural sciences
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Bibliographical note
Abstract for oral presentation by Charlotte K Hjulsager at 9th International Symposium on Avian Influenza, Athens, Georgia, US. April 12-15, 2015.
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Source-ID: 112051314
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Molecular Epidemiology and Evolution of Influenza Viruses Circulating within European Swine between 2009 and 2013
The emergence in humans of the A(H1N1)pdm09 influenza virus, a complex reassortant virus of swine origin, highlighted the importance of worldwide influenza virus surveillance in swine. To date, large-scale surveillance studies have been reported for southern China and North America, but such data have not yet been described for Europe. We report the first large-scale genomic characterization of 290 swine influenza viruses collected from 14 European countries between 2009 and 2013. A total of 23 distinct genotypes were identified, with the 7 most common comprising 82% of the incidence.
Contrasting epidemiological dynamics were observed for two of these genotypes, H1huN2 and H3N2, with the former showing multiple long-lived geographically isolated lineages, while the latter had short-lived geographically diffuse lineages. At least 32 human-swine transmission events have resulted in A(H1N1)pdm09 becoming established at a mean frequency of 8% across European countries. Notably, swine in the United Kingdom have largely had a replacement of the endemic Eurasian avian virus-like (“avian-like”) genotypes with A(H1N1)pdm09-derived genotypes. The high number of reassortant genotypes observed in European swine, combined with the identification of a genotype similar to the A(H3N2)v genotype in North America, underlines the importance of continued swine surveillance in Europe for the purposes of maintaining public health. This report further reveals that the emergences and drivers of virus evolution in swine differ at the global level.

IMPORTANCE The influenza A(H1N1)pdm09 virus contains a reassortant genome with segments derived from separate virus lineages that evolved in different regions of the world. In particular, its neuraminidase and matrix segments were derived from the Eurasian avian virus-like (“avian-like”) lineage that emerged in European swine in the 1970s. However, while large-scale genomic characterization of swine has been reported for southern China and North America, no equivalent study has yet been reported for Europe. Surveillance of swine herds across Europe between 2009 and 2013 revealed that the A(H1N1)pdm09 virus is established in European swine, increasing the number of circulating lineages in the region and increasing the possibility of the emergence of a genotype with human pandemic potential. It also has implications for veterinary health, making prevention through vaccination more challenging. The identification of a genotype similar to the A(H3N2)v genotype, causing zoonoses at North American agricultural fairs, underlines the importance of continued genomic characterization in European swine.
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.399 SNIP 1.288 CiteScore 5.37
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.532 SNIP 1.278
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 3.595 SNIP 1.307
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 3.803 SNIP 1.264
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 3.571 SNIP 1.311
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 3.76 SNIP 1.255
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 3.374 SNIP 1.243
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 3.382 SNIP 1.32
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 3.425 SNIP 1.331
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 3.242 SNIP 1.254
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 3.577 SNIP 1.357
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 3.543 SNIP 1.394
Web of Science (2000): Indexed yes
Original language: English
Electronic versions:
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Mutant stamme af PCV2: opdatering af tilgængelig viden

General information
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Organisations: National Veterinary Institute, Section for Virology
Authors: Larsen, L. E. (Intern), Hjulsager, C. K. (Intern)
Number of pages: 5
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Original language: Danish
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Source: PublicationPreSubmission
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Publication: Education › Compendium/lecture notes – Annual report year: 2015
New neonatal porcine diarrhoea syndrome in Danish pigs. Characterisation of viral findings in diseased and healthy control animals

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Bacteriology, Pathology and Parasitology, Pig Research Centre, Swedish University of Agricultural Sciences, Statens Serum Institut
Authors: Larsen, L. E. (Intern), Goecke, N. B. (Intern), Kongsted, H. (Ekstern), Boye, M. (Intern), Hjulsager, C. K. (Intern), Granberg, F. (Ekstern), Kølsen Fischer, T. (Ekstern), Midgley, S. (Ekstern)
Pages: 181-181
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Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

New reassortant and enzootic European swine influenza 1 viruses transmitted efficiently through direct contact in the ferret model

The reverse zoonotic events that introduced the 2009 pandemic influenza virus into pigs have drastically increased the diversity of swine influenza viruses in Europe. The pandemic potential of these novel reassortments is still unclear, necessitating enhanced surveillance of European pigs with additional focus on risk assessment of these new viruses. In this study, four European swine influenza viruses were assessed for their zoonotic potential. Two of the four viruses were enzootic viruses of subtype H1N2 (with avian-like H1) and H3N2 and two were new reassortants, one with avian-like H1 and human-like N2 and one with 2009 pandemic H1 and swine-like N2. All viruses replicated to high titers in nasal wash- and nasal turbinate samples from inoculated ferrets and transmitted efficiently by direct contact. Only the H3N2 virus transmitted to naïve ferrets via the airborne route. Growth kinetics using a differentiated human bronchial epithelial cell line showed that all four viruses were able to replicate to high titers. Further, the viruses revealed preferential binding to the α2,6-sialylated glycans and investigation of the antiviral susceptibility of the viruses revealed that all were sensitive to neuraminidase inhibitors. These findings suggest that these viruses have the potential to infect humans and further underline the need for continued surveillance as well as biological characterization of new influenza A viruses.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Bacteriology, Pathology and Parasitology, St. Jude Children’s Research Hospital
Authors: Fobian, K. (Intern), Fabrizio, T. (Ekstern), Yoon, S. (Ekstern), Hansen, M. S. (Intern), Webby, R. J. (Ekstern), Larsen, L. E. (Intern)
Pages: 1603-1612
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.93 SJR 1.499 SNIP 0.886
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.729 SNIP 1.007 CiteScore 3.26
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Overvågning af aviær influenza i vilde fugle i Danmark 2014

Overvågningen af aviær influenza (AI) virus i vilde fugle i Danmark i 2014 blev udført i samarbejde mellem Veterinærinstituttet, Danmarks Tekniske Universitet (DTU-VET), Fødevarestyrelsen (FVST) og Statens Naturhistoriske Museum, Københavns Universitet (SNM) i henhold til "Projektplan vedr. overvågningen af aviær influenza i vilde fugle i Danmark i 2014" (bilag 4). Overvågning af AI på EU niveau går tilbage til 2002, og Danmark er underlagt EU kommissionens bestemmelser for udføring af overvågningen, der dog har skiftet gennem årene i takt med indhastede erfaringer. I 2014 blev der udført passiv overvågning af døde vilde fugle, der blev fundet i naturen. Der blev testet 10 fugle,

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**Organisations:** National Veterinary Institute, Section for Virology, University of Copenhagen

**Authors:** Hjulsager, C. K. (Intern), Krog, J. S. (Intern), Madsen, J. J. (Ekstern), Thorup, K. (Ekstern), Larsen, L. E. (Intern)

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Overvågning af influenza afslører flere subtyper

Overvågning af influenza A virus i svin i 2014

Overvågning af influenza i wilde fugle i Danmark 2014 til ORBIT.pdf

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Scientific report
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Publication: Research - peer-review › Report – Annual report year: 2015

General information
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Organisations: National Veterinary Institute, Section for Virology
Authors: Krog, J. S. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
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Overvågning af influenza A virus i svin i 2014

Der er i 2014 gennemført en systematisk, prospektiv passiv overvågning af cirkulerende influenza virus subtyper i danske svin. Det overordnede formål med overvågningen var at identificere hvilke influenza virus subtyper og stammer, der cirkulerer blandt danske svin, og at kortlægge sygdomsårsager i svinepopulationen med henblik på at sikre det strategiske mål: at mindske antibiotikaforbruget i danske svinebesætninger. Overvågningen har bestået i: 1) Undersøgelse for influenza virus vha. pan-influenza A virus real time RT-PCR på brugerbetalte diagnostiske indsendelser til influenza virusundersøgelse på DTU-VET 2) Test af influenza virus positive prøver for pandemisk H1N1 (H1N1pdm09) ved real time RT-PCR der specifikt detekterer HA-genet i H1N1pdm09 virus 3) Isolering af virus i MDCK celler 4) Subtypning af positive virusisolater ved sekvensanalyse (HA og NA generne) 5) Komplet genom karakterisering af udvalgte virusisolater Der blev totalt i 2014 iværksat undersøgelse for influenza A virus på 1173 prøver fordelt på 538 indsendelser fra 422 besætninger. I alt var 435 (37 %) af prøverne positive og 239 (44 %) af indsendelserne havde minimum en positiv prøve fordelt på 199 forskellige besætninger. Indsendelserne fordelt sig over hele landet og over hele året. Der var flest indsendelser til undersøgelse i de kolde måneder, men influenza virus blev påvist med næsten samme hyppighed hele året. I alt blev 80 influenza virus positive indsendelser opdyrket i MDCK celler. De dyrkede virusisolater blev undersøgt ved sekvensanalyse for at bestemme subtypen. Disse analyser viste, at de to mest almindelige subtyper i danske svin i 2014 var den danske variant af H1N2 og H1N1pdm09. Praevalensen af det almindelige svineinfluenza virus “avian-like swine” H1N1 subtype er faldet drastisk og forekom i 2014 tilsyneladende mindre hyppigt end H1N1pdm09 subtypen. Influenza virus af subtypen H3N2, der har cirkuleret i Danmark siden 1990, blev påvist i en enkelt indsendelse i 2014, hvilket også var tilfældet i 2013. Den centraleuropæiske variant af H1N2, der har et human-like HA gen, er i lighed med tidligere år ikke påvist i danske svin. Virus med subtypen H1pdm09 blev påvist i 60 indsendelser fra 55 besætninger og udgjorde således 24 % af de influenza virus positive indsendelser. Dette er næsten en fordobling i forhold til 2013. Hos mennesker var 2014 domineret af H1pdm09 subtypen, men det er uklart om stigningen hos svin i 2014 skyldes øget smitteoverførsel fra mennesker til svin. Resultaterne af overvågningen i 2014 underbygger antagelsen om at de nye reassortments fra de foregående år: H1N2hu, H1pdmN2hu og H1pdmN2sw, nu er fast etableret i den danske svinepopulation, hvor den cirkulerer uafhængigt af den humane influenza virus sæson. Overvågningen har endvidere påvist adskillige nye virus reassortments, hvor gener fra H1pdm09 indgår, bl.a. tyder det på at H1N2 virus med interne gener fra H1pdm09 har etableret sig i den danske svinepopulation. Ud over disse subtyper blev der i 2014 fundet en helt ny reassortment: H3hu05N2sw. Dette virus bærer et human-like HA gen, der ligner dem, der cirkulerede i den danske befolkning i 2004-2005, samt et NA gen med stor lighed med NA genet i H1N2 virus fra danske svin. De interne gener stammer alle fra H1N1pdm09 subtypen. Der er i dette tilfælde tale om en triple-reassortment (blanding af tre forskellige influenza virus), men da HA genet har cirkuleret i den humane befolkning for nylig, må det formodes at der er stor grad af immunitet mod denne type. Resultaterne beskrevet i rapporten er vigtige i forhold til såvel zoonotiske som veterinære aspekter ved influenza A virus infektion i svin i Danmark. Undersøgelserne har med stor sandsynlighed vist, at H1N1pdm09, som stadig må betragtes som en zoonose, nu er etableret i den danske svinpopulation, hvor den cirkulerer uafhængigt af den humane influenza virus sæson. Overvågningen af influenza afslører flere subtyper
virus bliver etableret i danske svin. Fra et veterinært synspunkt er det vigtigt at få fastlagt hvilke(n) subtype(r), der cirkulerer i besætningen, da valg af vaccine er afhængig af denne information. Det er derfor positivt, at der over de senere år er sket en stigning i antal inddsendelser til influenzapåvisning i Danmark, da det øger muligheden for at vaccinere korrekt og derved nedsætte risikoen for antibiotika krævende sekundære infektioner. Det er også positivt at den H1N2 subtype (med human-like HA-gen), der er dominerende i andre dele af Europa, stadig ikke findes i Danmark. Introduktion af dette virus kan frygtes at få epizootisk karakter, da immuniteten i populationen mod dette virus er meget lille. Det kan konkluderes, at den iværksatte overvågning har givet et godt indblik i hvilke influenza A virus, der cirkulerer i danske svin, og at denne information dagligt bruges proaktivt ved håndtering af sygdom i besætningerne. Overvågningen har endvidere vist, at virus med nye genkombinationer er blevet etableret i danske svin, og der bør de kommende år holdes øje med, om disse virus smitter til mennesker.

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Organisations: National Veterinary Institute, Section for Virology
Authors: Krog, J. S. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
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Original language: English
Main Research Area: Technical/natural sciences
Electronic versions: Overvågning af influenza A virus i svin i 2014_ORBIT.pdf
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Publication: Research - peer-review › Report – Annual report year: 2015

PRRSV type 1 detection in aerosols from three swine herds in Denmark

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Technical University of Denmark, Boehringer Ingelheim Danmark A/S, Boehringer Ingelheim Vetmedica, Inc., Svinevet Pig Practise
Authors: Priebe, A. (Ekstern), Rathkjen, P. H. (Ekstern), Larsen, L. E. (Intern), Kvisgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Angulo, J. (Ekstern), Havn, K. (Ekstern)
Number of pages: 1
Publication date: 2015

Host publication information
Title of host publication: Proceedings of the 7th european symposium of porcine health management
Place of publication: Nantes, France
Article number: PO85
Main Research Area: Technical/natural sciences
Conference: 7th European Symposium of Porcine Health Management, Nantes, France, 22/04/2015 - 22/04/2015
Source: PublicationPreSubmission
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PRRSV type 1 detection in aerosols inside a PRRSV-positive swine herd in Denmark

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Technical University of Denmark, Boehringer Ingelheim Vetmedica, Inc., Technical University of Denmark, Boehringer Ingelheim Danmark A/S, Svinevet Pig Practise
Authors: Priebe, A. (Ekstern), Rathkjen, P. H. (Ekstern), Larsen, L. E. (Intern), Kvisgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Angulo, J. (Ekstern), Havn, K. (Ekstern)
Pages: 171-171
Publication date: 2015

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Main Research Area: Technical/natural sciences
Conference: 7th European Symposium of Porcine Health Management, Nantes, France, 22/04/2015 - 22/04/2015
Simultaneous vaccination with PRRS mlv against both PRRSV type 1 and type 2: duration of viraemia and level of clinical protection

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Technical University of Denmark, Danish Pig Production
Authors: Kristensen, C. S. (Ekstern), Kvisgaard, L. K. (Intern), Pawlowski, M. (Ekstern), Holmgaard Carlsen, S. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from 7th International Symposium on Emerging and Re-emerging Pig Diseases, Kyoto, Japan.
Main Research Area: Technical/natural sciences
Electronic versions:
ISERPD2015_abstract_Lindholm_final.pdf
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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Spatial analysis and temporal trends of porcine reproductive and respiratory syndrome in Denmark from 2007 to 2010 based on laboratory submission data
Porcine reproductive and respiratory syndrome (PRRS) has been a cause for great concern to the Danish pig industry since it was first diagnosed in 1992. The causative agent of PRRS is an RNA virus which is divided into different genotypes. The clinical signs, as well as its morbidity and mortality, is highly variable between herds and regions. Two different genotypes of PRRS virus (PRRSV) are found in Denmark: type 1 and type 2. Approximately 40 % of Danish swine herds are seropositive for one or both PRRSV types. The objective of this study was to describe the temporal trend and spatial distribution of PRRSV in Danish swine herds from 2007 to 2010, based on type-specific serological tests from the PRRS surveillance and control program in Denmark using the results stored in the information management system at the National Veterinary Institute, Technical University of Denmark (DTU Vet). The average monthly seroprevalence of PRRSV type 1 was 9 % (minimum of 5 %; maximum of 13 %) in breeding herds, and 20 % (minimum of 14 %; maximum of 26 %) in production herds; PRRSV type 2 had an average seroprevalence of 3 % (minimum of 1 %; maximum of 9 %) in breeding herds and of 9 % (minimum of 5 %; maximum of 13 %) within production herds. The seroconversion rate followed a similar and consistent pattern, being higher for type 1 than for type 2 for both PRRSV types. Regarding the spatiotemporal results, the relative risk distribution maps changed over time as a consequence of the changes in PRRSV seroprevalence, suggesting a general decline in the extent of areas with higher relative risk for both type 1 and 2. Local spatial analysis results demonstrated the existence of statistically significant clusters in areas where the relative risk was higher for both herds. PRRSV type 1 seroprevalence was constantly higher than for PRRSV type 2 in both herd types. Significant spatial clusters were consistently found in Denmark, suggesting that PRRSV is endemic in these areas. Furthermore, relative risk distribution maps revealed different patterns over time as a consequence of the changes in seroprevalence.

General information
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Section for Virology, Pig Research Centre
Authors: Lopes Antunes, A. C. (Intern), Hisham Beshara Halasa, T. (Intern), Lauritsen, K. T. (Intern), Kristensen, C. S. (Ekstern), Larsen, L. E. (Intern), Toft, N. (Intern)
Number of pages: 11
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Main Research Area: Technical/natural sciences
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Strain-specific serological response after simultaneous vaccination with PRRS MLV against

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Technical University of Denmark, Danish Pig Production
Authors: Kristensen, C. S. (Ekstern), Kvisgaard, L. K. (Intern), Pawlowski, M. (Ekstern), Carlsen, S. H. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from International Porcine Reproductive And Respiratory Syndrome Congress, Ghent, Belgium.
Main Research Area: Technical/natural sciences
Electronic versions:
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Source: PublicationPreSubmission
Source-ID: 2289946454
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Swine influenza viruses in circulation in European pigs exhibit an increasing genetic diversity since last pandemic 2009
Swine plasma Immunoglobulins for prevention and treatment of post-weaning diarrhoea: Safety and Preliminary results

Post-weaning diarrhoea (PWD) is a common condition in intensive swine production, resulting in reduced welfare of weaners and economic losses for the farmer as a result of illness, death, and treatment costs. It is also one of the main causes of antibiotics- and zinc use in the pig production industry. We aim at developing a sustainable product for protection against PWD based on natural antibodies (immunoglobulins) derived directly from inexpensive raw materials. The availability of such an inexpensive and highly active immunoglobulin product would allow swine producers to reduce expenses and minimize the on antibiotics and zinc usage. Swine immunoglobulins were isolated directly from slaughterhouse swine plasma-waste by expanded bed chromatography. It was shown that the isolated Immunoglobulin fraction bound enterotoxigenic Escherichia coli (ETEC) and Salmonella ssp. and inhibited their adhesion to porcine epithelial cells in vitro. As the immunoglobulin fraction is intended for oral use as a feed supplement, we also tested the safety of feeding 4 grams of natural immunoglobulins to 4-5 week old weaner piglets for 14 days and observed no adverse effects. In an experimental model of E. coli F4+ induced PWD, we observed that piglets given IgG as a feed supplement cleared the E. coli infection significantly faster than control weaner piglets not receiving an immunoglobulin feed supplement. Furthermore, deep sequencing of the ileal microbiota showed a significantly lowered colonization of the family Enterobacteriaceae in immunoglobulin fed piglets as compared to the control group. Thus pig slaughterhouse plasma is indicated as a potential source resource of antibodies for the control of PWD.
The immunity raised by recent European subtype 1 PRRSV strains allows a better replication of East European subtype 3 PRRSV strain Lena than the immunity raised by an older strain - increased risk for spatial expansion of PRRSV Lena-like strains

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Ghent University

The pig as a large animal model for influenza a virus infection
It is increasingly realized that large animal models like the pig are exceptionally human like and serve as an excellent model for disease and inflammation. Pigs are fully susceptible to human influenza, share many similarities with humans regarding lung physiology and innate immune cell infiltration of the respiratory system.

This study aimed at providing a better understanding of the involvement of innate immune factors and non-coding RNA in blood leukocytes during influenza A virus infection. By using the pig as a model we were able to perform highly controlled experimental infections and study early clinical signs of disease, viral titer, and transcriptional response of coding and non-coding RNA. This was completed during the first two weeks after experimental viral infection, generating information that would be difficult to obtain from human patients.

Expression of a wide range of immune factors including several genes known to be centrally involved in the viral defence was quantified by high throughput qPCR (BioMark, Fluidigm). Likewise, miRNAs were quantified using the BioMark (Fluidigm) as well as by MiRCURY LNA TM (Exiqon).

During the first 24 hours of infection we found the expression of several antiviral genes, including interferon and interferon-related genes, to mimic key findings from human studies. Finally, several circulating miRNAs isolated from blood leukocytes was found to hold great potential as biomarkers for progression of viral lung infection. These results further consolidate the pig as a valuable model for influenza A virus infection.

General information
State: Published
Organisations: National Veterinary Institute, Section for Immunology and Vaccinology, Section for Virology, Technical University of Denmark, IDT-Biologika GmbH

1. THE_PIG_AS_A_LARGE_ANIMAL_MODEL_FOR_INFLUENZA_A_VIRUS_INFECTION.pdf
Source: PublicationPreSubmission
Overvågning af aviser influenza i vilde fugle i Danmark 2013

Overvågningen af aviser influenza (AI) virus i vilde fugle i Danmark i 2013 blev udført i samarbejde mellem Fødevarestyrelsen (FVST), Veterinærinstituttet, Danmarks Tekniske Universitet (DTU-VET) og Statens Naturhistoriske Museum, Københavns Universitet (SNM) i henhold til "Aftale mellem Fødevarestyrelsen og Veterinærinstituttet om overvågning af aviser influenza i vilde fugle i Danmark i 2013" (bilag 4).

Overvågning af AI på EU niveau går tilbage til 2002, og Danmark er underlagt EU kommissionens bestemmelser for udførelse af overvågningen, der dog har skiftet gennem årene i takt med indhøstede erfaringer.

I 2013 blev der udført passiv overvågning af døde vilde fugle, der blev fundet i naturen. Der blev testet 10 fugle, og ingen af disse var positive for AI virus. Tre blev indsendt af Veterinærafdeling Øst, de øvrige var indsendt faldvildt fra private indsamler.

General information
State: Published
Organisations: National Veterinary Institute, Section for Public sector service and commercial diagnostics, Section for Virology, Natural History Museum of Denmark
Authors: Hjulsager, C. K. (Intern), Krog, J. S. (Intern), Madsen, J. J. (Ekstern), Thorup, K. (Ekstern), Larsen, L. E. (Intern)
Publication date: 15 Mar 2014

3 PRRS-stabile sohold leverede hver 10 hold PRRS-fri smågrise

I tre besætninger var det muligt at producere 10 PRRS-fri hold af smågrise i hver besætning over tid, selvom soholdet var PRRS-positivt. Dette var muligt på trods af forskelle i produktionssystemer, karantænebrug og PRRS-vaccinationsstrategier.

I undersøgelsen indgik tre besætninger. Besætningerne var deklareret PRRS-positive, hvilket betyder at der var påvist antistoffer mod PRRS i søernes blod, men besætningsejerne formodede, at de havde et PRRS-stabilt sohold (ingen cirkulation af PRRS-virus blandt søerne), så grisene var PRRS-fri (grise uden PRRS-virus) ved 30 kg. I hver besætning blev der taget blodprøver af 10 hold grise ved 30 kg.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Dansk Svineproduktion
Authors: Kristensen, C. S. (Ekstern), Larsen, L. E. (Intern), Hjulsager, C. K. (Intern)
Number of pages: 7
Publication date: 2014

Analysis of ORF5 and Full-Length Genome Sequences of Porcine Reproductive and Respiratory Syndrome Virus Isolates of Genotypes 1 and 2 Retrieved Worldwide Provides Evidence that Recombination Is a Common Phenomenon and May Produce Mosaic Isolates

Recombination is currently recognized as a factor for high genetic diversity, but the frequency of such recombination events and the genome segments involved are not well known. In the present study, we initially focused on the detection of recombinant porcine reproductive and respiratory syndrome virus (PRRSV) isolates by examining previously published data sets of ORF5 sequences (genotypes 1 and 2) obtained worldwide. We then examined full-length genome sequences in order to determine potential recombination breakpoints along the viral genome. For ORF5, 11 sets of genotype 1 sequences from different geographical areas, including 2 Asian, 1 American, and 7 European regions, and three sets of genotype 2, including sets from China, Mexico, and the United States, were analyzed separately. Potential recombination
breakpoints were detected in 10/11 genotype 1 sets, including 9 cases in which the clustering of at least one isolate was different before and after the breakpoints. In genotype 2, potential breakpoints and different tree clustering of at least one strain before and after the breakpoint were observed in 2 out of 3 sets. The results indicated that most of the ORF5 data sets contained at least one recombinant sequence. When the full-length genome sequences were examined, both genotype 1 and 2 sets presented breakpoints (10 and 9, respectively), resulting in significantly different topologies before and after the breakpoints. Mosaic genomes were detected in genotype 1 sequences. These results may have significant implications for the understanding of the molecular epidemiology of PRRSV. IMPORTANCE PRRSV is one of the most important viruses affecting swine production worldwide, causing big economic losses and sanitary problems. One of the key questions on PRRSV arises from its genetic diversity, which is thought to have a direct impact on immunobiology, epidemiology, diagnosis, and vaccine efficacy. One of the causes of this genetic diversity is recombination among strains. This study provides evidence that recombinant PRRSV isolates are common in most of the countries with significant swine production, especially PRRSV genotype 1. This observation has implications in the proper characterization of PRRSV strains, in the future development of phylogenetic studies, and in the development of new PRRSV control strategies. Moreover, the present paper emphasizes the need for a deeper understanding of the mechanisms and circumstances involved in the generation of genetic diversity of PRRSV.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Universidad Autonoma de Barcelona, The Pirbright Institute, Centro de Investigacion en Alimentacion y Desarrollo
Authors: Martín-Valls, G. E. (Ekstern), Kvisgaard, L. K. (Intern), Tello, M. (Forskerdatabase), Darwich, L. (Ekstern), Cortey, M. (Ekstern), Burgara-Estrella, A. J. (Ekstern), Hernández, J. (Forskerdatabase), Larsen, L. E. (Intern), Mateu, E. (Ekstern)
Pages: 3170-3181
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Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed Yes
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Scopus rating (2016): SJR 3.052 SNIP 1.131 CiteScore 4.42
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 3.286 SNIP 1.138 CiteScore 4.42
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 3.168 SNIP 1.219 CiteScore 4.4
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 3.468 SNIP 1.26 CiteScore 4.92
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 3.154 SNIP 1.227 CiteScore 5.2
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.399 SNIP 1.288 CiteScore 5.37
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.532 SNIP 1.278
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Assessment of zoonotic potential of four European swine influenza viruses in the ferret model

The reverse zoonotic events that introduced the 2009 pandemic influenza virus into swine herds have drastically increased the diversity of reassortants throughout Europe. The pandemic potential of these novel reassortments is unknown, hence necessitating enhanced surveillance of European swine herds and enhanced focus on risk assessment of these new viruses. In this study, four European swine influenza viruses were assessed for their zoonotic potential. Of the four viruses, two were enzootic viruses of subtype H1N2 (with avian-like H1) and H3N2 and two were new reassortants, one with avian-like H1 and human-like N2 and one with pandemic H1 and swine-like N2. All viruses replicated to high viral titers in nasal wash- and nasal turbinate samples from inoculated ferrets and transmitted efficiently by direct contact. Only the H3N2 virus transmitted to naive ferrets via respiratory droplets. Growth kinetics using human bronchial cells showed that all four viruses were able to replicate to high titers. Further, the viruses revealed preferential binding to the α2,6-sialylated glycans and investigation of the antiviral susceptibility of the viruses revealed that they were all sensitive to neuraminidase inhibitors. These findings suggest that the investigated viruses have the potential to infect humans and further underline the need for continued surveillance as well as pandemic and zoonotic assessment of new influenza reassortants.

General information

State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Bacteriology, Pathology and Parasitology, St. Jude Children’s Research Hospital, Korea Research Institute of Bioscience and Biotechnology
Authors: Fobian, K. (Intern), P. Fabrizio, T. (Ekstern), Yoon, S. (Ekstern), Hansen, M. S. (Intern), Webby, R. J. (Ekstern), Larsen, L. E. (Intern)
Publication date: 2014
Event: Abstract from Influenza 2014, Oxford, United Kingdom.
Main Research Area: Technical/natural sciences
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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014
Clinical characterization of a type 2 PRRSV causing significant clinical disease in the field in Denmark

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Immunology and Vaccinology, Section for Bacteriology, Pathology and Parasitology, Danvet K/S, Boehringer Ingelheim Danmark A/S, Technical University of Denmark
Authors: Larsen, L. E. (Intern), Kvitsgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Bøtner, A. (Intern), Rathkjen, P. H. (Ekstern), Heegaard, P. M. H. (Intern), Bisaard, N. (Ekstern), Hansen, M. S. (Intern), Nielsen, J. (Ekstern)
Publication date: 2014

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Main Research Area: Technical/natural sciences
Conference: 23rd IPVS Congress, Cancun, Mexico, 08/06/2014 - 08/06/2014
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PRRSV_BI_abstract_IPVS2014.pdf
Source: PublicationPreSubmission
Source-ID: 103450993
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Effects of level of social contact on dairy calf behavior and health
Housing preweaned dairy calves in pairs rather than individually has been found to positively affect behavioral responses in novel social and environmental situations, but concerns have been raised that close contact among very young animals may impair their health. In previous studies, the level of social contact permitted in individual housing has been auditory, visual, or physical contact. It is unclear how these various levels of social contact compare with each other and to pair housing, when their effects on behavior and health are considered, and whether the timing of pair housing has an effect. To investigate this, 110 Holstein calves (50 males, 60 females) in 11 blocks were paired according to birth date. Within 60 h of birth, each pair of calves was allocated to 1 of 5 treatments: individual housing with auditory contact (I), individual housing with auditory and visual contact (V), individual housing with auditory, visual, and tactile contact (T), pair housing (P), or individual housing with auditory and visual contact the first 2 wk followed by pair housing (VP). At 6 wk of age, calves were subjected to a social test and a novel environment test. In the social test, all pair-housed calves (P and VP) had a shorter latency to sniff an unfamiliar calf than did individually hosed calves (I, V; and T), whereas calves with physical contact (T, P, and VP) sniffed the unfamiliar calf for longer than calves on the remaining treatments (I and V). In the novel environment test, calves with physical contact (T, P, and VP) had a lower heart rate, and more of these calves vocalized during the test compared with calves without physical contact (I and V). No effect of treatment was found for clinical scores, levels of the 5 most common pathogens in feces, or in development of serum antibodies against the 3 most common respiratory pathogens. Calves housed individually are more fearful of unfamiliar calves than are pair-housed calves. Contrary to common belief, the allowance of physical contact and pair housing had no effects on the health of the calves.

General information
State: Published
Organisations: National Veterinary Institute, Aarhus University
Authors: Jensen, M. B. (Ekstern), Larsen, L. E. (Intern)
Pages: 5035-5044
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Main Research Area: Technical/natural sciences

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BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.66 SJR 1.304 SNIP 1.464
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.464 SNIP 1.498 CiteScore 2.63
Enteric porcine viruses in farmed shellfish in Denmark

Bivalve shellfish are at constant risk of being exposed to pathogens as a consequence of contamination of the shellfish beds with human or animal waste originating from sewage treatment plants or slurry fertilized fields. Consumption of contaminated oysters and mussels are frequently reported as causes of disease outbreaks caused by norovirus or hepatitis A virus. Other zoonotic pathogens such as hepatitis E virus (HEV), rotavirus (RV) and Salmonella from livestock may also be transmitted to shellfish via this route. In this study, 29 pooled samples from commercial Danish blue mussels were tested for porcine pathogens and indicator bacteria Escherichia coli (E. coli). All samples tested negative for HEV,
RV and Salmonella, whereas E. coli and the highly stable porcine circovirus type 2 (PCV2) were detected in eight and 12 samples, respectively. This is the first study to report the detection of PCV2 in commercial mussels. Based on the detection of PCV2 in clean areas with low prevalence of the normally applied fecal indicator E. coli, testing for PCV2 may be a more sensitive and robust specific porcine waste indicator in shellfish harvesting areas.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, National Food Institute, Division of Food Microbiology
Authors: Krog, J. S. (Intern), Larsen, L. E. (Intern), Schultz, A. C. (Intern)
Pages: 105-109
Publication date: 2014
Main Research Area: Technical/natural sciences

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Scopus rating (2016): CiteScore 3.97 SJR 1.462 SNIP 1.554
Web of Science (2016): Indexed yes
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Scopus rating (2015): SJR 1.628 SNIP 1.694 CiteScore 4.02
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.501 SNIP 1.711 CiteScore 3.62
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.602 SNIP 1.86 CiteScore 3.8
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.62 SNIP 1.709 CiteScore 3.7
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.595 SNIP 1.717 CiteScore 3.63
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.593 SNIP 1.665
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.458 SNIP 1.52
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.486 SNIP 1.511
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.33 SNIP 1.69
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.52 SNIP 1.794
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.494 SNIP 1.827
Web of Science (2005): Indexed yes
Swine influenza causes concern for global veterinary and public health officials. In continuing two previous networks that initiated the surveillance of swine influenza viruses (SIVs) circulating in European pigs between 2001 and 2008, a third European Surveillance Network for Influenza in Pigs (ESNIP3, 2010-2013) aimed to expand widely the knowledge of the epidemiology of European SIVs. ESNIP3 stimulated programs of harmonized SIV surveillance in European countries and supported the coordination of appropriate diagnostic tools and subtyping methods. Thus, an extensive virological monitoring, mainly conducted through passive surveillance programs, resulted in the examination of more than 9,000 herds in 17 countries. Influenza A viruses were detected in 31% of herds examined from which 1,887 viruses were preliminary characterized. The dominating subtypes were the three European enzootic SIVs: avian-like swine H1N1 (53.6%), human-like reassortant swine H1N2 (13%) and human-like reassortant swine H3N2 (9.1%), as well as pandemic A/H1N1 2009 (H1N1pdm) virus (10.3%). Viruses from these four lineages co-circulated in several countries but with very different relative levels of incidence. For instance, the H3N2 subtype was not detected at all in some geographic areas whereas it was still prevalent in other parts of Europe. Interestingly, H3N2-free areas were those that exhibited highest frequencies of circulating H1N2 viruses. H1N1pdm viruses were isolated at an increasing incidence in some countries from 2010 to 2013, indicating that this subtype has become established in the European pig population. Finally, 13.9% of the viruses represented reassortants between these four lineages, especially between previous enzootic SIVs and H1N1pdm. These novel viruses were detected at the same time in several countries, with increasing prevalence. Some of them might become established in pig herds, causing implications for zoonotic infections.
Gastric ulcers in nursery pigs.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Bacteriology, Pathology and Parasitology, Danish Agriculture and Food Council, Universidade Federal de Minas Gerais, National Veterinary Institute, University of Copenhagen
Authors: Pedersen, K. S. (Ekstern), Guedes, R. M. C. (Ekstern), Angen, Ø. (Intern), Ståhl, M. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Nielsen, J. P. (Ekstern), Bækbo, P. (Ekstern), Jensen, T. K. (Intern)
Publication date: 2014
Event: Abstract from 6th European Symposium of Porcine Health Management (ESPHM 2014), Italy.
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 103450889
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014
Genetic and antigenic drift of Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) in a closed population evaluated by full genome sequencing

Porcine Reproductive and Respiratory Syndrome (PRRS) viruses are divided into two major genotypes (Type 1 and Type 2) based on their genetic diversity. Type 1 PRRSV is further divided into at least 3 subtypes, but until now only subtype 1 has been detected in Western Europe and North America. Both genotypes are circulating in Denmark and since gilt vaccinations are widely used it is essential to monitor the diversity of circulating PRRS viruses. Prior to the present study, however, the diversity of circulating viruses in Denmark was virtually unknown. The main objective was to assess the diversity of circulating PRRS viruses in Danish pigs and to investigate the genetic drift of the virus in a closed population with very limited introductions of new animals. The study included phylogenetic analysis of full genome sequences of eight Type 1 and nine Type 2 PRRS viruses, including the very first Danish isolated Type 1 virus and the very first Danish Type 2 PRRS virus isolated from a non-vaccinated pig herd. Furthermore, by sequencing ORF5 and ORF7 of 43 Type 1 and 57 Type 2 viruses isolated between 2003 and 2013, the level of genetic diversity was assessed. The results showed a very high genetic diversity among the Danish viruses throughout the genome within the same genotype. A global phylogenetic analysis showed that the Danish Type 1 PRRSV formed two major clusters, one vaccine (Porcilis)-like clade exclusively containing viruses isolated after the Porcilis vaccine was introduced and another distinct clade consisting mainly of viruses isolated in Denmark. Phylogenetic analysis in a global Type 2 PRRSV framework classified all Danish Type 2 viruses to a single cluster (sub-lineage 5.1) which comprised viruses closely related to the Type 2 prototype isolate VR2332. Both Type 1 and Type 2 harbored deletions in the region encoding nsp2 and some significant amino acid changes were also seen in antigenic sites. Acknowledgement: The study was supported by EU Grant n° 245141 (New tools and approaches to control Porcine Reproductive and Respiratory Syndrome in the EU and Asia (PoRRSCon) coordinated by Prof. H. Nauwynck.

General information
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Organisations: National Veterinary Institute, Section for Virology
Authors: Kvisgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Publication date: 2014
Event: Abstract from 13th International Nidovirus Symposium, Salamanca, Spain.
Main Research Area: Technical/natural sciences
Electronic versions:
PRRSV_abstract_Lise_Kirstine_Kvisgaard_Nidovirus_2014.pdf

High-throughput gene expression analysis in pigs as model for respiratory infections

Animal models are essential in understanding the mechanisms involved in human infectious disease and for the development of effective prevention and treatment strategies. It is increasingly realized that large animal models like the pig are exceptionally human like and serve as an excellent model for disease and inflammation. Pigs are fully susceptible to human influenza, and have been demonstrated to be involved in influenza evolution and ecology. Pigs share many similarities with humans regarding lung physiology and innate immune cell infiltration of the respiratory system and thus seem to be an obvious large animal model for respiratory infections. This study aimed at providing a better understanding of the involvement of circulating non-coding RNA and innate immune factors in porcine blood leukocytes during influenza virus infection. By employing the pig as a model we were able to perform highly controlled experimental infections and to study changes of symptoms, viral titer, and expression of microRNAs/mRNAs as the influenza infection progresses in time, generating information that would be difficult to obtain from human patients.

General information
State: Published
Organisations: National Veterinary Institute, Section for Immunology and Vaccinology, Section for Bacteriology, Pathology and Parasitology, Section for Virology
Authors: Skovgaard, K. (Intern), Brogaard, L. (Intern), Schou, K. K. (Intern), Larsen, L. E. (Intern), Mortensen, S. (Intern), Dürrwald, R. (Ekstern), Schengel, M. (Ekstern), Heegaard, P. M. H. (Intern)
Publication date: 2014
Event: Abstract from Conferences and Workshops of COST Action BM1308, Munich, Germany.
Main Research Area: Technical/natural sciences
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High_throughput_gene_expression_analysis_in_pigs_as_model_for_respiratory_infections.pdf
Identification of swine influenza virus epitopes and analysis of multiple specificities expressed by cytotoxic T cell subsets

Background: Major histocompatibility complex (MHC) class I peptide binding and presentation are essential for antigen-specific activation of cytotoxic T lymphocytes (CTLs) and swine MHC class I molecules, also termed swine leukocyte antigens (SLA), thus play a crucial role in the process that leads to elimination of viruses such as swine influenza virus (SwIV). This study describes the identification of SLA-presented peptide epitopes that are targets for a swine CTL response, and further analyses multiple specificities expressed by SwIV activated CTL subsets. Findings: Four SwIV derived peptides were identified as T cell epitopes using fluorescent influenza: SLA tetramers. In addition, multiple CTL specificities were analyzed using peptide sequence substitutions in two of the four epitope candidates analyzed. Interestingly both conserved and substituted peptides were found to stain the CD4⁻CD8⁺ T cell subsets indicating multiple specificities. Conclusions: This study describes a timely and cost-effective approach for viral epitope identification in livestock animals. Analysis of T cell subsets showed multiple specificities suggesting SLA-bound epitope recognition of different conformations.
Locally increased mortality of harbour seals (Phoca vitulina) in the Danish Limfjord

At the end of August 2014 an aerial seal counting was done by Aarhus University (Galatius, A) and increased mortality was observed on a small island Ejerslev Røn (56° 56' N 0° 87' Ø) and a sand bank Blinderøn about 4 km south-east of Ejerslev Røn. Both islands/sandbanks are protected nature reserves. The islands were inspected the following day by boat/walking. In total, 56 dead seals were found on Ejerslev Røn and Blinderøn. Four were shot due to severe respiratory symptoms and these four seals did not escape into the water when approached.

All 60 seals except one with fishing net around the neck were dead within few days. One of the seals had a tag showing it had been through rehabilitation in the Netherlands (Zeehondencreche Pieterburen) in 2010, where it was treated for a lungworm infection (information from Lenie’t Hart about the tagged seal). This indicates the long distances seals are travelling and that lungworm infections can be successfully treated.

A field necropsy was done on the four shot seals and all suffered from pneumonia. Three of the seals had empty stomachs and intestines but all 4 seals were in good nutritional condition with blubber thickness ranging from 1.2 cm to 2.0 cm suggesting a short duration of the pneumonia. Influenza virus was found in the lungs, subtyping is pending.

At inspection, 12 days later only 1 recently dead seal was found indicating the mortality had peaked within a short time and only within a small geographic area.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Bacteriology, Pathology and Parasitology
Authors: Jensen, T. H. (Intern), Krog, J. S. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Chriél, M. (Intern), Holm, E. (Intern), Pedersen, K. (Intern), Hansen, M. S. (Intern)
Number of pages: 1
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Wildlife Disease Association Newsletter
Issue number: October
Original language: English
Links:
Source: PublicationPreSubmission
Source-ID: 103299966
Publication: Communication › Comment/debate – Annual report year: 2014

Overvågning af influenza A virus i svin i 2013. Slutrapport 2013: Opsummering og konklusion

Der er i 2013 gennemført en systematisk passiv overvågning af cirkulerende influenzavirus subtyper i danske svin. Det overordnede formål med overvågningen var at identificere hvilke influenzavirus subtyper og stammer, der cirkulerer blandt danske svin, og at kortlægge sygdomsårsager i svinepopulationen med henblik på at sikre det strategiske mål: at mindske antibiotikaforbruget i danske svinebesætninger.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology
Authors: Krog, J. S. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 3
Publication date: 2014

Publication information
Original language: English
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 93591825
Publication: Commissioned › Report – Annual report year: 2014

PRDC - Validation of a new diagnostic procedure for the diagnosis of PRDC in pigs

General information
Real-time PCR diagnostic package for diagnosis of porcine respiratory disease.

**General information**
State: Published
Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Section for Virology
Authors: Jorsal, S. E. L. (Intern), Hjulsager, C. K. (Intern), Kokotovic, B. (Intern), Larsen, L. E. (Intern)
Publication date: 2014
Event: Abstract from 6th European Symposium of Porcine Health Management (ESPHM 2014), Italy.
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 103450835
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014

Respiratory disease in finishers – comparisons of diagnostic tools

**General information**
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Section for Virology, Technical University of Denmark, Danish Agriculture and Food Council
Authors: Jakobsen, S. (Ekstern), Hjulsager, C. K. (Intern), Christensen, C. (Ekstern), Lind, P. (Intern), Bak, H. (Ekstern), Larsen, L. E. (Intern)
Publication date: 2014
Event: Poster session presented at 6th European Symposium of Porcine Health Management (ESPHM 2014), Italy.
Main Research Area: Technical/natural sciences
Electronic versions:
Publication: Research - peer-review › Poster – Annual report year: 2014
Surveillance programs in Denmark has revealed the circulation of novel reassortant influenza A viruses in swine

Swine influenza is a respiratory disease caused by multiple subtypes of influenza A virus. Swine influenza virus (SIV) is enzootic in swine populations in Europe, Asia, North and South America. The influenza A virus genome consist of eight distinct gene segments and SIV subtypes are defined by the combination of the gene segments hemagglutinin (HA) and neuraminidase (NA). In most European countries, the avian-like (av)H1N1, the 2009 pandemic variant (H1N1pdm09), H1N2 and H3N2 subtypes have constituted the dominating SIV subtypes during recent years. In Denmark, the H1N2 subtype is a reassortant between avH1N1 and H3N2 which is different from the dominating European H1N2 subtype (1). The prevalence of the H1N1pdm09 virus in swine has increased since 2009 in some countries including Denmark. Here we present the results of the national passive surveillance program on influenza in swine performed from 2009-13.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology
Authors: Larsen, L. E. (Intern), Hjulsager, C. K. (Intern), Trebbien, R. (Intern), Krog, J. S. (Intern), Breum, S. Ø. (Intern)
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 23rd IPVS Congress
Main Research Area: Technical/natural sciences
Conference: 23rd IPVS Congress, Cancun, Mexico, 08/06/2014 - 08/06/2014
Electronic versions:
SIV_abstract_IPVS2014.pdf
Source: PublicationPreSubmission
Source-ID: 103450987
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Svært at afgøre om grise smittes med PRRSV før eller efter fravænning

Til at afgøre om Porcin Reproduktions- og Respiratorisk Syndrom Virus (PRRSV) cirkulerer i farestalden eller kun i smågrisestalden kan næsesvaberprøver af alle grise ved fravænning være en hjælp. Resultatet fra et enkelt fravænningshold kan dog ikke stå alene, når det skal afgøres om en tømning af smågrisestalden er tilstrækkeligt for at der fremadrettet kan produceres PRRSV-negative grise ved 30 kg. Det vil ofte være nødvendigt at tage næsesvaberprøver af alle grise i flere fravænningshold.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Danish Agriculture and Food Council
Authors: Kristensen, C. S. (Ekstern), Larsen, L. E. (Intern), Hjulsager, C. K. (Intern)
Publication date: 2014

Publication information
Publisher: Videncenter for Svineproduktion
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Source: PublicationPreSubmission
Source-ID: 103490731
Publication: Commissioned › Report – Annual report year: 2014

Swine Influenza Viruses – Evolution and Zoonotic Potential

Influenza A virus (IAV) is an important respiratory pathogen with a broad host range. The natural reservoir for IAV is waterfowls, but both human and swine are considered natural hosts. During the past century IAV has caused severe pandemics as well as seasonal epidemics in the human population. In pigs, swine influenza virus (SIV) is endemic worldwide and is associated with economic losses for the farmer due to the impact on pig health causing lowered production. Swine has been shown to be susceptible to infection with IAVs of different host origin and has hence been considered as potential mixing vessels of new IAVs. Furthermore, transmission of IAVs from swine to human and vice versa has been documented on several occasions and further classifies this virus as a highly important zoonosis. This aspect enhances the possibility of the formation and establishment of new and potentially more virulent viruses with the capacity to cause severe pandemics. Therefore, it is important to gain a deeper understanding of the evolution of SIVs, their zoonotic potential as well as host-range characteristics and this PhD project aimed at elucidating parts of these important points.

The PhD thesis begins with a presentation of the aims and a brief introduction of the situation of SIV in Denmark. In the
A major outbreak of canine distemper virus (CDV) in Danish farmed mink (Neovison vison) started in the late summer period of 2012. At the same time, a high number of diseased and dead wildlife species such as foxes, raccoon dogs, and ferrets were observed. To track the origin of the outbreak virus full-length sequencing of the receptor binding surface protein hemagglutinin (H) was performed on 26 CDV's collected from mink and 10 CDV's collected from wildlife species. Subsequent phylogenetic analyses showed that the virus circulating in the mink farms and wildlife were highly identical with an identity at the nucleotide level of 99.45% to 100%. The sequences could be grouped by single nucleotide polymorphisms according to geographical distribution of mink farms and wildlife. The signaling lymphocytic activation molecule (SLAM) receptor binding region in most viruses from both mink and wildlife contained G at position 530 and Y at position 549; however, three mink viruses had an Y549H substitution. The outbreak viruses clustered phylogenetically in the European lineage and were highly identical to wildlife viruses from Germany and Hungary (99.29% - 99.62%). The study furthermore revealed that fleas (Ceratophyllus sciuorum) contained CDV and that vertical transmission of CDV occurred in a wild ferret. The study provides evidence that wildlife species, such as foxes, play an important role in the transmission of CDV to farmed mink and that the virus may be maintained in the wild animal reservoir between outbreaks.
Overvågning af aviær influenza i vilde fugle 2012 i Danmark

General information
State: Published
Organisations: National Veterinary Institute, Section for Public sector service and commercial diagnostics, Section for Virology, Natural History Museum of Denmark
Authors: Hjulsager, C. K. (Intern), Trebbien, R. (Intern), Madsen, J. J. (Ekstern), Thorup, K. (Ekstern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern)
Number of pages: 33
Publication date: 15 Mar 2013

Publication information
Place of publication: Frederiksberg
Publisher: Technical University of Denmark (DTU)
Original language: Danish
Applicant: Fødevarestyrelsen
Main Research Area: Technical/natural sciences

Bibliographical note
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Source: dtu
Source-ID: u::8481
Publication: Commissioned › Report – Annual report year: 2013

Overvågning af influenza i svin 2012

General information
State: Published
Organisations: National Veterinary Institute, Section for Public sector service and commercial diagnostics, Section for Virology
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 22
Publication date: 4 Mar 2013

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Place of publication: Frederiksberg
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Original language: Danish
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J.nr. 10/10489
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A fast and robust method for full genome sequencing of Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) Type 1 and Type 2
PRRSV is a positive-sense RNA virus with a high degree of genetic variability among isolates. For diagnostic sensitivity and vaccine design it is essential to monitor PRRSV genetic diversity. However, to date only a few full genome sequences of PRRSV isolates have been made publicly available. In the present study, fast and robust methods for long range RT-PCR amplification and subsequent next generation sequencing (NGS) were developed and validated on nine Type 1 and nine Type 2 PRRSV viruses. The methods generated robust and reliable sequences both on primary material and cell culture adapted viruses and the protocols performed well on all three NGS platforms tested (Roche 454 FLX, Illumina HiSeq2000, and Ion Torrent PGM™ Sequencer). These methods will greatly facilitate the generation of more full genome PRRSV sequences globally.
Detection of Porcine Circovirus Type 2 and Viral Replication by In Situ Hybridization in Primary Lymphoid Organs From Naturally and Experimentally Infected Pigs

Porcine circovirus type 2 (PCV2) infection is the cause of postweaning multisystemic wasting syndrome (PMWS). It has been speculated whether cell types permissive of replication are found in the primary lymphoid organs and whether infection of these tissues has an important role in the pathogenesis of PMWS. The aim of this study was to determine if primary lymphoid organ cells support viral replication during PCV2 infection. This was done by histopathological examination of thymus and bone marrow from pigs experimentally inoculated with PCV2 (n = 24), mock-infected pigs (n = 12), pigs naturally affected by PMWS (n = 33), and age-matched healthy control animals (n = 29). In situ hybridization (ISH) techniques were used to detect PCV2 nucleic acid irrespective of replicative status (complementary probe, CP) or to detect only the replicative form of the virus (replicative form probe, RFP). PCV2 was not detected in the experimentally PCV2-inoculated pigs or the control animals. Among the PMWS-affected pigs, 19 of 20 (95%) thymuses were positive for PCV2 by CP ISH, and 7 of 19 (37%) of these also supported viral replication. By CP ISH, PCV2 was detected in 16 of 33 (48%) bone marrow samples, and 5 of 16 (31%) of these also supported replication. The 2 ISH probes labeled the same cell types, which were histiocytes in both organs and lymphocytes in thymus. The RFP labeled fewer cells than the CP. Thus, PCV2 nucleic acids and replication were found in bone marrow and thymus of PMWS-affected pigs, but there was no evidence that primary lymphoid organ cells are major supporters of PCV2 replication.

General information

State: Published
Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Section for Virology, Universidad Autonoma de Barcelona, Centre de Recerca en Sanitat Animal, University of Copenhagen
Authors: Hansen, M. S. (Intern), Segalés, J. (Ekstern), Fernandes, L. (Forskerdatabase), Grau-Roma, L. (Ekstern), Bille-Hansen, V. (Intern), Larsen, L. E. (Intern), Nielsen, O. L. (Ekstern)
Pages: 20980-988
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Veterinary Pathology
Volume: 50
Issue number: 6
ISSN (Print): 0300-9858
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BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.923 SNIP 1.111 CiteScore 1.68
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.082 SNIP 1.329 CiteScore 2.05
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.914 SNIP 1.163 CiteScore 1.74
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.101 SNIP 1.278 CiteScore 2
ISI indexed (2013): ISI indexed yes
Diagnostic performance of fecal quantitative real-time polymerase chain reaction for detection of *Lawsonia intracellularis*–associated proliferative enteropathy in nursery pigs

Quantitative polymerase chain reaction (qPCR) tests for detection and quantification of *Lawsonia intracellularis* in feces from pigs have been developed. The objective of the current study was to evaluate the diagnostic performance of a fecal qPCR test for detection of nursery pigs with *L. intracellularis*–associated proliferative enteropathy (PE) under field conditions. Furthermore, the diagnostic performance for different subpopulations of pigs was investigated, including pigs infected or noninfected with Porcine circovirus-2, Brachyspira pilosicoli, and *Escherichia coli*. The diagnostic performance was evaluated in terms of diagnostic sensitivity and specificity. Data from pigs originating from 20 herds with antibiotic treatment requiring diarrhea outbreaks from a prior study were reused. Before treatment, pigs were randomly selected for histopathological and immunohistochemical examination of intestinal segments and fecal quantification of *L. intracellularis* by qPCR. A total of 313 pigs (157 without diarrhea, 156 with diarrhea) were included in the statistical analysis, and 37 pigs (11.8%) were classified as PE positives (defined as proliferative histological lesions in combination with *L. intracellularis* demonstration by immunohistochemistry). *Lawsonia intracellularis* was detected by qPCR in feces from 91 pigs (29.1%). A nonparametric receiver operating characteristic (ROC) analysis provided an area under the ROC curve (0.93) and an optimal cutoff value of 4.8 log10 *L. intracellularis* bacteria/g feces. This cutoff provided a diagnostic sensitivity of 0.84 and diagnostic specificity of 0.93. The diagnostic sensitivity and specificity were significantly different between herds (P < 0.0001). Numerically, diagnostic sensitivity and specificity were different between subpopulations of pigs, but no significant differences were demonstrated.

**General information**

State: Published

Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Section for Public sector service and commercial diagnostics, Section for Virology, Universidade Federal de Minas Gerais, University of Copenhagen

Authors: Pedersen, K. S. (Forskerdatabase), Stege, H. (Ekstern), Jensen, T. K. (Intern), Guedes, R. (Ekstern), Ståhl, M. (Intern), Nielsen, J. P. (Forskerdatabase), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Angen, Ø. (Intern)
Feces, Lawsonia intracellularis, Quantitative polymerase chain reaction, Pigs, Sensitivity, Specificity
Experimental Airborne Transmission of Porcine Postweaning Multisystemic Wasting Syndrome

The objective of these studies was to investigate if porcine postweaning multisystemic wasting syndrome (PMWS) could be induced in healthy pigs following contact with air from pigs with clinical signs of PMWS. The pigs were housed in different units. Either 31 (study I) or 25 (study II) pigs with clinical symptoms of PMWS from a PMWS-affected herd and 25 healthy pigs from a PMWS-free, but PCV2-positive, herd were housed in unit A. Fifty pigs from a PMWS-free herd were housed in unit B, which were connected by pipes to unit A. In unit C, 30 pigs from a PMWS-free herd were housed as controls. In study II, the pigs in units A and B from the PMWS-free herd developed clinical signs of PMWS 2-3 weeks after arrival. PMWS was confirmed at necropsy and the diseased pigs had increased PCV2 load and increased antibody titers against PCV2 in serum that coincided with the development of clinical signs typical of PMWS. Sequence analysis revealed that the PCV2 isolate belonged to genotype 2b. In conclusion, the present study showed that PMWS can be induced in pigs from a PMWS-free herd by airborne contact with pigs from a PMWS-affected herd.

General information

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Volume: 2013
ISSN (Print): 2090-3065
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Scopus rating (2016): SJR 0.125 SNIP 0 CiteScore 0
ISI indexed (2013): ISI indexed no
ISI indexed (2012): ISI indexed no
Original language: English
Electronic versions:
534342.pdf
DOIs:
10.1155/2013/534342

Bibliographical note

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Source-ID: n:oai:DTIC-ART:doaj/380024966::26643
Publication: Research - peer-review › Journal article – Annual report year: 2013

Experimental infection of pigs with two East European variants of Type 1 PRRSV

Porcine reproductive and respiratory syndrome viruses (PRRSV) have been divided into Type 1 (European) and Type 2 (North American) viruses. PRRSV are very diverse and Type 1 viruses have even been further divided into subtypes. While Type 1 viruses from Western Europe belong to subtype 1, viruses from Eastern Europe have been divided into at least 3 different subtypes based on the length of ORF7 and in addition, atypical Type 1 viruses do not readily group into the subtype groups. In experimental trials it has been shown that some of these viruses, e.g. strain Lena, are more virulent than the subtype 1 strains.

The aim of this project was to study the infection dynamics and clinical and pathological impact of two east European Type 1 strains. In an experimental trial, infection of pigs with the Russian subtype 2 strain “II6“ and the Belarusian atypical isolate “Bor59” were compared to an early “Lelystad-like” Danish subtype 1 isolate “18794". Groups of seven pigs of unique high sanitary status were infected with one of the three PRRSV isolates, and a fourth group served as sham-inoculated controls. The pigs were monitored for 24 days, and nasal swabs and blood samples were taken at 0, 3, 7, 10, 14, 17, 21 and 24 days post infection (dpi).
The pigs infected with the "Bor59" virus developed higher body temperature and more severe clinical symptoms compared to the other three groups, although the clinical signs in general were mild. The acute phase response was measured in serum samples as an objective indicator of infection. Acute phase protein C-reactive protein (CRP) showed an increase in levels in pigs infected with the Eastern European viruses with an earlier rise for Bor59 than for Ili6, both peaking at 10 dpi. In contrast, the CRP level did not increase significantly in neither the subtype 1 virus inoculated pigs nor the sham-inoculated controls. Acute phase protein haptoglobin showed a very early increase in Bor59 infected pigs, peaking at 3 dpi, while no increase was observed in Ili6 infected pigs.

All of the virus inoculated pigs seroconverted, as measured by IPMA and ELISA, around 7 dpi, and virus was detected by real-time RT-PCR in serum at various quantities and times after infection; detailed PCR analyses are ongoing.

Taken together, these preliminary data suggested that the east European subtype 2 isolate Ili6 and the atypical Bor59 strain induced more severe infection compared to the type 1 "Lelystad-like" virus isolate. This correlates with results obtained from studies of other east European PRRSV strains.

**Fast and robust methods for full genome sequencing of Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) Type 1 and Type 2**

The high level of diversity among PRRS viruses makes it very important to monitor the overall genetic variations in relation to the sensitivity of diagnostic tests and vaccination efficacy, but only few full genome sequences of PRRSV strains isolated in Europe have been made public available. In the present study, fast and robust methods for long range RT-PCR amplification and subsequent next generation sequencing (NGS) of PRRSV Type 1 and Type 2 viruses were developed and validated on nine Type 1 and nine Type 2 PRRSV viruses. The methods were shown to generate robust and reliable sequences both on primary material and cell culture adapted viruses and the protocols were shown to perform well on all three NGS platforms tested (Roche 454 FLX, Illumina HiSeq 2000, and Ion Torrent PGM™ Sequencer). To complete the sequences at the 5' end, 5' Rapid Amplification of cDNA Ends (5' RACE) was conducted followed by cycle sequencing of clones. The genome lengths were determined to be 14,876-15,098 and 15,342-15,408 nucleotides long for the Type 1 and Type 2 strains, respectively. These methods will greatly facilitate the generation of more complete genome PRRSV sequences globally which in turn may lead to identification of markers of virulence and improve our understanding of PRRSV evolution and pathogenesis.
Genetic and antigenic characterization of complete genomes of Type 1 Porcine Reproductive and Respiratory Syndrome viruses (PRRSV) isolated in Denmark over a period of 10 years

Porcine Reproductive and Respiratory Syndrome (PRRS) caused by the PRRS virus (PRRSV) is considered one of the most devastating swine diseases worldwide. PRRS viruses are divided into two major genotypes, Type 1 and Type 2, with pronounced diversity between and within the genotypes. In Denmark more than 50% of the herds are infected with Type 1 and/or Type 2 PRRSV. The main objective of this study was to examine the genetic diversity and drift of Type 1 viruses in a population with limited introduction of new animals and semen. A total of 43 ORF5 and 42 ORF7 nucleotide sequences were obtained from viruses collected from 2003 to February 2013. Phylogenetic analysis of ORF5 nucleotide sequences showed that the Danish isolates formed two major clusters within the subtype 1. The nucleotide identity to the subtype 1 protogenotype Lelystad virus (LV) spanned 84.9–98.8% for ORF5 and 90.7–100% for ORF7. Among the Danish viruses the pairwise nucleotide identities in ORF5 and ORF7 were 81.2–100% and 88.9–100%, respectively. Sequencing of the complete genomes, including the 5' and 3'-end nucleotides, of 8 Danish PRRSV Type 1 showed that the genome lengths differed from 14,876 to 15,098 nucleotides and the pairwise nucleotide identity among the Danish viruses was 86.5–97.3% and the identity to LV was 88.7–97.9%. The study strongly indicated that there have been at least two independent introductions of Type 1 PRRSV in Denmark and analysis of the full genomes revealed a significant drift in several regions of the virus.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics, Danish Agriculture and Food Council
Authors: Kvisgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Kristensen, C. (Forskerdatabase), Lauritsen, K. T. (Intern), Larsen, L. E. (Intern)
Pages: 197-205
Publication date: 2013
Main Research Area: Technical/natural sciences

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ISSN (Print): 0168-1702
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BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.179 SNIP 0.915 CiteScore 2.55
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.257 SNIP 0.915 CiteScore 2.56
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.213 SNIP 0.933 CiteScore 2.63
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.293 SNIP 1.113 CiteScore 2.94
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.202 SNIP 1.059 CiteScore 2.9
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.265 SNIP 1.216 CiteScore 3.04
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.217 SNIP 1.075
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.292 SNIP 1.038
Genetic and antigenic characterization of influenza A virus circulating in Danish swine during the past decade

Influenza A virus has been endemic in Danish swine for the last 30 years, with H1N1 and H1N2 being the dominating subtypes. The purpose of this study was to investigate the genetic and antigenic evolution of the influenza viruses found in Danish swine during the last 10 years. A total of 78 samples were isolated in MDCK cells, RNA extracted and the hemagglutinin and neuraminidase genes full length sequenced. In addition, the isolates were tested in hemagglutination inhibition (HI) tests against a panel of known antisera raised against a range of European swine influenza virus isolates. Phylogenetic analysis of the HA and NA genes revealed continuous evolutionary drift as expected for RNA viruses with low mutational selection pressure. Estimated selection pressures indicated that more purifying and less diversifying selection controlled the H1 evolution. The mean rates of synonymous and non-synonymous substitutions for H1, N1 and N2 were found to be in agreement with previously observed values for Eurasian swine lineages. Calculation of possible glycosylation sites in the hemagglutinin gene revealed that the H1N2 and H1N1 subtypes had three well conserved glycosylation sites in common. The results of the HI tests were analysed by antigenic cartography to quantify the antigenic relationship between the virus isolates. The antigenic cartography map showed that most of the Danish viruses were antigenic very similar, with only a few outliers. In conclusion, this study provided an important contribution to the complex epidemiology of circulating swine influenza virus in Denmark and indicates that vaccine development targeted against Danish H1N1 and H1N2 need only to include few components for the induction of cross protection against the predominant strains.

The study was supported by grants from “European surveillance network for influenza in pigs (ESNIP) 3” (http://www.esnip3.eu) and The Danish Veterinary and Food Administration.

General information

State: Published
Organisations: National Veterinary Institute, Section for Virology, Department of Systems Biology, Integrative Systems Biology, Molecular Evolutionary, Section for Public sector service and commercial diagnostics, University of Cambridge
Authors: Fobian, K. (Intern), Kirk, I. K. (Intern), Breum, S. Ø. (Intern), Lewis, N. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 1
Publication date: 2013
Event: Abstract from Influenza2013, Oxford, United Kingdom.
Main Research Area: Technical/natural sciences
Swine influenza, Phylogeny, Antigenic cartography
Electronic versions:
Oxford2013ver2_abstract.pdf

Bibliographical note
Genetic and biological characterisation of an avian-like H1N2 swine influenza virus generated by reassortment of circulating avian-like H1N1 and H3N2 subtypes in Denmark

BACKGROUND: The influenza A virus subtypes H1N1, H1N2 and H3N2 are the most prevalent subtypes in swine. In 2003, a reassorted H1N2 swine influenza virus (SIV) subtype appeared and became prevalent in Denmark. In the present study, the reassortant H1N2 subtype was characterised genetically and the infection dynamics compared to an “avian-like” H1N1 virus by an experimental infection study.

METHODS: Sequence analyses were performed of the H1N2 virus. Two groups of pigs were inoculated with the reassortant H1N2 virus and an “avian-like” H1N1 virus, respectively, followed by inoculation with the opposite subtype four weeks later. Measurements of HI antibodies and acute phase proteins were performed. Nasal virus excretion and virus load in lungs were determined by real-time RT-PCR.

RESULTS: The phylogenetic analysis revealed that the reassorted H1N2 virus contained a European “avian-like” H1-gene and a European “swine-like” N2-gene, thus being genetically distinct from most H1N2 viruses circulating in Europe, but similar to viruses reported in 2009/2010 in Sweden and Italy. Sequence analyses of the internal genes revealed that the reassortment probably arose between circulating Danish “avian-like” H1N1 and H3N2 SIVs. Infected pigs developed cross-reactive antibodies, and increased levels of acute phase proteins after inoculations. Pigs inoculated with H1N2 exhibited nasal virus excretion for seven days, peaking day 1 after inoculation two days earlier than H1N1 infected pigs and at a six times higher level. The difference, however, was not statistically significant. Pigs euthanized on day 4 after inoculation, had a high virus load in all lung lobes. After the second inoculation, the nasal virus excretion was minimal. There were no clinical sign except elevated body temperature under the experimental conditions.

CONCLUSIONS: The “avian-like” H1N2 subtype, which has been established in the Danish pig population at least since 2003, is a reassortant between circulating swine “avian-like” H1N1 and H3N2. The Danish H1N2 has an “avian-like” H1 and differs from most other reported H1N2 viruses in Europe and North America/Asia, which have H1-genes of human or “classical-swine” origin, respectively. The variant seems, however, also to be circulating in countries like Sweden and Italy. The infection dynamics of the reassorted “avian-like” H1N2 is similar to the older “avian-like” H1N1 subtype.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Immunology and Vaccinology, Section for Public sector service and commercial diagnostics, Statens Serum Institut, University of Copenhagen
Authors: Trebbien, R. (Intern), Bragstad, K. (Forskerdatabase), Larsen, L. E. (Intern), Nielsen, J. (Intern), Bøtner, A. (Intern), Heegaard, P. M. H. (Intern), Fomsgaard, A. (Forskerdatabase), Viuff, B. M. (Forskerdatabase), Hjulsager, C. K. (Intern)
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Scopus rating (2013): SJR 1.031 SNIP 0.981 CiteScore 2.44
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Scopus rating (2012): SJR 0.957 SNIP 0.866 CiteScore 2.37
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Scopus rating (2011): SJR 1.057 SNIP 0.9 CiteScore 2.65
Genetic characterization of canine distemper virus involved in outbreaks in farmed mink in Denmark 2012

Danish farmed mink herds experienced a large outbreak of canine distemper virus in 2012. Full-length sequence analysis (1824 nucleotides) of the variable hemagglutinin (H) gene were performed on 27 viruses collected from mink and on 7 viruses collected from wild foxes. Results of the study showed that the farmed mink and wild fox population were infected by identical viruses which strongly indicate an epidemiological link between these populations. Accordingly, diseased and dead foxes were observed in some of the mink herds in connection to the outbreak. The Danish virus strain clustered phylogenetically with other European canine distemper viruses and showed the highest level of similarity (99.3 - 99.6 %) to viruses isolated from wild foxes in Germany. The fox should therefore be considered as an important wild life reservoir of canine distemper virus and may also contribute to the transmission of the virus between mink farms during outbreaks.

Genetic dissection of complete genomes of Type 2 PRRS viruses isolated in Denmark over a period of 15 years

Type 2 Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) was first detected in Europe in 1996 co-incident with the introduction of a live attenuated vaccine. Since then, only limited ORF5 and ORF7 sequences of Type 2 PRRS viruses have been reported throughout Europe. In the present study, the genetic and antigenic diversity of 11 complete genomes and 49 ORF5 and 55 ORF7 nucleotide sequences obtained from 57 viruses in Denmark from 2003 to 2012 were examined. The genetic identity of the 11 complete genomes to the vaccine strain (Ingelvac PRRS MLV) ranged between 93.6 and 99.6% while the 49 ORF5 sequences examined were 94.0–99.8% identical to the vaccine strain. Among the Danish sequences, the pairwise nucleotide identity was 90.9–100% and 93.0–100.0% for ORF5 and ORF7, respectively. Analysis of the genetic region encoding NSP2 revealed high diversity among the Danish viruses with an 86.6–98.9% range in similarity. Furthermore, several of the sequenced viruses harbored deletions in the NSP2 coding region. Phylogenetic analysis in a global Type 2 PRRSV framework classified all Danish isolates to a single cluster (sub-lineage
5.1) which comprised strains closely-related to the Type 2 prototype isolate VR2332.

**General information**

State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics, University of Hong Kong
Authors: Kvisgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Brar, M. S. (Ekstern), Leung, F. C. C. (Ekstern), Larsen, L. E. (Intern)
Pages: 334-344
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BFI (2016): BFI-level 2
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Web of Science (2016): Indexed yes
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Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.281 SNIP 1.262 CiteScore 2.54
Web of Science (2014): Indexed yes
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Scopus rating (2013): SJR 1.438 SNIP 1.484 CiteScore 3
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
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Scopus rating (2012): SJR 1.437 SNIP 1.579 CiteScore 3.18
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.562 SNIP 1.738 CiteScore 3.27
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.371 SNIP 1.476
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.29 SNIP 1.472
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.169 SNIP 1.3
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.043 SNIP 1.322
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.022 SNIP 1.401
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.078 SNIP 1.262
Web of Science (2005): Indexed yes
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Hepatitis E virus: En overset zoonose, der smitter fra svin

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Organisations: National Veterinary Institute, Section for Virology, Statens Serum Institut
Authors: Krog, J. S. (Intern), Midgley, S. (Ekstern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern)
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BFI (2008): BFI-level 1
Original language: Danish
Source: PublicationPreSubmission
Source-ID: 97946961
Publication: Research - peer-review › Journal article – Annual report year: 2014

Hepatitis E Virus Variant in Farmed Mink, Denmark
Hepatitis E virus (HEV) is a zoonotic virus for which pigs are the primary animal reservoir. To investigate whether HEV occurs in mink in Denmark, we screened feces and tissues from domestic and wild mink. Our finding of a novel HEV variant supports previous findings of HEV variants in a variety of species.
Influenza A Virus with a Human-Like N2 Gene Is Circulating in Pigs

A novel reassortant influenza A virus, H1avN2hu, has been found in Danish swine. The virus contains an H1 gene similar to the hemagglutinin (HA) gene of H1N1 avian-like swine viruses and an N2 gene most closely related to the neuraminidase (NA) gene of human H3N2 viruses from the mid-1990s.

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Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Trebbien, R. (Intern), Larsen, L. E. (Intern)
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Scopus rating (2015): SJR 0.199 SNIP 0.077
Scopus rating (2014): SJR 0.218 SNIP 0.089
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Investigation of the association of growth rate in grower-finishing pigs with the quantification of Lawsonia intracellularis and porcine circovirus type 2

As a part of a prospective cohort study in four herds, a nested case control study was carried out. Five slow growing pigs (cases) and five fast growing pigs (controls) out of 60 pigs were selected for euthanasia and laboratory examination at the end of the study in each herd. A total of 238 pigs, all approximately 12 weeks old, were included in the study during the first week in the grower–finisher barn. In each herd, approximately 60 pigs from four pens were individually ear tagged. The pigs were weighed at the beginning of the study and at the end of the 6–8 weeks observation period. Clinical data, blood and faecal samples were serially collected from the 60 selected piglets every second week in the observation period. In the killed pigs serum was examined for antibodies against Lawsonia intracellularis (LI) and porcine circovirus
type 2 (PCV2) and in addition PCV2 viral DNA content was quantified. In faeces the quantity of LI cells/g faeces and number of PCV2 copies/g faeces was measured by qPCR. The objective of the study was to examine if growth rate in grower-finishing pig is associated with the detection of LI and PCV2 infection or clinical data. This study has shown that diarrhoea is a significant risk factor for low growth rate and that one log10 unit increase in LI load increases the odds ratio for a pig to have a low growth rate by 2.0 times. Gross lesions in the small intestine and LI load > log10 6/g were significant risk factors for low growth. No association between PCV2 virus and low growth was found.

**General information**

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- **Organisations:** National Veterinary Institute, Division of Veterinary Diagnostics and Research, Section for Veterinary Diagnostics, Bacteriology & Pathology, Adaptive Immunology & Parasitology, Virology, Danish Agriculture and Food Council
- **Authors:** Johansen, M. (Ekstern), Nielsen, M. (Ekstern), Dahl, J. (Ekstern), Svensmark, B. (Ekstern), Bækbo, P. (Ekstern), Kristensen, C. S. (Ekstern), Hjulsager, C. K. (Intern), Jensen, T. K. (Intern), Ståhl, M. (Intern), Larsen, L. E. (Intern), Angen, Ø. (Intern)
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- **Main Research Area:** Technical/natural sciences

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  - Scopus rating (2015): SJR 1.26 SNIP 1.23 CiteScore 2.1
  - Web of Science (2015): Indexed yes
  - BFI (2014): BFI-level 2
  - Scopus rating (2014): SJR 1.267 SNIP 1.421 CiteScore 2.37
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  - Scopus rating (2013): SJR 1.247 SNIP 1.552 CiteScore 2.49
  - ISI indexed (2013): ISI indexed yes
  - Web of Science (2013): Indexed yes
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  - Scopus rating (2012): SJR 1.274 SNIP 1.452 CiteScore 2.45
  - ISI indexed (2012): ISI indexed yes
  - Web of Science (2012): Indexed yes
  - BFI (2011): BFI-level 2
  - Scopus rating (2011): SJR 1.211 SNIP 1.303 CiteScore 2.24
  - ISI indexed (2011): ISI indexed yes
  - Web of Science (2011): Indexed yes
  - BFI (2010): BFI-level 2
  - Scopus rating (2010): SJR 1.155 SNIP 1.28
  - Web of Science (2010): Indexed yes
  - BFI (2009): BFI-level 2
  - Scopus rating (2009): SJR 1.022 SNIP 1.34
  - Web of Science (2009): Indexed yes
  - BFI (2008): BFI-level 2
  - Scopus rating (2008): SJR 1.066 SNIP 1.273
  - Web of Science (2008): Indexed yes
  - Scopus rating (2007): SJR 1.006 SNIP 1.36
Microbiological, pathological and histological findings in four Danish pig herds affected by a new neonatal diarrhoea syndrome

BACKGROUND: Neonatal diarrhoea is a frequent clinical condition in commercial swine herds, previously regarded to be uncomplicated to treat. However, since 2008 it seems that a new neonatal diarrhoeic syndrome unresponsive to antibiotics and common management practices has emerged. Routine laboratory examinations have not detected any pathogen related to this syndrome. The primary purpose of this study was to evaluate if well-known enteric pathogens could be associated with outbreaks of neonatal diarrhoea, thus question the hypotheses of a new syndrome. Furthermore, we wanted to evaluate macroscopic and microscopic findings associated with these outbreaks and if possible propose a preliminary piglet-level case-definition on syndrome New Neonatal Porcine Diarrhoea Syndrome (NNPDS).

RESULTS: Four well-managed herds experiencing neonatal diarrhoea with no previously established laboratory conclusion and suspected to suffer from New Neonatal Porcine Diarrhoea Syndrome, were selected. Within these herds, 51 diarrhoeic and 50 non-diarrhoeic piglets at the age of three to seven days were necropsied and subjected to histological and microbiological examination. Faeces were non-haemorrhagic. Neither enterotoxigenic E. coli, Clostridium perfringens type A or C, Clostridium difficile, rotavirus, coronavirus, Cryptosporidium spp, Giardia spp, Cystoisospora suis nor Strongyloides ransomi were associated with diarrhoea in the investigated outbreaks. Macroscopically, the diarrhoeic piglets were characterized by filled stomachs and flaccid intestines without mucosal changes. The predominant histological lesions were villous atrophy in jejunum and ileum. Epithelial lesions in colon were seen in one third of the case piglets.

CONCLUSIONS: The results of the study supported the hypothesis that a new neonatal porcine diarrhoea was present in the investigated herds, since no known pathogen(s) or management factors could explain the diarrhoeal outbreaks. Based on the findings in the four herds the following case-definition of NNPDS was suggested: Non-haemorrhagic diarrhoea during the first week of life, without detection of known infectious pathogens, characterized by milk-filled stomachs and flaccid intestines at necropsy.
Molekylær karakterisering af influenzavirus fra vilde fugle i Danmark i 2012

Aviær influenza (AI) virus indeholder 8 genom (RNA) segmenter, som koder for 13 proteiner. De mest variable proteiner er overflade glykoproteinene hemagglutinin (HA) og neuraminidase (NA), der kodes af hhv. HA og NA genom segmenterne. HA og NA danner basis for subtypeklassificering af AI virus. Vilde vandfugle anses for at være den naturlige vært for AI virus, og i forbindelse med flere udbrud af højpatogen aviær influenza (HPAI) virus i fjerræ er der fundet et tilsvarende lavpatogene aviær influenza (LPAI) virus i vilde vandfugle. AI virus kan spredes over lange afstande af vilde fugle, herunder potentielt også HPAI virus. Vilde fugle er derfor et oplagt mål for overvågning af AI virus, og Danmarks topologi...
Novel reassortant swine influenza viruses are circulating in Danish pigs

The Danish surveillance program for influenza A virus in pigs has revealed that two novel reassortant swine influenza viruses may now be circulating in the Danish swine population, since they each have been detected in at least two submissions from different herds in 2011 as well as in 2012. One of the reassortant viruses comprised a HA gene similar to H1 of H1N1 avian-like swine influenza virus (SIV) and a NA gene most closely related to N2 gene of human H3N2 influenza virus that circulated in humans in the mid 1990s. The internal genes of this reassortant virus with the subtype H1avN2hu all belonged to the H1N1 avian-like SIV lineages. Until now this novel virus H1avN2hu has only been detected in Danish swine. The other novel reassortant virus contained the HA gene from H1N1pdm09 virus and a NA gene similar to the N2 gene of H3N2 SIV that have been circulating in European swine since the mid 1980s. The N2 gene of this new reassortant virus could also have been donated by the reassortant H1N2 SIV with an avian-like HA gene which is very common in Danish pigs and has been circulating since 2003. The internal genes of this reassortant virus with the subtype H1pdm09N2sw all belonged to the pandemic H1N1pdm09 influenza virus lineage. Swine influenza virus with a similar subtype to H1pdm09N2sw has previously been found in pigs in Italy and Germany. Detailed analyses of viral genes will further elucidate the relationship between these new swine influenza viruses found in the different countries. In addition, several sporadic reassortant swine influenza viruses comprising different constellations of internal genes from known circulating swine influenza viruses were found. Future full genome studies will reveal if some of these reassortant viruses also will be established in the Danish pig population.
One health – One flu: Surveillance in pigs and mink has revealed extensive exchange of influenza A virus genes and viruses among animals and humans

General information
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Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Trebbien, R. (Intern), Fobian, K. (Intern), Larsen, L. E. (Intern)
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PMWS Development in Pigs from Affected Farms in Spain and Denmark
Postweaning multisystemic wasting syndrome (PMWS) is a worldwide spread condition that affects pigs in nursery and/or fattening units, and is considered to have a severe economic impact on swine production. The main clinical sign of PMWS is wasting, but can also include pallor of the skin, icterus, respiratory distress and diarrhoea. The main essential infectious agent for PMWS development is porcine circovirus type 2 (PCV2), but the exact cause of PMWS is still unclear. PCV2 is present in most pig herds, but the occurrence of PMWS is sporadic, and it is been difficult to reproduce PMWS by inoculating PCV2 alone. However, studies where co-infections have been applied have been more successful. Based on this, we modeled PMWS development based on longitudinal data on antibodies and PMWS status from herds in Denmark and Spain, where presence of a range of pathogens were considered as explanatory variables in the form of maternal immunity and the occurrence of seroconversion against the considered pathogens. However, maternal immunity could not be measured from mother animals due to cross fostering, no time points for seroconversion was available, and no case/control status could be assigned as PMWS do not have an 'infectious period' after which animals may be assigned control status. The talk will concentrate on the framework in which this was handled, which may be translated to similar settings for similar studies. We found that seroconversion towards PCV2 and Lawsonia intracellularis had a significant impact on PMWS in the Danish data, but it appears that the effect is positive, in the sense that seroconverted animals were less likely to develop PMWS. A number of maternal immunities also significantly affected PMWS development. Furthermore it was uncovered that most of these effects would not have been detected if pathogens were considered by themselves and not simultaneously.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, National Veterinary Institute, Section for Epidemiology, Section for Public sector service and commercial diagnostics, Section for Virology
Number of pages: 1
Porcine Reproductive and Respiratory Syndrome Virus (PRRSV)
This PhD thesis presents the diversity of Porcine Reproductive and Respiratory Syndrome viruses (PRRSV) circulating in the Danish pig population. PRRS is a disease in pigs caused by the PRRS virus resulting in reproductive failures in sows and gilts and respiratory diseases in pigs. Due to genetic heterogeneity, PRRSV is divided into two genotypes, Type 1 and Type 2. Type 1 PRRS viruses are further divided into at least 3 subtypes. The virus evolves rapidly and reports of high pathogenic variants of both Type 1 and Type 2 appearing in Europe, North America, and Asia have been reported within recent years. This abrupt occurrence of highly pathogenic PRRSV strains emphasizes the significance of monitoring the diversity of circulating strains around the world both in respect to the sensitivity and specificity of diagnostic tests as well as efficacy of available vaccines.

The aims and objectives of the PhD project will be introduced in the objectives section together with a short introduction to the situation of PRRSV in Denmark at the start of this study. The background chapter will provide a review on PRRSV with the emphasis on genetic diversity.

The results of the work performed during the PhD are presented in the four manuscripts included in the PhD thesis and a short summary of each manuscript is depicted below:

Manuscript I is focusing on the development of methods for complete genome sequencing of PRRSV. The sequencing strategy was based on the production of long range PCR fragments covering the PRRSV genome in two or four fragments with full-length cDNA as template. The sequencing of the PCR fragments was performed using Next Generation Sequencing (NGS) technologies and three different platforms were used. A total of 18 complete PRRSV genomes were obtained using this new method.

Manuscript II is focusing on the diversity of Type 1 PRRSV in Denmark. For the first time genetic and antigenic examinations of complete genomes of Danish isolated Type 1 PRRSV was conducted. Furthermore, extensive studies of ORF5 and ORF7 sequences were performed from 44 viruses collected from 2003 to February 2013. The diversity study confirmed that only Type 1 subtype 1 PRRSV is circulating in the Danish pig population. The examination of the Danish PRRS field viruses confirmed that there is a high overall diversity among Type 1 viruses in Europe. The phylogenetic study also indicated the presence of two Danish virus clusters, one dominating vaccine/LV like and one resembling an early introduced strain.

Manuscript III is focusing on the diversity of Type 2 PRRSV in Denmark. For the first time examinations of complete genomes of European isolated Type 2 PRRSV were performed. Furthermore, ORF5 and ORF7 sequences obtained from 57 viruses collected in the years 2003-2012 were examined. The diversity study confirmed that Danish Type 2 PRRS viruses share high genetic similarity to the vaccine strain and there was no obviously reason to believe that new Type 2 PRRSV strains have been introduced. However, a few viruses showed both a higher diversity to the other Danish viruses and to the vaccine strain and one virus harbored the largest deletion in NSP2 reported in Danish Type 2 PRRSV. Manuscript IV is focusing on an experimental infection study in pigs with a Type 2 PRRS virus causing significant clinical disease in the field. Genetic and antigenic examination of ORF5 and partial NSP2 sequences obtained from the case virus revealed several variations compared to the vaccine strain. However, complete genome comparison of the case virus to the vaccine strain showed high genetic similarity and no obvious virulence maker was found. The results of the experimental infection study revealed that the strain induced only sparse clinical symptoms and the magnitude and duration of viraemia was comparable to an older Danish Type 2 strain. The results emphasized that infections in the field is often more severe than in experimental studies due to the multifactorial nature of PRRSV. Furthermore, the study underlined the need for more research on virulence markers of PRRSV.
Spread of hepatitis E virus from pig slurry to the water environment

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Organisations: National Veterinary Institute, Section for Virology, National Food Institute, Division of Food Microbiology, University of Copenhagen
Authors: Krog, J. S. (Intern), Forslund, A. (Ekstern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern), Dalsgaard, A. (Ekstern), Schultz, A. C. (Intern)
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Swine Plasma Immunoglobulins for Prevention and Treatment of Post-Weaning Diarrhoea: Optimizing Stability Towards Gut Conditions

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Authors: Hedegaard, C. J. (Intern), Ballegaard, A. (Ekstern), Røjel, N. (Ekstern), Bendix Hansen, M. (Ekstern), Kjær Lindved, B. (Ekstern), Bisgaard Frantzen, K. (Ekstern), Larsen, L. E. (Intern), Lihme, A. (Ekstern), Heegaard, P. M. H. (Intern)
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Swine Plasma Immunoglobulins for Prevention and Treatment of Post-Weaning Diarrhoea: Optimizing Stability Towards Gut Conditions

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Authors: Hedegaard, C. J. (Intern), Ballegaard, A. (Ekstern), Røjel, N. (Ekstern), Bendix Hansen, M. (Ekstern), Kjær Lindved, B. (Ekstern), Bisgaard Frantzen, K. (Ekstern), Larsen, L. E. (Intern), Lihme, A. (Ekstern), Heegaard, P. M. H. (Intern)
Number of pages: 1
Swine plasma immunoglobulins for prevention and treatment of post-weaning diarrhoea: Optimizing stability towards gut conditions

Post-weaning diarrhoea (PWD) is a common condition in intensive swine production, resulting in reduced welfare of weaners and economic losses for the farmer as a result of illness, death, and treatment costs. It is also one of the main causes of antibiotics- and zinc use in the pig production. We aim at developing products for protection against PWD based on natural antibodies (immunoglobulins) derived directly from inexpensive raw materials.

Swine immunoglobulins (Igs) were isolated directly from slaughterhouse swine plasma-waste by expanded bed chromatography. The immunoglobulin product is intended for enteral administration and thus has to pass through the digestive system, thus we consequently cross-linked the Igs by a periodate based method. The formation of high molecular weight complexes were demonstrated by size exclusion chromatography. By imitating the gastrointestinal system we subjected the Igs to pepsin or trypsin/chymotrypsin and observed the degradation patterns of the cross-linked Igs compared to unmodified Igs, and optimized coupling conditions to achieve maximal stability with concurrent retention of antigen binding activity. The availability of such an inexpensive, stable and highly active Ig product would allow swine producers to reduce expenses and cut down on antibiotics and zinc usage.

General information
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Swine plasma immunoglobulins for prevention and treatment of post-weaning diarrhoea: Optimizing stability towards gut conditions

Brief description of research area:
A common problem in swine production is diarrhoea in newly weaned piglets, and huge quantities of antibiotics go to treat post-weaning diarrhoeas in pigs. The use of antibiotics can lead to the development of multi- and fully resistant bacteria, which consequently pose a great threat to human health. Therefore, sustainable alternatives for treating post-weaning diarrhoea without using antibiotics are in demand. Swine that are old (and big) enough for slaughter have during their upbringing been challenged by many different pathogens and thus have developed immunity towards these pathogens, which include pathogen-specific immunoglobulins (antibodies). We hypothesis that by harvesting natural immunoglobulins from porcine blood plasma, a waste product from swine slaughter, and feeding these immunoglobulins to the piglets this can subsequently (by passive immunisation) prevent and treat post-weaning diarrhoea.

Our challenge is to find a suitable method for stabilising the immunoglobulins for oral provision in order for the immunoglobulins to pass as unharmed as possible through the digestive system and still retaining their anti-pathogenic properties.

What we know:
It is possible to multimerise immunoglobulins, which results in an advantage when binding to their respective antigens in comparison to the non-multimerised immunoglobulins, but too high degree of multimerisation abates immunoglobulin reactivity. Unfortunately, a preliminary study showed that multimerisation destabilises the immunoglobulins. On the other hand, proteolytical resistance correlates with increased immunoglobulin concentration.
What we need:
To investigate the effect of increasing the concentration of multimerised immunoglobulins on proteolytical resistance.

To investigate multimerised immunoglobulins’ ability in inhibiting microbial (E. coli) adhesion on relevant matrices, such intestinal villi and/or intestinal cell lines.

A toxicological study on (if any) adverse side effects occurs when enteral providing immunoglobulins to piglets.

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The diversity of Porcine Reproductive and Respiratory Syndrome Virus Type 1 and 2 in Denmark
Both Type 1 and Type 2 PRRS viruses are circulating among Danish pigs. The first appearance of Type 1 PRRSV in Denmark was in 1992 whereas the Type 2 PRRSV was introduced in 1996 after the use of a live attenuated vaccine that reverted to virulence. Since then, vaccination to control the disease for both PRRSV genotypes has been widely used in Denmark and it is therefore highly relevant to monitor the diversity of currently circulating PRRSV strains. Only subtype 1 of the Type 1 PRRSV strains and vaccine-like Type 2 PRRSV strains were previously detected in Denmark, however, only few Danish PRRSV strains were sequenced. Denmark exports more than 50.000 living pigs each month. A portion of these pigs inevitably harbor PRRSV. Thus, the diversity of PRRSV in Denmark is of interest to other countries besides Denmark. The main objective of the present study was to close the gap in knowledge on the genetic diversity of currently circulating PRRSV strains in Danish pigs by sequencing ORF5 and ORF7 of approximately 41 Type 1 and 50 Type 2 strains isolated between 2003 and 2013. Furthermore, full genome analysis was performed on nine Type 1 and nine Type 2 selected strains. The preliminary assessment of the results showed that the Type 1 strains all belonged to subtype 1. Based on the ORF5 sequences, the Danish Type 1 viruses clustered into two groups. These two groups shared 84 % to 92 % and 94 % to 99 % nucleotide identity to the Lelystad virus, respectively. The sequenced Type 2 viruses showed a significant higher level of identity in that the ORF5 sequences were 94 - >99 % identical at the nucleotide level. Most of the Type 2 viruses, shared high level of identity to the VR2332 vaccine strain (Ingelvac MLV), but a few more diverse isolates were also identified, including strains with interesting deletions in NSP2 and other genes. The full genome sequences of Danish strains showed an overall nucleotide identity of 88-98% (Type 1) and 94 % to >99 % (Type 2). The impact of these results will be discussed.

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State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics, Danish Agriculture and Food Council, University of Hong Kong
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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2013
Zoonotic Aspects of Hepatitis E Virus in Denmark

In this thesis the epidemiology of hepatitis E virus (HEV) in Denmark was explored. Globally, four genotypes of HEV are recognized along with several species specific variants. Non-zoonotic genotypes of the virus are found in the developing world, where they cause epidemics due to fecal contaminated water resources. Zoonotic genotypes have a primary reservoir in pigs worldwide. Humans infected with HEV are often asymptomatic, but can experience an acute self-limiting hepatitis. Pigs are asymptomatic and only mild lesions have been observed in the liver of infected animals. In the developed world, sporadic cases of HEV induced disease have been more frequently reported as awareness of the disease increases, including human cases in Denmark where HEV is also prevalent in pigs.

The thesis consists of an introduction into HEV where the literature on specific subjects is reviewed. The results obtained during the work of this PhD are presented in the form of four manuscripts. Finally, the four manuscripts are discussed in a broader context.

In Manuscript I, the work performed to investigate if HEV was found in other animal reservoirs than pigs in Denmark is presented. The research focused on mink (Nevison vison), an economically important livestock in Denmark. The main finding was the discovery of a novel variant of HEV. The virus was found in four different locations in samples collected in 2008 and in samples collected in 2011 indicating that the virus is widespread and has been circulating in minks for years. The virus did not seem to cause clinical disease in mink, however, this should be investigated further.

Manuscript II describes the teaching of HEV along with rotavirus (RV), porcine circovirus type 2 (PCV2), somatic coliphages, E. coli and Enterococcus spp. through field soil into tile drains under natural conditions of field fertilization. The microorganisms were naturally present in the pig slurry applied to the field. The results showed that HEV along with the other five microorganisms were found in water drained from the field, indicating potential contamination of water reservoirs in connection with the untreated drainage runoff. Rotavirus was detected in deeper groundwater screen indicating the possibility of groundwater contamination of viruses originating from manure, posing a risk for the contamination of important drinking water reservoirs in Denmark.

Manuscript III focuses on the viral contamination of mussels farmed in Denmark. The mussels was assayed for HEV and Rotavirus, known to occur in shellfish and cause disease. Furthermore, PCV2 was also assayed as an indicator of porcine waste contamination. All samples analyzed were negative for HEV and RV, however, a large proportion of the samples tested positive for the PCV2. This is the first report that shows the potential of PCV2 as an indicator organism. The lack of HEV in the mussels is in accordance with previous studies, although shellfish has been reported as the source of multiple sporadic cases of HEV infection.

Manuscript IV report the results of a longitudinal study performed in a multi-site farm, where HEV development in 104 pigs followed from farrowing to 17 weeks of age. The pigs were divided into three groups according to the level of antibody titers of their sows. During the study, successful transfers of maternal antibodies were observed only for the pigs born to sows with the highest antibody level. Furthermore, a significant reduction of the number of pigs shedding HEV from approx. 70% to 50% was observed in the group that received maternal antibodies. Ten of the pigs that were shedding HEV at week 17 were necropsied at week 20 and three of these were still shedding HEV. Correspondingly, HEV was found in different tissues, e.g. liver, tonsils and lungs, of these three pigs. HEV was, however, not found in muscles. In addition, high level of HEV was found in 1 out of 73 Danish livers purchased at grocery stores in the larger Copenhagen area.

Based on these studies it could be concluded that HEV belongs to a diverse family of viruses with variants in multiple species, and there is a possibility that many more of these will be identified during the coming years. However, clinical illness have so far only been described in humans and birds. HEV is known to be present in the water environment of poorly sanitized regions of the world, however, our study also emphasized the need for better understanding of viral teaching as well as the need for diagnostic tools enabling survey of water to maintain high drinking water quality also in the developed part of the world. We did not find HEV or RV in shellfish although indications of porcine waste contamination of shellfish occurring were observed in though the detection of the porcine specific virus PCV2. This is an interesting finding and suggest that PCV2 may be utilized to monitor viral contamination of shellfish, which is completely lacking today. Lastly, high levels of maternal antibodies can diminish the number of pigs shedding or carrying infectious HEV when entering the food supply chain. This could be utilized by vaccinating sows prior to farrowing, ensuring transfer of maternal antibodies and thereby reducing human exposure to HEV.

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Organisations: National Veterinary Institute, Section for Virology, National Food Institute, Division of Food Microbiology
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Association between average daily gain, faecal dry matter content and concentration of Lawsonia intracellularis in faeces

Background
The objective of this study was to investigate the association between average daily gain and the number of Lawsonia intracellularis bacteria in faeces of growing pigs with different levels of diarrhoea.

Methods
A longitudinal field study (n=7150 pigs) was performed in a Danish herd from day 29 to 47 post weaning. Every third day all pigs were weighed, subjected to a clinical examination and faecal samples were obtained. Faecal samples were subjected to dry matter determination and absolute quantification by PCR for L. intracellularis and porcine circovirus type 2 (PCV2). Association between average daily gain, faecal dry matter content, numbers of L. intracellularis bacteria and PCV2 genome copies in faeces was investigated in a multilevel mixed-effects linear model.

Results
Increasing numbers of L. intracellularis log10 bacteria/g faeces were significantly associated with decreasing average daily gain (P<0.001). The association was decreasing with increasing faecal dry matter content (P<0.01). The number of PCV2 log10 copies/g faeces was not significantly associated with average daily gain of the pigs (P>0.5).

Conclusion
The results suggest a potential application of a PCR quantifying L. intracellularis in growing pigs. Faecal dry matter content must be taken into consideration in interpretation of such test results.

General information
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Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Section for Public sector service and commercial diagnostics, Section for Virology, University of Copenhagen
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Clinical and laboratory studies on herds affected with postweaning multisystemic wasting syndrome in Denmark, France, Spain, and Sweden: Disease progression and a proposal for herd case definition

Objectives: To propose and evaluate a protocol to establish a diagnosis of postweaning multisystemic wasting syndrome (PMWS) at herd level.

Materials and methods: The data used included both laboratory data from previous epidemiological studies carried out in Italy, Denmark, and Spain and original postweaning mortality data collected from several herds in Denmark, France, Spain, and Sweden. Statistical process control techniques were used to analyze the longitudinal evolution of mortality in each herd.

Results: The analysis of data sets from three different countries showed that to diagnose at least one PMWS-affected pig with a probability > 95%, it is necessary to study a minimum of three to five pigs. Longitudinally collected data showed that when > 20 data points were available, a significant increase in mortality was always detected at close to the time of PMWS diagnosis. When <10 points were available, a significant increase in mortality was detected in four of six studied herds, although mortality percentages were always higher at the time of PMWS diagnosis than before diagnosis.

Implications: These results suggest that two conditions must be fulfilled to diagnose PMWS in a herd. Firstly, a significant increase in postweaning mortality, compared to the historical background in the herd, must be observed in association with clinical signs compatible with PMWS. Secondly, PMWS must be diagnosed in at least one of three to five necropsied pigs concurrently with the increase in mortality. Ruling out other potential causes of increased mortality is also necessary.
Consequences of outbreaks of influenza A virus in farmed mink (Neovison vison) in Denmark in 2009 and 2010

Influenza in mink (Neovison vison) is assumed to be rare, but outbreaks have previously been reported in farmed mink. The first report was from Swedish mink farms in 1984 which was caused by influenza A virus H10N4 of avian origin. In 2009 and 2010 outbreaks of respiratory disease were seen in several Danish mink farms. In all of the farms, the clinical symptoms were upper respiratory tract symptoms with sneezing and coughing as the most dominant symptoms. Peracute deaths were seen in mink without any clinical symptoms. Influenza H3N2 was found detected by PCR in the lungs from diseased mink. The mean mortality rate was 1.20% (95% confidence intervals: 0.58–1.82) during the outbreak period.

Young mink and especially males were reported to be more likely to die. The outbreak in the farms varied from two to ten weeks. During the outbreak period most farms treated all mink with antimicrobials and four of these farms used feed medication in three weeks. The farmers, however, noted that the medication had little or no effect. The most plausible way of transmission of the influenza is from the raw untreated pig waste containing lungs used in the production of mink feed. Because the first clinical symptoms were observed few weeks after the raw pig waste was added to the wet mink feed.

General information
State: Published
Organisations: National Veterinary Institute, Section for Public sector service and commercial diagnostics, Division of Veterinary Diagnostics and Research, Virology, Section for Virology, Division of Poultry, Fish and Fur Animals, Section of Fur Animal Diseases and Wildlife, Holstebro Veterinary Clinic
Pages: 186-189
Publication date: 2012

Detection of PRRSV in 218 field samples using six molecular methods: What we are looking for?

Objectives
The purpose of this study was to determine the sensitivity and the specificity of six molecular methods used for the detection of porcine reproductive and respiratory syndrome virus (PRRSV).

Methods
218 field samples (serum, tissues) were collected between 2009 and 2011 from 50 PRRSV positive and 45 negative pig herds from Slovenia. Total viral RNA was extracted from original samples and stored in aliquots at -70 °C until analysis. RT-PCR and direct sequencing of positive samples was performed as described previously (Toplak et al., 2012). All field samples were analyzed with five commercial real-time RT-PCR kits (named as kit A to E) according to the instructions of producer.

Results
According to determined 258 nucleotides long sequences (ORF7) 102 PRRSV samples belong to Type I (identification of 12 different lineages of EU subtype 1 (a=1, b=8, c=1, d=1, e=61, f=8, g=2, h=4, i=3, j=4, k=1, m=8) with 85.7-93.8 % nucleotide identity between lineages and four samples belong to Type II. In total, 138 PRRSV positive samples were detected with broad range of PRRSV RNA in samples. The highest sensitivity was observed with kit E (96.3%) and with kit B (94.5%), followed by conventional RT-PCR (87.8%) and kit D (82.1%), while the lowest sensitivity was observed with kit A (55.3%) and kit C (53.8%). Reduced sensitivity was directly related to the genetic lineages.

Discussion and conclusion
The study showed that the performance of conventional RT-PCR assays are highly dependent on the genetic make-up of the target viruses and confirm findings of a previous study where we showed some commercial PCR kits failed to detect specific genetic linkages of PRRSV. Thus, these finding emphasise that it is crucial that the manifactors of diagnostic PCR kits (conventional and real-time) Continuously follow the genetic evaluation of especially Type I PRRSV subtype viruses and regularly update their primer sequences.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, University of Ljubljana, ADIAGENE, Faculty of Veterinary Science, Tetracore Inc
Diversity and zoonotic potential of rotaviruses in swine and cattle across Europe.

Group A rotaviruses can infect both humans and animals. Individual rotavirus strains can occasionally cross species barriers and might hereby contribute to the emergence of new genotypes in heterologous hosts. The incidence and impact of zoonotic rotavirus are not well defined, and one reason for this is a lack of data about strains circulating in suspected reservoir animal hosts. In this study we report the incidence, genetic diversity, and molecular epidemiology of rotaviruses detected in domestic cattle and swine in 6 European countries. From 2003 to 2007, 1101 and more than 2000 faecal specimens were collected from swine and cattle, both healthy and diarrhoeic, and tested for rotaviruses. Viruses from positive stools were genotyped and a subset of strains was characterized by nucleotide sequencing and phylogenetic analysis of the VP7 (G) and VP4 (P) genes. Rotaviruses were detected in 43% of bovine samples and in 14% of porcine samples. In cattle, 10 different combinations of G and P types were identified and the most common strains were G6P[11] and G6P[5]. In swine, the number of identified G–P combinations was higher (n = 21), however, no single combination was predominant across Europe. Newly described genotype specificities, P[27] and P[32], were identified in swine. When compared at the nucleotide sequence level, the identified porcine rotavirus strains and contemporary human strains grouped together phylogenetically, whereas bovine rotavirus strains formed separate clades. These data demonstrate large genetic diversity of porcine and bovine rotavirus strains across Europe, and suggest that livestock herds may serve as potential reservoirs for human infections.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Statens Serum Institut, Hungarian Academy of Sciences, University of Valencia, University of Zaragoza, Centre National de Référence des Virus Entériques, Istituto Superiore di Sanita, University of Ljubljana, National Institute of Public Health and the Environment, University of Pecs
Authors: Midgley, S. E. (Ekstern), Bányai, K. (Ekstern), Buesa, J. (Ekstern), Halaihel, N. (Ekstern), Hjulsager, C. K. (Intern), Jakab, F. (Ekstern), Kaplon, J. (Ekstern), Larsen, L. E. (Intern), Monini, M. (Ekstern), Poliššak-Prijatelj, M. (Ekstern), Pothier, P. (Ekstern), Ruggeri, F. M. (Ekstern), Steyer, A. (Ekstern), Koopmans, M. (Ekstern), Böttiger, B. (Ekstern)
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Diversity of type I porcine reproductive and respiratory syndrome virus (PRRSV) in Europe: A PORRSCON study

General Information
State: Published
Enabling Passive Immunization as an Alternative to Antibiotics for Controlling Enteric Infections in Production Animals

Enteric infections cause major problems in most intensive animal production sectors, including poultry, pigs and cattle, leading to disease, reduced production and compromised welfare. In addition some of these infections are zoonotic, and they are to a large extent responsible for the continued massive use of antibiotics in food animals. Thus there is a pressing need for economically feasible, efficient, non-antibiotics based means for controlling the problem. Passive immunization has been known for decades as an efficient way of endowing humans or animals with short-term (weeks) immunity. To control enteric infections by passive immunization a bolus of immunoglobulin may simply be administered orally. For this to work, large amounts of active immunoglobulins are needed. To be a real alternative to antibiotics the price of the immunoglobulin product needs to be low. We combined an efficient and mild high-capacity method for extracting immunoglobulins directly from raw materials like milk, whey and blood plasma with a novel method for stabilizing activity. In a first experiment a total of 15 kg unstabilized bovine immunoglobulin was purified from whey (35,000 liters) and administered to colostrum-deprived calves (225-300 g pr calf during the first 24 hours after birth). No difference in resulting immunoglobulin serum concentration, weight gain or disease frequency were seen in this group of calves compared to a control group given full access to high-quality colostrum. The effect of orally administered bovine immunoglobulin is currently being tested in a calf herd with persistent diarrhea problems. Furthermore, it was shown in a Campylobacter challenge model in chickens that caecal and faecal counts of Campylobacter were between 0.5 and 1.0 logs lower in birds when given 200 mg avian immunoglobulins orally together with the challenge (at day 21 of age) compared to a placebo group receiving immunoglobulin with no reactivity against Campylobacter. While clearly preliminary, these results show that immunoglobulin can be produced from renewable sources at a price enabling passive immunization as a viable strategy for control of infectious diseases in the intensive animal production, with the potential to significantly reduce antibiotics consumption.
European surveillance network for influenza in pigs 3 (ESNIP 3)

Objectives: The "European surveillance network for influenza in pigs (ESNIP) 3" continues a surveillance network previously established during concerted actions ESNIP 1 and ESNIP 2. Running from 2010-2013, ESNIP 3 represents the only organised surveillance network for influenza in pigs in Europe and seeks to strengthen formal interactions with human and avian surveillance networks.

Materials and Methods: The project consortium comprises 24 participants, contributing a variety of specialism's and skills ensuring multi-disciplinary cutting-edge outputs. Most partners are actively working with swine influenza virus (SIV) experimentally and in the field. Three work packages aim to increase knowledge of the epidemiology and evolution of SIV in European pigs to inform changes in disease trends and variation in contemporary viruses through organised field surveillance programmes.

Results: An inventory of the programmes that are currently active in fifteen of the partners showed that passive surveillance was primarily used. Detected virus strains will be characterised by antigenic cartography (informing better evidence-based approaches for selection of vaccine strains) and genetically through full genome sequencing using the latest technology. The virus bank and electronic database will be expanded and formally curated with relevant SIV isolates together with information for global dissemination within and out with the consortium to the wider scientific and veterinary community.

Conclusions: All data will improve SI diagnosis by updating reagents employed in the recommended techniques to define minimum datasets for standardised epidemiological analyses. These approaches will aid pandemic preparedness and planning for human influenza whilst providing an evidence base for decisions relating to veterinary health.
European surveillance network for influenza in pigs 3 (ESNIP 3)

General information
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Organisations: National Veterinary Institute, Section for Virology, Ploufragan-Pluzané Laboratory, Animal Health and Veterinary Laboratories Agency, Wellcome Trust Sanger Institute, Ghent University, IZLER, National Veterinary Research Institute, Laboratorio Central Veterinario-Sanidad Animal, IDT-Biologika GmbH, Finnish Food Safety Authority, Kimron Veterinary Institute, Veterinary Diagnostic Directorate, Central Veterinary Institute, University of Thessaly, Merial S.A.S., Hipra, University of Cambridge

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Main Research Area: Technical/natural sciences
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Simon et al European Surveillance network for influenza in pigs_Final.pdf

Genetic drift of HA and NA in Danish swine influenza virus from the period 2003-2012

The aim of this study is to analyze the genetic drift in hemagglutinin (HA) and neuraminidase (NA) genes from influenza viruses isolated from Danish swine over the past decade; the antigenic evolution and relatedness between swine influenza virus strains of the H1 subtype by antigenic cartography.
Currently at least three influenza A subtypes (H1N1, H1N2 and H3N2) are endemic in the Danish swine population, and since 2010 the pandemic virus (H1N1pdm09) have also frequently been detected. The focus in this study will be on H1N1 and H1N2, since the prevalence of H3N2 have declined over the past years.
Obtained isolates derived from diagnostic samples submitted to the Danish National Veterinary Institute for influenza A virus detection. Approximately eight isolates from each of the years 2003 to 2012 are examined by HA and NA full length sequencing and phylogenetic analyses. In addition, HI-titers obtained by testing against a panel of reference swine influenza virus antisera are used for antigenic cartography. Preliminary phylogenetic analyses indicate a higher degree of drift for H1 genes than N1 genes.
The antigenic and genetic characterization of the swine influenza virus isolates in this study will provide a more complete picture of the molecular epidemiology of the H1N1 and H1N2 swine influenza viruses in Denmark.
A thorough knowledge of the antigenic drift in surface genes is very important concerning evaluation of the zoonotic potential of existing and future swine influenza virus strains and along with the monitoring of antigenic changes in hemagglutinin subtypes it will be possible to ensure a continuous efficacy of influenza virus vaccines.

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Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics, Statens Serum Institut
Authors: Fobian, K. (Intern), Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Trebbien, R. (Intern), Larsen, L. E. (Intern), Bragstad, K. (Ekstern)

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Oral presentation
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Infectious risk factors for individual postweaning multisystemic wasting syndrome (PMWS) development in pigs from affected farms in Spain and Denmark

Two prospective longitudinal studies in 13 postweaning multisystemic wasting syndrome (PMWS)-affected farms from Spain (n = 3) and Denmark (n = 10) were performed. Blood samples from pigs were longitudinally collected from 1st week until the occurrence of the PMWS outbreak. Wasted and healthy age-matched pigs were euthanized, necropsied and histopathologically characterised. PMWS diagnosis was confirmed by means of lymphoid lesions and detection of porcine circovirus type 2 (PCV2) in these tissues by in situ hybridization or immunohistochemistry. Serological analyses were performed in longitudinally collected serum samples to detect antibodies against PCV2, porcine reproductive and respiratory syndrome virus (PRRSV), porcine parvovirus (PPV), swine influenza virus (SIV) and Lawsonia intracellularis (law), Mycoplasma hyopneumoniae, Aujeszky’s disease virus (ADV) and Salmonella spp. A Cox proportional hazards model was used to investigate the simultaneous effects of seroconversion and maternal immunity against the studied pathogens. Results showed that high levels of maternal immunity against PCV2 had a protecting effect in farms from both countries. Moreover, for the Danish dataset, seroconversion against law had an overall protecting effect, but for animals with very low levels of maternal antibody levels against this pathogen, the effect appeared neutral or aggravating. Otherwise, for the Spanish dataset, maternal immunity against PPV and PRRSV gave protective and aggravating effects, respectively. In conclusion, the present study reflects the complex interaction among different pathogens and their effects in order to trigger PMWS in PCV2 infected pigs.

General information
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Organisations: Department of Informatics and Mathematical Modeling, DTU Data Analysis, National Veterinary Institute, Division of Veterinary Diagnostics and Research, Section for Veterinary Epidemiology and public sector consultancy, Section for Veterinary Diagnostics, Division of Microbiology and Risk Assessment, Virology, Universidad Autonoma de Barcelona, Pig Research Centre
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Porcine reproductive and respiratory syndrome (PRRS) has for nearly 3 decades been economically one of the most important swine diseases. Despite intensive research focus, many unanswered questions remain regarding the pathogenesis of PRRSV. In situ hybridization (ISH) is generally considered a more useful diagnostic tool than immunohistochemistry (IHC) and may be helpful in further research of pathogenesis. ISH is able to detect virus in non-progressive stages therefore the length of successful detection after infection is expected. It is not widely used, however, because of problems with specificity of the oligonucleotide probe due to the pronounced diversity of the PRRSV genome.

The aim of the present study was to evaluate a PRRSV specific ISH protocol. Three, non-overlapping PRRSV specific 20 nucleotides, DIG labeled oligonucleotide probes were designed targeting the ORF7 region. The probes were specific designed to recognize PRRSV Type I isolates only. A total of 19 positive PRRSV paraffin blocks from different organs and infected with different strains were tested as well as a negative control. All samples were simultaneously tested by IHC using different anti-PRRSV monoclonal antibodies. Five experiments of ISH were performed, using a pool of 1 nmol of each of the three oligonucleotide probes with two different prehybridization temperature (105°C and 80°C) and time (5 and 10 min), using 0.5 nmol of each of the probes separately with prehybridization on 105°C during 5 min. Positive signals were detected in alveolar macrophages in lungs, in hystiocytes in lymph nodes, Payer patches and tonsils, in macrophages, on inflamed area in ileum and in glomerular cells. 58 EuroPRRS2012 Budapest, Hungary ISH showed better sensitivity than IHC while there was an obvious discrepancy between sensitivity among the probes.
Investigation of the presence of human or bovine respiratory syncytial virus in the lungs of mink (Neovison vison) with hemorrhagic pneumonia due to Pseudomonas aeruginosa

Background
Hemorrhagic pneumonia is a disease of farmed mink (Neovison vison) caused by Pseudomonas aeruginosa. The disease is highly seasonal in Danish mink with outbreaks occurring almost exclusively in the autumn. Human respiratory syncytial virus (RSV) has been shown to augment infection with P. aeruginosa in mice and to promote adhesion of P. aeruginosa to human respiratory cells.

Findings
We tested 50 lung specimens from mink with hemorrhagic pneumonia for bovine RSV by reverse transcriptase polymerase chain reaction (PCR) and for human RSV by a commercial real-time PCR. RSV was not found.

Conclusions
This study indicates that human and bovine RSV is not a major co-factor for development of hemorrhagic pneumonia in Danish mink.

General information
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Organisations: National Veterinary Institute, Section for Virology, Division of Poultry, Fish and Fur Animals, Section of Fur Animal Diseases and Wildlife, Copenhagen University Hospital
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Scopus rating (2011): SJR 0.649 SNIP 0.99 CiteScore 1.42
New influenza A virus reassortments have been found in Danish swine in 2011

In 2011 a passive surveillance for influenza A virus was conducted in Danish swine. Tested samples were clinical samples from affected pigs submitted to the Danish National Veterinary Institute for swine influenza virus detection. In total 713 samples from 276 herds were analysed and about 24% of the samples were positive for swine influenza virus. All influenza positive samples were tested for the H1N1pdm09 virus by a real time RT-PCR assay specific for the pandemic HA gene and 26% of the samples were positive. Subtyping of 90 samples by sequencing revealed the presence of; i) H1N1 "avian like" viruses which have been circulating in Danish pigs since it was found for the first time in 1981. ii) H1N2 reassortant viruses which comprise HA from "avian like" H1N1 and NA from swine H3N2. The reassortant H1N2 virus was discovered in Danish pig for the first time in 2003 and is now well established in the Danish pig population. iii) H1N1pdm09 viruses which were found the first time in Danish pigs in January 2010. iv) Three new subtype variants comprising H1 "avian like" together with N2 "human like", H1 pandemic with N2 "human like" and finally H1 pandemic with N2 from swine H3N2. The presence of N2 "human like" gene in Danish swine is new and genetic analysis indicate that it is most closely related to NA of human H3N2 viruses. In addition, full genome characterization of 40 viruses from the surveillance revealed the presence of additional new reassortments of which some have internal genes from the pandemic H1N1 virus.

This study contribute significantly to our knowledge of the epidemiology of swine influenza A virus circulating in Danish swine and the potential role of swine in the emergence of novel reassortant viruses.
Outbreaks of Influenza A Virus in Farmed Mink (Neovison vison) in Denmark: Molecular characterization of the involved viruses

Influenza in mink (Neovison vison) is assumed to be rare, but outbreaks have previously been reported in farmed mink. The first report was from Swedish mink farms in 1984 and the second was reported from Canadian mink farms.

In 2009, influenza A of the subtype H3N2 was detected in several Danish mink farms with respiratory symptoms. Full-genome sequencing showed that the virus was a human/swine reassortant, with the H and N gene most related to human H3N2 viruses circulating in 2005. The remaining 6 genes were most closely related to H1N2 influenza viruses circulating in Danish swine. This virus had not previously been described in swine, mink nor humans. PCRs assays specifically targeting the new reassortant were developed and used to screen influenza positive samples from humans and swine in Denmark with negative results. Thus, there was no evidence that this virus had spread to humans or was circulating in Danish pigs.

In 2010 and 2011, influenza virus was again diagnosed in diseased mink in a few farms. The genetic typing showed that the virus was similar to the pandemic H1N1 virus circulating in humans and swine. The H3N2 virus was not detected in 2010 and 2011.

Taken together, these findings indicate that mink is highly susceptible for influenza A virus of human and swine origin and may therefore act as a potential host/reservoir for influenza A viruses.

Outbreaks of influenza A virus in farmed mink (Neovison vison) in Denmark: molecular characterization of the viruses

Influenza in mink (Neovison vison) is assumed to be rare, but several outbreaks have been described during recent years in Europe and the North America. In 2009, influenza A of the subtype H3N2 was detected in several Danish mink farms with respiratory symptoms. Full-genome sequencing showed that the virus was a human/swine reassortant, with the H and N gene most related to human H3N2 viruses circulating in 2005. The remaining 6 genes were most closely related to H1N2 influenza viruses circulating in Danish swine. This virus had not previously been described in swine, mink or humans. PCRs assays specifically targeting the new reassortant were developed and used to screen influenza positive samples from humans and swine in Denmark with negative results. Thus, there was no evidence that this virus had spread
to humans or was circulating in Danish pigs. In 2010 and 2011, influenza virus was again diagnosed in diseased mink in a few farms. The genetic typing showed that the virus was similar to the pandemic H1N1 virus circulating in humans and swine. The H3N2 virus was not detected in 2010 and 2011. Taken together, these findings indicate that mink is highly susceptible for influenza A virus of human and swine origin and may therefore act as a potential host/reservoir for influenza A viruses.

General information
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Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics, Division of Veterinary Diagnostics and Research, Virology, Division of Poultry, Fish and Fur Animals, Section of Fur Animal Diseases and Wildlife, Statens Serum Institut, Holstebro Veterinary Clinic
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Overvågning af influenza i svin 2011

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Authors: Hjulsager, C. K. (Intern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern)
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PCR diagnosis of PRRS virus in oral fluids from weaned Danish pigs

Introduction
Oral fluid testing has been suggested as an alternative diagnostic approach for surveillance of pathogens in swine herds. In Denmark oral fluid has been used for detection of PCV2 and swine veterinarians are eager to use it for diagnosis of other pathogens. The aim of the present study was to evaluate the diagnostic performance of oral fluid testing for PRRSV by PCR under Danish conditions.

Materials and Methods
Five herds with PRRS positive nursery pigs were selected for sampling by convenience. Oral fluid and blood samples were collected from each of 10 pens in each of the 5 herds. Oral fluid was collected by providing 1 cotton rope in each selected pen for 30 minutes. Blood samples from 5 systematic randomly selected pigs in each pen were taken and the separated serum was pooled penwise. Different purification methods were tested in order to decrease the content of PCR inhibitors in the RNA extract of oral fluid. QIAamp Viral RNA Mini Kit (QIAGEN) was selected for purification of RNA from oral fluid and serum. Purified RNA was tested for PRRSV by real-time RT-PCR by a modified previously published assay.

Overall agreement, diagnostic sensitivity and diagnostic specificity were calculated in order to evaluate the performance of oral fluid as test material in comparison with penwise pooled sera. PCR results from serum samples were considered as gold standard.

Results
The detection of PRRSV in oral fluid and pooled serum is shown in figure 1 and 100% agreement was observed at the herd level. Pen level agreement between oral fluid and pooled serum samples for detection of PRRSV in the 50 pens is displayed in table 1. Overall agreement was 68%. The diagnostic sensitivity of oral fluid testing was 0.75 (95% CI= 0.55-0.89) and the diagnostic specificity of oral fluid testing was 0.95 (95% CI= 0.77-1.0).

Figure 1. Herd level detection of PRRSV based on samples from 50 pens

Table 1. 2x2 table of PRRSV real-time RT-PCR results, when testing pooled serum samples and oral fluid samples from 50 pens

Conclusions and Discussion
Agreement between oral fluid and serum testing at herd and pen level was promising. The present results indicate that oral fluid testing for PRRSV at pen level has a high diagnostic specificity and a somewhat lower, but acceptable diagnostic sensitivity. These findings suggest that oral fluid testing using the real-time RT-PCR procedure established in this study is applicable for PRRS surveillance and diagnosis under Danish conditions.

Porcine Circovirus Diseases: A review of PMWS
This article is a review on post‐weaning multisystemic wasting syndrome (PMWS), the first described disease among the porcine circovirus diseases (PCVD). Post‐weaning multisystemic wasting syndrome has, since its appearance in Canada in 1991, been seen in all major pig producing countries. To diagnose PMWS at herd level typical clinical appearance consisting of wasting and increased mortality must be combined with finding at autopsy of diseased pigs, where typical microscopic findings in the lymphatic tissue must be present. Post‐weaning multisystemic wasting syndrome significantly increases the mortality and reduces the daily weight gain in weaner pig and/or in finishing pigs. Post‐weaning multisystemic wasting syndrome can be transmitted by pig‐to‐pig contact and some studies point at airborne transmission as a possibility. Studies in Europe have shown several risk factors that either increase or decrease the risk for a pig herd to be affected by PMWS. At the pig level, studies have shown the importance of maternal immunity as protection for subsequent development of PMWS. To control PMWS, good production management and control of other diseases are
crucial. Since 2004, commercial vaccines against Porcine Circo Virus type 2 have been coming on the market and many studies have shown great benefits of these to control PMWS. Today, sow vaccines as well as piglet vaccines are available in most countries. An extensive meta-analysis of many of the vaccines has shown a comparable good efficacy of the vaccines in significantly reducing mortality and increasing weight gain of the pigs.
Real-time PCR testing for Porcine Circovirus Type 2 and Lawsonia intracellularis to assess diarrhoea status

Introduction
Real-time PCR tests have been developed to detect and quantify Porcine Circovirus type 2 (PCV2) and Lawsonia intracellularis in pigs’ faeces. Pooling of individual faecal samples is often used to reduce the costs of diagnostic testing. The objective of this study was to determine the association between quantities of PCV2 and L. intracellularis in pooled faecal samples and diarrhoea in pigs. Materials and Methods
Forty individual faecal samples were collected from grower (>10 weeks) pigs on five farms in Denmark. Each pig was described as having diarrhoea +/- Eighteen individual "diarrhoea" and 18 "non-diarrhoea" samples were randomly selected from each farm. Six "diarrhoea" and six "non-diarrhoea" pooled samples were made by combining three individual "diarrhoea/non-diarrhoea" samples. Individual and pooled samples were tested using real-time PCR specific for PCV2 and L. intracellularis. The associations between diarrhoea (+/-) and pooled faecal PCV2 and L. intracellularis quantity were analysed using logistic regression (Stata/IC 11.1). Results
Low quantities of L. intracellularis were detected in six non-diarrhoeic pigs. There was no association between PCV2 or L. intracellularis quantity in pooled faecal samples and diarrhoea (p>0.05). However, when moderate/massive categories for L. intracellularis were combined, there was a tendency toward significance (OR=4.9; 95%CI 0.9-26.0). Conclusions
PCV2 was not associated with diarrhoea in pigs on the five farms studied. Our results suggest that the quantity of L. intracellularis in pooled faecal samples may reflect diarrhoea status, however further research in this area is required. Subclinically-affected pigs shed low quantities of L. intracellularis.

Spread of Hepatitis E virus from pig slurry to the water environment

Objectives: Spread of pig slurry as an organic fertilizer is commonly used in Danish agriculture. The slurry is spread untreated so pathogens able to survive in slurry tanks will be widely distributed in the environment. The objective of this study was to examine if hepatitis E virus (HEV), which is known to be excreted in faeces from pigs, will be transported through the soil and into the drainage system of a field due to precipitation or will be retained in the soil matrix. Water from the drainage system is not treated before it is discharged into larger water reservoirs (lake, fjords, streams), and hence could present a risk for virus transmission to wildlife and shellfish. We tested the presence of HEV in water drained from a test field where slurry from a Danish pig farm had been applied and in mussels from different regions in Denmark with fields in close proximity.

Methods: Slurry from a Danish pig farm was spread on a tile-drained field of loamy soil. Water that arrived at the drainage system located 1 m below surface was collected over a time period of 4 month. Samples were collected on a weekly basis and when water flow in the drainage system exceeded a certain threshold (an event). In addition, samples of water collected from wells located along the field and groundwater. Archived mussels from different regions in Denmark were included in the study. Virus was concentrated from water using Poly Ethylene Glycol precipitation and virus from the digestive tissue of the mussels was extracted sing proteinase K treatment. Subsequently, viral genomic RNA, from both water and mussels, was purified using the NucliSENS miniMAG system and detection and quantification of HEV and
HEV was detected in the first event following spread of pig slurry. In agreement with this, the weekly sample of this period also tested positive. HEV was not found in any of the subsequent water samples. Of the 70 blue mussel samples, that mainly originated from fjords, none tested positive.

Conclusion: HEV is regarded as a zoonotic virus with pigs as the primary reservoir. The pathway to humans and other mammals is unclear. Here we show that under Danish conditions, spread of pig slurry can cause viral contamination of water reservoirs, making HEV accessible to the population and wildlife. This indicates a possible route of HEV transmission from pigs to other reservoirs. We also show that retention in soil matrix is at a minimum as HEV was detected at first rainfall after application of pig slurry. The viability of the viruses found in this study is still unclear since HEV cannot be cultivated in cells. We did not find any HEV positive mussel samples indicating that the release of HEV from fields is not a concern for shellfish production.

**General information**
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Organisations: National Veterinary Institute, Section for Virology, National Food Institute, Division of Food Microbiology, University of Copenhagen
Authors: Krog, J. S. (Intern), Forslund, A. (Ekstern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern), Schultz, A. C. (Intern)
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**Surveillance for avian influenza viruses in wild birds in Denmark and Greenland**
Avian influenza (AI) is a disease of major threat to poultry production. Surveillance of AI in wild birds contributes to the control of AI. In Denmark (DK) and Greenland (GL), extensive surveillance of AI viruses in the wild bird population has been conducted. The surveillance aimed at detecting viruses of both high pathogenic AI (HPAI) subtypes H5 and H7, and low pathogenic AI (LPAI). Captured live wild birds and shot game birds were sampled by swabbing of the oropharyngeal and/or cloacal tracts, or swabs were collected from faecal droppings. In DK, most samples were collected in major staging areas for migratory waterfowl, whereas in GL, samples were collected in breeding areas. Samples from birds found dead at scattered locations across DK were sampled by oropharyngeal swabbing. 17530 wild birds from DK were tested as part of the surveillance during 2006-2010, of which 1614 were birds found dead. During 2007-2010, 2926 live wild birds from GL were tested. Swab samples were tested by RT-PCR and culturing. Positive samples were subtyped and the pathogenicity was determined by HA cleavage site sequencing. HPAI H5N1 was detected only during spring 2006, in 44 wild birds from DK. LPAI H5 and H7 subtypes were detected throughout the period together with several other LPAI subtypes. In GL, HPAI was not detected, but few samples were PCR positive for AI. The occurrence of AI subtypes in the wild bird population correlates with concurrent outbreaks of LPAI in Danish poultry, which may suggest virus transmission between these populations.

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Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Aarhus University, United States Department of Agriculture, University of Copenhagen
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Surveillance for Avian Influenza Viruses in Wild Birds in Denmark and Greenland, 2007–10

In Denmark and Greenland, extensive surveillance of avian influenza (AI) viruses in wild bird populations has been conducted from 2007 through 2010. In Denmark, the surveillance consisted of passive surveillance of wild birds found dead or sick across Denmark and active surveillance of apparently healthy live birds in waterfowl reservoirs and along migratory flyways, birds living in proximity to domestic poultry, and hunted game birds. Dead birds were sampled by oropharyngeal swabbing. Healthy live wild birds were captured with nets, traps, or by hand and were sampled by swabbing of the oropharyngeal and cloacal tracts, or swabs were collected from fresh fecal droppings. Hunted game birds were delivered to game-handling establishments, where each bird was sampled by oropharyngeal and cloacal swabbing. During the 2007–10 period, a total of 11,055 wild birds were sampled in Denmark, of which 396 were birds that were found dead. In Greenland, samples were collected mainly from fecal droppings in breeding areas. Samples from 3555 live and apparently healthy wild birds were tested. All swab samples were tested by pan-influenza reverse transcriptase–PCR (RT-PCR), and the positive samples were further tested by H5/H7 specific RT-PCRs. H5/H7-positive samples were subjected to hemagglutination cleavage site sequencing for pathotyping. In addition, all RT-PCR–positive samples were subjected to virus isolation, and the virus isolates were subsequently subtyped. In Denmark, low pathogenic (LP) H5 viruses were detected throughout the period, in addition to a few LPAI H7 and several other subtypes. In Greenland, very few samples were positive for AI. None of them were found to be of the H5 or H7 subtypes by RT-PCR. Isolation of these viruses in eggs was unsuccessful; thus, they were not subtyped further. The findings did, however, demonstrate the presence of LPAI viruses in Greenland. For several water bird species overwintering in North America and northwest Europe, respectively, Greenland constitutes a common breeding area. This raises the possibility that viruses could be transmitted to North America via Greenland and vice versa. In Denmark, the screenings for AI showed LPAI viruses to be naturally occurring in the wild bird population, particularly in waterfowl. The occurrence of AI viruses in the wild bird population may pose a risk for AI infections in Danish poultry.

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Organisations: National Veterinary Institute, Section for Public sector service and commercial diagnostics, Section for Virology, United States Department of Agriculture, University of Copenhagen, Aarhus University Hospital, Aarhus University
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Scopus rating (2012): SJR 0.876 SNIP 0.985 CiteScore 1.75
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.802 SNIP 0.861 CiteScore 1.59
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Suspected zoonotic transmission of rotavirus group A in Danish adults

Group A rotaviruses infect humans and a variety of animals. In July 2006 a rare rotavirus strain with G8P[14] specificity was identified in the stool samples of two adult patients with diarrheoa, who lived in the same geographical area in Denmark. Nucleotide sequences of the VP7, VP4, VP6, and NSP4 genes of the identified strains were identical. Phylogenetic analyses showed that both Danish G8P[14] strains clustered with rotaviruses of animal, mainly, bovine and caprine, origin. The high genetic relatedness to animal rotaviruses and the atypical epidemiological features suggest that these human G8P[14] strains were acquired through direct zoonotic transmission events.

General information

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Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Statens Serum Institut
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Within-day repeatability for absolute quantification of Lawsonia intracellularis bacteria in feces from growing pigs

Absolute quantification of Lawsonia intracellularis by real-time polymerase chain reaction (PCR) is now possible on a routine basis. Poor repeatability of quantification can result in disease status misclassification of individual pigs when a single fecal sample is obtained. The objective of the current study was to investigate overall variation within a day for fecal numbers of L. intracellularis bacteria determined by real-time PCR in growing pigs. From each of 30 pigs with an infection of L. intracellularis, 5 fecal samples were collected within 1 day. A total of 150 fecal samples were obtained and subjected
to quantitative PCR (qPCR) testing. Mean fecal dry matter content was 14.3% (standard deviation = 4.5%). Two pigs (6.7%) alternated between being L. intracellularis qPCR positive and negative. For 28 pigs, the excreting levels of L. intracellularis were within the dynamic range of the qPCR assay at all sampling points. For these 28 pigs, the mean excretion level of L. intracellularis was 6.1 log10 bacteria/g feces (standard deviation = 1.2 log10 bacteria/g feces). The maximum observed difference between 2 fecal samples from the same pig was 1.1 log10 bacteria/g feces. The average standard deviation for individual pigs was 0.27 log10 bacteria/g feces. The average coefficient of variation within pigs was 0.04, ranging from 0.006 to 0.08. The results imply that absolute quantification of L. intracellularis by qPCR has acceptable repeatability within 1 day. However, a population-specific proportion of pigs alternating between positive and negative test results must be expected.

General information
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Organisations: Adaptive Immunology & Parasitology, National Veterinary Institute, Division of Veterinary Diagnostics and Research, Bacteriology & Pathology, Section for Veterinary Diagnostics, Virology, University of Copenhagen
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  - BFI (2009): BFI-level 1
  - Scopus rating (2009): SJR 0.717 SNIP 1.022
  - Web of Science (2009): Indexed yes
  - BFI (2008): BFI-level 1
  - Scopus rating (2008): SJR 0.794 SNIP 0.972
  - Web of Science (2008): Indexed yes
  - Scopus rating (2007): SJR 0.605 SNIP 0.773
  - Web of Science (2007): Indexed yes
You can pool faecal samples from individual pigs to test for Porcine Circovirus Type 2 and Lawsonia intracellularis using real-time PCRs

Introduction Real-time PCR tests have been developed to detect and quantify Porcine Circovirus type 2 (PCV2) and Lawsonia intracellularis in pigs' faeces. Pooling of individual faecal samples is often used to reduce the costs of diagnostic testing. The objective of this study was to evaluate any change in the test sensitivity of PCV2 and L. intracellularis real-time PCR when individual faecal samples were pooled. Materials and Methods Forty eight faecal samples were collected from the rectum of individual pigs (>10 weeks) from four farms. Faecal samples were classified as diarrhoea +/- based on subjective assessment of consistency. Three individual samples were combined to make 16 pooled samples (8 diarrhoea; 8 non-diarrhoea). Individual and pooled samples were tested using real-time PCR tests specific for PCV2 and L. intracellularis. A positive result in any of the three individual samples was deemed “group positive”. Changes in test sensitivity after combining the three individual samples were evaluated. Results The sensitivity and specificity of the pooled faecal samples for L. intracellularis were 86.4% and 100%, respectively. The sensitivity and specificity of the pooled faecal samples for PCV2 were 97% and 100%, respectively. Conclusions These preliminary results suggest that three individual faecal samples may be pooled for PCV2 or L. intracellularis testing using real-time PCR with minimal loss of sensitivity. Under the conditions of this study, the sensitivity of pooling was reduced when quantities of L. intracellularis or PCV2 in individual samples were low.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Bacteriology & Pathology, Queensland Department of Primary Industries, Pig Research Centre, University of Copenhagen
Authors: Holyoake, P. K. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Pedersen, K. S. (Ekstern), Johansen, M. (Ekstern), Stege, H. (Ekstern), Moore, K. (Ekstern), Ståhl, M. (Intern), Angen, Ø. (Intern), Nielsen, J. P. (Ekstern)
Publication date: 2012
Event: Abstract from 4th European Symposium of Porcine Health Management, Bruges, Belgium.
Main Research Area: Technical/natural sciences
Electronic versions:
ESPHabstraclpool12Dec11.pdf
Links:
Source: orbit
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Betydningen af Lawsonia og PCV2 virus for daglig tilvækst hos slagtesvin

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Bacteriology & Pathology, Virology, Videncenter for Svineproduktion, Landbrug & Fødevarer
Authors: Johansen, M. (Ekstern), Nielsen, M. B. F. (Ekstern), Dahl, J. (Ekstern), Svensmark, B. (Ekstern), Bækbo, P. (Ekstern), Kristensen, C. S. (Ekstern), Hjulsager, C. K. (Intern), Jensen, T. K. (Intern), Ståhl, M. (Intern), Larsen, L. E. (Intern), Angen, Ø. (Intern)
Number of pages: 13
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Publication information
Publisher: Videncenter for Svineproduktion
Original language: Danish
Series: Meddelelse
Number: 903
Main Research Area: Technical/natural sciences
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Detection and quantification of porcine circovirus type 2 (PCV2) and PCV2-antibodies in oral fluid from finisher pigs.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Danish Agriculture and Food Council, University of Copenhagen
Authors: Leth, S. C. (Ekstern), Pedersen, K. S. (Ekstern), Hjulsager, C. K. (Intern), Stege, H. (Ekstern), Kristensen, C. S. (Ekstern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern)
Number of pages: 121
Pages: P.040
Publication date: 2011

Host publication information
Title of host publication: 6th International Symposium on Emerging and Re-emerging Pig Diseases : Proceedings
Main Research Area: Technical/natural sciences
Conference: 6th International Symposium on Emerging and Re-emerging Pig Diseases, Barcelona, Spain, 12/06/2011 - 12/06/2011
Electronic versions:
Diagnosis of porcine respiratory disease with a real-time PCR diagnostic package

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Bacteriology & Pathology
Authors: Hjulsager, C. K. (Intern), Breum, S. Ø. (Intern), Jorsal, S. E. L. (Intern), Kokotovic, B. (Intern), Larsen, L. E. (Intern)
Publication date: 2011
Event: Abstract from 1st Congress of the European Association of Veterinary Laboratory Diagnosticians, Lelystad, Netherlands.
Main Research Area: Technical/natural sciences
Electronic versions:

Links:

Diagnostik af PCV-2 i svinebesætninger på spyt indsamlet ved hjælp af reb

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Technical University of Denmark, Videncenter for Svineproduktion, Landbrug & Fødevarer, University of Copenhagen
Authors: Christensen, S. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Pedersen, K. S. (Ekstern), Stege, H. (Ekstern), Kristensen, C. S. (Ekstern)
Pages: 35
Publication date: 2011
Main Research Area: Technical/natural sciences

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Journal: Dansk Veterinaertidsskrift
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BFI (2011): BFI-level 1
ISI indexed (2011): ISI indexed no
Distribution of influenza A viruses of avian and swine origin and their sialic acid receptors in experimentally influenza infected pigs

Background: Pigs are considered susceptible to influenza A virus infections from different host origins because earlier studies have shown that they have receptors for both avian (sialic acid-alpha-2,3-terminal saccharides (SA-alpha-2,3)) and swine/human (SA-alpha-2,6) influenza viruses in the upper respiratory tract. Furthermore, experimental and natural infections in pigs have been reported with influenza A virus from avian and human sources. Methods: This study investigated the receptor distribution in the entire respiratory tract of pigs using specific lectins Maackia Amurensis (MAA) I, and II, and Sambucus Nigra (SNA). Furthermore, the predilection sites of swine influenza virus (SIV) subtypes H1N1 and H1N2 as well as avian influenza virus (AIV) subtype H4N6 were investigated in the respiratory tract of experimentally infected pigs using immunohistochemical methods. Results: SIV antigen was widely distributed in bronchi, but was also present in epithelial cells of the nose, trachea, bronchioles, and alveolar type I and II epithelial cells in severely affected animals. AIV was found in the lower respiratory tract, especially in alveolar type II epithelial cells and occasionally in bronchiolar epithelial cells. SA-alpha-2,6 was the predominant receptor in all areas of the respiratory tract with an average of 80-100% lining at the epithelial cells. On the contrary, the SA-alpha-2,3 was not present (0%) at epithelial cells of nose, trachea, and most bronchi, but was found in small amounts in bronchioles, and in alveoli reaching an average of 20-40% at the epithelial cells. Interestingly, the receptor expression of both SA-alpha-2,3 and 2,6 was markedly diminished in influenza infected areas compared to non-infected areas. Conclusions: A difference in predilection sites between SIV and AIV virus was found, and this difference was in accordance with the distribution of the SA-alpha-2,6 and SA-alpha-2,3 receptor, respectively. The results indicated that the distribution of influenza A virus receptors in pigs are similar to that of humans and therefore challenge the theory that the pig acts as a mixing vessel between human and avian influenza viruses. Furthermore, it was shown that AIV prefers to infect alveolar type II epithelial cells in pigs. This corresponds with findings in humans emphasising the resemblance between the two species.
Does PCV2 reduce the impact of subsequent infection with Lawsonia intracellularis?

**General information**

State: Published
Organisations: National Veterinary Institute, Bacteriology & Pathology, Division of Veterinary Diagnostics and Research, Section for Veterinary Diagnostics, Adaptive Immunology & Parasitology, Sektion for Eksotiske Virussygdomme, Division of Virology, Virology
Authors: Hansen, M. S. (Intern), Jensen, T. K. (Intern), Hjulsager, C. K. (Intern), Angen, Ø. (Intern), Riber, U. (Intern), Nielsen, J. (Intern), Larsen, L. E. (Intern)
Number of pages: 103
Pages: P.022
Publication date: 2011

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Main Research Area: Technical/natural sciences
Conference: 6th International Symposium on Emerging and Re-emerging Pig Diseases, Barcelona, Spain, 12/06/2011 - 12/06/2011
Electronic versions:
Identification of an antigenically different porcine parvovirus (PPV) isolate in Denmark

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Chinese Academy of Agricultural Sciences, Intervet/Schering-Plough Animal Health
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Shangjin, C. (Ekstern), Larsen, K. V. (Ekstern), Larsen, L. E. (Intern)
Number of pages: 52
Publication date: 2011

Host publication information
Title of host publication: Proceedings of the 6th International Symposium on Emerging and Re-emerging Pig Diseases
Main Research Area: Technical/natural sciences
Conference: 6th International Symposium on Emerging and Re-emerging Pig Diseases, Barcelona, Spain, 12/06/2011 - 12/06/2011
Electronic versions: Identification.pdf
Links:
Source: orbit
Source-ID: 282038
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2011

Investigation of PCV2-status in Danish herds - One year longitudinal study

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Danish Agriculture and Food Council
Authors: Kristensen, C. S. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 104
Pages: P.023
Publication date: 2011

Host publication information
Title of host publication: 6th International Symposium on Emerging and Re-emerging Pig Diseases : Proceedings
Main Research Area: Technical/natural sciences
Conference: 6th International Symposium on Emerging and Re-emerging Pig Diseases, Barcelona, Spain, 12/06/2011 - 12/06/2011
Electronic versions: int02.pdf
Links:

Bibliographical note
Poster presentation.
Source: orbit
Source-ID: 282630
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2011

Pandemic H1N1 2009 virus in Danish pigs: Diagnosis and lack of surveillance

In March-April 2009, a novel pandemic H1N1 virus (H1N1v) of likely swine origin emerged in the human population globally. The first case in pigs was reported from Canada in May 2009 and presently almost all countries with pig production have reported cases. The emergence of a new influenza subtype in swine with a genetic profile similar to older circulating strains implied a challenge for the veterinary diagnostic laboratories. We report the development, validation and implementation of a diagnostic strategy for specific diagnosis of H1N1v in pigs and the results of tests of pigs performed in
Pandemic H1N1 2009 virus in Norwegian pigs naïve to influenza A viruses

In March-April 2009, a novel pandemic influenza A (H1N1) virus (pH1N1-09v) emerged in the human population. The first case of pH1N1v infection in pigs was reported from Canada in May 2009. In Norway, pH1N1v infection was recorded in a swine herd on the 10th of October of 2009. Here, we report results from the investigation performed during the outbreak and the follow up surveillance performed in the Norwegian pig population. Nasal swabs were collected from herds i) where pigs had been exposed to persons with verified pH1N1-09v infection or with influenza-like illness (ILI); ii) where pigs showed clinical signs or iii) with a history of close contact with or close proximity to infected herds. In addition, blood samples were collected from nucleus and multiplier breeding herds. Detection of pH1N1v was initially performed using a real-time RT-PCR targeted to detect influenza A virus. Positive samples were tested by a pH1N1-09v specific real-time RT-PCR. Blood samples were tested for presence of antibodies against influenza A virus by ELISA (DVET) and positive samples in the ELISA were tested by haemagglutinin inhibition test using A/California/07/09 as antigen. From the onset of the outbreak and until 31st of December 2009, the pH1N1-09v was detected in nasal swabs from 54 of 114 herds investigated tested, while 55 of 140 herds tested positive for antibodies against pH1N1-09v. No herd has been tested positive for pH1N1-09v since early January 2010, however, results of the Norwegian surveillance and control programme for specific swine herds for 2010 so far indicates that 40 % of the swine herds (154 herds) are positive for antibodies against pH1N1-09. Serological evaluation of swine herds and detailed back tracking of the outbreak indicated that the virus was introduced in September 2009. The Norwegian swine population has, until the outbreak of pH1N1-09v, been considered free from influenza A virus infection as documented through serological surveillance program running since 1997. Virus isolated from one of the herds positive for pH1N1-09v was fully identical across the full genome to virus published H1N1v strains and 80- 95% identity to classical-swine H1N1 which do not circulate in Denmark. In contrast, there was only 60-70% identity to the subtypes circulating in Denmark (H1N1, H3N2, and avian-like H1N2) indicating that these subtypes would not be detected by this assay. The negative outcome of the test of 76 Danish swine influenza virus positive samples in the H1N1v assay confirmed that the assay was specific for H1N1v. Test of dilution series of cell culture adapted strains revealed a sensitivity of 1-2 TCID50/ML. All influenza positive samples from swine submitted to NVI in 2009 (81 out of 299 submissions) have been tested for H1N1v with negative results. In 2010 (until the 24rd. of June) samples from 34 submissions have been tested and 5 herds were found positive for H1N1v (4 in January and 1 in June). The number of submissions for influenza diagnosis of swine have dropped significantly in 2010 compared to 2009 probably because the producers want to avoid the constraints put on the herd in case of a positive H1N1v result. In combination with the fact that Denmark does not have any formal surveillance program for swine influenza in place, we have currently no overview of the number of H1N1v positive swine in Denmark. However, the diagnosis of a positive herd in June 2010, outside the human influenza season, may indicate an ongoing swine to swine transmission of H1N1v in Denmark.
Pandemic Influenza A H1N1v circulates in Danish pigs

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Statens Serum Institut
Authors: Hjulsager, C. K. (Intern), Breum, S. Ø. (Intern), Nielsen, L. P. (Ekstern), Trebbien, R. (Intern), Larsen, L. E. (Intern)
Number of pages: 73
Publication date: 2011

Host publication information
Title of host publication: 6th International Symposium on Emerging and Re-emerging Pig Diseases: Proceedings
Main Research Area: Technical/natural sciences
Conference: 6th International Symposium on Emerging and Re-emerging Pig Diseases, Barcelona, Spain, 12/06/2011 - 12/06/2011
Electronic versions: 98FA82d01.pdf
Bibliographical note
Oral presentation.
Source: orbit
Source-ID: 282207
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2011

PRRSV outbreak with high mortality in northern part of Denmark

Porcine reproductive and respiratory syndrome virus (PRRSV) belongs to the Arteriviridae family and is the cause of significant respiratory and reproductive disease in swine worldwide. Strains of PRRSV are divided into two genotypes: type 1 and type 2, also referred to as EU and US type, respectively, due to their geographical origin. In Denmark the type 1 virus was first recognized in 1992, and since 1996 both types of PRRSV are widely spread. Approximately 50 % of the herds are seropositive for PRRSV antibodies against either or both types of PRRSV.

In November 2010, a severe case of PRRSV with high mortality rate in piglets occurred in Northern Jutland. PRRSV type 2 was detected by real-time RT-PCR in lung tissue from 10 days old piglets. The outbreak was treated by extensive vaccination with Ingelvac® PRRS MLV and strict management procedures. 6 weeks later, the mortality of liveborn piglets had dropped to normal levels. From week 6 until week 14 after the initial outbreak, up to 75 % of fetuses were born as mummified. PCV2 and PPV have not been detected in the fetuses. 15 weeks after the initial outbreak, the number of liveborn piglets and the mortality until weaning was back to normal. Total losses of piglets until weaning for the 15 week period were about 50 %. Losses in the nursery and finisher barn are still substantial 15 weeks after the initial outbreak. Sequencing of ORF5 and ORF7 confirmed the type of PRRSV to be type 2, and revealed distinct nucleotide differences compared to other Danish PRRSV type 2 sequences in the ORF5 region. We speculate that the virus causing this outbreak is more pathogenic than previously recognized Danish PRRSV type 2 strains.

General information
State: Published
Organisations: National Veterinary Institute, Section for Virology, Section for Public sector service and commercial diagnostics, Boehringer Ingelheim Danmark A/S
Authors: Kvisgaard, L. K. (Intern), Hjulsager, C. K. (Intern), Rathkjen, P. H. (Ekstern), Breum, S. Ø. (Intern), Trebbien, R. (Intern), Larsen, L. E. (Intern)
Number of pages: 1
Publication date: 2011
Event: Abstract from 12th International Nidovirus Symposium, Acme, Michigan, United States.
Screening of reservoirs for hepatitis E virus

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Krog, J. S. (Intern), Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Jensen, T. H. (Intern), Bøtner, A. (Intern), Larsen, L. E. (Intern)
Number of pages: 359
Pages: P.239
Publication date: 2011

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Title of host publication: 6th International Symposium on Emerging and Re-emerging Pig Diseases : Proceedings
Main Research Area: Technical/natural sciences
Conference: 6th International Symposium on Emerging and Re-emerging Pig Diseases, Barcelona, Spain, 12/06/2011 - 12/06/2011
Electronic versions:
Screening of reservoirs for hepatitis E virus.pdf
Links:
Source: orbit
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Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2011

The aetiological role of porcine circovirus type 2 in acute diarrhoea of weaners in Danish herds

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Universidade Federal de Minas Gerais, University of Copenhagen
Authors: Pedersen, K. S. (Ekstern), Hjulsager, C. K. (Intern), Guedes, R. (Ekstern), Jensen, T. H. (Intern), Jorsal, S. E. L. (Intern), Stege, H. (Ekstern), Nielsen, J. P. (Ekstern), Larsen, L. E. (Intern)
Number of pages: 131
Pages: P.050
Publication date: 2011

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998FA82d01.pdf
Links:
Source: orbit
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Undersøgelse af PCV2-status i to danske besætninger - et års opfølgning.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics
A preliminary study of the association between Porcine Circovirus Type 2, Lawsonia intracellularis and diarrhoea in growing pigs

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Bacteriology & Pathology, Wagga Wagga Agricultural Institute, Pig Research Centre, University of Copenhagen
Authors: Holyoake, P. K. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Pedersen, K. S. (Ekstern), Johansen, M. (Ekstern), Stege, H. (Ekstern), Orchard, B. (Ekstern), Ståhl, M. (Intern), Angen, Ø. (Intern), Nielsen, J. P. (Ekstern)
Number of pages: 284
Pages: O.252
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 21st International Pig Veterinary Society Congress
Main Research Area: Technical/natural sciences
Conference: 21st International Pig Veterinary Society Congress, Vancouver, Canada, 18/07/2010 - 18/07/2010
Links:
http://www.ipvs2010.com/
Source-ID: 282422
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2011

A preliminary study of the effects of treating diarrhoeic pigs with oxytetracycline on shedding of Porcine Circovirus Type 2 and Lawsonia intracellularis

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Bacteriology & Pathology, Wagga Wagga Agricultural Institute, Pig Research Centre, University of Copenhagen
Authors: Holyoake, P. K. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Pedersen, K. S. (Ekstern), Johansen, M. (Ekstern), Stege, H. (Ekstern), Orchard, B. (Ekstern), Ståhl, M. (Intern), Angen, Ø. (Intern), Nielsen, J. P. (Ekstern)
Number of pages: 464
Pages: P.158
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 21st International Pig Veterinary Society Congress
Main Research Area: Technical/natural sciences
Conference: 21st International Pig Veterinary Society Congress, Vancouver, Canada, 18/07/2010 - 18/07/2010
Links:
http://www.ipvs2010.com/
Source-ID: 282425
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2011
Detection of myxoma viruses encoding a defective M135R gene from clinical cases of myxomatosis; possible implications for the role of the M135R protein as a virulence factor

Background: Myxoma virus is a member of the Poxviridae and causes disease in European rabbits. Laboratory confirmation of the clinical disease, which occurs in the autumn of most years in Denmark, has been achieved previously using antigen ELISA and electron microscopy. Results: An unusually large number of clinically suspected cases of myxomatosis were observed in Denmark during 2007. Myxoma virus DNA was detected, using a new real time PCR assay which targets the M029L gene, in over 70% of the clinical samples submitted for laboratory confirmation. Unexpectedly, further analysis revealed that a high proportion of these viral DNA preparations contained a frame-shift mutation within the M135R gene that has previously been identified as a virulence factor. This frame-shift mutation results in expression of a greatly truncated product. The same frame-shift mutation has also been found recently within an avirulent strain of myxoma virus (6918). However, three other frame-shift mutations found in this strain (in the genes M009L, M036L and M148R) were not shared with the Danish viruses but a single nucleotide deletion in the M138R/M139R intergenic region was a common feature. Conclusions: It appears that expression of the full-length myxoma virus M135R protein is not required for virulence in rabbits. Hence, the frame-shift mutation in the M135R gene in the nonpathogenic 6918 virus strain is not sufficient to explain the attenuation of this myxoma virus but one/some of the other frame-shift mutations alone or in conjunction with one/some of the thirty two amino acid substitutions must also contribute. The real time PCR assay for myxoma virus is a useful diagnostic tool for laboratory confirmation of suspected cases of myxomatosis.
Diagnosis of Porcine Circovirus Diseases (PCVDs) by serology and qPCR

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Intervet/Schering-Plough Animal Health
Authors: Larsen, L. E. (Intern), Aastrup, P. (Ekstern), Hjulsager, C. K. (Intern), Larsen, K. V. (Ekstern)
Number of pages: 105
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 21st International Pig Veterinary Society Congress
Main Research Area: Technical/natural sciences
Conference: 21st International Pig Veterinary Society Congress, Vancouver, Canada, 18/07/2010 - 18/07/2010

Dynamics of swine influenza infections in the farrowing unit of a Danish sow herd

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Danish Agriculture and Food Council, Odder Dyreklinik, Merial Norden A/S, University of Copenhagen
Authors: Larsen, L. E. (Intern), Nielsen, C. K. (Ekstern), Aakerblom, S. (Ekstern), Hjulsager, C. K. (Intern), Nielsen, J. P. (Ekstern), Stege, H. H. (Ekstern), Kristensen, C. S. (Ekstern), Elvstrom, A. (Ekstern), Lau, L. (Ekstern)
Number of pages: 80
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 21st International Pig Veterinary Society Congress
Main Research Area: Technical/natural sciences
Conference: 21st International Pig Veterinary Society Congress, Vancouver, Canada, 18/07/2010 - 18/07/2010

Forskningsprojekt om ny spædgrisediarre i Danmark

General information
State: Published
Organisations: Bacteriology & Pathology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Microbial Ecology, Virology, Section for Veterinary Diagnostics, Videnscenter for svineproduktion
Authors: Angen, Ø. (Intern), Jensen, T. K. (Intern), Mølbak, L. (Intern), Larsen, L. E. (Intern), Jorsal, S. E. L. (Intern), Bækbo, P. (Ekstern)
Pages: 31
Publication date: 2010
Main Research Area: Technical/natural sciences
Hepatitis E virus is highly prevalent in the Danish pig population

The objective of this study was to examine the prevalence of Hepatitis E virus (HEV) in the Danish pig population. Faecal samples from 97 pigs, 1–5 months of age were analysed for HEV RNA by a new PriProET real time RT-PCR assay. In addition, serum samples from 71 sow herds were screened for the presence of anti-HEV IgG antibodies by ELISA. The genotype of the detected HEV positive samples was estimated based on the melting temperature obtained by the PriProET real time RT-PCR assay. The HEV prevalence of faecal samples was estimated based on the melting temperature obtained by the PriProET real time RT-PCR assay. The HEV prevalence of faecal samples was 55.0% and 49.5% for herds and animals, respectively. A HEV IgG prevalence of 91.5% was found for the sow herds which correspond to 73.2% of the sows. The PriProET assay indicated that all HEV positive samples belonged to genotype 3 or 4, which is consistent with the observation of genotype 3 as dominant in European pigs. This is the first study showing that HEV is highly prevalent in the Danish pig population. The abundant presence of HEV in Danish pigs and the known high similarity between HEV isolates from pigs and humans support previous reports indicating possible zoonotic transmission of HEV.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Universidad Autonoma de Barcelona
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Deus, N. D. (Ekstern), Segalès, J. (Ekstern), Larsen, L. E. (Intern)
Publication date: 2010
Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.65 SJR 1.326 SNIP 1.208
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.393 SNIP 1.21 CiteScore 2.56
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.281 SNIP 1.262 CiteScore 2.54
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.438 SNIP 1.484 CiteScore 3
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.437 SNIP 1.579 CiteScore 3.18
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.562 SNIP 1.738 CiteScore 3.27
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Incidence, Diversity, and Molecular Epidemiology of Sapoviruses in Swine across Europe

Porcine sapovirus is an enteric calicivirus in domestic pigs that belongs to the family Caliciviridae. Some porcine sapoviruses are genetically related to human caliciviruses, which has raised public health concerns over animal reservoirs and potential cross-species transmission of sapoviruses. We report on the incidence, genetic diversity and molecular epidemiology of sapoviruses detected in domestic pigs in a comprehensive study conducted in six European countries (Denmark, Finland, Hungary, Italy, Slovenia and Spain) between 2004 and 2007. A total of 1,050 swine fecal samples from 88 pig farms were collected and tested by reverse transcription-PCR for sapoviruses, and positive findings were confirmed by sequencing. Sapoviruses were detected in 80 (7.6%) samples collected on 39 (44.3%) farms and in every country. The highest prevalence was seen among piglets aged 2 to 8 weeks, and there was no significant difference in the proportion of sapovirus positive findings in healthy animals or animals with diarrhea in Spain and Denmark (the only countries where both healthy animals and animals with diarrhea were tested). On the basis of the RNA polymerase region, highly heterogeneous populations of viruses representing six differential genogroups (genogroups III, VI, VII, and VIII, including potential new genogroups IX and X) were identified, with a predominance of genogroup GIII (50.6%). Genogroup VIII, found in five of the six countries, had the highest degree of homology (up to 66% at the amino acid level) to human sapovirus strains. Sapoviruses are commonly circulating and endemic agents in swine herds throughout Europe. Highly heterogenous and potential new genogroups of sapoviruses were found in pigs; however, no "human-like" sapoviruses were detected.

General information

State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Authors: Reuter, G. (Ekstern), Zimsek-Mijovski, J. (Ekstern), Poljsak-Prijatelj, M. (Ekstern), Di Bartolo, I. (Ekstern), Ruggeri, F. (Ekstern), Kantala, T. (Ekstern), Maunula, L. (Ekstern), Kiss, I. (Ekstern), Kecskemeti, S. (Ekstern), Halaihel, N. (Ekstern), Buesa, J. (Ekstern), Johnsen, C. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern), Koopmans, M. (Ekstern), Bottiger, B. (Ekstern)
Publication information
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BFI (2016): BFI-level 1
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.204 SNIP 1.448 CiteScore 3.56
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.205 SNIP 1.538 CiteScore 3.84
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.414 SNIP 1.646 CiteScore 4.18
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.114 SNIP 1.632 CiteScore 4.11
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.336 SNIP 1.698 CiteScore 4.27
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.303 SNIP 1.727
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.173 SNIP 1.694
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.239 SNIP 1.621
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 2.202 SNIP 1.689
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 2.187 SNIP 1.642
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 2.012 SNIP 1.655
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.678 SNIP 1.701
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 1.845 SNIP 1.855
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 1.947 SNIP 1.722
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 2.076 SNIP 1.808
Infection dynamics of Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) in vaccinated and non-vaccinated pigs

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Danvet K/S, Odder Dyreklinitk, University of Copenhagen
Authors: Jessen, H. H. (Ekstern), Hjulsager, C. K. (Intern), Nielsen, J. P. (Ekstern), Stege, H. (Ekstern), Larsen, L. E. (Intern), Elvstrøm, A. (Ekstern)
Number of pages: 207
Pages: O.173
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 21st International Pig Veterinary Society Congress
Main Research Area: Technical/natural sciences
Conference: 21st International Pig Veterinary Society Congress, Vancouver, Canada, 18/07/2010 - 18/07/2010
Source: orbit
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Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2011

Infectious risk factors for postweaning multisystemic wasting syndrome (PMWS) development

General information
State: Published
Organisations: National Veterinary Institute, Section for Veterinary Epidemiology and public sector consultancy, Division of Veterinary Diagnostics and Research, Section for Veterinary Diagnostics, Virology, Centre de Recerca en Sanitat Animal, Danish Agriculture and Food Council
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Links: http://www.ipvs2010.com/
Source: orbit
Source-ID: 282423
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Lung pathology in slaughtered pigs from Norwegian herds naturally infected with pandemic influenza A (H1N1) 2009 virus

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, National Veterinary Institute
Authors: Valheim, M. (Ekstern), Gamlem, H. (Ekstern), Gjerset, B. (Ekstern), Larsen, L. E. (Intern), Lium, B. (Ekstern)
Replication, Pathogenesis and Transmission of Pandemic (H1N1) 2009 Virus in Non-Immune Pigs

The declaration of the human influenza A pandemic (H1N1) 2009 (H1N1/09) raised important questions, including origin and host range [1,2]. Two of the three pandemics in the last century resulted in the spread of virus to pigs (H1N1, 1918; H3N2, 1968) with subsequent independent establishment and evolution within swine worldwide [3]. A key public and veterinary health consideration in the context of the evolving pandemic is whether the H1N1/09 virus could become established in pig populations [4]. We performed an infection and transmission study in pigs with A/California/07/09. In combination, clinical, pathological, modified influenza A matrix gene real time RT-PCR and viral genomic analyses have shown that infection results in the induction of clinical signs, viral pathogenesis restricted to the respiratory tract, infection dynamics consistent with endemic strains of influenza A in pigs, virus transmissibility between pigs and virus-host adaptation events. Our results demonstrate that extant H1N1/09 is fully capable of becoming established in global pig populations. We also show the roles of viral receptor specificity in both transmission and tissue tropism. Remarkably, following direct inoculation of pigs with virus quasispecies differing by amino acid substitutions in the haemagglutinin receptor-binding site, only virus with aspartic acid at position 225 (225D) was detected in nasal secretions of contact infected pigs. In contrast, in lower respiratory tract samples from directly inoculated pigs, with clearly demonstrable
pulmonary pathology, there was apparent selection of a virus variant with glycine (225G). These findings provide potential clues to the existence and biological significance of viral receptor-binding variants with 225D and 225G during the 1918 pandemic [5].

**General information**

**State:** Published

**Organisations:** Innate Immunology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Veterinary Laboratories Agency, Philippus-Universität Marburg, Agence Francaise de Sécurite des Aliments, Merial S.A.S., Hipra, Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia, Central Veterinary Institute, Ghent University

**Authors:** Brookes, S. M. (Ekstern), Nunez, A. (Ekstern), Choudhury, B. (Ekstern), Matrosovich, M. (Ekstern), Essen, S. C. (Ekstern), Clifford, D. (Ekstern), Slomka, M. J. (Ekstern), Kuntz-Simon, G. (Ekstern), Garcon, F. (Ekstern), Nash, B. (Ekstern), Hanna, A. (Ekstern), Heggaard, P. M. H. (Intern), Queguiner, S. (Ekstern), Bublot, M. (Ekstern), Garcia, J. M. (Ekstern), Gardner, R. (Ekstern), Foni, E. (Ekstern), Loeffen, W. (Ekstern), Larsen, L. E. (Intern), Reeth, K. V. (Ekstern), Banks, J. (Ekstern), Irvine, R. M. (Ekstern), Brown, I. H. (Ekstern)

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**Main Research Area:** Technical/natural sciences

**Publication information**

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Web of Science (2016): Indexed yes

BFI (2015): BFI-level 1

Scopus rating (2015): SJR 1.414 SNIP 1.131 CiteScore 3.32

Web of Science (2015): Indexed yes

BFI (2014): BFI-level 1

Scopus rating (2014): SJR 1.545 SNIP 1.141 CiteScore 3.54

Web of Science (2014): Indexed yes

BFI (2013): BFI-level 1

Scopus rating (2013): SJR 1.74 SNIP 1.147 CiteScore 3.94

ISI indexed (2013): ISI indexed yes

Web of Science (2013): Indexed yes

BFI (2012): BFI-level 1

Scopus rating (2012): SJR 1.945 SNIP 1.142 CiteScore 4.15

ISI indexed (2012): ISI indexed yes

Web of Science (2012): Indexed yes

BFI (2011): BFI-level 1

Scopus rating (2011): SJR 2.369 SNIP 1.23 CiteScore 4.58

ISI indexed (2011): ISI indexed no

Web of Science (2011): Indexed yes

BFI (2010): BFI-level 1

Scopus rating (2010): SJR 2.631 SNIP 1.161

Web of Science (2010): Indexed yes

BFI (2009): BFI-level 1

Scopus rating (2009): SJR 2.473 SNIP 0.985

Web of Science (2009): Indexed yes

BFI (2008): BFI-level 1

Scopus rating (2008): SJR 2.323 SNIP 0.96

Web of Science (2008): Indexed yes

Scopus rating (2007): SJR 1.289 SNIP 0.525
Selection of method is crucial for the diagnosis of porcine circovirus type 2 associated reproductive failures
During a 2-month period a newly repopulated Danish pig herd experienced an increase in numbers of stillborn and mummies, caused by porcine circovirus type 2 (PCV2) associated reproductive failure. Based on recordings of data over time, the progression of the clinical outbreak was studied and the diagnostic value of different techniques was evaluated. Foetal hearts (38 cases and 13 controls) were examined by immunohistochemistry (IHC) and real-time polymerase chain reaction (PCR) for the detection of PCV2; and total immunoglobulin G (IgG) was measured in pleura cavity fluid. PCV2 IHC was positive in 14/38 of the case foetuses, which were delivered during a 9 days period early in the outbreak. On the basis of the results obtained by IHC and PCR, the foetuses were divided into 3 categories: PCV2 negative; moderately positive (10⁴ to 10⁷ copies per 500ng DNA); and massively positive for PCV2 (>10⁷ copies per 500ng DNA). All control- and IHC positive foetuses were included in the negative and massively positive groups, respectively. Ten case foetuses had elevated IgG levels, which did not correlate with the IHC or PCR results. Based on the clustering of the IHC positive foetuses, it is suggested that IHC only is suited for diagnosing acute stages of reproductive failure, whereas quantitative PCR can be used as a sensitive diagnostic method within a wider time span. It seems that IgG measurements are unpredictable as indication of intrauterine infection with PCV2. Copyright © 2010 Elsevier B.V. All rights reserved.
Serological response and influence on virus load in pigs vaccinated with Porcilis PCV

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Intervet/Schering-Plough Animal Health, OE-Vet, Danvet K/S
Authors: Astrup, P. (Ekstern), Haugegaard, S. (Ekstern), Larsen, C. B. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Number of pages: 360
Pages: P.054
Publication date: 2010

Host publication information
Title of host publication: Proceedings of the 21st International Pig Veterinary Society Congress
Main Research Area: Technical/natural sciences
Strategies for subtyping influenza viruses circulating in the Danish pig population

Influenza viruses are endemic in the Danish pig population and the dominant circulating subtypes are H1N1, a Danish H1N2 reassortant, and H3N2. Here we present our current and future strategies for influenza virus subtyping. For diagnostic and surveillance of influenza subtypes circulating in the Danish pig population functional and rapid subtyping assays are required. The conventional RT-PCR influenza subtyping assays developed by Chiapponi et al. (2003) have been implemented and used for typing of influenza viruses found positive in a pan influenza A real time RT-PCR assay. The H1 and N1 assays were specific when applied on Danish influenza positive samples, whereas the N2 assay consistently showed several unspecific PCR products. A subset of positive influenza samples detected by the real time RT-PCR screening assay could not be subtyped using these assays. Therefore, new influenza subtyping assays based on RT-PCR and subsequent sequencing were implemented for the four subtypes H1, H3, N1, and N2. The assays were based on primer sets published by the WHO, but slightly modified for improved detection of Danish subtype variants. Sequencing of circulating influenza viruses is beneficial since it provides information about the genetic drift of influenza in the Danish pig population. Finally, we will present preliminary results of the performance of new real time RT-PCR assays for rapid subtyping of the most common subtypes circulating in Danish pigs. These real time RT-PCR assays would provide a simpler and faster tool for routine diagnostic influenza subtyping.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Trebbien, R. (Intern), Larsen, L. E. (Intern)
Pages: P-033
Publication date: 2010

Host publication information
Title of host publication: The International Symposium on Neglected Influenza Viruses : Final Programme & Abstracts
Volume: Poster Presentations
Main Research Area: Technical/natural sciences
Conference: The International Symposium on Neglected Influenza Viruses, Amelia Island, Florida, USA, 01/01/2010
Source: orbit
Source-ID: 265784
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2010

Svineinfluenza – status og afklaring af nomenklatur

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics
Authors: Larsen, L. E. (Intern), Hjulsager, C. K. (Intern)
Publication date: 2010
Main Research Area: Technical/natural sciences

Publication information
Journal: Dansk Veterinærtidsskrift
Volume: 93
Issue number: 10
ISSN (Print): 1600-2032
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BFI (2008): BFI-level 1
Web of Science (2004): Indexed yes
Original language: Danish
Source: orbit
Source-ID: 282203
Publication: Research - peer-review › Journal article – Annual report year: 2011
Vaccination med Porcilis PCV i to danske svinebesætninger: Vaccination gav et ensartet serologisk respons

In two pig farms with clinical symptoms of PCVD and circulation of PCV2, vaccination was instituted with 2 ml of Porcilis PCV given once at around 4 (3-5) weeks of age. Vaccinations resulted in a uniform serological response. In one farm, where vaccinated pigs were reared separated from non-vaccinated from weaning through to slaughter, the viraemia was prevented. In the other farm viraemia was reduced with at least 2 log(10) units, even though pigs were housed in the same pen as non-vaccinated and viraemic pigs. In this herd a statistically significant (+ 39 g) average daily weight gain was accomplished in vaccinated pigs compared to non-vaccinated during the period 8-16 weeks after weaning. It was concluded that vaccination with Porcilis PCV reduced the virus load in infected pigs, and vaccination had a positive impact on daily weight gain.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Intervet/Schering-Plough Animal Health, OE-Vet, Danvet K/S
Authors: Haugegaard, J. (Ekstern), Astrup, P. (Ekstern), Haugegaard, S. (Ekstern), Larsen, C. B. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Pages: 24-28
Publication date: 2010
Main Research Area: Technical/natural sciences

Endemic Hepatitis E in two Nordic Countries
Antibodies against hepatitis E virus (anti-HEV) were found in 248 Swedish and Danish patients between 1993 and 2007. Most patients were symptomatic and tested for anti-HEV due to travel abroad. Among patients with known country of infection, most were infected in Asia, mainly on the Indian subcontinent. However, 29 patients were infected in Europe, nine of these had HEV IgM and/or HEV RNA in serum. In sera from 65 of 141 tested patients HEV RNA could be detected, and 63 strains could be typed by limited sequencing within ORF2. HEV RNA was found in sera from 71% of the patients with HEV IgM and IgG and in 18% of the patients with only detectable HEV IgG. It was also found up to three weeks after the onset of disease in 67% of the patients with known date of onset. Patients infected in Europe were infected by genotype 3, and were older than those infected by genotype 1 (mean age 55.3 vs 30 years, p

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics
Authors: Norder, H. (Ekstern), Sundqvist, L. (Ekstern), Magnusson, L. (Ekstern), Breum, S. Ø. (Intern), Lofdahl, M. (Ekstern), Larsen, L. E. (Intern), Hjulsager, C. K. (Intern), Magnius, L. (Ekstern), Bottiger, B. (Ekstern), Widen, F. (Ekstern)
H1N1 Influenza A hos mennesker og svin

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern)
Pages: 80
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: Hyologisk
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Ratings:
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HEPATITIS E VIRUS IS PREVALENT IN THE DANISH PIG POPULATION

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Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Universidad Autonoma de Barcelona, Swedish Institute for Infectious Disease Control, Statens Serum Institut
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Deus, N. D. (Ekstern), Segalès, J. (Ekstern), Norder, H. (Ekstern), Böttiger, B. (Ekstern), Larsen, L. E. (Intern)
Number of pages: 114
Publication date: 2009

Host publication information
Title of host publication: 8th International Congress of Veterinary Virology : Integrating classical and molecular virology
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 254908
Publication: Research - peer-review › Article in proceedings – Annual report year: 2009

Induction of porcine post-weaning multisystemic wasting syndrome (PMWS) in pigs from PMWS unaffected herds following mingling with pigs from PMWS-affected herds

In this paper we present the results from two experimental studies (I and II) investigating whether post-weaning multisystemic wasting syndrome (PMWS) can be induced in pigs from PMWS unaffected herds by mingling with pigs from PMWS-affected herds and to observe whether transportation and/or mingling of healthy pigs from unaffected herds could induce PMWS. The studies comprised pigs from 12 different herds. Eight herds had PMWS while four were unaffected. All 12 herds were found to be infected with PCV2. Pigs from PMWS-affected herds were mingled with pigs from unaffected herds in four separate compartments in both study I and study II. In addition, in study II, four groups of pigs from unaffected herds were included. Two groups with pigs transported and mingled from unaffected herds and two groups with pigs which were only transported. The PMWS diagnoses on the individual pigs were based on lymphoid depletion, histiocytic proliferation and the presence of giant cells or inclusion bodies together with the demonstration of PCV2 in lymphoid tissue. Healthy pigs, in both studies, developed PMWS 4–5 weeks after mingling with pigs clinically affected with PMWS. None of the pigs from unaffected herds which had no contact with pigs from PMWS-affected herds developed clinical signs of PMWS. Transportation and mingling of pigs from PMWS unaffected herds in combination or alone was insufficient to provoke PMWS.

General information
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Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology, Division of Microbiology and Risk Assessment, National Food Institute, Section for Veterinary Epidemiology and public sector consultancy, Virology, Danish Pig Production
Authors: Kristensen, C. S. (Ekstern), Bækbo, P. (Ekstern), Bille-Hansen, V. (Intern), Bøtner, A. (Intern), Vigre, H. (Intern), Enøe, C. (Intern), Larsen, L. E. (Intern)
Pages: 244-250
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: Veterinary Microbiology
Volume: 138
ISSN (Print): 0378-1135
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Infection, excretion and seroconversion dynamics of porcine circovirus type 2 (PCV2) in pigs from post-weaning multisystemic wasting syndrome (PMWS) affected farms in Spain and Denmark

Longitudinal case-control studies were performed in post-weaning multisystemic wasting syndrome (PMWS) affected farms from Denmark and Spain using similar designs. Fourteen independent batches of 100-154 pigs per batch were monitored from birth to PMWS outbreak occurrence. Pigs displaying PMWS-like signs and matched healthy cohorts were euthanized during the clinical outbreak. PMWS was diagnosed according to internationally accepted criteria and pigs were classified as: (i) PMWS cases, (ii) wasted non-PMWS cases and (iii) healthy pigs. Porcine circovirus type 2 (PCV2) quantitative PCR (qPCR) and serology techniques were applied to analyse longitudinally collected sera and/or nasal and rectal swabs. Results showed that PCV2 load increased in parallel to waning maternal antibody levels, reaching the maximum viral load concurrent with development of clinical signs. PMWS affected pigs had higher PCV2 prevalence and/or viral load than healthy pigs in all collected samples at necropsy (p <0.0001-0.05) and even in sera and nasal swabs at the sampling prior to PMWS outbreak (p <0.01-0.05). Danish farms had a higher PCV2 prevalence in young piglets as well as an earlier PMWS presentation compared to Spanish farms. PMWS diagnoses were confirmed by laboratory tests in only half of pigs clinically suspected to suffer from PMWS. Positive and significant correlations were found among PCV2 viral loads present in sera, nasal swabs, rectal swabs and lymphoid tissues (R = 0.289-0.827, p <0.0001-0.01), which indicates that nasal and rectal swabs were suitable indicators of PCV2 excretion. Sensitivity and/or specificity values observed from both tests used separately or combined suggested that qPCR and/or serology tests are not apparently able to substitute histopathology plus detection of PCV2 in tissues for the individual PMWS diagnosis within PMWS affected farms. However, qPCR appears to be a potential reliable technique to diagnose PMWS on a population basis.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Epidemiology and public sector consultancy, Sektion for Ekstotiske Virussygdomme, Division of Virology, Virology
Authors: Grau-Roma, L. (Ekstern), Hjulsager, C. K. (Intern), Sibila, M. (Ekstern), Kristensen, C. S. (Ekstern), Lopez-Soria, S. (Ekstern), Eneæ, C. (Intern), Casal, J. (Ekstern), Bøtner, A. (Intern), Nofrarias, M. (Ekstern), Bille-Hansen, V. (Intern), Fraile, L. (Ekstern), Bækbo, P. (Ekstern), Segales, J. (Ekstern), Larsen, L. E. (Intern)
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Main Research Area: Technical/natural sciences

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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.393 SNIP 1.21 CiteScore 2.56
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.281 SNIP 1.262 CiteScore 2.54
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.438 SNIP 1.484 CiteScore 3
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.437 SNIP 1.579 CiteScore 3.18
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.562 SNIP 1.738 CiteScore 3.27
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Influenza A (H1N1) infection in pigs

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Main Research Area: Technical/natural sciences

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Volume: 164
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Ratings:
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.442 SNIP 0.692 CiteScore 0.3

Original language: English
Epidemiology, Longitudinal case-control study, Quantitative real-time PCR (qPCR), Porcine circovirus type 2 (PCV2), Post-weaning multisystemic wasting syndrome (PMWS)

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Source: orbit
Source-ID: 243930
Publication: Research - peer-review ➔ Journal article – Annual report year: 2009
Influenzavirus hos svin

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Dansk Veterinaertidsskrift
Authors: Dalsgård, A. (Ekstern), Larsen, L. E. (Intern)
Inter-laboratory and inter-assay comparison on two real-time PCR techniques for quantification of PCV2 nucleic acid extracted from field samples

Several real-time PCR assays for quantification of PCV2 DNA (qPCR) have been described in the literature, and different in-house assays are being used by laboratories around the world. A general threshold of 10^6 copies of PCV2 per millilitre serum for postweaning multisystemic wasting syndrome (PMWS) diagnosis has been suggested. However, neither inter-laboratory nor inter-assay comparisons have been published so far. In the present study two different qPCR probe assays used routinely in two laboratories were compared on DNA extracted from serum, nasal and rectal swabs. Results showed a significant linear association between the assays (p < 0.0001) and a systematic difference of 1.4 log(10) copies of PCV2 per millilitre of sample (p < 0.0001). This difference indicated that the assay from laboratory 1 yielded a higher output than the one from laboratory 2. Results also showed that there was no linear association between the amount of PCV2 DNA and the amount of total DNA, neither in nasal (p = 0.86) nor in rectal (p=0.78) swabs, suggesting that normalizing of PCV2 DNA load in swab samples to total DNA concentration is not suitable. The present exploratory study highlights the need for the performance of ring trials on qPCV2 protocols between laboratories. Meanwhile, the proposed thresholds for PMWS diagnosis should only be considered reliable for each particular laboratory and each particular assay.
Ny mulighed for at undersøge svinediarre

General information
State: Published
Organisations: Bacteriology & Pathology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Virology
Authors: Angen, Ø. (Intern), Jorsal, S. E. L. (Intern), Larsen, L. E. (Intern), Hjulsager, C. K. (Intern), Ståhl, M. (Intern)
Pages: 30
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication: Research - peer-review › Journal article – Annual report year: 2009
Phylogenetic Analysis of PRRSV from Danish Pigs

Introduction and Objectives
Porcine reproductive and respiratory syndrome virus (PRRSV) is a single-stranded RNA virus belonging to the Arteriviridae family. It is the causative agent of significant respiratory and reproductive disease in swine worldwide. The virus is a recently emerged pathogen, being first identified as a cause of clinical disease in 1991. The disease spread simultaneously in North America and Europe to gain global residence in a short time-span. Two genotypes of PRRSV are currently recognized due to profound genomic and antigenic differences: PRRSV EU type and PRRSV US type, named from their geographic origin of identification. Great diversity within the two genotypes exists, and further division of PRRSV EU type into at least 3 subtypes has been suggested (Stadejek et al. 2006, 2008). In Denmark PRRSV EU type was first identified in 1992 and a few years later the US type also was recognized. According to serologic testing, both types are prevalent in the Danish pig population. However, the genetic drift of the virus during the past 10 years has not been determined. The objective of this study was to examine the genetic diversity and evolution of PRRSV in Danish pigs by phylogenetic analysis, in order to assess the applicability of vaccines currently used to control PRRSV infection in Danish pig herds. Materials and methods Lung tissue from samples submitted to the National Veterinary Institute during 2003-2008 for PRRSV diagnosis were screened for PRRSV by real-time RT-PCR, essentially as described by Egli et al. 2001, on RNA extracted with RNeasy Mini Kit (QIAGEN). Complete open reading frames (ORF) ORF5 and ORF7 were PCR amplified as described (Olekisiewicz et al. 1998) and sequenced. Sequences were aligned and Neighbour-Joining trees were constructed with ClustalX. Trees were visualized with NJ-plot software. Genbank entries of Danish PRRSV
The aim of the present longitudinal study was to assess the evolution of two acute phase proteins (APPs), pig-major acute phase protein (pig-MAP) and haptoglobin (HPT), in serum from pigs that developed postweaning multisystemic wasting syndrome (PMWS) in comparison to healthy and wasted non-PMWS affected pigs. In addition, evidence of infection with other pathogens and its relation with variations in APP's concentrations was also assessed. Fourteen independent batches of 100 to 154 pigs were monitored from birth to PMWS outbreak occurrence in 11 PMWS affected farms. Pigs diagnosed according to internationally accepted criteria and pigs were classified as: i) PMWS cases, ii) wasted non-PMWS affected pigs, iii) healthy pigs. At the moment of PMWS occurrence, pig-MAP and HPT concentration in PMWS affected pigs were higher than in healthy ones (p>0.001). No differences in APPs serum concentrations between subclinically PCV2 infected pigs and healthy non-PCV2 infected pigs (based on quantitative PCR on serum results) were detected. Results showed a significant correlation between PCV2 loads and both pig-MAP (R=0.487 to 0.602, p>0.001) and HPT (R=0.326 to 0.550, p>0.05 to 0.0001) concentrations in serum of PMWS affected pigs, indicating that the acute phase response in PMWS affected pigs occurred concomitantly to PCV2 viremia. No other pathogen, apart from PCV2, caused changes in antigenicity of viruses. Antigenic differences between EU subtypes have been demonstrated (Stadejek et al. 2008). PRRSV is a very diverse virus with a high mutation rate. It is therefore extremely important to continuously monitor and sequence the virus. The present data suggests, that the PRRSV vaccines used for the moment are adequate for control of PRRSV infection in the Danish pig population. References: 1.Egli et al. 2001 J.Vir.Methods 98:63-75. 2.Oleksiewicz et al. 1998, Vet.Microbiol. 64:7-22. 3.Stadejek et al. 2006, J.Gen.Vir. 87:1835-41. 4.Stadejek et al. 2008, Arch.Virol. 153:1479-88.

**Genera information**

**State:** Published

**Organisations:** Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology

**Authors:** Hjulsager, C. K. (Intern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern)

**Publication date:** 2009

**Event:** Abstract from 8th International Congress of Veterinary Virology, Budapest, Hungary.

**Main Research Area:** Technical/natural sciences

**Sequence analysis, Porcine reproductive and respiratory syndrome virus, PRRSV, swine**

**Source:** orbit

**Source-ID:** 250015

**Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2009**

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### Pig major acute-phase protein and haptoglobin serum concentrations correlate with PCV2 viremia and the clinical course of postweaning multisystemic wasting syndrome

The aim of the present longitudinal study was to assess the evolution of two acute phase proteins (APPs), pig-major acute phase protein (pig-MAP) and haptoglobin (HPT), in serum from pigs that developed postweaning multisystemic wasting syndrome (PMWS) in comparison to healthy and wasted non-PMWS affected pigs. In addition, evidence of infection with other pathogens and its relation with variations in APP's concentrations was also assessed. Fourteen independent batches of 100 to 154 pigs were monitored from birth to PMWS outbreak occurrence in 11 PMWS affected farms. Pigs displaying PMWS-like signs and age-matched healthy controls were euthanized during the clinical outbreak. PMWS was diagnosed according to internationally accepted criteria and pigs were classified as: i) PMWS cases, ii) wasted non-PMWS affected pigs and iii) healthy pigs. At the moment of PMWS occurrence, pig-MAP and HPT concentration in PMWS affected pigs were higher than in healthy ones (p>0.001). No differences in APPs serum concentrations between subclinically PCV2 infected pigs and healthy non-PCV2 infected pigs (based on quantitative PCR on serum results) were detected. Results showed a significant correlation between PCV2 loads and both pig-MAP (R=0.487 to 0.602, p>0.001) and HPT (R=0.326 to 0.550, p>0.05 to 0.0001) concentrations in serum of PMWS affected pigs, indicating that the acute phase response in PMWS affected pigs occurred concomitantly to PCV2 viremia. No other pathogen, apart from PCV2, caused changes in antigenicity of viruses. Antigenic differences between EU subtypes have been demonstrated (Stadejek et al. 2008). PRRSV is a very diverse virus with a high mutation rate. It is therefore extremely important to continuously monitor and sequence the virus. The present data suggests, that the PRRSV vaccines used for the moment are adequate for control of PRRSV infection in the Danish pig population. References: 1.Egli et al. 2001 J.Vir.Methods 98:63-75. 2.Oleksiewicz et al. 1998, Vet.Microbiol. 64:7-22. 3.Stadejek et al. 2006, J.Gen.Vir. 87:1835-41. 4.Stadejek et al. 2008, Arch.Virol. 153:1479-88.

**General information**

**State:** Published

**Organisations:** Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology

**Authors:** Grau-Roma, L. (Ekstern), Heegaard, P. M. H. (Intern), Hjulsager, C. K. (Intern), Sibila, M. (Ekstern), Kristensen, C. S. (Ekstern), Allepuz, A. (Ekstern), Pineiro, M. (Ekstern), Larsen, L. E. (Intern), Segales, J. (Ekstern), Fraile, L. (Ekstern)

**Pages:** 53-61

**Publication date:** 2009

**Main Research Area:** Technical/natural sciences

**Journal:** Veterinary Microbiology
Respiratory disease in calves: Microbiological investigations on trans-tracheally aspirated bronchoalveolar fluid and acute phase protein response

General information
State: Published
Organisations: Bacteriology & Pathology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Innate Immunology, Technical University of Denmark
Authors: Angen, Ø. (Intern), Thomsen, J. (Ekstern), Larsen, L. E. (Intern), Larsen, J. (Ekstern), Kokotovic, B. (Intern), Heegaard, P. M. H. (Intern), Enemark, J. M. D. (Ekstern)
Pages: 165-171
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: Veterinary Microbiology
Volume: 137
Issue number: 1-2
ISSN (Print): 0378-1135
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.65 SJR 1.326 SNIP 1.208
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.393 SNIP 1.21 CiteScore 2.56
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.281 SNIP 1.262 CiteScore 2.54
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.438 SNIP 1.484 CiteScore 3
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.437 SNIP 1.579 CiteScore 3.18
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.562 SNIP 1.738 CiteScore 3.27
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.371 SNIP 1.476
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.29 SNIP 1.472
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.169 SNIP 1.3
Web of Science (2008): Indexed yes
Transmission of different variants of PCV2 and viral dynamics in a research facility with pigs mingled from PMWS-affected herds and non-affected herds

Post-weaning Multisystemic Wasting Syndrome (PMWS) has been identified in most swine-producing countries worldwide. The disease has resulted in significant health challenges and economic damage to the swine industry. The aim of this study was to determine horizontal transmission of porcine circovirus type 2 (PCV2) and to examine viral dynamics in pigs in a controlled PMWS transmission study. In the study pigs from PMWS-affected herds and non-affected herds were permitted to have close contact (same pen), nose-to-nose contact (to pigs in neighbouring pens) or no physical contact (pen across the aisle and pens in other compartments). By DNA sequence analysis, eight variants of genotype PCV-2b were identified in the research facility. From the spread of these PCV2-variants it was concluded that PCV2 primarily infects through close contact and nose-to-nose contact. PCV2 genome sequences were obtained from selected pigs at arrival to the research facility and again when the same pigs developed PMWS. This analysis showed that pigs from PMWS-affected herds developed PMWS caused by the same variant of PCV2 as they carried when entering the research facility. In contrast, pigs from non-affected herds developed PMWS with PCV2-variants identified in pigs from PMWS-affected herds. This was probably connected to at least 103 higher mean serum titer of PCV2 in pigs from PMWS-affected herds as compared to pigs from non-affected herds at the beginning of the transmission study. The study further showed that pigs able to control the PCV2 infection, as measured by the PCV2-titer in serum, recovered clinically (pigs from PMWS-affected herds) or stayed healthy (pigs from non-affected herds). Likewise, pigs with a PCV2 titer below 5 \times 10^8 copies/ml serum during the study period had a chance of recover from the PCV2 infection whereas pigs with PCV2 titers above 5 \times 10^8 copies/ml serum at any time point generally died from PMWS.

General information
State: Published
Organisations: Microbial Ecology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Virology, Danish Pig Production
Authors: Dupont, K. (Intern), Hjulsager, C. K. (Intern), Kristensen, C. (Ekstern), Baekbo, P. (Ekstern), Larsen, L. E. (Intern)
Pages: 219-226
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: Veterinary Microbiology
Volume: 139
Issue number: 3-4
ISSN (Print): 0378-1135
Ratings:
BFI (2017): BFI-level 2
Vaccination af slagtekalve mod BRSV: Et feltforsøg i 16 danske slagtekalvebesætninger i perioden 2006 - 2008

General information
State: Published
Organisations: National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology, AgroTech
Authors: Graumann, A. M. (Ekstern), Larsen, L. E. (Intern)
Number of pages: 45
Publication date: 2009

Host publication information
Title of host publication: Slagtekalveproduktion - Temanede
Volume: 16
Place of publication: Århus
Publisher: Det Jordbrugsvidenskabelige Fakultet, Århus Universitet
Edition: 16
Main Research Area: Technical/natural sciences
Conference: Slagtekalveproduktion - Temanede, 01/01/2009
Source: orbit
Source-ID: 244550
Publication: Research › Article in proceedings – Annual report year: 2009

Antibody titers against swine influenza subtypes determined by the hemagglutination inhibition test are highly dependent on the strain

In Denmark there are three circulating strains of swine influenza H1N1, H1N2 and H3N2. The H1N2 is different from the H1N2 subtypes circulating in other European countries. The Danish subtype is a reassortment between the two Danish circulating swine influenza subtypes H1N1 and H3N2. From a diagnostic and epidemiological point of view it is crucial to clarify whether the immunological response to one subtype protects against infection with the other subtype. The hemagglutination inhibition test (HI-test) has been used widely to determine the presence of antibodies in serum against influenza viruses. In the present study the HI-test was used to determine antibody response from experimental infected pigs. The aim of the study was to evaluate the antibody response against the new Danish influenza subtype H1N2 (H1N2dk) and to examine the level of crossprotection/reaction between the two influenza subtypes.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section of Swine fever etc., Division of Virology, Section for Veterinary Diagnostics
Authors: Trebbien, R. (Intern), Nielsen, J. (Intern), Bøtner, A. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Publication date: 2008
Event: Abstract from 20th International Pig Veterinary Society Congress, Durban, South Africa.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 224311
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2008

Årsager til luftvejsinfektioner hos kalve

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, AgroTech A/S, Dansk Kvæg
Authors: Sloth, K. H. (Ekstern), Fisker, I. (Ekstern), Larsen, L. E. (Intern)
Pages: 14 - 17
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: Kalveproducenten
Issue number: Maj
ISSN (Print): 0109-3800
Ratings:
ISI indexed (2013): ISI indexed no
ISI indexed (2012): ISI indexed no
Årsager til luftvejsinfektioner hos kalve

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, AgroTech A/S, Dansk Kvæg
Authors: Sloth, K. H. (Ekstern), Fisker, I. (Ekstern), Larsen, L. E. (Intern)
Pages: 1 - 5
Publication date: 2008
Main Research Area: Technical/natural sciences

Comparison of two quantitative PCR techniques for porcine circovirus Type 2 (PCV2) nucleic acid in field samples
Porcine circovirus type 2 (PCV2) is considered the essential infectious agent of postweaning multisystemic wasting syndrome (PMWS), a global swine disease of devastating economic and animal welfare impact. Most pigs become infected with PCV2 during their life, but only a proportion of them develop PMWS (1). PMWS is associated with a high PCV2 load, and a general threshold of 10^7 copies of PCV2 per ml serum has been suggested for PMWS diagnosis (2,3). The objective of this study was to compare the performance of two different real-time quantitative polymerase chain reaction (qPCR) assays for PCV2 used routinely in two laboratoires located in Denmark (lab 1) and Spain (lab 2), respectively.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Epidemiology and public sector consultancy, Virology, Universidad Autonoma de Barcelona
Authors: Hjulsager, C. K. (Intern), Grau-Roma, L. (Ekstern), Sibila, M. (Ekstern), Enøe, C. (Intern), Larsen, L. E. (Intern), Segales, J. (Ekstern)
Publication date: 2008
Event: Abstract from 20th International Pig Veterinary Society Congress, Durban, South Africa.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 224289
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2008

Danske aktiviteter vedr. mitteovervågning og forskning

General information
State: Published
Organisations: National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology, Section for Veterinary Epidemiology and public sector consultancy
Authors: Larsen, L. E. (Intern), Badker, R. (Intern)
Publication date: 2008
Event: Poster session presented at RUFF-møde om klimaændringer, Krogerup Avlsgård, Humlebæk,
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 222701
Publication: Research › Poster – Annual report year: 2008

Dynamics of porcine circovirus type 2 infection and excretion in pigs from postweaning multisystemic wasting syndrome affected farms from Spain and Denmark
Serological and non-quantitative DNA detection techniques (PCR) have been widely used to monitor porcine circovirus type 2 (PCV2) infection dynamics (1,2). In spite of available epidemiological information, very few data on PCV2 load dynamics of Postweaning multisystemic wasting syndrome (PMWS) affected and non-affected pigs in PMWS affected farms are available. The present longitudinal study describes the evolution of PCV2 infection and excretion in pathologically characterized pigs from PMWS affected farms from two different countries, namely Denmark and Spain.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Epidemiology and public sector consultancy, Section of Swine fever etc., Division of Virology, Section for Veterinary Diagnostics, Universidad Autonoma de Barcelona, Danish Meat Association, Institut de Recerca i Tecnologia Agroalimentàries
Authors: Grau-Roma, L. (Ekstern), Hjulsager, C. K. (Intern), Sibila, M. (Ekstern), Kristensen, C. (Ekstern), Lopez-Soria, S. (Ekstern), Enne, C. (Intern), Batner, A. (Intern), Nofrarias, M. (Ekstern), Bille-Hansen, V. (Intern), Fraile, L. (Ekstern), Baekbo, P. (Ekstern), Segales, J. (Ekstern), Larsen, L. E. (Intern)
Publication date: 2008
Event: Abstract from 20th International Pig Veterinary Society Congress, Durban, South Africa.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 224295
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2008

Er der sammenhæng mellem PMWS og salmonella?
General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Dansk Svineproduktion, Centre de Recerca en Sanitat Animal
Authors: Kristensen, C. S. (Ekstern), Roma, L. G. (Ekstern), Larsen, L. E. (Intern)
Pages: 1-4
Publication date: 2008
Main Research Area: Technical/natural sciences
Publication information
Journal: Dansk Svineproduktion
Issue number: Erfaring nr. 0806
Original language: English
Source: orbit
Source-ID: 231892
Publication: Communication › Journal article – Annual report year: 2008

Hepatitis E virus - en ny zoonose?
General information
State: Published
Organisations: National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology, Section for Veterinary Diagnostics
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Publication date: 2008
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 232979
Publication: Research › Conference abstract for conference – Annual report year: 2008

Hepatitis E Virus i danske grise
General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Publication date: 2008
Main Research Area: Technical/natural sciences
Hepatitis E virus is prevalent in the Danish pig population

Hepatitis E virus (HEV) is responsible for major outbreaks of acute hepatitis in humans from developing countries, but evidence increases that also in industrialized countries locally acquired HEV infections occur. The disease usually affects young adults and has a relatively high mortality in infected pregnant women. HEV sequences worldwide can be classified into four major genotypes. Genotypes 1 and 2 are causing the majority of HEV infections in humans in hyper-endemic areas. In contrast, HEV genotypes 3 and 4 identified in cases of human hepatitis with increasing prevalence in countries such as USA, Europe, Japan and China. There is increasing evidence for the zoonotic origin of infections with HEV genotypes 3 and 4. Swine HEV sequences closely related to human HEV sequences have been detected in many countries and in several cases the source of infection has been linked to contact with swine or ingestion of undercooked swine meat. The aim of this study was to clarify if HEV is prevalent in the Danish pig population. Presence of HEV was examined by detection of HEV by real time RT-PCR or serological screening for HEV antibodies.

General information

State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Section for Veterinary Epidemiology and public sector consultancy, Universidad Autonoma de Barcelona
Authors: Breum, S. Ø. (Intern), Hjulsager, C. K. (Intern), De Deus, N. (Ekstern), Segales, J. (Ekstern), Enøe, C. (Intern), Larsen, L. E. (Intern)
Publication date: 2008
Event: Abstract from 20th International Pig Veterinary Society Congress, Durban, South Africa.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 224421
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2008

Hepatitis E virus is prevalent in the Danish pig population

Hepatitis E virus (HEV) is responsible for major outbreaks of acute hepatitis in humans from developing countries, but evidence increases that also in industrialized countries locally acquired HEV infections occur. The disease usually affects young adults and has a relatively high mortality in infected pregnant women. HEV sequences worldwide can be classified into four major genotypes. Genotypes 1 and 2 are causing the majority of HEV infections in humans in hyper-endemic areas. In contrast, HEV genotypes 3 and 4 identified in cases of human hepatitis with increasing prevalence in countries such as USA, Europe, Japan and China. There is increasing evidence for the zoonotic origin of infections with HEV genotypes 3 and 4. Swine HEV sequences closely related to human HEV sequences have been detected in many countries and in several cases the source of infection has been linked to contact with swine or ingestion of undercooked swine meat. The aim of this study was to clarify if HEV is prevalent in the Danish pig population. Presence of HEV was examined by detection of HEV by real time RT-PCR or serological screening for HEV antibodies.

General information
Identification of a new porcine circovirus type 2 (PCV2) genotype in Danish archive pig samples

PCV2 is the major causative agent of postweaning multisystemic wasting syndrome (PMWS) in pigs. Two genotypes of PCV2 have been identified: genotype 1 and 2 (Olvera et al., 2007). PCV2 genotype 2 was involved in the first cases of PMWS in Canada (Hamel et al., 1998). PCV2 genotype 1 may be more pathogenic than PCV2 genotype 2, as a recent study from Grau-Roma et al. (2007) showed that genotype 2 primary was found in non-PMWS affected herds in Spain, while genotype 1 was found in PMWS affected herds.

General information

Longitudinal determination of haptoglobin and pigmap concentrations in PMWS affected and non-affected pigs

PCV-2 genotype definition and nomenclature

General information
Porcine Reproductive and respiratory syndrome virus (PRRSV) is a single-stranded RNA virus and a worldwide cause of significant respiratory disease and reproductive failure in swine. Two different types of PRRSV, the European (EU) and North American (US) type exist. Boar semen can harbor PRRSV (1) and the virus can be transmitted by this route, creating a need for diagnostic tests to ensure a PRRSV-free semen supply. PCR is an obvious method for such testing, and especially nested and TwoStep RT-PCR methods have been extensively used for this purpose. However, OneStep RT-PCR offers a more convenient and safe diagnostic procedure, since cDNA synthesis and PCR is performed sequentially without inbetween opening of the PCR-tubes, thus eliminating a substantial contamination risk. The aim of the present study was to validate a real-time OneStep RT-PCR assay for the simultaneous detection and discrimination of PRRSV EU and US types in semen.
Real-time onestep RT-PCR for the detection and differentiation of European and North American types of PRRSV in boar semen

Porcine Reproductive and respiratory syndrome virus (PRRSV) is a single-stranded RNA virus and a worldwide cause of significant respiratory disease and reproductive failure in swine. Two different types of PRRSV, the European (EU) and North American (US) type exist. Boar semen can harbor PRRSV (1) and the virus can be transmitted by this route, creating a need for diagnostic tests to ensure a PRRSV-free semen supply. PCR is an obvious method for such testing, and especially nested and TwoStep RT-PCR methods have been extensively used for this purpose. However, OneStep RT-PCR offers a more convenient and safe diagnostic procedure, since cDNA synthesis and PCR is performed sequentially without inbetween opening of the PCR-tubes, thus eliminating a substantial contamination risk. The aim of the present study was to validate a real-time OneStep RT-PCR assay for the simultaneous detection and discrimination of PRRSV EU and US types in semen.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Authors: Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Publication date: 2008
Event: Abstract from 20th International Pig Veterinary Society Congress, Durban, South Africa.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 224420
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2008

Sapovirus fundet i danske grise

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Authors: Hjulsager, C. K. (Intern), Breum, S. Ø. (Intern), Larsen, L. E. (Intern)
Pages: 41
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: Dansk Veterinærtidsskrift
Issue number: 18
ISSN (Print): 0106-6854
Ratings:
BFI (2017): BFI-level 1
BFI (2016): BFI-level 1
BFI (2015): BFI-level 1
BFI (2014): BFI-level 1
BFI (2013): BFI-level 1
ISI indexed (2013): ISI indexed no
BFI (2012): BFI-level 1
ISI indexed (2012): ISI indexed no
BFI (2011): BFI-level 1
ISI indexed (2011): ISI indexed no
BFI (2010): BFI-level 1
BFI (2009): BFI-level 1
BFI (2008): BFI-level 1
Original language: Danish
Source: orbit
Source-ID: 232976
Publication: Communication › Journal article – Annual report year: 2008

Vacciner til kvæg - status og perspektiver

General information
State: Published
Validation of real time PCR assays for use in routine diagnostics of pig diarrhoea

At the National Veterinary Institute in Denmark we want to optimize routine diagnostic analyses by screening samples simultaneously for several agents by real time PCR. Here we present the validation of real time PCR assays for E. coli F4, E coli F18 and Lawsonia intracellularis2 in pig feces. The validation is based on feces samples spiked with a serial dilution of the respective bacteria for determination of PCR efficiencies, dynamic ranges and detection limits. In addition, the effect of the PCR assays of different concentrations of feces and pig to pig variation have been evaluated.

Airborne transmission of PMWS between pig units located at close range

Airborn transmission of PMWS between pig units located at close range
Calves health and welfare

General information
State: Published
Organisations: National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology
Authors: Larsen, L. E. (Intern)
Publication date: 2007
Event: Abstract from CCDays, Nyborg, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 242164
Publication: Research › Conference abstract for conference – Annual report year: 2007

Dynamics in PMWS positive herds

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Microbial Ecology, Division of Microbiology and Risk Assessment, National Food Institute, Section for Veterinary Epidemiology and public sector consultancy, Virology
Publication date: 2007
Event: Abstract from 5th International Symposium on Emerging and Re-emerging Pig Diseases, Krakow, Poland.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 241481
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2007

Faktorer af betydning for sundheden hos kalve

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern)
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: KvægInfo
Volume: 1808
Original language: Danish
Source: orbit
Source-ID: 242199
Publication: Research › Journal article – Annual report year: 2007

Mingling of PMWS-affected pigs with non-affected pigs: a PCV2 sequence study

General information
State: Published
Organisations: Microbial Ecology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Virology
Authors: Dupont, K. (Intern), Kristensen, C. S. (Ekstern), Hjulsager, C. K. (Intern), Bækbo, P. (Ekstern), Bille-Hansen, V. (Intern), Larsen, L. E. (Intern)
Publication date: 2007
Event: Poster session presented at 5th International Symposium on Emerging and Re-emerging Pig Diseases, Krakow, Poland.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240808
Publication: Research - peer-review › Poster – Annual report year: 2007
Myxomatose hos kaniner

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern)
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: Dansk Veterinærtidsskrift
Volume: 21
ISSN (Print): 1600-2032
Ratings:
BFI (2008): BFI-level 1
Web of Science (2004): Indexed yes
Original language: Danish
Source: orbit
Source-ID: 242189
Publication: Research › Journal article – Annual report year: 2007

Norovirus hyppig hos kalve

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Authors: Kristensen, S. L. S. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: Norovirus hyppig hos kalve
Volume: 10
ISSN (Print): 0106-6854
Ratings:
BFI (2017): BFI-level 1
BFI (2016): BFI-level 1
BFI (2015): BFI-level 1
BFI (2014): BFI-level 1
BFI (2013): BFI-level 1
ISI indexed (2013): ISI indexed no
BFI (2012): BFI-level 1
ISI indexed (2012): ISI indexed no
BFI (2011): BFI-level 1
ISI indexed (2011): ISI indexed no
BFI (2010): BFI-level 1
BFI (2009): BFI-level 1
BFI (2008): BFI-level 1
Original language: English
Source: orbit
Source-ID: 240505
Publication: Research › Journal article – Annual report year: 2007

Norovirus, Sapovirus, rotavirus and hepeviruses in animal samples. Norovirus surveillance humans. Sapovirus surveillance humans

General information
State: Published
PCV2 dynamics in PMWS positive Herds

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Microbial Ecology, Division of Microbiology and Risk Assessment, National Food Institute, Section for Veterinary Epidemiology and public sector consultancy, Virology
Publication date: 2007
Event: Paper presented at 5th International Symposium on Emerging and Re-emerging Pig Diseases, Krakow, Poland.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240510
Publication: Research › Paper – Annual report year: 2007

Seological testing for Porcine circovirus type 2 in Danish pig herds with and without PMWS

General information
State: Published
Organisations: Section for Veterinary Epidemiology and public sector consultancy, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Section for Veterinary Diagnostics
Authors: Enæe, C. (Intern), Bækbo, P. (Ekstern), Vigre, H. (Intern), Larsen, L. E. (Intern), Jorsal, S. E. L. (Intern), Nielsen, E. (Ekstern)
Publication date: 2007
Event: Abstract from 5th International Symposium on Emerging and Re-emerging Pig Diseases, Krakow, Poland.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240809
Publication: Research › Conference abstract for conference – Annual report year: 2007

Validation of real-time one-step RT-PCR assays for detection of influenza a virus subtypes H5 and H7 in pigs

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Section of Poultry Diseases, Division of Poultry, Fish and Fur Animals
Authors: Trebbien, R. (Intern), Hjulsager, C. K. (Intern), Handberg, K. (Intern), Larsen, L. E. (Intern)
Publication date: 2007
Event: Paper presented at 5th International Symposium on Emerging and Re-emerging Pig Diseases, Krakow, Poland.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240810
Publication: Research › Paper – Annual report year: 2007

What do we know on epidemiology, control and prevention of porcine circovirus diseases

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Segalés, J. (Ekstern), Larsen, L. E. (Intern), Wallgren, P. (Ekstern), Rose, N. (Ekstern), Grau-Roma, L. (Ekstern), Sibila, M. (Ekstern), Fraile, L. (Ekstern), Casal, J. (Ekstern), Bækbo, P. (Ekstern)
Aviær influenza i svin

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics
Authors: Larsen, L. E. (Intern), Hjulsager, C. K. (Intern)
Pages: 2-4
Publication date: 2006
Main Research Area: Technical/natural sciences

Publication information
Journal: Dyrlægemagasinet for Praktiserende Dyrlæger
Volume: 1/6 2006
ISSN (Print): 1603-8002
Ratings:
- ISI indexed (2013): ISI indexed no
- ISI indexed (2012): ISI indexed no
- ISI indexed (2011): ISI indexed no
Original language: English
Source: orbit
Source-ID: 240506
Publication: Research › Journal article – Annual report year: 2006

Circulation of bovine respiratory syncytial virus in Brazil

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Almeida, R. (Ekstern), Domingues, H. (Ekstern), Spilki, F. (Ekstern), Larsen, L. E. (Intern), Hagglund, S. (Ekstern), Belak, S. (Ekstern), Arns, C. (Ekstern)
Pages: 632-634
Publication date: 2006
Main Research Area: Technical/natural sciences

Publication information
Journal: Veterinary Record
Volume: 158
Issue number: 18
ISSN (Print): 0042-4900
Ratings:
- BFI (2017): BFI-level 1
- Web of Science (2017): Indexed Yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): SJR 0.442 SNIP 0.692 CiteScore 0.3
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 0.509 SNIP 0.794 CiteScore 0.39
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 0.469 SNIP 0.839 CiteScore 0.41
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 0.474 SNIP 0.821 CiteScore 0.5
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
**Diagnosis and epidemiology of bovine coronavirus in Swedish neonatal dairy and beef calves**

**General information**
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Tråvén, M. (Ekstern), Verdier, K. (Ekstern), Larsen, L. E. (Intern), Thorén, P. (Ekstern)
Publication date: 2006
Event: Abstract from 7th International Congress of Veterinary Virology, Lisboa, Portugal, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 230105
Publication: Research - peer-review › Journal article – Annual report year: 2006

**Histopathologic findings in a case control study of PMWS in Danish pig herds**

**General information**
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Authors: Bille-Hansen, V. (Intern), Jorsal, S. E. L. (Intern), Vigre, H. (Intern), Larsen, L. E. (Intern)
Publication date: 2006
Event: Abstract from 19th International Pig Veterinary Society Congress, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240803
Publication: Research › Conference abstract for conference – Annual report year: 2006

Isolation and genetic characterization of new reassortant H1N2 swine influenza a virus from pigs in Denmark

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology, Virology
Authors: Hjulsager, C. K. (Intern), Bragstad, K. (Ekstern), Bøtner, A. (Intern), Larsen, L. E. (Intern)
Publication date: 2006
Event: Poster session presented at 7th International Congress of Veterinary Virology, Lisboa, Portugal.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240806
Publication: Research - peer-review › Poster – Annual report year: 2006

Molecular epidemiology of bovine coronavirus on the basis of comparative analyses of the S gene

Bovine coronavirus (BCoV), a group 2 member of the genus Coronavirus in the family Coronaviridae, is an important pathogen in cattle worldwide. It causes diarrhea in adult animals (winter dysentery), as well as enteric and respiratory diseases in calves. The annual occurrence of BCoV epidemics in Sweden and Denmark led to this investigation, with the aim to deepen the knowledge of BCoV epidemiology at the molecular level. A total of 43 samples from outbreaks in both countries were used for PCR amplification and direct sequencing of a 624-nucleotide fragment of the BCoV S gene. Sequence comparison and phylogenetic studies were performed. The results showed (i) identical sequences from different animals in the same herds and from paired nasal and fecal samples, suggesting a dominant virus circulating in each herd at a given time; (ii) sequence differences among four outbreaks in different years in the same herd, indicating new introduction of virus; (iii) identical sequences in four different Danish herds in samples obtained within 2 months, implying virus transmission between herds; and (iv) that at least two different virus strains were involved in the outbreaks of BCoV in Denmark during the spring of 2003. This study presents molecular data of BCoV infections that will contribute to an increased understanding of BCoV epidemiology in cattle populations.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Liu, L. (Ekstern), Hägglund, S. (Ekstern), Hakhverdyan, M. (Ekstern), Alenius, S. (Ekstern), Larsen, L. E. (Intern), Belak, S. (Ekstern)
Pages: 957-960
Publication date: 2006
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Clinical Microbiology
Volume: 44
Issue number: 3
ISSN (Print): 0095-1137
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.57 SJR 2.14 SNIP 1.417
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.204 SNIP 1.448 CiteScore 3.56
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
New swine influenza A H1N2 re-assortment found in Danish swine

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology, Division of Microbiology and Risk Assessment, National Food Institute, Section for Veterinary Epidemiology and public sector consultancy, Virology
New swine influenza A H1N2 reassortment found in Danish swine

**General information**
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Publication date: 2006
Event: Paper presented at 19th International Pig Veterinary Society Congress, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240512
Publication: Research - peer-review › Paper – Annual report year: 2006

Norovirus i danske køer

**General information**
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Authors: Kristensen, S. S. (Ekstern), Hjulsager, C. K. (Intern), Larsen, L. E. (Intern)
Publication date: 2006
Main Research Area: Technical/natural sciences

**Publication information**
Journal: Dansk Veterinærtidsskrift
Volume: 18
ISSN (Print): 1600-2032
Ratings:
BFI (2008): BFI-level 1
Web of Science (2004): Indexed yes
Original language: English
Source: orbit
Source-ID: 242186
Publication: Research › Journal article – Annual report year: 2006

PMWS in Denmark: Epidemiology, diagnosis and control

**General information**
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Division of Microbiology and Risk Assessment, National Food Institute, Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, Virology, Section for Veterinary Epidemiology and public sector consultancy
Authors: Bøtner, A. (Intern), Vigre, H. (Intern), Jorsal, S. E. L. (Intern), Nielsen, J. (Intern), Lohse, L. (Intern), Bille-Hansen, V. (Intern), Larsen, L. E. (Intern), Baekbo, P. (Ekstern), Kristensen, C. S. (Ekstern), Nielsen, E. O. (Ekstern), Enøe, C. (Intern)
Publication date: 2006

**Host publication information**
Title of host publication: PCVD…Coming Full Circle
Place of publication: Merial Write Book
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 242195
Publication: Research › Book chapter – Annual report year: 2006
The use of different diagnostic tests in a herd with an unexpected case of a BVD virus positive calf.

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Holm, E. (Intern), Voss, H. (Intern), Jensen, N. (Ekstern), Larsen, L. E. (Intern), Uttenthal, Å. (Intern)
Publication date: 2006
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240805
Publication: Research › Conference abstract for conference – Annual report year: 2006

Transmission of PMWS between pen mates

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology, Section for Veterinary Epidemiology and public sector consultancy, Virology
Authors: Kristensen, C. (Ekstern), Bille-Hansen, V. (Intern), Vigre, H. (Intern), Bøtner, A. (Intern), Bækbo, P. (Ekstern), Enøe, C. (Intern), Larsen, L. E. (Intern)
Publication date: 2006
Event: Abstract from 19th International Pig Veterinary Society Congress, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240802
Publication: Research › Conference abstract for conference – Annual report year: 2006

Vaccination af Kalve mod lungebetændelse

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern)
Publication date: 2006

Vertical transmission of bovine viral diarrhoea virus (BVDV) in mousedeer (Tragulus javanicus) and spread to domestic cattle
This study investigates the transmission of bovine viral diarrhoea virus (BVDV) 1f from a persistently infected (PI) lesser Malayan mousedeer to two bovine calves. Different contact routes to two calves were analysed: 1) aerosol contact between two adjacent pens without physical contact; 2) indirect contact by use of common utensils; 3) direct nose-to-nose contact for 30 seconds. One of the calves was infected either by aerosol or indirect contact. The virus sequence in 247 nucleotides in the 5’-UTR was 100% identical in mousedeer and calf. To elucidate the distribution of BVDV within the affected mousedeer family the captive population in a Zoo was analysed. The maternal line of PI animals was maintained, whereas a PI male was able to reproduce and have a non-PI calf. As a consequence of this, six female PI mousedeer were killed; subsequent autopsies did not reveal any lesions. Sequencing mousedeer BVD virus in the E2 region (420 nucleotides) through 4 generations showed only 7 mutations, which were maintained from mother to offspring.

General information
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research
Authors: Uttenthal, Å. (Intern), Høyer, M. (Ekstern), Grøndahl, C. (Ekstern), Houe, H. (Intern), van Maanen, C. (Ekstern), Rasmussen, T. B. (Intern), Larsen, L. E. (Intern)
Veterinary and medical aspects of abortion in Danish sheep

The Danish sheep population totals around 144,000 animals, but little is known of the causes and prevalence of diseases. This study focuses on the causes of abortion in Danish sheep. During one breeding season, aborted foetuses and stillbirths with signs of intrauterine death or malformation were submitted for laboratory examination from a population of 3,758 breeding ewes. Samples from 24 incidents of abortion and 21 ewes delivering malformed lambs or lambs with ante partum decomposition were submitted. A specific aetiology was established in 66.7% and 14.3% of the cases, respectively. Bacterial pathogens were the most prevalent cause of abortion. Several of the abortifacients were zoonotic microorganisms, for example Listeria monocytogenes, Campylobacter fetus subsp. fetus, Yersinia pseudotuberculosis and Toxoplasma gondii. The identified microorganisms probably represent the most common causes of abortion in Danish sheep but occurrence in Denmark of other pathogens such as Coxiella burnetii and Chlamydia abortus cannot be excluded. Due to the high prevalence of zoonotic microorganisms, precautions must be taken in handling abortions or assisting lambing, especially for pregnant women.

General information
State: Published
Organisations: Microbial Ecology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section for Veterinary Diagnostics, Virology, Royal Veterinary and Agricultural University
Pages: 146-152
Publication date: 2006
Main Research Area: Technical/natural sciences

Publication information
Journal: Acta Pathologica Microbiologica et Immunologica Scandinavica
Volume: 114
Issue number: 2
ISSN (Print): 0903-4641
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.87
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 1.92
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 1.95
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 2.07
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 2.06
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 1.97
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Web of Science (2008): Indexed yes
Age-dependent differences in cytokine and antibody responses after experimental RSV infection in a bovine model

Respiratory syncytial virus (RSV) causes severe respiratory disease in both infants and calves. As in humans, bovine RSV (BRSV) infections are most severe in the first 6 months of life. In this study, experimental infection with BRSV was performed in calves aged 1-5, 9-16 or 32-37 weeks. Compared to younger animals, older calves showed significantly less fever and lower TNFα levels and less virus-specific IFN gamma release. In addition, blood from older animals had more mononuclear cells, more B cells and stronger BRSV-specific IgA and neutralising antibody responses to infection. A strong "inflammatory" but weak humoral antiviral response in very young animals suggests that enhanced inflammation contributes to disease during RSV infection during the early postnatal period.

General information
State: Published
Organisations: Adaptive Immunology & Parasitology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Ekotiske Virussygdomme, Division of Virology, Virology, Innate Immunology, Technical University of Denmark
Authors: Grell, S. (Ekstern), Riber, U. (Intern), Tjørnehøj, K. (Intern), Larsen, L. E. (Intern), Heegaard, P. M. H. (Intern)
Pages: 3412-3423
Publication date: 2005
Main Research Area: Technical/natural sciences

Publications
Journal: Vaccine
Volume: 23
Issue number: 26
ISSN (Print): 0264-410X
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.33 SJR 1.956 SNIP 1.155
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.068 SNIP 1.259 CiteScore 3.45
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.05 SNIP 1.231 CiteScore 3.57
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.73 SNIP 1.126 CiteScore 3.43
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.634 SNIP 1.159 CiteScore 3.56
ISI indexed (2012): ISI indexed yes
Diagnostik af svineinfluenza

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Bøtner, A. (Intern)
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Dansk Veterinaertidsskrift
ISSN (Print): 1600-2032
Ratings:
BFI (2008): BFI-level 1
Web of Science (2004): Indexed yes
Original language: Danish
Source: orbit
Source-ID: 230273
Publication: Research - peer-review › Journal article – Annual report year: 2005
Evaluation of a single-tube fluorogenic RT-PCR assay for detection of bovine respiratory syncytial virus in clinical samples

Bovine respiratory syncytial virus (BRSV) causes severe disease in naive cattle of all ages and is a common pathogen in the respiratory disease complex of calves. Simplified methods for rapid BRSV diagnosis would encourage sampling during outbreaks and would consequently lead to an extended understanding of the virus. In this study, a BRSV fluorogenic reverse transcription PCR (fRT-PCR) assay, based on TaqMan principle, was developed and evaluated on a large number of clinical samples, representing various cases of natural and experimental BRSV infections. By using a single-step closed-tube format, the turn-around time was shortened drastically and results were obtained with minimal risk for cross-contamination. According to comparative analyses, the detection limit of the fRT-PCR was on the same level as that of a nested PCR and the sensitivity relatively higher than that of a conventional PCR, antigen ELISA (Ag-ELISA) and virus isolation (VI). Interspersed negative control samples, samples from healthy animals and eight symptomatically or genetically related viruses were all negative, confirming a high specificity of the assay. Taken together, the data indicated that the fRT-PCR assay can be applied to routine virus detection in clinical specimens and provides a rapid and valuable tool in BRSV research.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Hakhverdyan, M. (Ekstern), Hägglund, S. (Ekstern), Larsen, L. E. (Intern), Belák, S. (Ekstern)
Pages: 195-202
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Virological Methods
Volume: 123
Issue number: 2
ISSN (Print): 0166-0934
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.87 SNIP 0.736 CiteScore 1.78
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.868 SNIP 0.799 CiteScore 1.68
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.893 SNIP 0.952 CiteScore 1.87
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.861 SNIP 0.91 CiteScore 1.99
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.869 SNIP 0.935 CiteScore 2.08
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.907 SNIP 0.994 CiteScore 2.23
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.892 SNIP 0.998
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.964 SNIP 1.061
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Marked induction of IL-6, haptoglobin and IFN gamma following experimental BRSV infection in young calves

Bovine respiratory syncytial virus (BRSV) has been identified worldwide as an important pathogen associated with acute respiratory disease in calves. An infection model has been developed reflecting accurately the clinical course and die, development of pathological signs during a natural BRSV-infection. In the experiments described in the present study, calves were infected at 13-21 weeks of age and reinfectected 14 weeks later. Blood samples from the entire infection period were analysed for acute phase protein (haptoglobin) by ELISA and for expression (mRNA level in peripheral blood mononuclear cells) of the cytokines interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-6 (IL-6) and interferon-gamma (IFNgamma) by quantitative real-time reverse transcribed polymerase chain reaction (RT-PCR). IFNgamma, interleukin-6 and haptoglobin were markedly induced to-ether with development of clinical signs in response to the first infection with BRSV. The IFNgamma response was biphasic, with an early peak at day 1-3 post infection (p.i.) and a later increase between day 5 and 8 p.i. Reinfection also resulted in an induction of IFNgamma, but without induction of clinical signs, IL-6 and haptoglobin. These results indicate that early mediators connected with the innate responses are induced on a first encounter with the pathogen, but not on a second encounter (reinfection) where the adaptive immune system may act as the first line defence.

General information
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research, Innate Immunology
Authors: Grell, S. N. (Ekstern), Tjørnehøj, K. (Intern), Larsen, L. E. (Intern), Heegaard, P. M. H. (Intern)
Pages: 235-245
Publication date: 2005
Main Research Area: Technical/natural sciences

Publication information
Journal: Veterinary Immunology and Immunopathology
Volume: 103
Issue number: 3-4
ISSN (Print): 0165-2427
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.63 SJR 0.73 SNIP 0.704
Web of Science (2016): Indexed yes
Persistent BVDV infection in mousedeer infects calves - Do we know the reservoirs for BVDV?

Bovine virus diarrhoea virus (BVDV)-1f was isolated from a Lesser Malayan Mousedeer in Copenhagen Zoo during a routine screening. Analysis of animals related to the Copenhagen mousedeer revealed that its mother and all siblings were virus positive, a pattern also seen for persistently infected (PI) cattle. BVDV could be transmitted from the PI mousedeer to a calf after indirect contact. The host spectrum for BVDV seems to be even wider than expected; the
implications for BVDV control are discussed. (c) 2005 Elsevier B.V. All rights reserved.

**General information**
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Division of Microbiology and Risk Assessment, National Food Institute, Virology, Division of Veterinary Diagnostics and Research
Authors: Uttenthal, Å. (Intern), Grøndahl, M. (Ekstern), Houe, H. (Intern), Van Maanen, C. (Ekstern), Rasmussen, T. B. (Intern), Larsen, L. E. (Intern)
Pages: 87-91
Publication date: 2005
Main Research Area: Technical/natural sciences

**Publication information**
Journal: Preventive Veterinary Medicine
Volume: 72
Issue number: 1-2
ISSN (Print): 0167-5877
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.2 SJR 1.185 SNIP 1.329
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.26 SNIP 1.23 CiteScore 2.1
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.267 SNIP 1.421 CiteScore 2.37
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.247 SNIP 1.552 CiteScore 2.49
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.274 SNIP 1.452 CiteScore 2.45
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.211 SNIP 1.303 CiteScore 2.24
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.155 SNIP 1.28
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.022 SNIP 1.34
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.066 SNIP 1.273
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.006 SNIP 1.36
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.056 SNIP 1.305
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.926 SNIP 1.438
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.807 SNIP 1.147
Persistent BVDV infection in Mousedeer infects calves. Do we know the reservoirs for BVDV?

**General information**
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research
Authors: Uttenthal, Å. (Intern), Grandahl, C. (Ekstern), Hoyer, M. (Ekstern), Houe, H. (Intern), van Maanen, K. (Ekstern), Rasmussen, T. B. (Intern), Larsen, L. E. (Intern)
Publication date: 2005
Event: Abstract from European symposium on BVDV control, Portugal.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 233574
Publication: Research - peer-review › Journal article – Annual report year: 2005

Porcine Circovirus Type 2 Enteritis is an Important Differential Diagnosis to Porcine Proliferative Enteropathy caused by Lawsonia Intracellularis

**General information**
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Division of Microbiology and Risk Assessment, National Food Institute, Virology
Authors: Jensen, T. K. (Intern), Vigre, H. (Intern), Svensmark, B. (Ekstern), Larsen, L. E. (Intern), Bille-Hansen, V. (Intern)
Publication date: 2005
Event: Abstract from International Conference on "Animal Circoviruses and Associated Diseases", Belfast, UK.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 241475
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2005

Smitterisiko ved separering af gylle

**General information**
State: Published
Organisations: Division of Microbiology and Risk Assessment, National Food Institute, Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Adaptive Immunology & Parasitology, Section for Veterinary Epidemiology and public sector consultancy
Publication date: 2005
Main Research Area: Technical/natural sciences
A real-time RT-PCR SYBR Green-I assay for detection of porcine reproductive and respiratory syndrome virus

General information
State: Published
Organisations: Section for Veterinary Diagnostics, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Section of Poultry Diseases, Division of Poultry, Fish and Fur Animals, Virology, Stald/vægterservice, Division of Virology, Sektion for Eksotiske Virussygdomme
Authors: Hjulsager, C. K. (Intern), Jørgensen, P. H. (Intern), Larsen, L. E. (Intern), Storgaard, T. (Ekstern), Bøtner, A. (Intern)
Publication date: 2004
Event: Poster session presented at International qPCR Symposium & Application Workshop, Freising-Weihenstephan, Germany.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240993
Publication: Research - peer-review › Poster – Annual report year: 2004

Bestemmelse af immunoglobulin (IgG) niveau i kalve med henblik på evaluering af råmælksoptagelse

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Laboratory Service, Division of Virology
Authors: Larsen, L. E. (Intern), Pedersen, R. E. (Ekstern), Lauridsen, B. H. (Ekstern), Steffensen, M. A. (Intern), Trinderup, M. (Ekstern), Jensen, A. M. (Ekstern)
Publication date: 2004
Main Research Area: Technical/natural sciences

Bovine respiratory syncytial virus ISCOMs - protection in the presence of maternal antibodies

The protection induced by immunostimulating complexes (ISCOMs) against bovine respiratory syncytial virus (BRSV) was evaluated and compared to that of a commercial inactivated vaccine (CV) in calves with BRSV-specific maternal antibodies. Following experimental challenge, controls (n = 4) and animals immunized with CV (n = 5) developed moderate to severe respiratory disease, whereas calves immunized with ISCOMs (17 = 5) remained clinically healthy. BRSV was re-isolated from the nasopharynx of all controls and from all calves immunized with CV, but from none of the calves immunized with ISCOMs. BRSV-RNA was detected by real-time PCR from a single animal in this group. Significantly higher BRSV-specific nasal IgG, serum IgG(1) and IgG(2) titers were detected before and after challenge in animals immunized with ISCOMs versus CV. In conclusion, the ISCOMs overcame the suppressive effect of maternal
antibodies in calves and induced strong clinical and virological protection against a BRSV challenge.
Microbiological investigations on trans-tracheal aspirated bronchoalveolar fluid from clinically normal calves and calves with pneumonia

An experimental infection model for reproduction of calf pneumonia with bovine respiratory syncytial virus (BRSV) based on one combined exposure of calves

Microbiological investigations on trans-tracheal aspirated bronchoalveolar fluid from clinically normal calves and calves with pneumonia

General information
State: Published
Organisations: Bacteriology & Pathology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Virology
Authors: Angen, Ø. (Intern), Enemark, J. M. (Ekstern), Larsen, L. E. (Intern), Thomsen, J. (Ekstern)
Publication date: 2004
Event: Abstract from ASM General Meeting,
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 229506
Publication: Research - peer-review › Journal article – Annual report year: 2004

An experimental infection model for reproduction of calf pneumonia with bovine respiratory syncytial virus (BRSV) based on one combined exposure of calves

Bovine respiratory syncytial virus (BRSV) has been recognised as an important pathogen in calf pneumonia for 30 years, but surprisingly few effective infection models for studies of the immune response and the pathogenesis in the natural host have been established. We present a reproducible experimental infection model for BRSV in 2-5-month-old, conventionally reared Jersey calves. Thirty-four colostrum-fed calves were inoculated once by aerosol and intratracheal injection with BRSV. Respiratory disease was recorded in 91% of the BRSV-inoculated calves, 72% had an accompanying rise in rectal temperature and 83% exhibited >5%, consolidation of the lung tissue. The disease closely resembled natural outbreaks of BRSV-related pneumonia, and detection of BRSV in nasal secretions and lung tissues confirmed the primary role of BRSV. Nine mock-inoculated control calves failed to develop respiratory disease. This model is a valuable tool for the study of the pathogenesis of BRSV and for vaccine efficacy studies.

General information
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research
Authors: Tjørnehøj, K. (Intern), Uttenthal, Å. (Intern), Viuff, B. (Ekstern), Larsen, L. E. (Intern), Rontved, C. (Ekstern), Ronsholt, L. (Ekstern)
Pages: 55-65
Publication date: 2003
Main Research Area: Technical/natural sciences

Publication information
Journal: Research in Veterinary Science
Volume: 74
Issue number: 1
ISSN (Print): 0034-5288
Ratings:
BFI (2017); BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016); BFI-level 2
Bovine respiratory syncytial virus immunostimulating complexes (BRSV-ISCOMS) provided protection against a virulent challenge

**General information**

State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Willman, S. (Ekstern), Hu, K. (Ekstern), Hakhverdyan, M. (Ekstern), Larsen, L. E. (Intern), Morein, B. (Ekstern), Belák, S. (Ekstern), Alenius, S. (Ekstern)
Publication date: 2003
Event: Abstract from 6th International Congress of Veterinary Virology, St.Malo, France,
Characterisation of a pestivirus isolated from persistently infected mousedeer (Tragulus javanicus)

Serum samples from the male Mousedeer A and the mother, father and sister of A were tested for bovine virus diarrhoea viruses (BVDV) by isolation, and for BVDV antibodies by blocking ELISA and homologous neutralisation test. Further, RNA was extracted and tested by RT-PCR protocol analysing the 5'-untranslated region and the E2 gene of pestivirus. The RT-PCR products were subsequently sequenced. Mousedeer A was positive in virus isolation on three occasions (days 1, 19 and 40) and by RT-PCR. The sister and mother of Mousedeer A were also found virus positive by isolation and RT-PCR. Mousedeer A, its sister and its mother, all had an antibody neutralisation titer below 10. The father of A was virus negative but was positive in the blocking antibody ELISA and had a high neutralisation antibody titer. The repeated detection of BVDV in Mousedeer A, the high amount of virus in serum, the lack of antibodies and the virus positive family members documented that the mousedeer were persistently infected with a pestivirus. The father of A probably had an acute infection resulting in antibodies to pestivirus and viral clearance. Sequence analysis and phylogenetic analysis revealed that the mousedeer pestivirus was closely related to BVDV Type 1f. The existences of persistently infected animals in non-domestic species have great implications for BVDV eradication campaigns in cattle.

General information
State: Published
Organisations: Sektion for Eksotiske Vrussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research
Authors: Grøndahl, C. (Ekstern), Uttenthal, Å. (Intern), Houe, H. (Intern), Rasmussen, T. B. (Intern), Hoyer, M. (Ekstern), Larsen, L. E. (Intern)
Pages: 1455-1463
Publication date: 2003
Main Research Area: Technical/natural sciences

Publication information
Journal: Archives of Virology
Volume: 148
Issue number: 8
ISSN (Print): 0304-8608
Ratings: 
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.948 SNIP 0.879 CiteScore 2.16
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.083 SNIP 0.89 CiteScore 2.16
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.096 SNIP 1.041 CiteScore 2.37
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.002 SNIP 0.961 CiteScore 2.26
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.888 SNIP 0.943 CiteScore 2.12
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.902 SNIP 1.045 CiteScore 2.17
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.001 SNIP 0.98
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.904 SNIP 0.926
Web of Science (2009): Indexed yes
Detection of persistent infection with pestivirus (BVDV) in a mousedeer (Tragulus Javanicus) and experimental transmission to cattle

General information
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research
Authors: Grøndahl, C. (Ekstern), Uttenthal, Å. (Intern), Houec, H. (Ekstern), Rasmussen, T. B. (Intern), Høyer, M. J. (Ekstern), Larsen, L. E. (Intern)
Publication date: 2003
Event: Abstract from International Congress for Zoo Animals, Rom, Italy, 
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 229768
Publication: Research - peer-review › Journal article – Annual report year: 2003

BRSV - Danske erfaringer

General information
State: Published
Organisations: National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology
Authors: Larsen, L. E. (Intern)
Publication date: 2002
Event: Abstract from Svenska Djurhälsovårdens Fortbindingskonferens, Stockholm, Sverige, 
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 242162
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2002

Immune response to bovine respiratory syncytial virus (BRSV) following immunisation with a commercial inactivated BRSV vaccine

General information
State: Published
Replication and clearance of respiratory syncytial virus - Apoptosis is an important pathway of virus clearance after experimental infection with bovine respiratory syncytial virus

Human respiratory syncytial virus is an important cause of severe respiratory disease in young children, the elderly, and in immunocompromised adults. Similarly, bovine respiratory syncytial virus (BRSV) is causing severe, sometimes fatal, respiratory disease in calves. Both viruses are pneumovirus and the infections with human respiratory syncytial virus and BRSV have similar clinical, pathological, and epidemiological characteristics. In this study we used experimental BRSV infection in calves as a model of respiratory syncytial virus infection to demonstrate important aspects of viral replication and clearance in a natural target animal. Replication of BRSV was demonstrated in the luminal part of the respiratory epithelial cells and replication in the upper respiratory tract preceded the replication in the lower respiratory tract. Virus excreted to the lumen of the respiratory tract was cleared by neutrophils whereas apoptosis was an important way of clearance of BRSV-infected epithelial cells. Neighboring cells, which probably were epithelial cells, phagocytized the BRSV-infected apoptotic cells. The number of both CD4+ and CD8+ T cells increased during the course of infection, but the T cells were not found between the epithelial cells of the bronchi up until apoptosis was no longer detected, thus in the bronchi there was no indication of direct contact-dependent T-cell-mediated cytotoxicity in the primary infection.
Bovine respiratory syncytial virus (BRSV) pneumonia in beef calf herds despite vaccination
The present report describes the clinical, pathological, serological and virological findings in calves from 2 larger Danish beef herds experiencing outbreaks of pneumonia. The calves had been vaccinated with an inactivated bovine respiratory syncytial virus (BRSV) vaccine 2 months prior to the outbreak. The clinical signs comprised nasal discharge, pyrexia, cough and increased respiratory rates. A total of 28 calves died in the 2 herds. The laboratory investigations revealed that BRSV was involved and probably initiated both outbreaks. Furthermore, the serological results suggested that the vaccine induced only sparse levels of antibodies probably due to the presence of maternally derived antibodies at the time of vaccination. Necropsy findings in 5 calves revealed changes typical for infectious pneumonia with involvement of BRSV. In conclusion, vaccination of calves against BRSV in 2 Danish beef herds failed to protect the calves against severe or even fatal BRSV mediated respiratory disease 2 months later.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Technical University of Denmark
Authors: Larsen, L. E. (Intern), Tegtmeier, C. (Ekstern), Pedersen, E. (Ekstern)
Pages: 113-121
Publication date: 2001
Main Research Area: Technical/natural sciences

Publication information
Journal: Acta Veterinaria Scandinavica (Print Edition)
Volume: 42
Issue number: 1
ISSN (Print): 0044-605X
Ratings:
Web of Science (2017): Indexed Yes
Scopus rating (2016): CiteScore 1.01
Scopus rating (2015): CiteScore 0.98
Scopus rating (2014): CiteScore 1.54
Scopus rating (2013): CiteScore 1.41
Scopus rating (2012): CiteScore 1.26
Web of Science (2012): Indexed yes
Scopus rating (2011): CiteScore 1.42
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
BFI (2008): BFI-level 1
BRSV Infektionsdynamik - perspektiver for sundhedsstyringen

General information
State: Published
Organisations: National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology
Authors: Larsen, L. E. (Intern)
Publication date: 2001
Event: Abstract from Boologisk Selskab : Efterårsseminar, Brædstrup, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 242158
Publication: Research › Conference abstract for conference – Annual report year: 2001

Does BRSV persist in calves

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Tjørnehøj, K. (Intern), Viuff, B. (Ekstern), Røntved, C. (Ekstern)
Publication date: 2001
Event: Abstract from RSV after 45 Years Symposium, Sergovia, Spanien, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240797
Publication: Research › Conference abstract for conference – Annual report year: 2001

Forekomst og betydning af bovin coronavirus

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern)
Pages: 6-7
Publication date: 2001
Main Research Area: Technical/natural sciences

Publication information
Journal: SVS/SVIV Information
Volume: 21
Issue number: 72
Original language: Danish
Source: orbit
Source-ID: 242168
Publication: Research › Journal article – Annual report year: 2001
**Herpeslammelse og vaccination**

**General information**
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern), Hoff-Jørgensen, R. (Intern)
Publication date: 2001
Main Research Area: Technical/natural sciences

**Publication information**
Journal: DANSK VETERINÆRTIDSSKRIFT
Volume: 84
Issue number: 16
ISSN (Print): 0106-6854
Ratings:
- BFI (2017): BFI-level 1
- BFI (2016): BFI-level 1
- BFI (2015): BFI-level 1
- BFI (2014): BFI-level 1
- BFI (2013): BFI-level 1
- ISI indexed (2013): ISI indexed no
- BFI (2012): BFI-level 1
- ISI indexed (2012): ISI indexed no
- BFI (2011): BFI-level 1
- ISI indexed (2011): ISI indexed no
- BFI (2010): BFI-level 1
- BFI (2009): BFI-level 1
- BFI (2008): BFI-level 1
Original language: Danish
Source: orbit
Source-ID: 242175
Publication: Research › Journal article – Annual report year: 2001

**Imunitetsstyring i slægtekalvebesætninger**

**General information**
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Viuff, B. (Ekstern), Tjørnehøj, K. (Intern), Røntved, C. (Ekstern)
Pages: 1-6
Publication date: 2001
Main Research Area: Technical/natural sciences

**Publication information**
Journal: Kalveproducenten
Volume: 19
ISSN (Print): 0109-3800
Ratings:
- ISI indexed (2013): ISI indexed no
- ISI indexed (2012): ISI indexed no
- ISI indexed (2011): ISI indexed no
Original language: Danish
Source: orbit
Source-ID: 242173
Publication: Research › Journal article – Annual report year: 2001

**Nye ELISA-tests for antistoffer mod bovint PI-3, BRS -og coronavirus**

**General information**
State: Published
Phylogenetic characterisation of the G(L) sequences of equine arteritis virus isolated from semen of asymptomatic stallions and fatal cases of equine viral arteritis in Denmark

The study describes for the first time the phylogenetic relationship between equine arteritis virus (EAV) isolated from asymptomatic virus-shedding stallions and fatal cases of equine viral arteritis (EVA) in an European country. EAV was isolated from three dead foals and an aborted foetus during three different outbreaks of EVA. From these fatalities, the complete open reading frame 5, encoding the EAV GL protein, was amplified by reverse transcription-polymerase chain reaction and subjected to nucleotide sequence analysis. Furthermore, DNA sequences were obtained from virus isolated from semen samples of seven virus-shedding, but clinically healthy, Danish stallions. DNA sequence alignment revealed an overall divergence of 0-14 and 0-10% at the nucleotide and amino acid levels, respectively. Phylogenetic analysis including 24 previously published sequences revealed that European as well as North American "types" of EAV were present in the semen of asymptomatic carrier stallions and in fatal cases of EVA. Our results reveal that the presence of EAV-shedding stallions in Denmark represents a potential source of severe EVA.
Antibody dynamics in BRSV-infected Danish dairy herds as determined by isotype-specific immunoglobulins

Using specific ELISAs, antibody levels of four different isotypes to bovine respiratory syncytial virus (BRSV) were determined in calves, following experimental BRSV infection. Most calves experienced an increase in the specific IgM and IgG1 titres about 6-10 days after infection with BRSV. The IgM titre was transient showing positive titres for only 5-10 days, while specific IgG1 was present for a longer time. IgA was detected concomitantly with IgM but at a lower level. Production of IgG2 anti-BRSV antibodies was detected from 3 weeks after infection. In two closed herds, repeated blood samplings were performed on young stock to analyse maternal immunity. The passively transferred antibodies were mainly of the IgG1 isotype and the half-life of IgG1 to BRSV was estimated to be 26.6 days. One of the herds had an outbreak of enzootic pneumonia, diagnosed to be caused by BRSV. Furthermore, another herd with acute BRSV was followed by weekly blood samples in six calves; in both herds IgM and IgG1 was detected shortly after the appearance of clinical signs. Serum samples from 50 Danish dairy herds (453 samples) were tested for immunoglobulins of the isotypes IgG1, IgG2 and IgM. The presence of antibodies to BRSV was widespread and more than 54% of the samples had BRSV antibodies of both the IgG1 and IgG2 isotypes indicating a high herd prevalence to BRSV. Test samples from two herds out of 50 were free from all isotypes to BRSV.

General information

State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research, Secretariat
Authors: Uttenthal, Å. (Intern), Larsen, L. E. (Intern), Philipsen, J. (Ekstern), Tjørnehøj, K. (Intern), Viuff, B. (Ekstern), Nielsen, K. (Ekstern), Nielsen, T. K. (Intern)
Bovine respiratory syncytial virus (BRSV): A review

Bovine respiratory syncytial virus (BRSV) infection is the major cause of respiratory disease in calves during the first year of life. The study of the virus has been difficult because of its lability and very poor growth in cell culture. However, during the last decade, the introduction of new immunological and biotechnological techniques has facilitated a more extensive study of BRSV as illustrated by the increasing number of papers published. Despite this growing focus, many aspects of the pathogenesis, epidemiology, immunology etc., remain obscure. The course and outcome of the infection is very complex and unpredictable which makes the diagnosis and subsequent therapy very difficult. BRSV is closely related to human respiratory syncytial virus (HRSV) which is an important cause of respiratory disease in young children. In contrast to BRSV, the recent knowledge of HRSV is regularly extensively reviewed in several books and journals. The present paper contains an updated review on BRSV covering most aspects of the structure, molecular biology, pathogenesis, pathology, clinical features, epidemiology, diagnosis and immunology based on approximately 140 references from international research journals.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern)
Pages: 1–+
Publication date: 2000
Main Research Area: Technical/natural sciences

Publication information
Journal: Acta Veterinaria Scandinavica
Volume: 41
Issue number: 1
ISSN (Print): 0044-605X
Ratings:
Web of Science (2017): Indexed Yes
Scopus rating (2016): CiteScore 1.01
Scopus rating (2015): CiteScore 0.98
Scopus rating (2014): CiteScore 1.54
Scopus rating (2013): CiteScore 1.41
Scopus rating (2012): CiteScore 1.26
Web of Science (2012): Indexed yes
Scopus rating (2011): CiteScore 1.42
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
BFI (2008): BFI-level 1
Web of Science (2006): Indexed yes
Web of Science (2005): Indexed yes
Web of Science (2004): Indexed yes
Web of Science (2003): Indexed yes
Web of Science (2002): Indexed yes
Web of Science (2001): Indexed yes
Web of Science (2000): Indexed yes
Extensive sequence divergence among bovine respiratory syncytial viruses isolated during recurrent outbreaks in closed herds

The nucleotides coding for the extracellular part of the G glycoprotein and the full SH protein of bovine respiratory syncytial virus (BRSV) were sequenced from viruses isolated from numerous outbreaks of BRSV infection. The isolates included viruses isolated from the same herd (closed dairy farms and veal calf production units) in different years and from all confirmed outbreaks in Denmark within a short period. The results showed that identical viruses were isolated within a herd during outbreaks and that viruses from recurrent infections varied by up to 11% in sequence even in closed herds. It is possible that a quasispecies variant swarm of BRSV persisted in some of the calves in each herd and that a new and different highly fit virus type (master and consensus sequence) became dominant and spread from a single animal in connection with each new outbreak. Based on the high level of diversity, however, the most likely explanation was that BRSV was (re)introduced into the herd prior to each new outbreak. These findings are highly relevant for the understanding of the transmission patterns of BRSV among calves and human respiratory syncytial virus among humans.
Increased pulmonary secretion of tumor necrosis factor-alpha in calves experimentally infected with bovine respiratory syncytial virus

Bovine respiratory syncytial virus (BRSV) is an important cause of respiratory disease among calves in the Danish cattle industry. An experimental BRSV infection model was used to study the pathogenesis of the disease in calves. Bronchoalveolar lung lavage (BAL) was performed on 28 Jersey calves, of which 23 were experimentally infected with BRSV and five were given a mock inoculum. The presence of the cytokine tumor necrosis factor alpha (TNF-alpha) in the BAL fluids was detected and quantified by a capture ELISA. TNF-alpha was detected in 21 of the infected animals. The amount of TNF-alpha in the BAL fluid of calves killed post inoculation day (PID) 2 and 4 was at the same very low level as in the uninfected control animals. Large amounts of TNF-alpha were detected on PID 6, maximum levels of TNF-alpha were reached on PID 7, and smaller amounts of TNF-alpha were seen on PID 8. The high levels of TNF-alpha appeared on the days where severe lung lesions and clinical signs were obvious and the amounts of BRSV-antigen were at their greatest. Although Pasteurellaceae were isolated from some of the BRSV-infected calves, calves treated with antibiotics before and through the whole period of the infection, as well as BRSV-infected calves free of bacteria reached the same level of TNF-alpha as animals from which bacteria were isolated from the lungs. It is concluded that significant quantities of TNF-alpha are produced in the lungs of the calves on PID 6–7 of BRSV infection. The involvement of TNF-alpha in the pathogenesis of, as well as the anti-viral immune response against, BRSV infection is discussed.
Infection with bovine respiratory syncytial virus in calves is accompanied by a significant pulmonary secretion of tumor necrosis factor-alpha

General information
State: Published
Organisations: Sektion for Eksotiske Virussygdomme, Division of Virology, National Veterinary Institute, Virology, Division of Veterinary Diagnostics and Research
Authors: Rontved, C. (Ekstern), Tjørnehøj, K. (Intern), Viuff, B. (Ekstern), Larsen, L. E. (Intern), Godson, D. (Ekstern), Ronsholt, L. (Ekstern), Alexandersen, S. (Intern)
Pages: A1039-A1039
Publication date: 2000
Main Research Area: Technical/natural sciences

Publication information
Journal: Faseb Journal
Volume: 14
Issue number: 6
ISSN (Print): 0892-6638
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.68 SJR 2.57 SNIP 1.22
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.788 SNIP 1.249 CiteScore 4.68
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.993 SNIP 1.342 CiteScore 4.92
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 3.116 SNIP 1.4 CiteScore 5.5
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 3.071 SNIP 1.441 CiteScore 5.6
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.042 SNIP 1.525 CiteScore 5.4
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Serological responses of calves to experimental infection and reinfection with bovine respiratory syncytial virus (BRSV)

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Tjørnehøj, K. (Intern), Viuff, B. (Ekstern), Røntved, C. (Ekstern), Blixenkrone-Møller, M. (Ekstern), Rønsholt, L. (Ekstern)
Publication date: 2000
Event: Abstract from international Congress of Veterinary Virology, Bresia, Italien, .
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 230824
Publication: Research › Conference abstract in journal – Annual report year: 2000

The acute phase response of haptoglobin and serum amyloid A (SAA) in cattle undergoing experimental infection with bovine respiratory syncytial virus

The ability of a pure virus infection to induce an acute phase protein response is of interest as viral infections are normally considered to be less efficient in inducing an acute phase protein response than bacterial infections. This was studied in a bovine model for infection with bovine respiratory syncytial virus (BRSV), analysing the induction of the two most dominant bovine acute phase proteins haptoglobin and serum amyloid A (SAA). Strong and reproducible acute phase responses were detected for both proteins, peaking at around 7-8 days after inoculation of BRSV, while no response was seen in mock-inoculated control animals. The serum concentrations reached for SAA and haptoglobin during the BRSV-induced acute phase response were generally the same or higher than previously reported for bacterial infections in calves. The magnitude and the duration of the haptoglobin response was found to correlate well with the severity of clinical signs (fever) and with the extent of lung consolidation while SAA responded most rapidly to infection.

General information
State: Published
Organisations: Innate Immunology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Heegaard, P. M. H. (Intern), Godson, D. (Ekstern), Toussaint, M. (Ekstern), Tjørnehøj, K. (Intern), Larsen, L. E. (Intern), Viuff, B. (Ekstern), Rønsholt, L. (Ekstern)
Pages: 151-159
Publication date: 2000
Main Research Area: Technical/natural sciences

Publication information
Journal: Veterinary Immunology and Immunopathology
Volume: 77
Issue number: 1-2
ISSN (Print): 0165-2427
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.63 SJR 0.73 SNIP 0.704
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.856 SNIP 0.752 CiteScore 1.67
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.768 SNIP 0.719 CiteScore 1.6
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.808 SNIP 0.805 CiteScore 1.89
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.837 SNIP 0.922 CiteScore 2.15
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.849 SNIP 0.996 CiteScore 2.16
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.77 SNIP 0.945
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 0.768 SNIP 0.852
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 0.69 SNIP 0.866
Scopus rating (2007): SJR 0.77 SNIP 0.925
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.784 SNIP 0.993
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.676 SNIP 0.937
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.742 SNIP 0.984
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.659 SNIP 0.757
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.64 SNIP 0.915
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.63 SNIP 0.84
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.569 SNIP 0.807
Web of Science (2000): Indexed yes
Diagnosis of enzootic pneumonia in Danish cattle: reverse transcription-polymerase chain reaction assay for detection of bovine respiratory syncytial virus in naturally and experimentally infected cattle

A reverse transcription-polymerase chain reaction (RT-PCR) assay was developed for detection of bovine respiratory syncytial virus (BRSV) in lung tissue of naturally and experimentally infected cattle. Primers were selected from the gene coding the F fusion protein, which is relatively conserved among BRSV isolates. The RT-PCR assay was highly specific, it yielded positive reactions only when performed on BRSV-infected cell cultures or tissues. The detection limit of the RT-PCR assay was assessed as 5 TCID50. BRSV was detected in tissues of the respiratory tract and in the tracheobronchial lymph node of calves euthanized 2-8 days after experimental infection with BRSV, whereas samples of other tissues and samples from mock-infected animals were negative at all time points. Examination of lung samples from 8 different regions of the lungs revealed that although the virus was most often found in the cranioventral lobules, it was frequently present in all lung lobules. Microbiologic examinations of all acute fatal cases of pneumonia (135 animals) in cattle submitted for diagnostic purposes during 1 year revealed that Actinomycetes pyogenes (11%), Haemophilus somnus (10%), Pasteurella sp. (7%), and Pasteurella haemolytica (7%) were the most common bacterial agents found in the lungs. BRSV was identified using a conventional antigen enzyme-linked immunosorbent assay (ELISA) in 23 (17%) animals. The established BRSV-specific RT-PCR assay yielded positive results for the same 23 animals, in addition, 10 animals that were negative with the ELISA were positive with the RT-PCR assay. These results indicates that the RT-PCR assay can be a sensitive, reliable alternative to conventional diagnostic procedures.
Eksperimentel afprøvning af Triangle RSV vaccine mod bovint respiratorisk syncytial virus (BRSV) i konventionelt opdrættede kalve: Foreløbige resultater

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Tjørnehøj, K. (Intern), Rønsholt, L. (Ekstern), Viuff, B. (Ekstern)
Pages: 13-15
Publication date: 1999
Main Research Area: Technical/natural sciences
Geno-epidemiological investigations of bovine respiratory syncytial virus (brsv) strain differences and quasispecies during recurrent outbreaks: no evidence of herd persistence, but high level of identity between virus strains isolated in the same geographic region at a given time.

Lungebetændelse hos kalve og BRS-virus: Fup eller fakta?

Møglicheder for at vaccination af danske kalve mod respirationsvejs virus

Påvisning af equin arteritis virus i et aborteret hestefoster
Afprøvning af vacciner mod bovint respiratorisk syncytial virus (BRSV) hos kalve

Isotype specifikke ELISAs for BRSV antistoffer

Luftvejslidelser hos kalve, ætiologi og diagnostik
Molecular biological studies on Bovine Respiratory Syncytial Virus Infections in Calves

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Larsen, L. E. (Intern)
Publication date: 1998

Publication information
Original language: English
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 241771
Publication: Research › Journal article – Annual report year: 1998

Serological and genetic characterisation of bovine respiratory syncytial virus (BRSV) indicates that Danish isolates belong to the intermediate subgroup: no evidence of a selective effect on the variability of G protein nucleotide sequence by prior cell culture adaption and passages in cell culture or calves

Danish isolates of bovine respiratory syncytial virus (BRSV) were characterised by nucleotide sequencing of the G glycoprotein and by their reactivity with a panel of monoclonal antibodies (MAbs). Among the six Danish isolates, the overall sequence divergence ranged between 0 and 3% at the nucleotide level and between 0 and 5% at the amino acid level. Sequence divergences of 7-8%, 8-9% and 2-3% (nucleotide) and 9-11%, 12-16% and 4-6% (amino acid) were obtained in the comparison made between the group of Danish isolates and the previously sequenced 391-2USA, 127UK and 220-69Bel isolates, respectively. Phylogenetic analysis showed that the Danish isolates formed three lineages within a separate branch of the phylogenetic tree. Nevertheless, the Danish isolates were closely related to the 220-69Bel isolate, the prototype of the intermediate antigenic subgroup. The sequencing of the extracellular part of the G gene of additional 11 field BRSV viruses, processed directly from lung samples without prior adaption to cell culture growth, revealed sequence variabilities in the range obtained with the propagated virus. In addition, several passages in cell culture and in calves had no major impact on the nucleotide sequence of the G protein. These findings indicated that the previously established variabilities of the G protein of RS virus isolates were not attributable to mutations induced during the propagation of the virus. The reactivity of the Danish isolates with G protein-specific MAbs were similar to that of the 220-69Bel isolate. Furthermore, the sequence of the immunodominant region was completely conserved among the Danish isolates on one side and the 220-69Bel isolate on the other. When combined, these data strongly suggested that the Danish isolates belong to the intermediate subgroup.

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virusygdormme, Division of Virology
Authors: Larsen, L. E. (Intern), Uttenthal, Å. (Intern), Arctander, P. (Ekstern), Tjærnehoj, K. (Intern), Viuff, B. (Ekstern), Rantzved, G. (Ekstern), Ransholt, L. (Ekstern), Alexandersen, S. (Intern), Blixenkrone-Moller, M. (Ekstern)
Vaccination af staekekalve mod bovin respiratorisk syncytial virus (BRSV)

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Tjørnehøj, K. (Intern)
Pages: 4-6
Publication date: 1998
Main Research Area: Technical/natural sciences

Publication information
Journal: SVS/SVIV Information
Volume: 63
Original language: Danish
Source: orbit
Source-ID: 241779
Publication: Research › Journal article – Annual report year: 1998

Variability of the G-protein of Bovine respiratory syncytial virus

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Jensen, N. E. (Ekstern), Tjørnehøj, K. (Intern), Viuff, B. (Ekstern), Nielsen, T. (Ekstern), Uttenthal, Å. (Intern)
Publication date: 1997
Event: Abstract from 4th International Congress of Veterinary Virology, Edinburgh, United Kingdom.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240791
Publication: Research › Conference abstract for conference – Annual report year: 1997

Variability of the G-protein of Bovine respiratory syncytial virus

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Uttenthal, Å. (Intern), Archtander, P. (Ekstern), Tjørnehøj, K. (Intern), Viuff, B. (Ekstern), Røntved, C. (Ekstern), Rensholt, L. (Ekstern), Axandersen, S. (Intern), Blixenkrone-Møller, M. (Ekstern)
Publication date: 1997
Event: Abstract from International Congress on Negative Strand Viruses, Dublin, Ireland.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 240793
Publication: Research › Conference abstract for conference – Annual report year: 1997
Diagnosis of BRSV infections in calves

General information
State: Published
Organisations: Virology, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Sektion for Eksotiske Virussygdomme, Division of Virology
Authors: Larsen, L. E. (Intern), Utenthal, Å. (Intern), Viuff, B. (Ekstern), Røntved, C. (Ekstern), Rønsholt, L. (Ekstern), Tjørnehøj, K. (Intern), Alexandersen, S. (Intern)
Publication date: 1996
Event: Abstract from First Nordic Veterinary Immunology Meeting, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 241770
Publication: Research › Conference abstract for conference – Annual report year: 1996

Projects:

Impact of low-grade inflammation on influenza
National Veterinary Institute
Period: 01/12/2016 → 30/11/2019
Number of participants: 5
Phd Student:
Starbæk, Sofie Maiken Riisgård (Intern)
Supervisor:
Heegaard, Peter Mikael Helweg (Intern)
Jungersen, Gregers (Intern)
Larsen, Lars Erik (Intern)
Main Supervisor:
Skovgaard, Kerstin (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Animal Influenza Viruses - Impacts of influenza virus in Danish swine herds
National Veterinary Institute
Period: 01/10/2016 → 30/09/2019
Number of participants: 5
Phd Student:
Ryt-Hansen, Pia (Intern)
Supervisor:
Plósz, Benedek G. (Intern)
Krog, Jesper Schak (Intern)
Larsen, Inge (Ekstern)
Main Supervisor:
Larsen, Lars Erik (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Samfinansierede - Virksomhed
Project: PhD

Host range selection, virulence determinants and pathogenesis of influenza A viruses: Towards the identification of new antiviral drugs and vaccines
National Veterinary Institute
Period: 01/08/2015 → 31/07/2018
Number of participants: 3
Phd Student:
Andersen, Malene Rask (Intern)
Supervisor:
Kvisgaard, Lise Kirstine (Intern)
Main Supervisor:
Larsen, Lars Erik (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Optimeret sygdomsforebyggelse i slagtesvinebesætninger
National Veterinary Institute
Diagnostic & Development
Virology
Innate Immunology
SEGES Pig Research Center
Period: 01/01/2015 → 31/12/2017
Number of participants: 5
Number of related Ph.D. students: 1
Project participant:
Larsen, Lars Erik (Intern)
Hjulsager, Charlotte Kristiane (Intern)
Skovgaard, Kerstin (Intern)
Phd Student:
Goecke, Nicole Bakkegård (Intern)
Project Manager, academic:
Jorsal, Sven Erik Lind (Intern)

Financing sources
Source: Private funding (private)
Name of research programme: Svineafgiftsfonden
Amount: 1,776,000.00 Danish Kroner
Year of approval: 2014
Documents:
Optimeret sygdomsforebyggelse i slagtesvinebesætninger
Project

Diagnostic methods for veterinary pathogens
National Veterinary Institute
Period: 15/12/2014 → 16/05/2018
Number of participants: 4
Phd Student:
Goecke, Nicole Bakkegård (Intern)
Supervisor:
Hjulsager, Charlotte Kristiane (Intern)
Skovgaard, Kerstin (Intern)
Main Supervisor:
Larsen, Lars Erik (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Samfinansieret - Andet
Project: PhD

A plant-produced immunoenhanced pig vaccine against PRRS
National Veterinary Institute
Section for Immunology and Vaccinology
Section for Virology
Center for Electron Nanoscopy
Aarhus University
Boehringer Ingelheim Vetmedica, Inc.
Period: 01/01/2014 → 31/12/2018
Number of participants: 3
Acronym: Pigvac
Project participant:
Sørensen, Maria Rathmann (Intern)
Larsen, Lars Erik (Intern)
Approving authority:
Jungersen, Gregers (Intern)
Project

Lab-on-chip system for virus detection in water

Department of Micro- and Nanotechnology
Period: 01/10/2013 → 11/01/2017
Number of participants: 7
Phd Student:
Kirkegaard, Julie (Intern)
Supervisor:
Larsen, Lars Erik (Intern)
Svendsen, Winnie Edith (Intern)
Main Supervisor:
Rozlosnik, Noemi (Intern)
Examiner:
Emnéus, Jenny (Intern)
Heegaard, Niels H.H. (Ekstern)
Merkoçi, Arben (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Anden EU-finansiering

Relations
Publications:
Aptasensor development for detection of virus in water
Project: PhD

Functional analysis of replication determinants in classical swine fever virus

National Veterinary Institute
Period: 01/09/2013 → 05/04/2017
Number of participants: 6
Phd Student:
Hadsbjerg, Johanne (Intern)
Supervisor:
Rasmussen, Thomas Bruun (Intern)
Main Supervisor:
Belsham, Graham (Intern)
Examiner:
Larsen, Lars Erik (Intern)
Becher, Paul (Ekstern)
Knudsen, Charlotte Rohde (Ekstern)
Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)

Relations
Publications:
Functional analysis of replication determinants in classical swine fever virus
Project: PhD

Tailored Design of Innovative Vaccine against PRRSV
National Veterinary Institute
Period: 01/09/2013 → 11/03/2017
Number of participants: 7
Phd Student:
Welner, Simon (Intern)
Supervisor:
Jungersen, Gregers (Intern)
Lund, Ole (Intern)
Main Supervisor:
Larsen, Lars Erik (Intern)
Examiner:
Rasmussen, Thomas Bruun (Intern)
Graham, Simon Paul (Ekstern)
Lundegaard, Claus (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)

Relations
Publications:
Design, development and experimental trial of a tailored cytotoxic T-cell vaccine against Porcine Reproductive and Respiratory Syndrome Virus-2
Project: PhD

Identification of risk factors for acquiring ADV in Danish mink farms
Department of Bio and Health Informatics
Period: 01/08/2013 → 06/06/2017
Number of participants: 7
Phd Student:
Hagberg, Emma Elisabeth (Intern)
Supervisor:
Krarup, Anders (Ekstern)
Larsen, Lars Erik (Intern)
Main Supervisor:
Pedersen, Anders Gorm (Intern)
Examiner:
Sicheritz-Pontén, Thomas (Intern)
Decaro, Nicola (Ekstern)
Fischer, Thea Kølsen (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Industrial PhD
Project: PhD

Non-coding RNA mediated gene regulation during in fluenza infection
National Veterinary Institute
Period: 15/07/2013 → 15/10/2017
Number of participants: 6
Phd Student:
Brogaard, Louise (Intern)
Supervisor:
Larsen, Lars Erik (Intern)
Main Supervisor:
Skovgaard, Kerstin (Intern)
Examiner:
Lorenzen, Niels (Intern)
Salicio, Susanna Cirera (Ekstern)
Tchilian, Elma Z. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Swine plasma immunoglobulins against post-weaning diarrhoea
National Veterinary Institute
Division of Veterinary Diagnostics and Research
Innate Immunology
Virolgy
Section for Immunology and Vaccinology
KiBif ApS
Videncenter for Svineproduktion, Landbrug & Fødevarer
Period: 01/10/2012 → 30/09/2015
Number of participants: 3
Project ID: 22619
Project participant:
Larsen, Lars Erik (Intern)
Hedegaard, Chris Juul (Intern)
Project applicant:
Heegaard, Peter Mikael Helweg (Intern)

Financing sources
Source: Public research council
Name of research programme: GUDP - Projekt. Udviklings- og demonstrationsprojekt med forskningsandel
Amount: 5,017,193.00 Danish Kroner
Year of approval: 2012

Relations
Activities:
5th European Veterinary Immunology Workshop
Mucosal Vaccines, Adjuvants & Delivery
15th International Conference on Production Diseases in Farm Animals
10th International Veterinary Immunology Symposium
10th Workshop in Protein.DTU
2nd international symposium on alternatives to antibiotics (ATA)
11th International Veterinary Immunology Symposium
Project

Bayesian statistical analysis to assess serological testing strategies for avian influenza surveillance in Europe
Club 5 Joint Research 2012
National Veterinary Institute
Cooperative refining of the BioChip microarray into a routine investigative tool to address emerging viral diseases
Club 5 project

In two previous projects, UK BioChip and EU NoE project Epizone, we have established micro-array principles to detect rare or newly emerging viruses. In the UK BioChip project we established the technology and successfully provided evidence for its feasibility (Gurrala et al., 2009). In the latter, we extended the approach and adopted the technology to in situ synthesis printing for its punctuality, higher density and lower background.

The key aim of the proposes project is to refine the microarray probe coverage for transfer into a regular investigatative tool, particularly addressing avian diseases. The array will also be used to investigate several Diagnosis Not Reached (DNR) cases where multiple infections or emerging/novem viruses are suspected.

European Surveillance Network for Influenza in Pigs 3

This "European surveillance network for influenza in pigs 3 (ESNIP 3)" is in part a continuation of a surveillance network that was established during a previous EC concerted action (ESNIP 2, SSPE-022749). This second co-ordination action, which ran from 2005 until 2008, sought to achieve a better understanding of the epidemiology of swine influenza in Europe. Ten partners from eight different European countries (Belgium, The Netherlands, Italy, France, Germany, Spain, Bulgaria and UK) were involved including two industrial partners. Seven of these ESNIP 2 partners are members of the current ESNIP 3 consortium. ESNIP 3 will build upon the achievements of ESNIP 1 and 2 which were:
1) The standardisation of protocols for swine influenza (SI) virus (SIV) isolation, serology, antigenic and genetic typing of SIV isolates.
2) The selection and production of reference virus strains and (hyperimmune) sera. These were made available to all participants for preliminary sub typing of SIV isolates.
3) The establishment of a central SIV bank with a collection of recent isolates from various geographical areas in Europe.
4) The establishment of an electronic database with relevant information on the SIV isolates that were obtained in different countries during the life of the network.
5) The antigenic and genetic characterisation of a number of recent H1N1, H3N2 and H1N2 SIV isolates from different European countries.
6) The organisation of a serological survey to obtain preliminary data on the prevalence of different SIV subtypes in various European countries.
Optimizing the bulk milk tank surveillance in Danish dairy cattle
National Veterinary Institute
Period: 01/07/2010 → 09/03/2015
Number of participants: 7
Phd Student:
Foddai, Alessandro (Intern)
Supervisor:
Hisham Beshara Halasa, Tariq (Intern)
Uttenthal, Åse (Intern)
Main Supervisor:
Lind, Peter (Intern)
Examiner:
Larsen, Lars Erik (Intern)
Houe, Hans (Ekstern)
Lindberg, Ann (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut, samfinansiering
Project: PhD

Porcine Reproductive and respiratory Syndrome Virus (PRRSV)
National Veterinary Institute
Period: 01/07/2010 → 30/09/2013
Number of participants: 6
Phd Student:
Kvisgaard, Lise Kirstine (Intern)
Supervisor:
Hjulsager, Charlotte Kristiane (Intern)
Main Supervisor:
Larsen, Lars Erik (Intern)
Examiner:
Rasmussen, Thomas Bruun (Intern)
Bækbo, Poul (Ekstern)
Stadejek, Tomasz (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Anden EU-finansiering
Project: PhD

Animale influenza virus
National Veterinary Institute
Period: 01/06/2010 → 05/11/2014
Number of participants: 6
Phd Student: Fobian, Kristina (Intern)
Supervisor: Breum, Solvej Østergaard (Intern)
Main Supervisor: Larsen, Lars Erik (Intern)
Examiner: Belsham, Graham (Intern)
Bragstad, Karoline (Ekstern)
Harder, Timm Clemens (Ekstern)

**Financing sources**
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

**Hepatitis E virus i svin**
National Veterinary Institute
Period: 01/06/2010 → 30/09/2013
Number of participants: 6
Phd Student: Krog, Jesper Schak (Intern)
Supervisor: Breum, Solvej Østergaard (Intern)
Schultz, Anna Charlotte (Intern)
Main Supervisor: Larsen, Lars Erik (Intern)
Examiner: Ethelberg, Steen (Ekstern)
Poel, Wim H. M. Van der (Ekstern)

**Financing sources**
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

**Identification of the determinants of efficient pestivirus replication**
National Veterinary Institute
Period: 01/01/2010 → 18/12/2013
Number of participants: 6
Phd Student: Risager, Peter Christian (Intern)
Supervisor: Rasmussen, Thomas Bruun (Intern)
Belsham, Graham (Intern)
Examiner: Larsen, Lars Erik (Intern)
Becher, Paul (Ekstern)
Lindberg, Michael (Ekstern)

**Financing sources**
Source: Internal funding (public)
Name of research programme: Institut, samfinansiering
Project: PhD
New tools and approaches to control Porcine Reproductive and Respiratory Syndrome in the EU and Asia

Virology
Division of Veterinary Diagnostics and Research
National Veterinary Institute
Ghent University
Consejo Superior de Investigaciones Científicas
Centre de Recerca en Sanitat Animal
Parco Tecnologico Padano
Eidgenossisches Volkswirtschaftsdepartement
Panstwowy Instytut Weterynaryjny
University of Edinburgh
Secretary of State for Environment, Food and Rural Affairs
Stichting Dienst Landbouwkundig Onderzoek
Chinese Academy of Agricultural Sciences
Ministry of Agriculture and Rural Development

Boehringer Ingelheim Vetmedica, Inc.
Period: 01/01/2010 → 31/12/2014
Number of participants: 24
Contact person:
Rodrigo, Rafael (Ekstern)
Sanchez-Serrano, Jose Juan (Ekstern)
Domingo, Mariano (Ekstern)
Taranzi, Luigi (Ekstern)
Piatti, Giancarlo (Ekstern)
Griot, Christian (Ekstern)
Summermatter, Kathrin (Ekstern)
Wijaszka, Tadeusz (Ekstern)
Kotelba, Barbara (Ekstern)
Waddell, Derek (Ekstern)
Campbell, Fiona (Ekstern)
Boriello, Peter (Ekstern)
Thorns, Christopher (Ekstern)
Bianchi, Andre (Ekstern)
vn Zijderveld, Fred (Ekstern)
Tong, Guangzhi (Ekstern)
Lin, Jiaojiau (Ekstern)
Bui, Quang Anh (Ekstern)
Hoang, Van Nam (Ekstern)
Seidler, Randolph (Ekstern)
Papp, Hubert (Ekstern)

Project participant:
Trebbien, Ramona (Intern)

Project Manager, organisational:
Nauwynck, Hans (Ekstern)
Larsen, Lars Erik (Intern)

Financing sources
Source: Forsk. EU - Rammeprogram
Name of research programme: Forsk. EU - Rammeprogram
Amount: 1.921 Danish Kroner
Project
Ny spædgrisediarre i Danmark. Afklaring af årsagsforhold og diagnostik samt effekt af behandlinger.

Division of Veterinary Diagnostics and Research
National Veterinary Institute

Videncenter for Svineproduktion, Landbrug & Fødevarer
Period: 01/01/2010 → 31/12/2013
Number of participants: 7
Project ID: 22438
Project Manager, organisational:
Angen, Øystein (Intern)
Jensen, Tim Kåre (Intern)
Mølbak, Lars (Intern)
Kokotovic, Branko (Intern)
Larsen, Lars Erik (Intern)
Jorsal, Sven Erik Lind (Intern)
Bækbo, Pou (Ekstern)

Financing sources
Source: Forskningsprojekter - Fødevareministeriet
Name of research programme: Forskningsprojekter - Fødevareministeriet
Amount: 3,867,668.00 Danish Kroner

Zoonotiske aspekter af Hepatitis E i Danmark

Virology
Division of Veterinary Diagnostics and Research
National Veterinary Institute
National Food Institute
FoodDTU
Statens Seruminstitute
Period: 01/01/2010 → 31/12/2012
Number of participants: 4
Project ID: 22442
Project participant:
Christensen, Laurids Siig (Intern)
Böttiger, Blenda (Ekstern)
Larsen, Hans Henrik (Ekstern)
Project Manager, organisational:
Larsen, Lars Erik (Intern)

Financing sources
Source: Forskningsprojekter - Fødevareministeriet
Name of research programme: Forskningsprojekter - Fødevareministeriet
Amount: 917,000.00 Danish Kroner

Betydning af tidlig kontakt for kalvens velfærd

Virology
Division of Veterinary Diagnostics and Research
National Veterinary Institute
Aarhus University
Period: 01/01/2009 → 31/12/2012
Number of participants: 2
Project ID: 22394
Project participant:
Larsen, Lars Erik (Intern)
Project Manager, organisational:
Jensen, Margit Bak (Ekstern)

Financing sources
Source: Forsk. Private danske - Fonde
Name of research programme: Forsk. Private danske - Fonde
Amount: 536,213.00 Danish Kroner

Indsættelsesstrategi, lungebetændelse eller intensiv fodring som årsag til leverbylder
Virology
Division of Veterinary Diagnostics and Research
National Veterinary Institute
AgroTech A/S
Period: 01/01/2009 → 12/07/2014
Number of participants: 3
Project ID: 22393
Project participant:
Larsen, Lars Erik (Intern)
Graumann, Anne Mette (Ekstern)
Project Manager, organisational:
Jungersen, Mogens Vestergaard (Intern)

Financing sources
Source: Forsk. Private danske - Fonde
Name of research programme: Forsk. Private danske - Fonde
Amount: 168,000.00 Danish Kroner

Velfærdsmæssige behov omkring kælvning og umiddelbart efter fødsel hos malkekvæg
Division of Veterinary Diagnostics and Research
National Veterinary Institute
Period: 01/01/2009 → 31/12/2012
Number of participants: 3
Project ID: 22441
Project Manager, organisational:
Larsen, Lars Erik (Intern)
Heegaard, Peter Mikael Helweg (Intern)
Jungersen, Gregers (Intern)

Financing sources
Source: Forskningsprojekter - Fødevareministeriet
Name of research programme: Forskningsprojekter - Fødevareministeriet
Amount: 727,799.00 Danish Kroner

PCV2 award 2008 fra Boehringer Ingelheim
Section for Veterinary Diagnostics
Division of Veterinary Diagnostics and Research
Development of methods for in-line detection and identification of viruses in water

National Food Institute
Period: 01/08/2008 → 27/06/2012
Number of participants: 7
Phd Student: Uhrbrand, Katrine (Intern)
Supervisor: Hedlund, Kjell-Olof (Ekstern)
Myrmel, Mette (Ekstern)
Main Supervisor: Christensen, Laurids Siig (Intern)
Examiner: Larsen, Lars Erik (Intern)
Cook, Nigel (Ekstern)
Simonsson, Magnus (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Offentlig finansiering
Project: PhD

Activities:

One Health International Summer Course 2017
Period: 8 May 2017 → 18 Aug 2017
Tine Hald (Organizer)
Maria Vang Johansen (Organizer)
Liza Rosenbaum Nielsen (Panel member)
Lars Erik Larsen (Organizer)
Anders Dalsgaard (Organizer)

National Food Institute
Research Group for Genomic Epidemiology
National Veterinary Institute
Virology

Description
One Health International Summer Course 2017
5-week elearning part + 1-week on campus paert, a total of 5 ECTS
Degree of recognition: International

Related event
One Health International Summer Course 2017
08/05/2017 → 18/08/2017
Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

One Health International Summer Course 2016
Period: 9 May 2016 → 23 Aug 2016
Tine Hald (Organizer)
Maria Vang Johansen (Organizer)
Liza Rosenbaum Nielsen (Organizer)
Lars Erik Larsen (Organizer)
Anders Dalsgaard (Organizer)
National Food Institute
Research Group for Genomic Epidemiology
National Veterinary Institute
Virology

Description
One Health International Summer Course 2016
5-week elearning part + 1-week on campus part, a total of 5 ECTS
Degree of recognition: International

Related event
One Health International Summer Course 2016
09/05/2016 → 23/08/2016
Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

One Health International Summer Course 2015
Period: 13 Apr 2015 → 21 Aug 2015
Tine Hald (Organizer)
Maria Vang Johansen (Organizer)
Liza Rosenbaum Nielsen (Organizer)
Lars Erik Larsen (Organizer)
Anders Dalsgaard (Organizer)
National Food Institute
Research Group for Genomic Epidemiology
National Veterinary Institute
Virology

Description
One Health International Summer Course 2015
6-week elearning part + 2 week on campus part, a total of 5 ECTS
Degree of recognition: International

Related event
One Health International Summer Course 2015
13/04/2015 → 21/08/2015
Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.
Diagnosis of PRRSV – a review
Period: 24 Jul 2008 → 25 Jul 2008
Lars Erik Larsen (Speaker)
National Veterinary Institute
Division of Veterinary Diagnostics and Research
Virology

Related event
Diagnosis of PRRSV – a review: EuroPRRSnet workshop
24/07/2008 → 25/07/2008
Brussels
Activity: Talks and presentations › Conference presentations

Press clippings:

Svin smitter svin med influenza
Lars Erik Larsen
01/08/2009
National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology

Media contribution (1)

Svin smitter svin med influenza
01/08/2009
Print
http://www.dyrlaegemagasinet.dk
PUB-OA
Lars Erik Larsen
National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology
Press / Media

Valle mod Kalvediarré
Lars Erik Larsen
01/01/2008
National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology

Media contribution (1)

Valle mod Kalvediarré
01/01/2008
Print
Lars Erik Larsen
National Veterinary Institute, Division of Veterinary Diagnostics and Research, Virology
Press / Media