Rescue of the highly virulent classical swine fever virus strain "Koslov" from cloned cDNA and first insights into genome variations relevant for virulence

Classical swine fever virus (CSFV) strain "Koslov" is highly virulent with a mortality rate of up to 100% in pigs. In this study, we modified non-functional cDNAs generated from the blood of Koslov virus infected pigs by site-directed mutagenesis, removing non-synonymous mutations step-by-step, thereby producing genomes encoding the consensus amino acid sequence. Viruses rescued from the construct corresponding to the inferred parental form were highly virulent, when tested in pigs, with infected animals displaying pronounced clinical symptoms leading to high mortality. The reconstruction therefore gave rise to a functional cDNA corresponding to the highly virulent Koslov strain of CSFV. It could be demonstrated that two single amino acid changes (S763L and P968H) in the surface structural protein E2 resulted in attenuation in the porcine infection system while another single amino acid change within the nonstructural protein NS3 (D2183G) reduced virus growth within cells in vitro.

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