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 that 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 SLAs 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 ubiquiting, 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.