



## Reconstructing the highly virulent Classical Swine Fever Virus strain Koslov

Fahnøe, Ulrik; Pedersen, Anders Gorm; Nielsen, Jens; Höper, Dirk; Beer, Martin; Rasmussen, Thomas Bruun

*Publication date:*  
2013

[Link back to DTU Orbit](#)

*Citation (APA):*

Fahnøe, U., Pedersen, A. G., Nielsen, J., Höper, D., Beer, M., & Rasmussen, T. B. (2013). *Reconstructing the highly virulent Classical Swine Fever Virus strain Koslov*. Abstract from SMBE 2013 – Annual Meeting of the Society for Molecular Biology and Evolution, Chicago, IL, United States.

---

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Abstract intended for SMBE, Chicago, July 2013:

Title: Reconstructing the highly virulent Classical Swine Fever Virus strain Koslov

Ulrik Fahnøe<sup>1</sup>, Anders Gorm Pedersen<sup>2</sup>, Jens Nielsen<sup>1</sup>, Dirk Höper<sup>3</sup>, Martin Beer<sup>3</sup>, Thomas Bruun Rasmussen<sup>1</sup>

<sup>1</sup>DTU National Veterinary Institute, Technical University of Denmark, Lindholm, Denmark

<sup>2</sup>Center for Biological Sequence Analysis, DTU Systems Biology, Technical University of Denmark, Denmark

<sup>3</sup>Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, Greifswald-Insel Riems, Germany

Classical swine fever virus (CSFV) may be highly virulent in pigs with a mortality rate close to 100%. The CSFV “Koslov strain” is known to be one of the most virulent CSFV, but so far a functional cloned cDNA of this strain has not been described. We suggest that this may be due to the error-prone nature of the RNA-dependent RNA polymerase resulting in the majority of circulating forms being non-functional. However, since any infectious virus particle should necessarily be the offspring of a functional virus, we hypothesized that it should be possible to synthesize a highly virulent form by reconstructing ancestral sequences. To test this hypothesis, we inferred sequences that correspond to ancestral nodes in a phylogenetic tree built from full-length nucleotide sequences of non-functional Koslov cDNAs and then proceeded to test the reconstructions. Specifically, we altered a non-functional cDNA by site directed mutagenesis, removing non-synonymous mutations step by step. In vitro testing of modified constructs did indeed lead to fully functional viruses with similar growth kinetics as the wild-type strain. Moreover, viruses rescued from the construct had the ancestral amino acid sequence and, when tested in pigs, were at least as virulent as the Koslov strain. The ancestral reconstruction therefore proved to give rise to a functional cDNA of the highly virulent Koslov strain. In vivo studies confirmed our methods and enabled us to identify nucleotide positions within the viral genome important for virulence.