MELATIN-PRV

Mechanisms contributing to pseudorabies virus latency induction in domestic pigs in vivo

DURATION
1/10/2013 - 31/12/2015

BUDGET
139.063 €

PROJECT DESCRIPTION

Pseudorabies virus (PRV) causes Aujeszky's disease in its reservoir hosts, pigs and wild boar. PRV has evolved over the years and strains differ in their capacity to cause clinical disease. The mechanistic basis for this variation in in vivo virulence is largely unknown. Since PRV was eradicated from the domestic pig population in Belgium in 2010, PRV strains circulating in wild boar are considered as a possible source for reintroduction of the disease and knowledge of their virulence is important for the control policy of the federal government.

Preliminary results of an in vivo infection experiment conducted beginning 2013 at CODA-CERVA with the virulent NIA3 reference strain and a Belgian PRV isolate from wild boar in 2 and 14 week old domestic pigs underlined the capability of the wild boar strain to cause disease and economic losses. Striking differences were however found between systemic and neurological spread of both strains in an age dependent way. Our objective is to use the collected samples to study differences in in vivo virulence of the Belgian wild boar PRV strain and the NIA3 strain.

In a first work package, it will be examined if differences exist between both strains in their capacity to replicate at the nasal mucosa, to cross the basement membrane and to spread via neurons to the trigeminal ganglion and further on to the central nervous system. This will mainly be done by detection of viral and/or host proteins using confocal microscopy and detection of viral genomic material via qPCR assays.

In a second work package, it will be examined if a correlation exists between the ability of the PRV strains to spread in the nervous system and towards the internal organs and the local (nasal mucosa and trigeminal ganglion) and systemic immune response elicited upon PRV infection. It will be examined which immune cells infiltrate at the nasal mucosa and the trigeminal ganglion via immunofluorescence stainings and confocal microscopy and if differences in cytokine expression can be found. ELISAs will be used to study cytokine kinetics over time in serum of infected animals.

Since this project aims to study immunological and neurological aspects related to alpaherpesvirus infections that are largely unknown, the gathered knowledge will be of interest to a broad scientific community.

Knowledge of immune mechanisms responsible for latency induction in the homologous PRV-pig model can help to develop in vitro latency models which could be helpful in finding new antiviral drugs that can interfere with the latency/reactivation cycle. Such knowledge could also aid in the development of vaccines that do not progress to latency themselves or new therapies capable to activate specific components of the immune system to avoid latency induction or to prevent reactivation (Chentoufi & BenMohamed, 2012).

Knowledge of which barriers play a role in the observed differences between the capacities of PRV strains to induce clinical disease in vivo will provide clues to which viral proteins are responsible for these differences and can open new directions for future research.

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From a government perspective, knowledge of the virulence of wild boar PRV strains is very important since these form the major risk for reintroduction of the disease in the domestic pig population. The results from the in vivo infection experiment show that the Belgian wild boar PRV strain is capable to infect domestic pigs and to potentially cause important economic damage. This project will allow studying the differences between the wild boar strain and NIA3 in more detail which will yield valuable information that will help the government to take decisions about the necessity of preventive actions in a knowledge driven way. Furthermore, knowledge of important in vivo barriers that can explain differences between the virulence of strains will stimulate the development of representative in vitro models that allow the rapid evaluation of the virulence of newly isolated strains from the field in order to assess the risk they pose to the domestic pig population.

CONTACT INFORMATION

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