

Characterization of immune evasion strategies of classical swine fever virus in dendritic cells with potential application as *in vitro* model for virulence studies

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Schlüsselwörter

Classical swine fever virus, CSFV, pestivirus, virulence, dendritic cell, interferon

Problemstellung und Zielsetzung

A major problem with classical swine fever virus (CSFV) is the persistence of the virus in wild boar, which represents a continuous threat for domestic pigs. The degree of disease in pigs depends on the virulence of a particular isolate. Infections with low and moderately virulent strains are often not recognized early enough in the field. Therefore it is important to characterize the virulence of CSFV isolates circulating in wild boar. This can so far only be achieved with infection studies in pigs. An *in vitro* assay to define the potential virulence of a CSFV isolate would greatly improve diagnosis. The aim of this project was to identify viral and host response parameters of virulence that would eventually lead to the establishment of such an assay.

Material und Methoden

The experiments were performed essentially with primary cell culture systems derived from SPF pigs held at the IVI. The CSFV mutants were engineered using the reverse genetics technology developed at the IVI.

Ergebnisse und Bedeutung

We identified viral triggers and inhibitors of CSFV-mediated innate immune activation. Our results lead to a model for CSF pathogenesis in which CSFV prevents interferon- α/β (IFN- α/β) induction by the means of the viral N^{pro} at the initial sites of virus replication involving essentially macrophages, conventional dendritic cells (DC) and epitheloid cells. This allows the virus to efficiently replicate and spread within the organism with kinetics and levels that depend on strain-specific virulence factors. The virus then infects plasmacytoid DC, resulting in massive IFN- α and pro-inflammatory cytokine release, which eventually leads to the multiple haemorrhages and oedema observed with CSF. In fact, we found a clear correlation of viremia, leukopenia and level of IFN- α/β secretion *in vivo* with the virulence of a particular strain. These data serve as a valuable basis for a current 3R research project (# 105-06) entitled "Establishment of an *in vitro* system for the prediction of the degree of virulence of classical swine fever virus isolates" (see <http://www.forschung3r.ch/>).

Publikationen

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