

# Rift Valley fever

## - Consequences of virus-host interactions

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**Abstract**

Rift Valley fever virus (RVFV) is a mosquito-borne virus which can infect many animals including humans. The abortion rate among non-human animals are ~100%, and are often lethal in young animals. In humans, Rift Valley fever (RVF) presents in most cases as a mild illness with influenza-like symptoms. However, it can progress into a more severe disease with a high case fatality rate. Since there is such a high abortion rate among infected animals, a link between human miscarriage and RVFV has been suggested, but never proven.

We could in paper I for the first time show an association between acute RVFV infection and miscarriage in humans. We observed an unexpected increase in pregnant women arriving at the Port Sudan Hospital with fever of unknown origin, and several of the patients experienced miscarriage. When we analysed their blood samples for several viral diseases we found that many had an acute RVFV infection and of these, 54% experienced a miscarriage. The odds of having a miscarriage was 7 times higher for RVFV patients compared to the RVFV negative women. These results indicated that RVFV infection could be a contributing factor to miscarriage.

RVFV is an enveloped virus containing the viral glycoproteins n and c (Gn and Gc respectively), where Gn most likely is responsible for the initial cellular contact. Charge is a driving force for molecular interaction and has been shown to be important for cellular attachment of several viruses, and in paper II we could show that when the charge around the cells was altered, the infection was affected. We also showed that Gn most likely has a positive charge at a physiological pH. When we added negatively charged molecules to the viral particles before infection, we observed a decreased infection efficiency, which we also observed after removal of carbohydrate structures from the cell surface. Our results suggested that the cellular interaction partner for initial attachment is a negatively charged carbohydrate. Further investigations into the mechanisms of RVFV cellular interactions has to be undertaken in order to understand, and ultimately prevent, infection and disease.

There is currently no vaccine approved for human use and no specific treatments for RVF, so there is a great need for developing safe effective drugs targeting this virus, something we aimed to achieve in paper III. We designed a whole-cell based high-throughput screen (HTS) assay which we used to screen libraries of small molecular compounds for anti-RVFV properties. After dose-response and toxicity analysis of the initial hits, we identified six safe and effective inhibitors of RVFV infection that with further testing could become drug candidates for treatment of RVF. This study demonstrated the application of HTS using a whole-cell virus replication reporter gene assay as an effective method to identify novel compounds with potential antiviral activity against RVFV.

**Keywords**

Rift Valley fever, Rift Valley fever virus, viral haemorrhagic fever, miscarriage, entry, charge, carbohydrates, high-throughput screening, antiviral, cell-based assay

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