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## Abstract

The projects of the Unit deal with Rift Valley fever virus, which represents a model to study an hemorrhagic fever. The aim is to identify determinants of virulence, to decipher their mode of action and to produce an attenuated virus which could be utilized as a vaccin candidate.

## Annual Report

### Role of Interferon and NSs in pathogenesis

Rift Valley fever virus is an arbovirus of the Bunyviridae family (Phlebovirus genus) transmitted by mosquitoes. It is endemic in sub-saharian Africa where it provokes many epizootics /epidemics. Recently it spread to Middle East. Ruminants are severely affected with a high mortality rate, abortions and teratogenesis. In humans, infection can lead to a fatal hemorrhagic fever with an acute hepatitis. The role of the non structural protein NSs has been determined only very recently. Studies on this phosphoprotein which forms filamentous structures in the nucleus whereas every step of the viral cycle occurs in the cytoplasm, represent our main axis of research. Genetic analysis of Clone 13, a naturally avirulent mutant, which possesses a large internal deletion in the NSs gene helped to show that NSs plays a major role in virulence and to demonstrate that NSs prevents the host antiviral response by blocking type I interferon production. Analysis of infected cells indicated that NSs prevents activation of transcription of Interferon beta mRNA. Attempts are being made to determine the mechanism utilized by NSs to act as antagonist of interferon production.

### Studies on transcription and replication with minigenomes.

To develop a system for reverse genetics, we established a basic transcription system in which viral proteins and RNAs were expressed from cDNA sequences cloned in plasmids. In a first step, the system was tested with a minigenome consisting in a viral like-RNA carrying the non coding sequences of the L, M or S genomic segments and the Chloramphenicol acetyl transferase gene in the antisense orientation. These RNA molecules were synthesized from plasmids under the control of the cellular Pol I promoter. Plasmids carrying the S-CAT, M-CAT and L-CAT sequences were constructed and these genome-like RNAs were efficiently recognized and transcribed by the viral complex composed of the L polymerase and the N nucleoprotein.

**Keywords:** Bunyviridae, arbovirus, reverse genetics, haemorrhagic fever, innate immunity

## Publications

> [Publications of the unit on Pasteur's references database](#)

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