

Molecular and serological techniques to study Lassa virus ecology (ECOLASSA)

Overview of results and conclusions

Lassa virus causes hemorrhagic fever in humans — Lassa fever — which is associated with case fatality rates between 20% and 60%. The disease is endemic in West Africa. The virus is transmitted to humans by the rodent *Mastomys natalensis*. The general objective of this proposal was to enhance our knowledge on Lassa virus circulation in the natural host population by combining field studies with serological and molecular epidemiological studies.

Workpackage 1: Temporal and spatial pattern of Lassa virus infection in rodents

The Lassa virus-specific antibody prevalence in the rodent population in various locations in Guinea was determined by indirect immunofluorescence (antibodies demonstrate past or present infection with the virus). A total of 1551 rodent sera were tested. The serological data were used together with PCR data (demonstrating presence of virus in the rodent) and ecological data (season, age, sex) to develop a model for Lassa virus circulation in the natural host population.

Of the 1551 animals tested, 129 were positive for arenavirus antibodies: 109 *M. natalensis*, 7 *M. erythroleucus*, 4 *L. striatus*, 4 *P. daltoni*, 3 *M. minutoides*, and 2 *P. rostratus*. They were mainly captured in the villages Bantou, Gbetaya, and Tanganya, where Lassa virus was previously described. The overall seroprevalence in *M. natalensis* was 18%. It was higher in the Faranah area with 21% in Bantou, 12% in Gbetaya, and 39% in Tanganya. Of the 108 seropositive animals, 11 were also PCR-positive.

The implementation of different variables into a logistical regression analysis indicates three significant factors influencing seroprevalence: the village, the habitat, and the age (Figure 1). Sex and season had no effect on the seroprevalence.

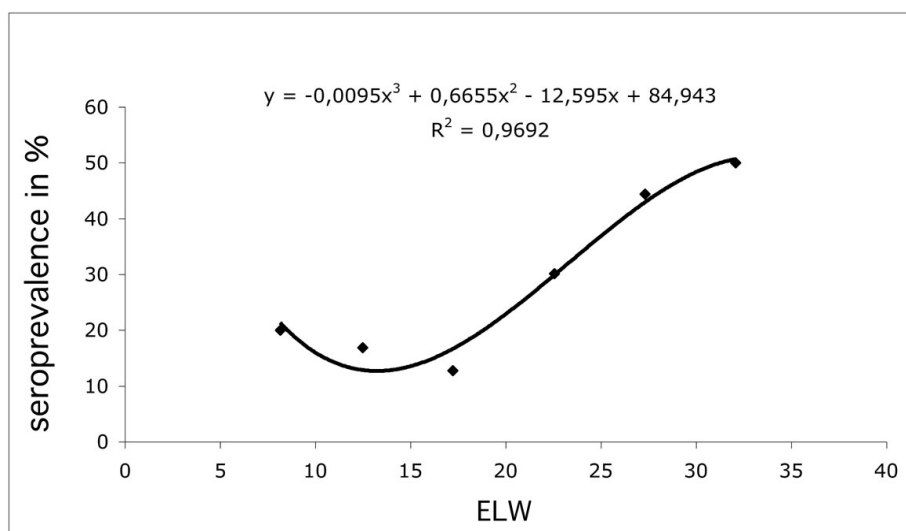


Figure 1: Age effect as measured by eye lens weight (ELW) on seroprevalence of *Mastomys natalensis*.

The correlation between infection rate and age suggests that Lassa virus is transmitted horizontally (that means through fighting/biting or virus-contaminated environment, but not from mother to newborn) in the natural host population. This finding has relevance for the design of strategies to control Lassa virus in the rodent population.

Workpackage 2: Temporal and spatial pattern of Lassa virus phylogeny in rodents

Aim of this task was to reconstruct the phylogenetic evolution of Lassa virus over time in Guinea. Virus was available from *M. natalensis* sampled in field studies conducted from 2003 to 2005 in Guinea. A total of 80 virus-positive animals had been captured. An additional field trip to the same sites was conducted in 2011, which yielded another 14 Lassa virus-positive *M. natalensis* (Figure 2).



Figure 2: Field trip to Guinea in 2011. Left, necropsies in the field; middle, preparation of the bait to capture the rodents; right, village of Tanganya.

From these specimens, sequences of the S segment of Lassa virus were generated and used for reconstructing the phylogeny over a period of 9 years. This analysis revealed that Lassa virus clusters strongly with the geographic location and that the virus rapidly evolves. The geographical clustering of virus strains on small scale indicates that Lassa virus is transmitted mainly locally and that the natural host of Lassa virus is not spreading the virus over large distances in short periods of time.

Workpackage 3: Complete sequencing of representative Lassa virus isolates from Guinea

For the first time, the complete sequence of large and small segments of a Lassa virus strain from Upper Guinea was determined. This is also the first full-length sequence of a Lassa virus strains isolated from *M. natalensis*. Phylogenetic reconstruction using strains from several West Africa countries indicates that the virus is ancestral to (older than) the virus strains from Liberia and Sierra Leone (Figure 3).

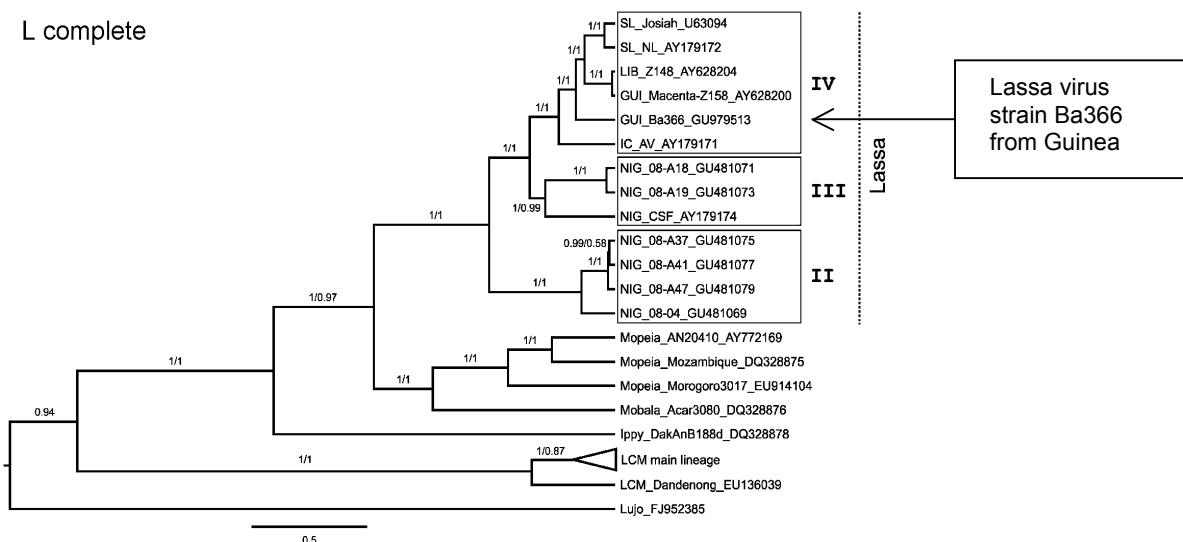


Figure 3: Phylogeny of Lassa virus in West Africa using full-length L segment sequences. The newly sequenced Lassa virus strain from Bantou village is marked with an arrow.

Socio-economic impacts

Understanding the ecology of Lassa virus in its natural reservoir *M. natalensis* and the evolution of the virus are prerequisites for the design of rational strategies to control virus transmission in the natural host population. Based on the data generated by this project, it will be feasible to test hypotheses to reduce the circulation of Lassa virus in nature. In future, these strategies may lead to a reduction of Lassa fever cases in West Africa and reduce the burden of a life threatening neglected tropical disease.

Contact details

Research fellow: Dr. Elisabeth Fichet-Calvet
Supervisor: Prof. Dr. Stephan Günther

ecalvet@club-internet.fr
guenther@bni.uni-hamburg.de

Bernhard-Nocht-Institute for Tropical Medicine, Department of Virology
Bernhard-Nocht-Str. 74, 20359 Hamburg, Germany
Phone: +49 40 42818 930, Fax: +49 40 42818 931