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Characterization of viral factors responsible for Arenavirus-host barriers in *M. natalensis*

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Lassa virus (LASV) outbreaks cause up to 18,000 annual deaths in West Africa. Transmission mainly occurs through contact with infected rodents, with *Mastomys natalensis* as the primary reservoir host. Prior studies showed that homologous LASV strains (isolated from *M. natalensis*) cause persistent infections in Mastomys, while heterologous strains (isolated from other rodent species) are cleared rapidly. To identify viral factors driving these host restrictions, we created LASV chimeras by inserting single protein sequences from a heterologous strain into a homologous backbone.

The growth kinetics of chimeric and wild-type viruses were compared *in vitro*. Furthermore, one-week old Mastomys were inoculated with the different chimeras and monitored for four weeks. Virus titers in organs, as well as viral RNA levels and antibody presence in blood were analyzed.

All four chimeric viruses showed attenuated growth *in vitro* on Vero and Mastomys-derived cells. The homologous wild-type control caused strong systemic infections *in vivo*. The chimera with a heterologous Z protein showed a similar infection phenotype, however, it also caused pathogenicity. In contrast, the chimeras with the heterologous GP, NP, or L protein only led to low virus titers and rapid clearance, like the heterologous wild-type virus.

Our findings indicate that the LASV GP, NP, and L protein play important roles in the observed virus-host barriers, while the Z protein has minimal effect on host restrictions.

Keywords

Lassa virus, *Mastomys natalensis*, virus-host barriers

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Junior Scientist Status

Yes, I am a Junior Scientist.

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