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Proof-of-concept For A Transmissible Lassa Virus Vaccine In The Rodent Mastomys Natalensis Reservoir: A Strategy To Mitigate Spillover Risk Of Highly Pathogenic Zoonotic Viruses From Animal Reservoirs To Humans

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The Problem: Most emerging viruses with high human disease potential are a result of zoonotic transmission from an animal reservoir or transmission/amplification species, primarily wildlife (especially rodents, non-human primates and bats) and domestic livestock. This emergence of highly pathogenic viruses from their animal host is a serious threat to US military operations and warfighters around the world.
Our Approach: Self-disseminating (transmissible) vaccination is an innovative technology with the potential to provide localized population level immunity among key animal reservoir species involved in zoonotic transmission of emerging viruses.

Our Project: Our 'proof-of concept' project focuses on Lassa virus (LASV), which causes Lassa hemorrhagic fever disease across much of western Sub-Saharan Africa resulting in an estimated 100,000 human cases and approximately 5,000 deaths annually. A commonplace rodent found across the region, the multimammate rat (Mastomys natalensis), is the primary reservoir host for the virus, and most human infections are a result of contact with virus contaminated rodent urine, feces and saliva.

Project Design: Our project focuses on the detection, prediction, and modeling of LASV and Mastomys natalensis cytomegalovirus (MasCMV) and the development of novel vaccine countermeasures for zoonotic virus animal reservoir species. Central to this goal is a transmissible MasCMV-based vaccine to block LASV zoonotic transmission from the Mastomys natalensis reservoir. Our team utilized long-standing research collaborations to extensively assess the ecology of LASV and CMVs among rodents in Sierra Leone, West Africa. Our project was multi-disciplinary and was integrated across stakeholder engagement, field studies, and genomic and mathematical modeling analyses. The project was further integrated with molecular virology to understand the underlying viral ecology and to develop prototype transmissible MasCMV-based vaccine candidates for LASV.

Current Status: Initial studies in colony-reared Mastomys natalensis under experimental biologically contained conditions demonstrated the ability of our lead vaccine candidate to establish a non-pathogenic systemic infection and to be shed into saliva of vaccinated animals. Ongoing and upcoming studies will further explore immunogenicity, efficacy and transmission of these vaccine candidates; these studies will also assess the effectiveness of an intrinsic control system to provide environmental control of the vaccine. Together with the development of additional critical implementation tools, our project provides a well-informed blueprint for application of transmissible CMV-based vaccines against current and future biological threats.

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