Development of Arenavirus Vaccines through Codon Deoptimization

A novel strategy for developing safe and effective live-attenuated arenavirus vaccines.

Problem Solved by This Technology
Arenaviruses have a significant impact on public health and pose a credible threat to biodefense. There are four arenaviruses that cause severe hemorrhagic fever in humans (Lassa virus, endemic to Africa; and Machupo, Junin, and Guanarito viruses endemic to South America). A fifth arenavirus, lymphocytic choriomeningitis virus (LCMV), is found throughout the world and it is particularly troublesome for immunocompromised individuals. Safe and effective arenavirus vaccines have remained elusive and none are currently available. Therapy is limited to off-label use of ribavirin, which is only partially effective and carries many undesired side-effects.

Applications
Researchers at the University of Rochester are developing a codon deoptimization (CD) -based approach as a novel strategy for live-attenuated arenavirus vaccines. This approach is based on recoding certain proteins of the virus with least frequently used codons in mammalian cells. Research has shown that a recoded LCMV is genetically and phenotypically stable during serial passages in FDA vaccine development-approved Vero cells. In vivo experiments in a LCMV-infected mouse model have shown that the recoded viruses were highly attenuated and conferred complete protection against a subsequent lethal challenge with wild-type LCMV. These results indicate the safety, efficacy, and stability of this CD-based approach for developing live-attenuated vaccine candidates against human pathogenic arenaviruses.

Intellectual Property Status
U.S. and international patent applications pending.

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Publications
Cheng BY et al. “Generation of recombinant arenavirus for vaccine development in FDA-approved Vero cells,” J Vis Exp. 2013 Aug 1; (78). PMID: 23928556

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