EVALUATION OF A RECOMBINANT RIFT VALLEY FEVER VIRUS NUCLEOCAPSID PROTEIN AS A VACCINE AND AN IMMUNODIAGNOSTIC REAGENT

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ABSTRACT

The serodiagnosis of Rift Valley fever (RVF) relies on the use of inactivated whole virus based reagents which present biosafety, financial and operational constraints. There are no vaccines for humans, the availability of animal vaccines is limited and they have several drawbacks. The aim of this study was to evaluate a bacterially expressed recombinant RVF virus (RVFV) nucleocapsid protein (recNP) as a safe immunodiagnostic reagent, and an immunogen in a mouse and host animal model. Several enzyme-linked immunosorbent assays (ELISAs) were developed in this study, enabling sensitive and specific detection of antibodies and RVFV antigen in human and animal specimens. The recNP was combined with different adjuvants and used to immunize mice and sheep subsequently challenged with a virulent wild type RVFV strain. Depending on the recNP/adjuvant combination, protection against disease in mice ranged between 17 and 100%, with sterilizing immunity elicited in some experimental groups, compared to 100% morbidity/mortality and excessive viral replication in adjuvant and PBS control mice. Immunization with recNP combined with Alhydrogel, an adjuvant that biases immunity towards Th2 humoral immunity, that yielded 100% protection, induced an earlier and stronger type I interferon response in mice after challenge, compared to repression of the same gene in adjuvant and PBS control mice. There was massive activation of pro-inflammatory responses and genes with pro-apoptotic effects in the livers of control mice at the acute phase of infection, accompanied by high viral replication, possibly contributing to the pathology of the liver. There was also evidence of activation and repression of several genes involved in activation of B- and T-cell immunity in control mice, some indicating possible immune evasion by the challenge virus. Immunization of sheep with the same recNP/adjuvant combinations were, however, not able to decrease replication of challenge virus. The recNP based ELISAs are an important addition to and improvement of the currently available serodiagnostic tests for RVF. The mechanism by which recNP immunization protects mice from developing severe disease during the acute phase of infection is now better understood, but the mechanism for earlier clearance of the virus needs further investigation.