Characterization of Immune Responses Induced by IntramuscularVaccination with DNA Vaccines Encoding Measles Virus Hemagglutinin and/or Fusion Proteins

Man Ki Song

International Vaccine Institute, Seoul, Korea

Measles virus (MV) remains a major cause of infant morbidity and mortality in many regions of the world. An estimated 700,000 deaths occur worldwide per year, the overwhelming majority clustered in developing countries. Given at 9 months of age or above, the existing licensed live attenuated MV vaccines are safe and have been highly effective in eliminating measles where they have been used programmatically in industrialized and middle-income countries. In contrast, in many less-developed countries, particularly in Africa, measles has remained a public health problem, despite moderate levels of coverage with attenuated measles vaccine. A specific high-risk group has been young infants who are too young (less than 9 months of age) to respond reliably to the current attenuated measles vaccine but who can develop severe, often fatal clinical measles upon exposure to wild-type virus.

DNA vaccines encoding measles antigens induce both humoral and cell-mediated immune responses. MV-H or MV-F DNA vaccines induce neutralizing antibodies in macaques and confer protection against experimental challenge with wild-type measles virus. Notably, an MV DNA vaccine containing the H, F, and nucleoprotein (N) genes induced protective immunity to MV in infant rhesus macaques even in the presence of maternal antibody and protected against experimental challenge. However, there is debate as to whether coimmunization with DNA vaccines encoding MV-H and MV-F has an additive or a suppressive effect on the generation of protective immunity against MV and whether the presence of both proteins modulates the immune responses. Coimmunizing with a combination of two DNA vaccines encoding MV-H and MV-F, Polack et al. reported that MV-specific cytotoxic T-lymphocyte responses were slowed and plaque reduction neutralizing (PRN) antibodies were decreased compared to responses elicited by MV-H. These investigators subsequently showed that vaccination with DNA vaccines encoding MV-H and MV-F prime Th2 and Th1 cytokine production in macaques, respectively, following challenge with MV. Coimmunization with MV-H and MV-F induced higher gamma interferon (IFN-r) production by phytohemagglutinin- stimulated peripheral blood lymphocytes than vaccination with MV-H alone. To characterize the immune responses elicited following parenteral administration of DNA vaccines encoding MV proteins, we engineered Sindbis virus-based DNA replicon pSINCP constructs to encode MV-H or MV-F alone or both MV-H and MV-F (thereby ensuring expression of both MV-H and MV-F proteins within the same transfected cell and eliminating any possible competition involving separate plasmids). Herein, we present data on the MV-specific immune responses elicited by the measles virus DNA vaccine constructs in mice and monkeys.