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IMMUNE-PROFILING OF INNATE AND ADAPTIVE IMMUNITY FOLLOWING THREE VACCINATIONS OF THE MERS VACCINE CANDIDATE MVA-MERS-S

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Middle East Respiratory Syndrome (MERS) is a respiratory disease caused by MERS coronavirus (MERS-CoV). In follow-up to a phase 1 trial, we performed a longitudinal analysis of immune responses following immunization with the Modified Vaccinia virus Ankara (MVA)-based vaccine MVA-MERS-S encoding MERS-CoV-spike protein. Three homologous intramuscular immunizations were administered on days 0 and 28 with a late booster vaccination at 12±4 months. Vaccination with MVA-MERS-S revealed a benign safety profile. No serious or severe adverse events were reported. Here, we analyzed innate and adaptive immune responses to the MVA-MERS-S in ten vaccinees. For this approach, blood samples were collected frequently for a period of about three years. Serum, plasma and PBMCs were analyzed at multiple time points using different techniques, which allowed an in-depth characterization of immune responses elicited by MVA-MERS-S.

Innate immune responses were analyzed using flowcytometry, Luminex and RNA Sequencing to gain a comprehensive insight into the activation status of innate immune cells, the secretion of signaling molecules and the transcriptome dynamics following vaccination. Adaptive immunity was evaluated by ELISA, ELISpot and flowcytometry to evaluate the induction and persistence of antigen-specific T and B cells as well as antibodies. Besides binding and neutralizing antibodies, antibody isotypes and subclasses were monitored.

The first and third, but not the second vaccination stimulated a notably enhanced innate immune response and underlined a greater frequency of activated monocytes and T cells; a higher concentration of plasma IP10; and an upregulation of mRNAs related to innate antiviral immunity. Vaccination resulted in a robust and long-lasting production of binding and neutralizing antibodies against MERS-CoV-S. The late booster immunization significantly increased frequency and persistence of MERS-CoV-S-specific B cells and IgG1 antibodies. Additionally, vaccination induced MERS-CoV-S specific CD8+ T cells secreting IFNg.

Collectively, our data underline the potential of a late boost to enhance long-term antibody and B cell immunity against MERS-CoV. Our approach of investigating multiple time points and different types of blood samples (serum, plasma, PBMC) using a variety of technologies provides a comprehensive overview of the immunogenicity induced by MVA-MERS-S. Our findings underscore the ability of the MVA platform to be used as a vaccine candidate against coronaviruses. Further, MVA represents an attractive vaccine platform for emerging viruses due to its plug-in potential and the immunogenic and favorable safety profile.