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New vaccines against emerging zoonotic infections: From animal models to clinical evaluation

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Modified Vaccinia virus Ankara (MVA) is a licensed third-generation smallpox vaccine and a potent vector platform for developing vaccines against infectious diseases and cancer. Developed by serial passage in chicken cells, MVA lost replication ability in mammalian hosts and many orthopoxvirus virulence genes, enhancing its safety profile. MVA-based vaccines have demonstrated safety, immunogenicity, and protective efficacy in animal models, including an MVA-MERS-S candidate tested successfully in dromedary camels—the primary MERS-CoV reservoir—supporting its use as a One Health strategy to prevent zoonotic transmission. Clinical safety and immunogenicity of MVA-MERS-S were confirmed in a phase I human trial, with phase II studies underway in Europe. Recent preclinical work on MVA-based COVID-19 vaccines showed that a recombinant MVA expressing stabilized SARS-CoV-2 spike protein (MVA-SARS-2-ST) elicited superior S1 surface expression and stronger neutralizing antibody responses across variants compared to the native S protein. Intramuscular vaccination with MVA-SARS-2-ST protected mice and hamsters from disease and lung pathology upon challenge. These results support MVA-SARS-2-ST as an improved clinical vaccine candidate, highlighting the importance of membrane-bound S1 for protective immunity.

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