The Role Of Vaccination Route With An Adenovirus-Vectored Vaccine In Protection, Viral Control, And Transmission In The SARS-Cov-2/K18-Hace2 Mouse Infection Model.

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Abstract:

Vaccination is the most effective mechanism to prevent severe COVID-19. However, breakthrough infections and subsequent transmission of SARS-CoV-2 among vaccinated and unvaccinated persons remains a significant problem. Intranasal delivery has the potential to be more effective in preventing disease and limiting transmission between individuals compared to an intramuscular route as the vaccine can induce responses at mucosal sites. Utilizing a replication-deficient adenovirus serotype 5-vectored vaccine expressing the SARS-CoV-2 RBD (AdCOVID) in homozygous and heterozygous transgenic mice expressing different levels of human angiotensin converting enzyme-2 in epithelial cells (K18-hACE2), we investigated the impact of the administration route on vaccine immunogenicity, transmission of SARS-CoV-2, and survival. The mice were vaccinated with AdCOVID via the intramuscular or intranasal route and subsequently challenged with SARS-CoV-2. The study results show that intranasal vaccinated animals had improved mucosal antibody responses, viremic control, and protection from lethal infection compared to intramuscular vaccinated animals. Intranasal vaccination also resulted in reduced viral transmission to naive co-housed mice compared to intramuscular vaccination in a highly sensitive homozygous K18-hACE2 mouse model. Overall, our data provides convincing evidence for the use of intranasal vaccination in protecting against SARS-CoV-2 infection and transmission.