Intranasal Immunization of HD-Ad-FS Induces Robust Systemic and Airway Mucosal Immunities Against SARS-CoV-2 and Variant Infection in Mice and Hamsters

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Introduction

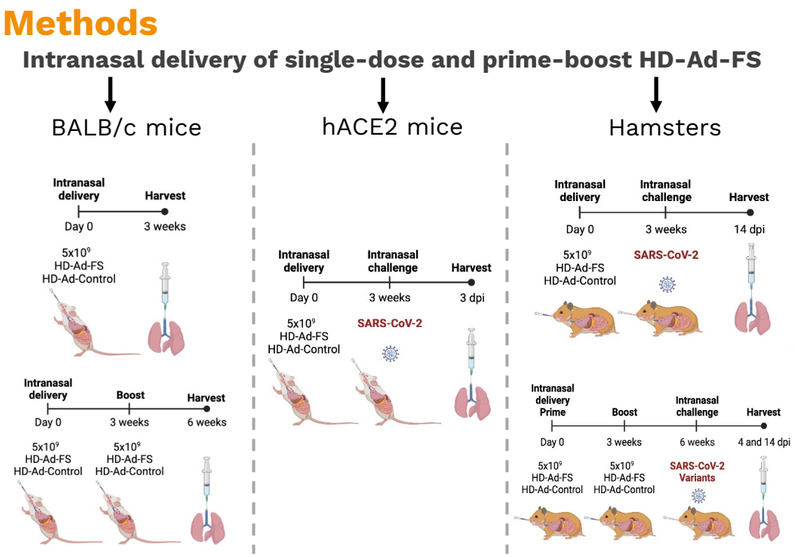
The coronavirus disease 2019 (COVID-19) is caused by aerosol transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is generally perceived that the generation of adequate airway mucosal immunity can protect the host from SARS-CoV-2 infection. However, current parenteral COVID-19 vaccines are administrated via an intramuscular route and elicit limited mucosal immunity. **Mucosal vaccine** has the potential to prevent SARS-CoV-2 infection of respiratory tract and stop transmission.

Objective

We developed a candidate mucosal vaccine, HD-AD-FS. It is a replication-deficient helper-dependent adenoviral vector encoding a full-length SARS-CoV-2 spike protein. We aimed to evaluate the safety and protective activity of HD-Ad-FS in animals challenged with SARS-CoV-2 and variants.

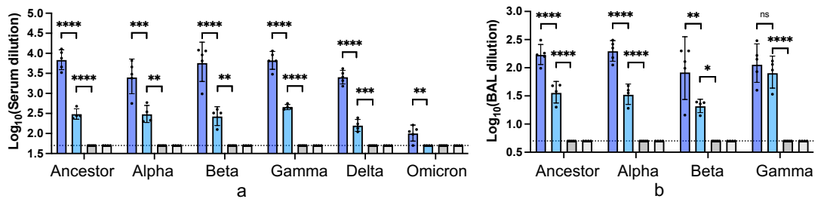
Methods

Intranasal delivery of single-dose and prime-boost HD-Ad-FS

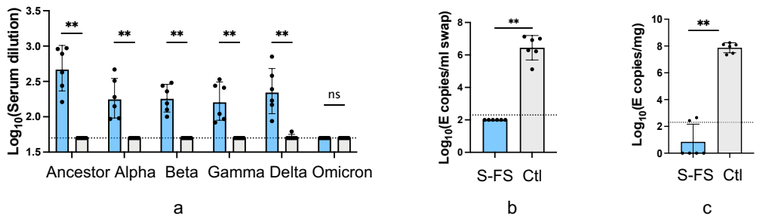


Results

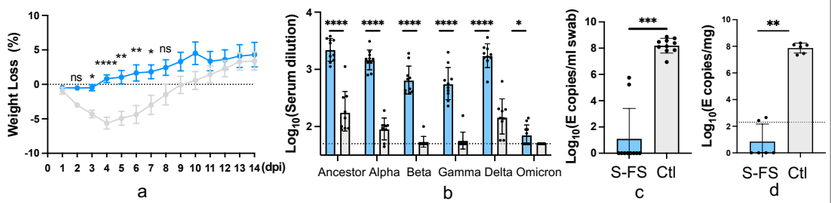
Result 1. Single-dose and prime-boost HD-Ad-FS induced neutralizing antibodies in sera and BALs of vaccinated BALB/c mice. (a) Serum neutralizing antibody levels. **(b)** Bronchoalveolar lavage (BAL) neutralizing antibody levels.



Result 2. Single-dose HD-Ad-FS protected hACE2 mice from SARS-CoV-2 challenge. **(a)** Serum neutralizing antibody titers. **(b)** Levels of SARS-CoV-2 RNA of oropharyngeal swabs. **(c)** Levels of SARS-CoV-2 RNA in lungs. Mann–Whitney test.

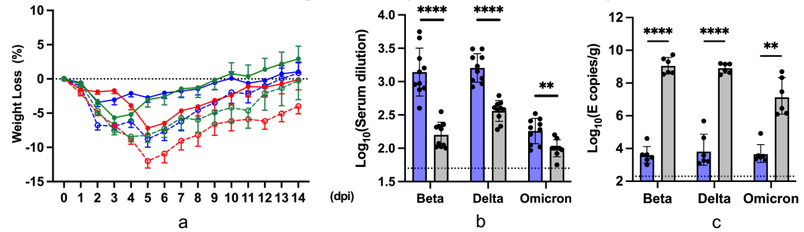


Result 3. Single-dose HD-Ad-FS protected hamsters from SARS-CoV-2 challenge. **(a)** Body weight was monitored after challenging. Two-way ANOVA. **(b)** Serum neutralizing antibody titers. **(c)** Levels of SARS-CoV-2 RNA of oropharyngeal swabs. **(d)** Levels of SARS-CoV-2 RNA in lungs. Mann–Whitney test.

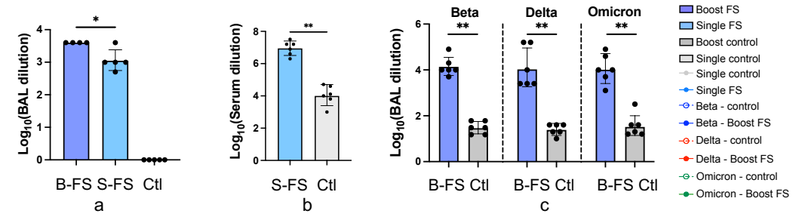


Results

Result 4. Prime-boost HD-Ad-FS protected hamsters from SARS-CoV-2 variant infection. (a) Body weight was monitored after challenging. Two-way ANOVA. **(b)** Serum neutralizing activities at 14 dpi. **(c)** Levels of SARS-CoV-2 RNA in lungs at 4 dpi. Mann–Whitney test.



Result 5. Vaccination of HD-Ad-FS elicited FS-specific secretory IgA (sIgA) responses in BALs and IgG responses in sera and BALs. (a) sIgA in BALs of BALB/c mice. **(b)** IgG in sera of single-dose hamsters. **(c)** IgG in BALs of prime-boost hamsters. Mann–Whitney test.



Conclusions

Our unpublished results demonstrated that the HD-Ad is a promising platform for SARS-CoV-2 vaccine. In challenged animals, intranasal immunization of HD-Ad-FS was safe and induced potent systemic and airway mucosal immunities. The airway mucosal immunities protected against SARS-CoV-2 in the upper and lower airways and against variants in the lower airways.

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