Spike-V987H Vaccination Protects Animal Models From SARS-CoV-2 Induced Severe Disease

392

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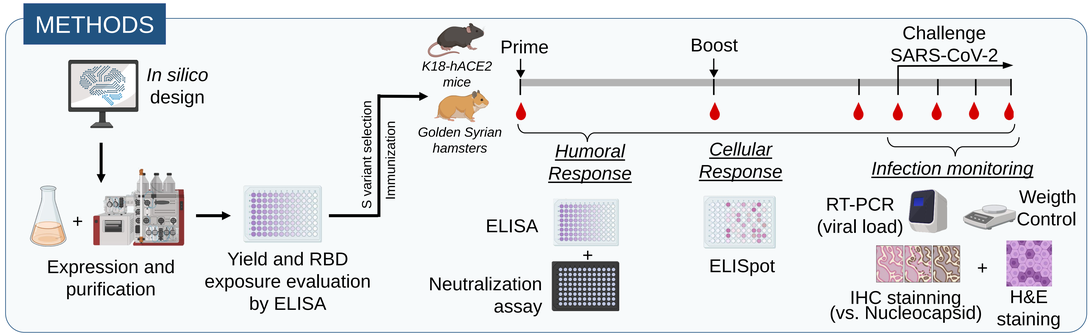
BACKGROUND

- Most SARS-CoV-2 vaccines are based on the Spike (S) glycoprotein and include a double mutation to stabilize its prefusogenic conformation (K986P/V987P, S-2P). These mutations improve stability, yield, and immunogenicity.
- However, S-2P is still poorly produced and maintains some structural motility, and the RBD can be found in an up or down conformation.

OBJECTIVES

- To perform an *in silico* design of novel stabilized S glycoproteins and evaluate their *in vitro* production and RBD exposure.
- To evaluate the *in vivo* immunogenicity and efficacy of a novel stabilized S glycoprotein against SARS-CoV-2 infection and induced disease.

METHODS



RESULTS

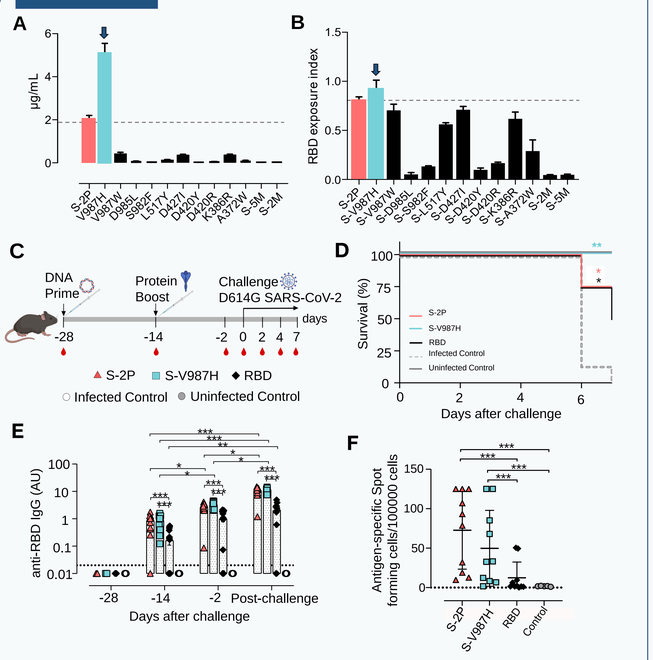


Figure 1. S-V987H immunization protects K18-hACE2 mice against SARS-CoV-2 D614G variant. a Production of recombinant proteins. **b** RBD exposure index. **c** Overview of vaccination and infection strategy. Blood drops indicate collection of biological sample. **d** Survival rate of mice after infection. **e** Kinetics of anti-RBD IgGs. **f** Spike-specific T cell responses determined by ELISpot as IFN-γ producing splenocytes.

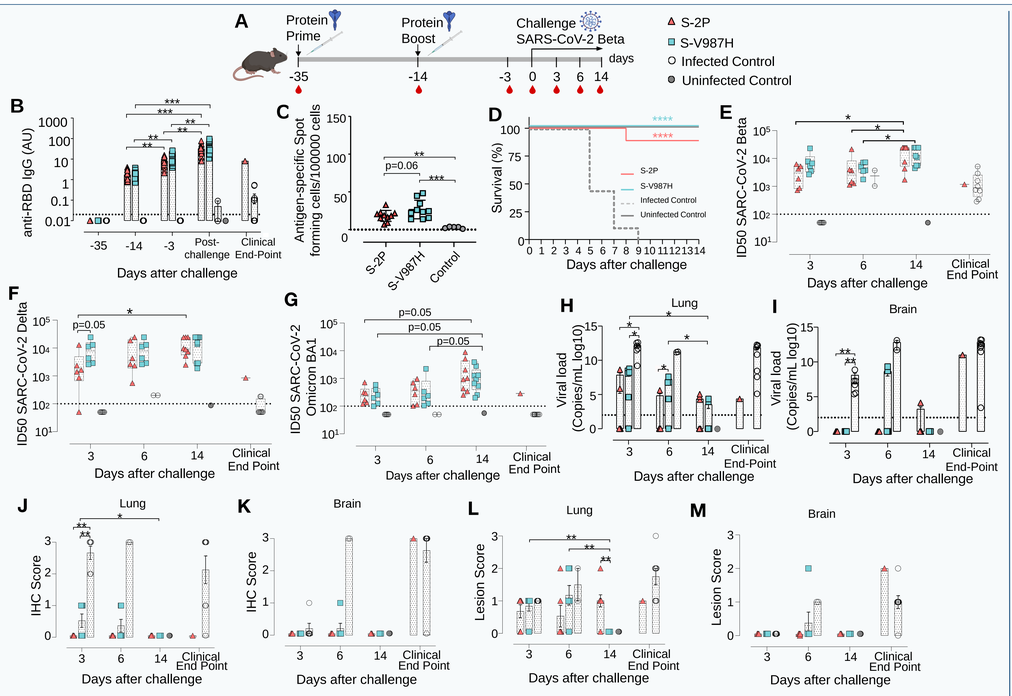


Figure 2. S-V987H immunization protects K18-hACE2 mice against SARS-CoV-2 Beta variant infection. **a** Vaccination and infection timeline. **b** Levels of anti-RBD IgGs. **c** Spike-specific T cell responses determined by ELISpot as IFN-γ producing splenocytes. **d** Survival rate of mice after infection. **e** Neutralization levels against SARS-CoV-2 Beta, **f** Delta, and **g** Omicron. **h** Levels of SARS_CoV-2 gRNA in lung and **i** brain. **j** SARS-CoV-2 N protein levels determined by immunohistochemistry in lung and **k** brain. **l** Histopathological analysis in lung and **m** brain.

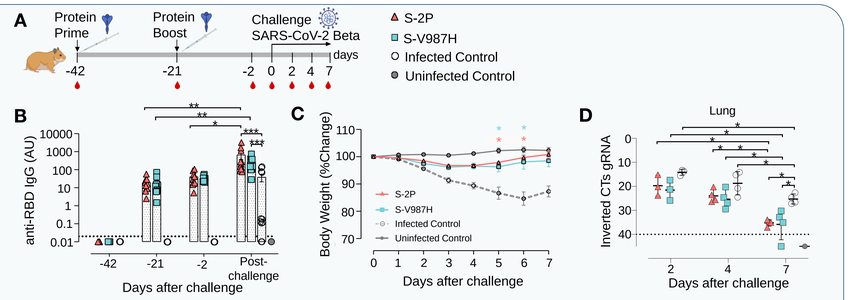


Figure 3. S-V987H immunization protects golden Syrian hamsters upon SARS-CoV-2 Beta variant challenge. a Overview of vaccination and challenge strategy. **b** Kinetics of anti-RBD IgGs. **c** Weight variation after SARS-CoV-2 Beta challenge. **d** Levels of SARS-CoV-2 gRNA expressed as cycles threshold (CTs) in lung

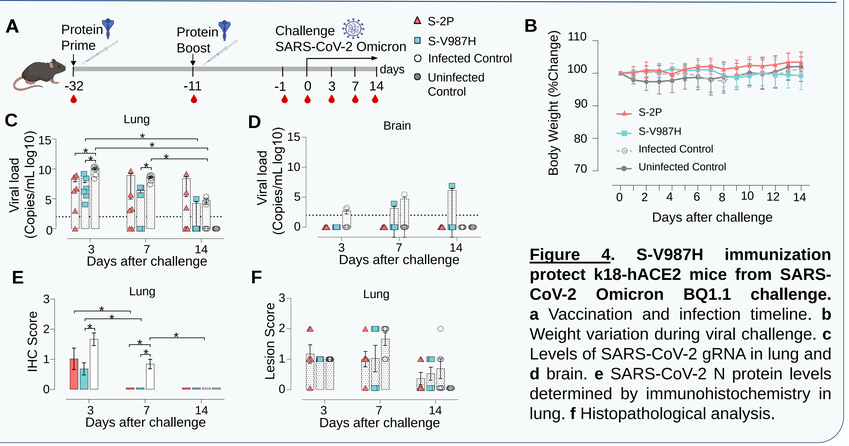


Figure 4. S-V987H immunization protect k18-hACE2 mice from SARS-CoV-2 Omicron BQ1.1 challenge. a Vaccination and infection timeline. **b** Weight variation during viral challenge. **c** Levels of SARS-CoV-2 gRNA in lung and **d** brain. **e** SARS-CoV-2 N protein levels determined by immunohistochemistry in lung. **f** Histopathological analysis.

CONCLUSIONS

We described the mutation V987H that increased S glycoprotein production compared with the S-2P and maintained the immunogenicity elicited by the S-2P variant. S-V987H immunization conferred a higher degree of protection against SARS-CoV-2-induced disease in K18-hACE2 mice and golden Syrian hamsters. Thus, these novel S protein may provide an alternative to S-2P to be used in future SARS-CoV-2 vaccine strategies.

TAKE HOME MESSAGE

S-V987H showed **high yield** and **protects** K18-hACE2 mice and hamsters from SARS-CoV-2 induced disease

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