

# RECOMBINANT VSV VECTOR FOR COVID-19 VACCINE OR DRUG SCREENING

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**Background:** Recombinant vesicular stomatitis virus (VSV) has successfully been used to create a vaccine for Ebola virus that is currently on the market. Previously, Professor Sean Whelan and colleagues have exploited the VSV platform to create similar vectors for both SARS and MERS.

**Technology:** The Whelan Lab has now genetically engineered a potential VSV vaccine candidate for COVID-19 by replacing the single viral envelope glycoprotein (G) of VSV with a modified version of the spike protein (S) of SARS-CoV-2. This replication-competent chimeric VSV-SARS-CoV2 virus has demonstrated immunogenicity and efficacy in mice with high titers of neutralizing antibodies. Overall, it protects against severe SARS-CoV-2 infection and lung disease, supporting its further development as an attenuated vaccine with the potential for low-cost manufacturing.

In addition, a related GFP-VSV reporter construct could be used as a screening platform for COVID-19 drug candidates (e.g., new antibody therapies or small molecule entry inhibitors).

## **In vivo efficacy in mice:**

- **High titers:**
  - the recombinant virus produces high titers of neutralizing antibodies that target both the SARS-CoV-2 spike protein and the receptor binding domain subunit
  - median and mean serum neutralizing titers of greater than 1/5,000
  - two doses induced higher neutralizing titers (1/2,700,000) with more rapid onset
- **Protection:**
  - immunized mice challenged with human SARS-CoV-2: had profoundly reduce viral infection; had decreased induction of pro-inflammatory cytokines; and were protected from lung inflammation and viral pneumonia
  - passive transfer of sera from immunized mice protected naïve mice (decreased viral burden and lung inflammation)
- **Research in progress** includes experiments on non-human primates.

## **Value proposition**

- **Robust response:**
  - strong neutralizing antibody responses which are boosted by a second dose
  - protects against infection, inflammation and pneumonia
- **Potential for simple, large-scale manufacturing:** grows efficiently in mammalian cell culture with high titers (e8 infectious units per ml in Vero cells) which could provide a cost-efficient and effective route for vaccine development
- **Advantages of VSV Vaccine Platform:**
  - established efficacy in humans with Ebola vaccine
  - stimulates both humoral and cellular immunity
  - little pre-existing human immunity

- **Related reporter construct** that could be used to screen for therapeutics

**Publications:**

- Case, J. B., Rothlauf, P., Chen, R. E., Kafai, N., Fox, J. M., Shrihari, S., ... & Bloyet, L. M. (2020). [Replication-competent vesicular stomatitis virus vaccine vector protects against SARS-CoV-2-mediated pathogenesis](#). bioRxiv.
- Case, J. B., Rothlauf, P. W., Chen, R. E., Liu, Z., Zhao, H., Kim, A. S., ... & Ilagan, M. (2020). [Neutralizing antibody and soluble ACE2 inhibition of a replication-competent VSV-SARS-CoV-2 and a clinical isolate of SARS-CoV-2](#).

**Patent status:** Application filed

**Related Web Links:** [Sean Whelan profile](#)