Washington University in St. Louis
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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