Washington University in St. Louis
Office of Technology Management

ADENOVIRUS- HUMAN ACE2 TRANSDUCTION SYSTEM TO SENSITIZE MICE TO SARS-COV-2

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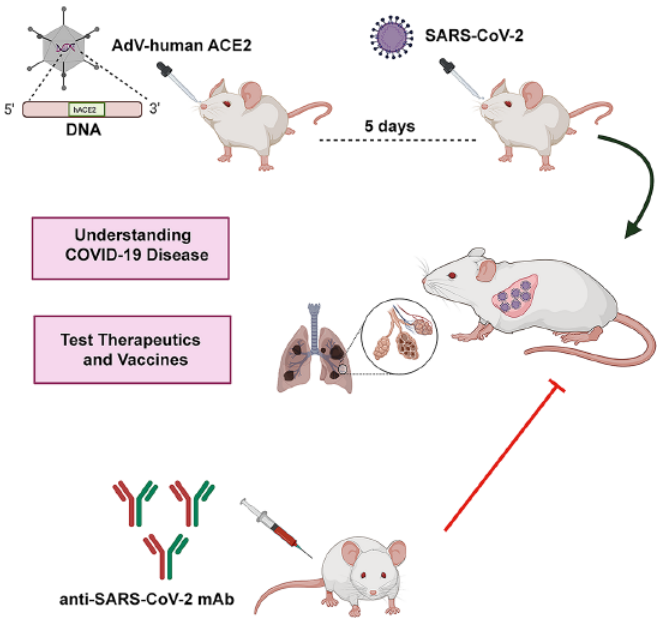
T-019482

Technology Description

Researchers at Washington University in St. Louis have developed a method to sensitize commercially available laboratory mice to SARS-CoV-2 infection. SARS-CoV-2 is the cause of the coronavirus disease 2019 (COVID-19) pandemic that has had severe morbidity and mortality impacts and destabilized society. There is an urgent need for antiviral therapeutics and protective vaccines. However, development of treatments has been hampered by a lack of readily available mouse models to test therapeutics. This is due to species specific differences between human and mouse angiotensin-converting enzyme 2 (ACE2). SARS-CoV-2 binds human ACE2 as a cellular receptor for viral entry and infection, however it does not bind mouse ACE2. Thus, easily accessible laboratory mice cannot be used as testing models. To overcome this limitation the inventors have developed a method to sensitize commercially available mice to SARS-CoV-2. They have transduced replication-defective adenoviruses encoding human ACE2 (hACE2) via intranasal administration into BALB/c mice, which sensitized them to productive SARS-CoV-2 infection and pneumonia. This technology provides the means to create accessible mouse models for studying SARS-CoV-2 infection.



Mice transduced with adenoviruses encoding human ACE2 are permissive for SARS-CoV-2 and develop pneumonia. Passive transfer of neutralizing monoclonal antibody reduces lung infection, inflammation and disease.

Stage of Research

The inventors have shown that their adenovirus- human ACE2 (AdV-hACE2) transduction system renders commercially available mice susceptible to SARS-CoV-2 lung infection, clinical disease and pathology.

Publications

- Hassan, A.O., Case, J.B., Winkler, E.S., Thackray, L., Kafai, N.M., Bailey, A.L., McCune, B.T., Fox, J.M., Chen, R.E., Al Soussi, W.B., Turner, J.S., Schmitz, A.J., Lei, T., Shrihari, S., Keeler, S.P., Fremont, D.H., Greco, S., McCray Jr., P.B., Perlman, S., Holtzman, M.J., Ellebedy, A.H., Diamond, M.S., A SARS-CoV-2 infection model in mice demonstrates protection by neutralizing antibodies, Cell (2020), doi: https://doi.org/10.1016/j.cell.2020.06.011.
- Bhandari, T. COVID-19 mouse model will speed search for drugs, vaccines. The Source from Washington University in St. Louis, June 10, 2020.

Related technology

The adenovirus- human ACE2 (AdV-hACE2) transduction system has been used to sensitize mice to SARS-CoV-2 to aid in the development of a chimpanzee adenovirus-based vaccine for COVID-19 (see WUSTL technology T-019478).

Applications

- Create mouse models of SARS-CoV-2 infection
    - Accelerate development and testing of therapeutics and vaccines
    - Study COVID-19 disease

Key Advantages

- Enables creation of accessible mouse models for studying SARS-CoV-2 pathogenesis
- Transduction system can be used immediately in a variety of mouse models
- Can accelerate the pace of screening, identification and development of therapeutics and vaccines to fight SARS-CoV-2infection

Related Web Links

Dr. Diamond profile