Single Domain Antibodies (Nanobodies) Targeting SARS-CoV-2 for treating COVID-19

Summary (1024-character limit)
The National Cancer Institute (NCI) seeks research co-development partners and/or licensees for a panel of single domain antibodies (nanobodies) that target the spike (S) protein of SARS-CoV-2.

NIH Reference Number
E-253-2020

Product Type
• Therapeutics

Keywords
• SARS-CoV-2, COVID-19, Spike Protein, S Protein, Nanobody, Antibody, Antigen-binding Fragment, Coronavirus, Respiratory Infection, Ho

Collaboration Opportunity
This invention is available for licensing and co-development.

Contact
• John D. Hewes
  NCI - National Cancer Institute
  240-276-5515
  John.Hewes@nih.gov

Description of Technology
The COVID-19 pandemic is a worldwide public health crisis with over 100 million confirmed cases and 2.4 million deaths as of February 2021. COVID-19 is caused by a novel coronavirus called SARS-CoV-2. SARS-CoV-2 infects hosts via its spike (S) protein. The S protein contains the receptor binding domain (RBD) that binds to the angiotensin converting enzyme 2 (ACE2) receptor on human cells to facilitate viral entry and infection. There are few therapeutics available for COVID-19 patients that directly target SARS-CoV-2.

Investigators at the National Cancer Institute (NCI) have isolated a panel of anti-RBD single domain antibodies (also called ‘nanobodies’) from camel single domain (VHH) phage display libraries. RBD is an ideal target as it is the key virus-host contact region required for viral entry and infection. There are 3 lead nanobodies, 7A3, 1B5, and 2F7, which were found to be the most potent RBD-ACE2 blockers. Interestingly, the 1B5 nanobody can cross react with the S protein of the previous 2002-2003 SARs-CoV coronavirus. This indicates that this nanobody targets a conserved region of the S protein and may be
useful for treatments against other coronavirus variants that may emerge.

Nanobodies are the smallest known antigen-binding fragments of antibodies and have several advantages. Due to their small size, high solubility, thermal stability, refolding capacity, and relatively easy tissue penetration, they have great potential as medical applications and research tools. These nanobodies can be used as either independent agents or targeting domains in recombinant immunotoxins (RITs), antibody-drug conjugates (ADCs), and chimeric antigen receptors (CARs). Due to their small size and high stability, the nanobodies may have the ability to be administered by an inhaler making them uniquely attractive therapeutics for respiratory infections such as COVID-19.

The NCI seeks licensing and/or co-development research collaborations for these SARS-CoV-2 targeting nanobodies.

**Potential Commercial Applications**
- Neutralizing nanobodies
- Nanobody-Fc fusion proteins as standard antibody therapy
- Antibody-drug conjugates (ADCs)
- Immunotoxins
- Diagnostic reagents (in vivo virus imaging)
- CARs (CAR T, NK, and macrophage)

**Competitive Advantages**
- The nanobodies directly target the receptor binding domain (RBD) of the SARS-CoV-2 spike (S) protein, which blocks the virus-host contact region required for viral entry and infection
- Due to their small size and high stability, the nanobodies may be administered by an inhaler making them ideal for respiratory infections such as COVID-19

**Inventor(s)**
Mitchell Ho Ph.D. (NCI), Jessica Hong (NCI)

**Development Stage**
- Discovery (Lead Identification)

**Patent Status**
- **U.S. Provisional:** U.S. Provisional Patent Application Number 63/105,769, Filed 26 Oct 2020

**Therapeutic Area**
- Infectious Diseases