BROAD-SPECTRUM THERAPEUTICS FOR VIRAL DISEASES: A MEDICAL COUNTERMEASURE PLATFORM FOR EMERGING THREATS

Treatment And Prevention Of Respiratory Pathogens By Use Of A Modified Mannose Binding Lectin Based Aerosolized Nasal Spray

David Trudil New Horizons Diagnostics Corp **Michael Super** Wyss Institute for Biologically Inspired Engineering at Harvard University **Larry Loomis** New Horizons Diagnostics Corp **Richard Ascione** Georgetown Medical University

To counter the spread of respiratory virus including Covid-19 and enable its immediate treatment as a localized infection, we are evaluating the use of an easily applied, natural-protein-based aerosolized nasal spray that would bind many varieties of respiratory virus including all coronavirus, irrespective of mutations and thus neutralize and reduce viral spread. Importantly for those who appear asymptomatic, as well as for the further systemic spread within the lungs of self-same individual, this therapeutic activates the users innate immune systems immediately even before antibody production. Further, the therapeutic subsequently triggers signals activating the multiple arms of our immune system including: the innate immune system; the mucosal immune system; the serum antibody system; as well as theour Natural Killer (NK) and T-cell system.

The respiratory virus enters the body by the nasal (nasopharyngeal) route ultimately expanding into our lungs causing, too often, lethal disease. Thus, the Nasal Therapeutic by blocking the pathogen at its portal deploys a natural protein designed to do just that. The nasal therapeutic's immediate action – via the innate immune system, uses a modified mannose-binding lectin (mMBL), that has been scientifically established as an important class of first-line inhibitors, which are unique defensive proteins present in all species of animals. Mannose is a sugar-type molecule commonly found as the terminal sugar on glycoproteins in all pathogenic (bacterial and viral) microorganisms and not present on healthy human cells. MBL's are capable of recognizing these foreign targets, and bind to the mannosylated glycosyl(sugar)-linked proteins that cover the surfaces of these invaders e.g. SARS CoV-2 spike proteins, thereby blocking them from entering the cells. The MBL's have a unique capability to signal our innate immunity within minutes, by chemical alarms, calling on the other immune systems for help; informing it that we have encountered invaders that might harm us and alerting our entire immune systems to deter entry, establishment and damage by "foreign" entities; by stimulating potent interdiction with killer-phagocytic circulating cells and by neutralizing/blocking antibodies.

The utilization of the MBL was developed under a DARPA contract for response to sepsis. In this project FcMBL was conjugated to a dialysis filter at up to 400 mL /min (2400 mL/hr). Clearance of live pathogens as well as dead pathogen debris/PAMPs from blood in vitro and in sepsis animal models (Rat and pig) was demonstrated. The FcMBL was tested binding to clinical pathogen isolates and it was established that FcMBL binds > 120 different pathogen species – bacteria (e.g. MRSA, E. coli, M. tuberculosis, K. pneumoniae, P. aerugionosa), viruses (e.g. SARS Cov-2, HIV, CMV, HSV), Fungi (e.g. C. albicans, C. auris) and parasites (e.g. P. vivax, S. gambiense)and toxins, (e.g. LPS endotoxin from Gram negative, WTA wall teichoic acid from Gram positive bacteria). CGMP material was produced ans phase 1 trails conducted.

The Therapeutic will be a nanoparticulate, aerosolized easily deliverable substance, easy to manufacture and distribute, without need of syringes, extensive refrigeration, or highly skilled health care workers to administer.

MBL developed under DoD projects::
DARPA DLT1 (Dialysis -Like Therapeutic): BAA-11-30 (Grant #N66001-11-1-4180)
DARPA DLT2: BAA-12-36 (Contract #HR001-13-C-0025)
DARPA THOR (Technologies for Host Resilience): BAA-15-21(Grant #W9111NF-16-C-0050)
The modified Stem FcMBL can be found in WO2017024114-APBDY-20170209-6056. (The Harvard number is HU5789).