Welcome to the third installment of DARPA’s ongoing web series highlighting the agency’s active programs focused COVID-19 medical countermeasure technologies.

DARPA has several programs actively engaged in developing safe and efficacious treatments for COVID-19, including:

**Electrical Prescriptions (ElectRx)**

The Electrical Prescriptions (ElectRx) program aims to support military operational readiness by reducing the time to treatment, logistical challenges, and potential off-target effects associated with traditional medical interventions for a wide range of physical and mental health conditions commonly faced by our warfighters. ElectRx seeks to deliver non-pharmacological treatments for pain, general inflammation, post-traumatic stress, severe anxiety, and trauma that employ precise, closed-loop, non-invasive modulation of the patient’s peripheral nervous system.

ElectRx performers at GE and the University of Minnesota are using non-invasive ultrasound that has previously been demonstrated in humans to modulate immune response to now treat patients diagnosed with COVID-19. A new clinical study is planned at the University of Minnesota to demonstrate that the non-invasive ultrasound, delivered for a few minutes each day, triggers specific gene expression pathways to ensure patients do not develop an overwhelming immune response.

**INTERfering and Co-Evolving Prevention and Therapy (INTERCEPT)**

DARPA’s INTERfering and Co-Evolving Prevention and Therapy (INTERCEPT) program aims to harness viral evolution to create a novel, adaptive form of medical countermeasure – therapeutic interfering particles (TIPs) – that outcompetes viruses in the body to prevent or treat infection.

INTERCEPT researchers at Los Alamos National Laboratory are currently collaborating with experimental labs to develop state-of-the-art methods to computationally model the spread of COVID-19, while performers at Autonomous Therapeutics Inc., are working to develop novel medical countermeasures to combat the disease and other respiratory infections.

**Panacea**

Panacea aims to generate a platform capability that enables rapid discovery of novel drug targets, and to provide the means to synthesize molecules to effectively engage those targets.
As part of the program, an international team of more than 120 scientists has detailed the impact of 75 over-the-counter prescription and development-stage drug compounds on SARS-CoV-2, the virus that causes COVID-19. Several of these agents show promise in blocking SARS-CoV-2 replication in laboratory experiments. One compound investigated in the research, a common ingredient in over-the-counter cough medicines, appears to have the potential to promote the growth of the virus.

The collaborative study, published in Nature on April 30, 2020, was assembled and led by Nevan Krogan, PhD, director of the Quantitative Biosciences Institute at UC San Francisco and a senior investigator at Gladstone Institutes. Rather than focusing on an antiviral approach to block SARS-CoV-2, the researchers first combined biological and computational techniques to create a “blueprint” of more than 300 human proteins that the virus requires to infect human cells and to thrive and replicate in the body. They then explored the question of which drugs, both those that are currently marketed as well as those in development, might be repurposed to treat SARS-CoV-2 infection by targeting those human proteins.

These same teams also published research in Cell (June 28, 2020) demonstrating that SARS-2 rewires cellular pathways interfering with the function of kinase-induced activity called phosphorylation – the addition of a phosphoryl group to a protein by an enzyme class called kinases, plays a pivotal role in the regulation of most cell processes including the production of the cytoskeleton, protein function, cell-to-cell communication, cell growth and cell death. They also identified that virally infected cells exhibit long filopodia, stringy arm-like extensions, which may explain [rapid] viral spread throughout the body.

PREPARE

Also mentioned in our piece on virus detection, the PREPARE program is leveraging investments towards the development of CRISPR-based antivirals that can directly neutralize and “shred” viral genomes to defeat SARS-CoV-2. Efforts are also exploring simple delivery to the tissue and organs where the countermeasures can be most effective. CRISPR-based antivirals offer a platform with the potential to be quickly re-programmed to defeat emergent viral threats based on pathogen sequence alone.

A recent piece in the New York Times entitled “Old Drugs May Find a New Purpose: Fighting the Coronavirus” features some PREPARE and Panacea performers.

Pandemic Prevention Platform (P3)

P3 focuses on rapid discovery, characterization, production, testing, and delivery of efficacious DNA- and RNA-encoded medical countermeasures against infectious disease, a foundational technology pioneered by DARPA under the Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program that provides the body with instructions on how to immediately begin producing protective antibodies against a given threat.
Just two years into a four-year program, P3 has performers at Abcellera Biologics, AstraZeneca, Duke University and Vanderbilt University, all of whom have been able to quickly pivot to rapidly identify antibodies for COVID-19 in less than 90-days. This process traditionally takes several years to complete.

Abcellera announced in June that their DARPA-funded rapid pandemic response platform contributed to the world’s first clinical trial for a potential monoclonal antibody therapy that targets the SARS-2 virus. Abcellera was able to obtain a sample of blood at the end of February via an intergovernmental panel, and identified over 1,000 potential candidates. They, along with the other performers, began testing for how well these antibodies bind to the virus, how well they neutralize the virus (to prevent them from entering human cells), and how well they can be manufactured/grown. As part of this work, they were able to hone in on one antibody they felt would best to take forward to Phase I clinical trials.

The performers have initiated ongoing testing in animal models, including a novel golden hamster model, and anticipate starting a Phase I therapy study in hospitalized patients with moderate disease in the next 1-2 months, moving on to patients with more severe symptoms.

Abcellera has since entered into a manufacturing agreement with Eli Lilly separate from their agreement with DARPA’s P3, and on August 3 announced that LY-CoV555, a human antibody discovered by AbCellera in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC) and co-developed with Eli Lilly and Company (Lilly) as a potential treatment and prophylaxis for COVID-19, has progressed to Phase 3 clinical trials.

For more information on the highlighted programs, we invite you to visit the appropriate program page.

Please continue to follow this space for timely updates on DARPA’s portfolio of pandemic prevention efforts, including installments focused on the prevention and manufacture of medical countermeasures to combat COVID-19.