Damon Runyon Scientists Help in the Global Effort Against COVID-19

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Since COVID-19 cases escalated to pandemic levels worldwide, Damon Runyon scientists are contributing to the unprecedented global effort to stop the disease by investigating how this specific coronavirus enters human cells, developing more efficient testing and searching for a treatment. While Damon Runyon's focus is on cancer, these projects demonstrate how our approach of funding brilliant scientists doing cutting-edge basic, laboratory research can result in benefits for patients in all areas of health.

Researchers Find that New York City Coronavirus Strains of European Descent

A team led by Former Damon Runyon Fellow Adriana Heguy, PhD, has sequenced the genetic code for SARS-CoV-2 viruses taken from 91 New York City patients to determine the origins of the city's COVID-19 outbreak and spread. The latest research from New York University's Grossman School of Medicine found that the new coronavirus strains began to circulate in the New York area weeks before the first confirmed case on March 1 and that travelers brought in the virus mainly from Europe. Independently, another group from Mount Sinai reached similar conclusions about the origin of the New City outbreak.

Identifying greater numbers of local SARS-CoV-2 genome sequences allows better monitoring of the spread and severity of the disease, and clarifies which drugs, vaccines, or social interventions are most effective here, said Dr. Heguy, director of the Genome Technology Center at NYU Langone.

The genetic code of SARS-CoV-2 is contained in a strand of RNA (similar to DNA) with 29,900 chemical letters called nucleotides. Viruses must invade a host cell and take over its molecular machinery to make new virus copies. During this replication process, changes (mutations) occur in the genetic code, causing viral genomes to continually, randomly evolve.

Once researchers have sequenced the genomes of many virus samples, they can compare their mutations using computer programs. As viruses evolve during transmission from person to person,

the differences in their sequences can help zero in on where the virus originated and how it traveled geographically.

As new genomes are identified, researchers from around the world upload them to an online database called GISAID. Experts are analyzing the growing collection of genomes in a global effort called Nextstrain, which continually updates the coronavirus family tree.

Dr. Heguy's future plans include sequencing 192 viral samples per week in order to collect thousands of viral sequences for future analysis.

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How You Can Help Scientists Understand COVID-19

Without widespread testing, researchers and physicians have faced challenges in developing an accurate picture of coronavirus symptoms and spread in the United States. Former Damon Runyon Clinical Investigator Andrew T. Chan, MD, MPH, at Massachusetts General Hospital, is leading an effort to stay a step ahead of COVID-19 by using a new free app that will gather information from millions of people to help identify those at risk sooner and help slow the outbreak of the disease.

Information about those who remain symptom-free while others become severely ill or die will support a better understanding of COVID-19. The app also includes questions for cancer patients and survivors, who may be at increased risk for getting COVID-19.

"This may be a better way to find out where hot spots of spread are, new symptoms to look out for, and use as a planning tool to target quarantines, send ventilators and medical equipment and provide real-time data to plan for future outbreaks," said Chan.

The COVID Symptom Tracker asks contributors to answer a few simple questions about themselves and their current health, then check-in every day to say whether they're feeling fine or have noticed any new symptoms. Anyone can take part by downloading the free COVID Symptom Tracker app on iOS from the Apple App Store or Android from the Google Play store through https://covid.joinzoe.com/.

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Scientists Develop More Efficient Diagnostic Tests

Diagnostic tests for COVID-19 are a top priority to track the spread of the disease. A new test based on the CRISPR machinery's ability to recognize specific genetic sequences and cut them is being developed at the Broad Institute of Massachusetts Institute of Technology (MIT) and Harvard. Former Damon Runyon Innovator Feng Zhang, PhD, has co-developed SHERLOCK to

quickly detect SARS-CoV-2, the new coronavirus which causes COVID-19. When CRISPR recognizes the genetic material of the coronavirus, it cuts a 'reporter' molecule added to the reaction, which appears as a line on a paper strip, indicating a positive reaction. The test has worked with Zika virus detection previously and can be completed in less than an hour. Zhang has sent some 1,600 kits to a dozen labs around the world to validate and optimize the test.

Former Damon Runyon Fellow Pardis C. Sabeti, MD, DPhil, and colleagues at the Broad Institute are designing sensitive tests for detecting 67 viruses including SARS-CoV-2. The researchers have created a website containing CRISPR-Cas13-based test designs to detect respiratory viruses, which is accessible to all researchers. The research team hopes these design resources and protocols are a useful step toward creating a system for detecting COVID-19 in patient samples using a simple readout.

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Understanding How SARS-CoV-2 Infects Cells

Just as important as efficient, reliable test kits is understanding how the coronavirus infects cells. Damon Runyon Fellow Jose M. Ordovas-Montanes, PhD, and colleagues at the Broad Institute of Massachusetts Institute of Technology and Harvard, discovered new mechanisms of how SARS-CoV-2 takes advantage of ACE2 and another protein called TMPRSS2 on respiratory cells to promote infection. ACE2 reduces blood pressure and inflammation, but also provides a "door" for the virus to insert its genes into a host cell and co-opt the cell's genetic machinery to produce viral proteins that come together forming millions of new virus particles. Stopping the virus from infecting cells may be one way of treating COVID-19.

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The Search for Treatments

Sponsor Kevan M. Shokat, PhD, Damon Runyon Fellow Ziyang Zhang, PhD, and Former Damon Runyon Fellow Brian K. Shoichet, PhD, are part of a large collaboration at the University of California, San Francisco, looking for drugs that can block the interaction between viral and human proteins. Focusing on 26 of the coronavirus's 29 genes that produce viral proteins related to infection, the researchers uncovered 332 human proteins targeted by the coronavirus.

They used this information to find drugs that latch onto the human proteins to prevent SARS-CoV-2 entry and replication in human cells. The team identified 24 FDA-approved drugs to treat such seemingly unrelated diseases as cancer, Parkinson's disease and hypertension. Repurposing known drugs holds the advantage that they have already gone through safety trials. If the research effort succeeds, it will significantly shorten the drug discovery process.

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