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Commentary

NCI's Work to Advance Cancer Research while Responding to the COVID-19 Pandemic

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During the COVID-19 pandemic, the National Cancer Institute (NCI) is bringing to bear its considerable expertise and capabilities to understand, treat, and prevent the disease. While responding to the pandemic, NCI's priority remains the advancement of cancer research. NCI has implemented many flexibilities for grantees and trainees.

We are in the midst of an unprecedented deadly pandemic that has caused tremendous upheaval. As scientists, as public servants, and as human beings, we at NCI embrace what we consider a moral obligation to respond to this global public health crisis to the extent that we are able.

Like many government agencies and research institutions around the world, we are adapting to the situation and contributing to efforts to tackle the novel coronavirus, SARS-CoV-2. NCI has brought to the fore considerable expertise in virology and numerous unique research capabilities and capacities to contribute to the worldwide effort to better understand and mitigate COVID-19.

However, cancer has not come to a halt during this period, nor have the needs of people with cancer. As the world's largest cancer research organization, we remain committed to sustaining progress against cancer. While acting quickly to address COVID-19, one of the newest diseases of humankind, NCI's number one priority is, and always will be, advancing cancer research and reducing the burden of cancer.

Frederick National Laboratory for Cancer Research Central to SARS-CoV-2 Research

In particular, we have pivoted some of the capacities and resources of the Frederick National Laboratory for Cancer Research (FNLCR), which houses cutting-edge technologies and research resources dedicated to biomedical research that are directly relevant and tailor-made to respond to this viral pandemic. FNLCR scientists have worked on earlier virus epidemics, including SARS, Ebola, and Zika,

in collaboration with experts from the National Institute of Allergy and Infectious Diseases (NIAID).

FNLCR recently worked closely with NIAID, the Centers for Disease Control and Prevention (CDC), and several academic medical centers on the recent clinical trial of the antiviral remdesivir for patients who are seriously ill with COVID-19. NCI, in partnership with NIAID and the National Human Genome Research Institute, has also begun a series of genomics studies at FNLCR to identify genetic variants associated with outcomes in both cancer and non-cancer patients with COVID-19. The goal is to identify potential targets for new treatments and provide valuable insights that can be used for screening purposes.

The HPV Serology Lab at FNLCR has been temporarily repurposed to work on antibody testing for the novel coronavirus. Outside scientists and companies developing tests to identify antibodies in the blood of those who have been infected and have evidence of immunity against COVID-19 have submitted tests to the Food and Drug Administration (FDA). Within a month, FNLCR became a major testing site to rapidly and rigorously validate the performance of those tests on behalf of FDA. It is still not clear whether the presence of positive antibodies in the blood is indicative of resistance to reinfection with the virus. This is the subject of ongoing research.

The clear potential of this serological work has resulted in an additional \$306M in supplemental funding to NCI from Congress to support further serology research to develop, validate, improve, and implement serological testing.

A Nationwide Infrastructure that Facilitates COVID-19 Research

While NCI has moved swiftly, sometimes in a matter of days, to develop and launch new research efforts to address the pandemic, we understand that we won't be successful alone. That's why we are expanding our robust partnerships and collaborative relationships with other federal entities, public health institutions, and private sector companies to expedite progress in understanding, treating, and preventing the deadly viral disease. Many scientists and clinicians within NCI's large networks of academic centers are experienced in conducting complex clinical trials and are temporarily pivoting some cancer research activities, including clinical trials, epidemiological studies, and basic research, to examine the impact of SARS-CoV-2 on cancer.

Based on the widespread reports of cytokine storm associated with COVID-19, NCI is conducting a compassionate-use trial of tocilizumab (Actimra), which blocks the inflammatory protein IL-6. Cytokine release syndrome, a hyperactive immune response, is one of the potentially fatal adverse effects of cancer immunotherapies that NCI researchers are familiar with and are studying. Given their experience with this syndrome, NCI quickly launched the trial and is conducting it with adult and pediatric patients affected by cancer and COVID-19 who have severe respiratory complications thought to be caused by cytokine storm. The protocol will evaluate whether the anti-IL6R antibody will reduce time on ventilators and time in the intensive care unit for these patients. Genentech, the drug manufacturer, is making the drug



Box 1. NCI COVID-19 Funding Opportunities

Availability of Competitive Revision SBIR/STTR Supplements on Coronavirus Disease 2019 (COVID-19): NOT-CA-20-043
 Availability of Urgent Competitive Revision and Administrative Supplements on Coronavirus Disease 2019 (COVID-19): NOT-CA-20-042
 Participation in PA-18-935 “Urgent Competitive Revision to Existing NIH Grants and Cooperative Agreements (Urgent Supplement - Clinical Trial Optional)”: NOT-CA-20-048
 Contributing to the Global COVID-19 Crisis Response by Allowing Some NCI-Supported Projects to be Redirected to COVID-19-Related Research during the Crisis: NOT-CA-20-054
 Please visit <https://www.cancer.gov/coronavirus-researchers> for more information.

available to up to 200 patients who are not able to enroll in their ongoing phase III clinical trials of the drug.

NCI is initiating a longitudinal cohort of cancer patients infected with SARS-CoV-2, called NCI COVID-19 in Cancer Patients Study (NCCaPS). Working through the NCI clinical trials networks and NCI-designated cancer centers, our target is to enroll more than 2,000 patients of all ages with the goal of generating a comprehensive dataset of cancer types, treatments, medications, symptoms, and outcomes. The study will follow the patients for an extended period and will inform our understanding of the risks and course of the virus in people with cancer.

Many NCI-designated cancer centers, on their own or in collaboration with other cancer centers, have also moved rapidly to launch novel therapeutic clinical trials involving cancer patients with COVID-19. One example is the COVID-19 and Cancer Consortium led by the Vanderbilt-Ingram Cancer Center. Because cancer patients may be at increased risk of developing complications from SARS-CoV-2, Vanderbilt has galvanized a group of more than 80 cancer centers and other organizations that are collecting clinical data on cancer patients who have been infected with COVID-19. The intent is to accumulate data as rapidly as possible on this vulnerable population and disseminate the data immediately via an open-access database, since some of what is learned from the data may have practice-changing implications.

In some centers, serology testing is being used to screen blood from those who have had and recovered from COVID-19 for the production of convalescent plasma, antibody-rich blood products that may be potential blood-based thera-

pies for others with serious disease. There is some evidence that convalescent plasma may benefit people who are infected with COVID-19.

Another example of COVID-19 research being conducted in the context of NCI-funded work is the Cancer Moonshot-funded Cellular Immunotherapy Data Resource (CIDR) program, which collects patient metadata associated with cellular therapies. In response to the COVID-19 crisis, CIDR has expanded its focus to collect data on COVID-19 infections and deaths among patients receiving cellular therapy.

Impact of COVID-19 on Cancer Research

Although NCI is responding to the COVID-19 crisis, NCI’s mission, first and foremost, is cancer research and care. NCI is taking steps to help keep the nation’s cancer research enterprise operating to the fullest extent possible. Nonetheless, it’s undeniable that the COVID-19 pandemic has caused an unprecedented disruption throughout the cancer research community, slowed down cancer clinical trial operations, and limited the healthcare system’s resources.

It has indeed become a delicate balancing act to advance cancer science while keeping cancer patients, many of whom are immunosuppressed, and staff safe and protected. Many researchers and institutions have had to pause their laboratory work during this period. Although clinical trials accrual has sharply declined, NCI is working to ensure that cancer center trials offering potentially life-saving therapies and trials where there are no other viable treatment options beyond a clinical trial for patients remain available.

To minimize disruptions to ongoing trials, NCI has worked with FDA’s and

NCI’s clinical trials networks to enable greater flexibility in trial operations. A few of the many adaptations that have been made to enable trials to continue include the following:

- Allowing patients’ local healthcare providers to conduct some study activities that typically require in-person visits to the trial site, such as testing and assessment, under the guidance of the trial investigators.
- Shipping orally administered investigational drugs directly to patients or their local healthcare providers.
- Obtaining informed consent remotely, based on guidance from the central institutional review board.

Supporting Grantees and Trainees during These Uncertain Times

The research of many NCI grantees and intramural researchers has been upended by the pandemic and the need for physical distancing. NCI will exercise all available options to support the cancer research community throughout this difficult period.

We understand that many cancer scientists may want to temporarily focus their attention on contributing to COVID-19 research. To facilitate such work where appropriate, we have announced several funding opportunities and the option of for redirecting current grant resources to COVID-19-related projects that are cancer relevant and can be initiated immediately (Box 1).

We are also aware that the research community is experiencing considerable stress and anxiety about the consequences of COVID-19 on their research grants and careers. NCI is committed to keeping cancer research moving forward. New policies have been

implemented during this crisis with safety and flexibility as priorities. Some of the newly instituted flexible policies include the following:

- Extending deadlines for applications.
- Allowing institutions to use NCI grant funds to maintain salaries and stipends.
- Extending project timelines and reporting requirements.
- Extending eligibility periods for early-stage investigators and trainees.

This flexibility will help sustain progress in cancer research and permit normal activities to resume to their full extent once the pandemic subsides.

Can the Pandemic Have a Silver Lining?

We are undoubtedly living through a terrible time in human history; however, some unexpected positive developments have emerged. The accelerated adoption of telehealth has provided patients and providers with new options and presents a unique implementation science opportunity. We are already seeing that many cancer patients find telehealth more convenient for some aspects of health-care delivery and may want to continue with it in the post-pandemic future. We can examine the impact that telehealth is having on our ability to manage patient care during the pandemic and how telehealth can be most effectively used, and expanded, going forward.

We recognize that the pandemic has disrupted life around the world, and that includes the cancer research enterprise. The novel virus continues to challenge us in unconventional ways and likewise pushes us to be ever more creative and flexible in how we address those challenges. This creativity and flexibility are evident in our research, in how we support grantees and trainees, and in how we communicate.

Our lives will return to normal, albeit a different normal. This disruption in cancer research should be viewed as only a temporary pause. But one fact has and always will remain permanent—NCI's commitment to advancing cancer research and care.