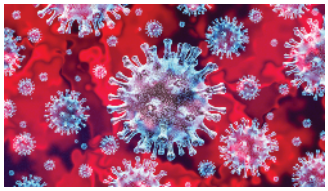
Cancer Labs Pivot to Battle COVID-19

Researchers bring expertise to challenges of diagnostics, treatment, and biospecimen collection

Although most cancer researchers have shuttered their labs to comply with COVID-19–related work restrictions, some have received permission to turn their attention, resources, and technical know-how to tackling the deadly coronavirus (Cancer Discov 2020 Mar 24 [Epub ahead of print]).

Scientists who normally study tumor biomarkers are now pivoting to develop better techniques for diagnosing COVID-19; those with drug-screening experience are exploring therapeutic options; and cancer center biobanks are adapting protocols to allow for safe and timely biospecimen collection from infected patients.



"When there's an important scientific and public health problem—and you have expertise—you think about how you can be helpful," says Wafik El-Deiry, MD, PhD, of the Warren Alpert Medical School of Brown University in Providence, RI.

An expert in cell death signaling, El-Deiry studies the links between *TP53* and the TRAIL pathway in the innate immune control of cancer. Among other experiments, he intends to modify assays for studying natural killer cells and T-cell responses to tumors to explore the role of TRAIL signaling in the immune-mediated clearance of SARS-CoV-2 infections. "There are a lot of open questions," El-Deiry says, "and I think we can have meaningful contributions at the bench."

CRUNCH TIME

With most cancer labs closed for now—save for bare-bones operations to ensure irreplaceable research is not lost—many scientists are catching up on manuscript preparation, grant proposals, and other tasks that can be done at home.

In addition to manuscript writing, Randy Sweis, MD, of the University of Chicago in Illinois, is prioritizing his clinical work, caring for patients with cancer, and covering for colleagues who have been exposed to the virus. However, his laboratory research has not stopped entirely.

When Sweis's research technician, Jeffrey Bloodworth, goes into the lab to maintain colonies of genetically engineered mice, he also develops tests for antibodies to the coronavirus or inhibitors of viral entry. Sweis's group had been developing a high-throughput ELISA-based assay for a project studying FGFR3 activation as a sign of resistance to immune checkpoint blockade. Bloodworth is modifying the technique to identify immune indicators of SARS-CoV-2 exposure.

Working with the human immunologic monitoring facility at his cancer center, Sweis and his colleagues also plan to bank blood, urine, and stool from COVID-19–infected patients. "We have all the infrastructure in place to pretty rapidly collect samples, store them, isolate DNA, and freeze things," he says. "We want to get this going ASAP."

SCIENCE, REPOSITIONED

Displaced from the bench, Feixiong Cheng, PhD, of the Cleveland Clinic in Ohio, turned to computer modeling to find approved therapies that might interfere with human–SARS-CoV-2 interactions. His analysis of drug targets and virus–host interactions found several older cancer drugs—including the chemotherapeutic dactinomycin, the selective estrogen receptor modulator toremifene, and the antineoplastic agent mercaptopurine—that might work (Cell Discov 6, 14 [2020]).

Other modeling efforts have highlighted the anti-coronavirus potential of newer targeted cancer drugs, such as afatinib (Gilotrif; Boehringer Ingelheim), and proteasome inhibitors, such as carfilzomib (Kyprolis; Amgen) and ixazomib (Ninlaro; Takeda; ChemRxiv 2020 Feb 21; ResearchGate 2020 Mar 18).

As described in another report, a team led by members of the Quantitative Biosciences Institute (QBI) Coronavirus Research Group, based at the University of California, San Francisco, experimentally cloned and expressed predicted SARS-CoV-2 proteins to elucidate their physical binding capacity with human proteins (bioRxiv 2020 Mar 27). Among their findings: the virus's envelope protein interacts with BET protein bromodomains. Building on that result, Gerald Denis, PhD, co-director of the Boston University Cancer Center in Massachusetts, says he now hopes to test novel BET inhibitors in human lung cells infected with SARS-CoV-2 as part of a larger drug-screening effort happening at a biosafety level 4 facility.

Meanwhile, a team led by virologist Adolfo García-Sastre, PhD, of the Icahn School of Medicine at Mount Sinai in New York, NY, is evaluating several approved cancer drugs identified by the QBI team in infected monkey cells. However, "it is still early in the game," García-Sastre says, noting that his group still needs to evaluate the drugs in tissue culture before animal testing and any human trials could begin.

The preliminary nature of most drug-screening studies hasn't stopped some clinicians on the front lines of the COVID-19 crisis from forging ahead with giving cancer therapeutics to their patients. In China, for example, trials are under way with the blood vessel growth inhibitor bevacizumab (Avastin; Roche), the myeloma drug thalidomide (Thalomid; Celgene), the PD-1 inhibitor camrelizumab (AiRuiKa; Jiangsu Hengrui Medicine), and the anti-IL6 drug tocilizumab (Actemra; Roche).

The recent shortages of chloroquine and hydroxychloroquine—antimalarial drugs touted as potential remedies for COVID-19—have led some oncologists to worry that off-label prescribing could leave patients with cancer in the lurch. Drug makers have sought to allay those concerns. For example, Roche announced that it has strategies in place to ensure that current supplies of tocilizumab are not impacted by COVID-19–related demand.

Cancer biologists are undoubtedly looking forward to resuming their research. But with COVID-19 cases ballooning, El-Deiry advises against becoming complacent. "It's a mistake to sit around and wait," he says. "We have got to act now." *–Elie Dolgin* ■