Viral Analysis: Early Detection of HCC

A test that analyzes patients’ exposure to viruses can detect hepatocellular carcinoma (HCC) before standard diagnostic techniques, a study reveals (Cell 2020;182:317–28). The approach may allow earlier detection of HCC, enabling more patients to receive potentially lifesaving treatments such as surgery and transplantation.

For patients who are at risk of HCC, current guidelines recommend twice-yearly screening with ultrasound, often combined with tests for the tumor biomarker alpha-fetoprotein. However, most HCCs are not diagnosed until they have reached an advanced stage.

Xin Wei Wang, PhD, of the NCI and colleagues suspected that a patient’s history of viral infections could reveal HCC earlier. Based on previous research, they hypothesized that viruses alter the immune system, thus decreasing or increasing its ability to combat HCC tumors. A variety of viruses—not just the ones that cause hepatitis B and C and promote liver tumors—could affect risk, Wang notes.

To detect viral exposures, the scientists used a method developed by other researchers called VirScan, which checks blood for antibodies against nearly 94,000 epitopes from almost all known human viruses. First, the team analyzed blood samples from a case-control study that included 899 participants who had HCC, were at risk for it, or were healthy. The researchers used 90% of the samples to discover patterns of viral infection and 10% of the samples to validate those results. They found that exposure to 61 viral strains could discriminate patients with HCC from at-risk and healthy individuals. Moreover, the technique could distinguish patients with HCC from healthy controls with about 90% accuracy for the discovery samples and about 70% accuracy for the validation samples.

However, the results indicate that not all 61 viruses affect HCC risk by promoting cancer. Exposure to hepatitis B or C viruses, two influenza strains, and cytomegalovirus correlated with increased HCC risk. By contrast, patients with HCC were less likely to have been infected by 43 of the viruses, including respiratory syncytial virus. Thus, the absence of these viruses appears to increase the likelihood of developing the disease, suggesting that they may play a protective role. “It is worth speculating that cancer-prone individuals may perceive viral epitopes differently compared to healthy individuals,” the authors wrote, adding that additional research on the relationship between viruses and an individual’s genome and immune profile is needed to
understand mechanisms of antitumor immunity.

The scientists also evaluated their approach by studying a different group of 173 at-risk individuals who were tracked for up to 20 years; 44 developed HCC. Wang and colleagues tested blood samples collected before diagnosis for exposure to the 61 viral strains. The results suggest that this method could uncover a patient’s cancer a median of 8.8 years earlier than conventional screening techniques. “This is a proof-of-concept study,” Wang says. “The real test,” he adds, will be to evaluate whether the method can reduce mortality in a randomized clinical trial.

Researchers who weren’t connected to the study are enthusiastic about the prospects for viral profiling. Augusto Villanueva, MD, PhD, of the Icahn School of Medicine at Mt. Sinai in New York, NY, says that the approach is immunologically sound and praises its novelty. “It’s a breath of fresh air,” he says. A clinical trial now needs to determine whether it allows earlier detection of HCC, he says.

Jonathan Schwartz, MD, of the Montefiore Medical Center at Albert Einstein College of Medicine in New York, NY, adds that “if this could be validated prospectively, it could be a game changer” for HCC screening.

-Mitch Leslie

COVID-19 Challenges Status Quo for Cancer Care

Due to the COVID-19 pandemic, oncologists have had to balance patients’ need for treatment with the risk of contracting the disease, sometimes prompting them to adjust standard treatment and/or rethink its timing. Further complicating the situation, many hospitals have limited surgeries when COVID-19 cases surge and a surgical backlog once cases decrease, requiring tough decisions about the timing of operations.

Several organizations have published recommendations to help with these decisions. But Daniel Spratt, MD, of the University of Michigan School of Medicine in Ann Arbor, notes that such guidelines are typically developed for specific cancers, making it difficult to determine which surgeries should take priority or how to use other shared hospital resources.

To aid in decision-making, Spratt and his team developed oncCOVID (see http://onccovid.med.umich.edu). The tool—linked to multiple large cancer registries and the Johns Hopkins COVID-19 dashboard—assesses more than 40 factors, including patients’ type and stage of cancer, age, preexisting conditions, geographic location, and the potential length of the delay. It then estimates the risk associated with delayed versus immediate treatment. “The motive behind oncCOVID is to integrate this massive amount of data into a quantitative estimate” so that patients can receive personalized care during the pandemic, Spratt explains.

Hospitals have also developed strategies for determining how to alter treatment to minimize hospital visits without compromising care. At Dana-Farber Cancer Institute in Boston, MA, for example, Ann Partridge, MD, MPH, and her colleagues developed guidelines for breast cancer care (available at www.dana-farber.org/covidmd). “Our principles were to assure [positive] long-term clinical outcomes for patients with breast cancer, minimize the risk of infection or exposure among patients and staff, avoid immunosuppression, and preserve vital resources within the healthcare system,” Partridge explains.

In practice, when Dana-Farber postponed nonurgent surgeries due to COVID-19, Partridge used hormone therapy in patients with breast cancer awaiting surgery, a strategy often used in higher-risk situations. Partridge says they were careful about choosing which treatment regimens to adjust, relying on data from patients with advanced disease: “We didn’t do anything crazy.”

Stephanie Wethington, MD, of Johns Hopkins University School of Medicine in Baltimore, MD, made similar decisions to delay surgery in her patients. For example, she prescribed hormone therapy for some patients with endometrial cancer so that they could delay a hysterectomy—an accepted, although less common, approach. She also recommended neoadjuvant chemotherapy for patients with ovarian cancer and rescheduled surgeries for precancers and early-stage, less-aggressive malignancies.

Centers have further reduced in-person visits by extending the time between surveillance exams, as well as maintenance treatments, when possible. “I do think it’s forced us to ask the question, ‘What is truly necessary, and what is actually optional?’” Wethington posits. “It is a very fluid process that evolved over time and continues to evolve.”

Wethington says she—and likely every oncologist—has had patients opt out of office visits due to fear of COVID-19 transmission, even in situations meriting in-person examinations. Thus, she has emphasized shared decision-making with patients, talking through patient-, cancer-, and COVID-19–specific considerations. “For some patients it can be a very complex dynamic—there is significant variation in terms of what patients feel comfortable with,” she says.

However, an important question remains: Will these changes to care negatively affect patients? “As of yet, we don’t have any good data to tell us what the impact, if any, has been—we’re still at a place where there is a theoretical concern,” Wethington says. “I think any damage done, we won’t really know for a long time,” Partridge agrees. –Catherine Caruso

Vor Nets $110m to Make Anti-CD33 Drugs Safer

Vor Biopharma secured $110 million in July to move its lead stem-cell therapy into clinical testing. The financing—added to $42 million raised last year—will support first-in-human trials of VOR33, an engineered cell product that employs CRISPR/Cas9 to inactivate CD33 from healthy donor hematopoietic stem cells (HSC).

The hope is that patients with high-risk acute myeloid leukemia (AML) who receive VOR33—manufactured for each individual—will better tolerate therapies that destroy cells expressing