Professor Allison M. Cushman-Vokoun is the medical director of the UNMC Molecular Diagnostics and Personalized Medicine Laboratory.

What Nebraska knows about better precision oncology

A solid history of sequencing and a dedication to patients ensures the University of Nebraska Medical Center offers the best care

ALTHOUGH OMAHA, NEBRASKA LIES more than 1000 miles from major cities on the East Coast, the University of Nebraska Medical Center (UNMC) has long been a destination for leading-edge medicine. UNMC took in Ebola virus patients during the 2014 outbreak and processed samples from some of the first COVID-19 patients aboard the *Diamond Princess* cruise ship.

Biocontainment units and emerging infectious diseases aside, this academic medical center also stands out in oncology. At UNMC, professor Allison M. Cushman-Vokoun is the medical director of the Molecular Diagnostics and Personalized Medicine Laboratory, which focuses primarily on precision oncology.

Even in the days before next-generation sequencing (NGS) was widely in use, Cushman-Vokoun and her colleagues had hoped to build what they thought could be a program in molecular oncology. With support from UNMC and Nebraska Medicine, its teaching hospital, they were able to adopt the technology early—and they've never looked back.

Benefits of a comprehensive approach

In 2014, the department was using single-gene assays and began testing tumor samples with small panels. They built on their experience and expertise over time, laying the groundwork for more advanced technologies and workflows. Two years ago, the lab implemented comprehensive genomic profiling (CGP), an NGS approach that assesses hundreds of cancer-causing genes in a single assay, including relevant cancer biomarkers, for therapy guidance. CGP can detect most major genomic variant classes (single-nucleotide variants, indels, copy number increases, fusions, and splice variants) as well as genomic signatures such as tumor mutational burden and microsatellite instability. The comprehensive assay eliminates the need for sequential testing, potentially providing faster results and limiting the use of precious biopsy samples.

Through CGP, Cushman-Vokoun's lab has been able to identify biomarkers they wouldn't have found otherwise—genes involved in homologous recombination deficiency (HRD), for example, or a gene that qualified a patient for a clinical trial or an off-label therapy.

She explains that simply examining a tumor is not enough, since it may look like another kind of tumor under the microscope: "It can be tricky—we have had

1. illumina.com/areas-of-interest/cancer/ngs-in-oncology/cgp.html

cases where you think it's one thing and then you look at the genomic profile of the tumor and it's something else."

Cushman-Vokoun can recall a case when CGP changed a cancer patient's diagnosis—and therapy. "For instance, clear cell sarcoma can look a lot like a melanoma," she says. "Sometimes it's hard to differentiate those even with staining. There's a particular fusion that you can have with clear cell sarcoma that's pretty much diagnostic of that entity. If you do CGP, for instance, you're going to find a fusion signaling that entity. That can change treatment for the patient, and it definitely makes a difference."

> "It's never going to be boring. There's always a new protein, pathway, or gene function, and a new drug that can affect that. You're always learning something new, and that's part of the fulfillment, reward, and excitement."
>
> *—Prof. Allison Cushman-Vokoun*

Testing in-house: Protecting tissue, relationships, and training

The hospital and the university department are aligned in their desire to keep the lab operations and testing under one roof. They are committed to maintaining tissue provenance and ensuring its security. "We take care of the tissue because it's a valuable resource for clinical care and even down the road for potential research purposes," Cushman-Vokoun says.

She points out that it takes far fewer resources to order the tests to be done in-house than it would to send out a block to another lab, hire people to coordinate the transfer, and follow up (sometimes more than a few times) on what might be an extended turnaround time. By processing the sample in-house, the oncologist can have test results by the patient's next appointment.

Cushman-Vokoun has also noticed improved relationships with physicians. "As the pathologist, I think it's really important to be able to discuss the results and explain the findings," she says. "I know my oncologists well; I know what they're thinking. Being able to interact with them, if I see something unusual or something that is at a low level, it helps to have trust—especially knowing the results might change things for the patient."

A third benefit of in-house testing is being able to train and educate the next wave of pathologists and oncologists. "There's only so much time in medical school to train in molecular pathology and genomics, but we've really tried to increase that, and in the residency programs as well," she explains. UNMC offers molecular genetic pathology and laboratory genetics and genomics fellowship programs. They train residents and fellows, as well as the occasional medical student who comes through their doors. They end up hiring many of the fellows they train, which has been useful in developing the molecular program.

Putting on her professor hat, Cushman-Vokoun warns not to overlook the impact that keeping CGP in-house has on training future generations in the field: "If all medical institutions send their samples out, then how are we going to train people to do this? There are lots of reasons to keep it in-house: It's good for the program; it's good for the patients. Yes, it's a big investment, but our hospital realizes the value of it, and I'm very appreciative of that."

Nebraska Medicine is a National Cancer Institute–designated cancer center, and it considers cancer care one of its most important pillars.

"If you want to have cutting-edge care for your patients, and you want to be able to interact with your oncologist and provide that testing, it's best to do it in-house," Cushman-Vokoun says, noting that more labs and clinics need to adopt the technology. "There is such a great need. Sadly, cancer is not going away, and it only seems to be increasing in number, and in younger populations. People want answers; they want to get started on the treatments. So the more institutions that can do it and the faster we can do it, the better it is for all patients."

Looking ahead, the lab hopes to increase the number of samples they run, and routinely test for HRD. Eventually, they would like to implement methylation for brain tumors, a circulating tumor DNA assay, and a lymphoma panel. Ambitious? Maybe. But it's for the patients. Don't discount Nebraska. ◆