Revolutionizing Treatment for Cancer Care

New Circulating Cell-Free Tumor DNA (ctDNA) Technology

Mary P. Bronner, MD, ARUP Laboratories' division chief of Anatomic Pathology and Oncology, discusses using circulating cell-free tumor DNA (ctDNA) for cancer testing. This break-through technology is now entering the clinical realm. In this Q & A, Dr. Bronner explains its application and advantages.

Dr. Bronner is the inaugural Carl R. Kjeldsberg presidential endowed professor of pathology at the University of Utah School of Medicine. She was awarded the Arthur Purdy Stout Prize in 2005, recognizing her work as a surgical pathologist under the age of 45 whose research publications have had a major impact on diagnostic pathology. This is just one of many honors recognizing her expertise and commitment to anatomic pathology and molecular oncology.

Q: What are the advantages of circulating cell-free tumor DNA testing over previous method(s) for solid tumor testing?

A: ctDNA is far less invasive and expensive than existing biopsies, surgeries, and imaging modalities. It is also more sensitive, allowing earlier detection. By virtue of blood circulating throughout the body, ctDNA samples all tumor locations as compared to targeted biopsies and resections.

Current methods of molecular tumor testing remove only a tiny fraction for analysis, since whole tumor testing is cost prohibitive. Because most tumors and their metastases are highly variable in their genetic makeup, important alterations are missed through these multiple forms of sampling error. ctDNA will likely dramatically improve this because the blood samples essentially all cells through perfusion and allows for more comprehensive testing.

Finally, ctDNA, as a minimally invasive and cost-effective test, can be done at far shorter serial intervals than current radiologic methods to detect not only earlier recurrence but also specific chemotherapy resistance mutations.

Q: How does circulating tumor DNA (ctDNA) testing differ from circulating tumor cell (CTC) testing?

A: ctDNA is over 100 times more sensitive than CTC testing, permitting much earlier detection.

Q: What does this technology mean for clinicians and their patients?

A: Clinicians and cancer patients can look forward to fewer invasive and costly biopsies, surgeries, and CT and MRI scans, to be replaced by ctDNA blood tests for earlier and more comprehensive detection of molecular alterations in tumors. Improved treatment will ensue by detection of chemotherapy-resistant mutations to redirect therapy.

Q: What are some future possibilities involving circulating cell-free DNA testing?

A: The future of ctDNA holds a tremendous amount of clinical trial work. It could help determine the extent and significance of improved tumor sampling, whether ctDNA can be used for cancer screening, the optimal blood draw intervals to detect recurrence and resistance, and ultimately whether these variables improve survival.

Q: Where is this application being used now?

A: ctDNA tests for the above applications are now in clinical use. ARUP Laboratories' initial ctDNA test targets non-small cell lung cancer (NSCLC) by identifying circulating EGFR T790M mutations that confer resistance to early generation NSCLC chemotherapy drugs. Virtually all treated patients develop drug resistance, with two-thirds due to the T790M mutation, for which new targeted therapies have been approved.

ARUP's test utilizes digital droplet PCR for exquisitely sensitive (<0.5%) mutant allele detection. This targeted test is highly cost effective to enable serial testing for early resistance and therapeutic intervention in lung cancer, the most common and deadly cancer in the world.