The New Bold Frontier of the "War on Cancer"

Peg Ford

When the fourth Illumina Discovery Symposium was presented in San Diego in conjunction with the 2014 meeting of the American Association for Cancer Research (AACR), I was fortunate to be invited to attend. The symposium focused on the progress being made in monitoring cancer through next-generation sequencing technologies. From my perspective as a patient advocate, there were several issues, concerns, and insights presented that caught my attention.

I thought the presentation by Shashikant Kulkarni, PhD, set the stage well. Dr Kulkarni is head of Clinical Genomics, Genomics and Pathology Services and director of Cytogenomics and Molecular Pathology, Washington University School of Medicine, Saint Louis, Missouri. His presentation specified the following challenges in cancer diagnosis:

1. Sample procurement and analytic issues: samples vary in quantity, quality, and purity
2. Almost all diagnostic cancer biopsies are formalin-fixed, paraffin-embedded (FFPE) tissue
3. Complexity of cancer genomes
4. Heterogeneity of genomic aberrations (abnormalities found at low levels)

Dr Kulkarni's facility is focused on patient care, cost-effectiveness, and ascertaining the right drug at the right dose for the right patient at the right time. Due to funding requirements, he focuses on the clinically actionable genes in cancer cells that have prior payer approval for reimbursement.

David S. Hoon, PhD, chief of Scientific Intelligence and director of Molecular Oncology at the John Wayne Cancer Institute, Santa Monica, California, presented information concerning circulating cell-free DNA (cfDNA) and circulating tumor cells (CTCs) in the blood of cancer patients. He discussed how the detection, prognostic, and predictive value of circulating cfDNA analysis is more powerful than protein assay and that it requires no repetitive biopsies but instead uses cfDNA blood tests for monitoring. He questioned the use of tumor samples as to size of the slice and whether the sample covered all the tumor and possible variants. He discussed several factors regarding CTCs: CTCs are shed into the vascular system depending on doubling time, which is a major unknown factor; CTCs occur at low molecular levels in blood; and methods exist to authenticate low-level validations. Also, there would be fewer CTCs in early-stage disease, thus requiring more sampling than at stage III or stage IV. However, he concluded each has its own merit—cfDNA for evidence of tumor or CTCs confirming a metastasized event.

During the AACR meeting, I was invited, along with the advocates participating in AACR's Scientist↔Survivor Program, to attend "Night at the Lab" at Scripps Research Institute to see firsthand what happens in a cancer research lab. Peter Kuhn, PhD, confirmed that CTCs exist in the peripheral blood of cancer patients in low concentrations, making their isolation and identification a difficult task. However, their lab has developed a reliable way to detect and characterize CTCs isolated from the blood of cancer patients—a step toward

ultimately reaching the goal of making cancer a managed disease.

It was an eventful evening that included an interactive session with physicians, advocates, and scientists discussing ways to navigate treatment pathways and biological pathways. In addition, advocates were placed in small groups and escorted to the lab rooms by one of the researchers, who described the facility and answered questions.

When I contacted Dr Kuhn about Dr Hoon's comments in reference to CTCs, he responded, "Solid tumors often have direct access to the blood supply through tumor vascularization, which in many cancers is disregulated to provide the tumor with additional blood supply for growth. This process also allows for tumor-derived cells to enter the blood circulation. These cells can serve as a liquid biopsy and be used to characterize the disease at many time points along the path of the disease evolution. Many but not all tumors shed cells into the blood, and not all of these cells survive. While generally an increased metastatic tumor burden results in more cells in the circulatory system, there is increasing evidence that some patients with seemingly early-stage disease also have cells in the circulation. This observation also makes sense in the description of the continuum of disease evolution in which one would expect cells to exist in the blood prior to clinically evident distant metastasis."

Laura MacConaill, PhD, shared the importance of standardizing the quality of tissue collection throughout the system.

He concluded, "Establishing both the broader biological context and the patient-specific use of these liquid biopsies is under intense study. It has opened new fields of rare cell biology that can indeed provide quantitative insights into the temporal evolution of the disease in patients under treatment pressures. The liquid biopsies will be an important complement to current standard of care diagnostic, prognostic, and predictive methods in patient care. The main advantage is of course the ability of directly accessing tumor tissue at multiple, clinically relevant time points to aid in the treatment decision-making process."

Laura MacConaill, PhD, scientific director, Center for Cancer Genome Discovery, Dana-Farber Cancer Institute and scientific director, Brigham and Women's Hospital, Boston, Massachusetts, addressed not only the quality of tissue samples but also the collection process. Stressing the significance of matching patient personalized cancer treatment to the driver mutation, she shared the importance of standardizing the quality of tissue collection throughout the system, indicating that currently 33% of samples are of low quality, inadequate, and/or too small. Possibly, in the past, the need for standardization was not as major an issue as it is today, but the world of genomic science has changed this fact. Standards

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from labs can vary greatly, affirming the need for the Clinical Laboratory Improvement Amendments (CLIA) program. CLIA labs are required to be certificated by their state as well as by the Center for Medicare and Medicaid Services (CMS) before they can accept human samples for diagnostic testing. Three federal agencies are responsible and have unique roles in assuring quality laboratory testing for CLIA: CMS, the US Food and Drug Administration, and the Centers for Disease Control and Prevention. In addition, Dr MacConaill discussed the importance of simplifying consent and enrollment forms, recommending a 2-page basic form that patients would find easier to complete. I briefly discussed these issues with Dr MacConaill regarding the next steps in setting standards for tissue collection and supporting the need to simplify the consent and enrollment forms for patients. Both these conditions are vital to the advancement of genomic science and, without question, are important to the patient community.

The last to speak was Richard Klausner, Sr, PhD, vice president and chief medical officer of Illumina. I was prepared to hear a brand pitch for the company's products from him, but I was wrong! Instead, he shared his vision of a Global Initiative—quite a hopeful end to a most interesting day for an advocate. He spoke of his commitment to bring all stakeholders (pharma, industry, academia, Congress, physicians, healthcare providers, payers, and the patient community) to the table for the benefit of humankind by open and transparent collaboration, communication, and sharing all findings with equal access for everyone. Prior to joining Illumina in 2013, Rick (as he likes to be called) filled many roles, for instance, as executive director for Global Health at the Bill and Melinda Gates Foundation and as the eleventh director of the National Cancer Institute between 1995 and 2001. Listening to his vision of the transformation of medicine through technology, and considering his enthusiasm and confidence as well as his impressive background, I was moved to expect that if anyone could be the bridge to conquer this challenge, it just might be Rick! It is an idea I feel the patient community desires and is hoping to see happen in which all aspects of medicine work harmoniously together, rather than with any form of competition, to benefit the individual as well as humankind. Perhaps we are on the cusp of a paradigm shift, and I personally applaud Rick's passion and dedication to make this transformation happen in the not-too-distant future! I look forward with hope to observing his progress in this dynamic initiative!

Richard Klausner, Sr, PhD, vice president and chief medical officer of Illumina, with Peg Ford at the Illumina Discovery Symposium held in conjunction with the 2014 meeting of the American Association for Cancer Research.

Yes, we certainly continue to face challenges, but as reported here, researchers are making bold steps into the new frontier of science and medicine. I see greater promise than ever before to finally move closer to achieving what President Richard Nixon declared as the "War on Cancer," when he signed the National Cancer Act into law on December 23, 1971, stating, "I hope in the years ahead we will look back on this action today as the most significant action taken during my Administration." ●