Q&A

How is molecular genetics changing the course of oncology?

Dr. Robert Decker
Hematologist/Oncologist
Cedars-Sinai Tower Hematology Oncology Medical Group

The 21st century has seen a revolution in understanding not just cancer, but cardiovascular, rheumatic disease and more. The ability to rapidly sequence genes and genomes (the entire DNA sequence of an organism or animal), has facilitated the identification of genetic variants and mutations, thereby allowing researchers to direct their efforts at very specific features of malignant cells. This has also allowed for the identification of certain patient populations who may be at increased risk for some malignancies, and thus improving screening and prevention approaches.

When tumor-specific mutations are recognized, we can selectively attack those cells with either oral medications that typically bind to and inactivate the mutated protein, or with a custom-made antibody directed against that protein also blocking its activity.

The first of these products, Gleevec (imatinib), a pill for chronic myeloid leukemia, and Herceptin, a man-made antibody that fights a growth-promoting protein in some breast cancers, were developed almost twenty years ago. These compounds proved to be incredibly successful, reinforcing this "targeted therapy" approach as an exciting and novel way to treat cancer more successfully and specifically. The current thrust toward activating the immune system to attack the cancer cells is another form of such targeting, wherein certain proteins (PDL-1, CTLA-4) that have inhibited the attack are now being blocked, allowing the patient's own immune system to spearhead the attack on the malignant cells.

Understanding what drives malignancies at the molecular genetic level can provide a giant step towards our goal of controlling and curing cancer. It is indeed an exciting and stimulating time to be an oncologist!

"Patient J.R. presented with a new lung cancer, and while working him up we found it to be very aggressive, growing rapidly and spreading quickly.

While contemplating what systemic therapy to start, chemo vs. targeted therapy, pathology results told us he did not have any of the "conventional" lung markers mutated in his case, namely EGFR, ALK, ROS-1. His PDL1 was highly expressed, except things like nivolumab (Opdivo) and pembrolizumab (Keytruda) usually work pretty slowly, not good for his situation.

Found from next generation sequencing (NGS, testing for a variety of tumor mutations, not just the "usual") revealed a BRAF mutation; common in melanoma, but seen in only about 2% of lung cancers.

We scrambled to get the two pills we use for this mutation, got them after about 4-5 days, and within about 7-10 days of starting therapy he looked and felt 100% better, and labs and X rays demonstrated a dramatic reduction in the tumor activity. Truly remarkable, but just one of many stories we see these days."

Dr. Robert Decker