Working toward personalized cancer treatment

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Prof. Yardena Samuels wants to reveal the big cancer picture. Credit: Weizmann Institute of Science

"We don't just want to find the genes involved in cancer," says Prof. Yardena Samuels of the Weizmann Institute of Science's Department of Molecular Cell Biology, "we want to understand what those genes do. We want to reveal the complete picture of a cancer genome."

That is something of a tall order, considering that cells from melanoma, the cancer Prof. Samuels is researching, can contain anywhere from tens to thousands of mutations. On average, melanoma – the deadliest form of skin cancer – has more mutations in the DNA of its cells than any other solid tumor. Among other things, this range of mutations explains why a recent treatment designed to target melanoma will only help around 50% of those with the disease, despite representing a large step forward.

Prof. Samuels first came to the Weizmann Institute at age 17, when she attended the Bessie F. Lawrence International Summer Science Institute. That encounter left her aspiring to one day run her own lab. The Israeli-born Samuels grew up in Israel, France, Mexico, and the United Kingdom: Her mother is a diplomat, and her father is Director for International Relations of the Simon Wiesenthal Centre. After completing her BSc at Cambridge University, Prof. Samuels returned to Israel to serve in the IDF Medical Corps labs. She went on to receive an MSc from Hebrew University/Hadassah Medical School and a Ph.D. from Imperial College London. Prof. Samuels then went to Johns Hopkins University to pursue her postdoctoral research in the lab of one of the preeminent cancer genetics researchers in the world: Prof. Bert Vogelstein. There, she identified a gene called PIK3CA, which is one of the most highly mutated oncogenes (cancer-causing genes) in human malignancies. These studies put PIK3CA in the spotlight of both clinical and basic cancer research.

Her postdoctoral experience inspired her to focus on personalized medicine for cancer: Investigating cancer biology using genomic tools and managing malignancies by tailoring treatment to personal genomic profiles. In 2006, Prof. Samuels established an independent research program as a tenure-track investigator at the National Institutes of Health (NIH) in Baltimore where, together with colleagues, she established a unique tumor bank of 120 matched normal and tumor tissue samples. This allowed her group to comprehensively analyze mutations in melanomas, identify possible new drug targets, and lay the groundwork for future personalized therapies.

One of these analyses revealed that a protein called ERBB4 is highly mutated in melanoma. Furthermore, she found that treatment with lapatinib – an FDA-approved drug already being used for breast cancer patients – suppresses the proliferation of ERBB4-mutant melanoma cells. This study paved the way to a clinical trial in melanoma patients, recruited from the NIH's National Cancer Institute and Memorial Sloan Kettering Cancer Center, who harbored ERBB4 mutations. The results are currently being

analyzed.

Prof. Samuels is expanding her tumor bank work in her role as director of the Weizmann Brazil Tumor Bank, a core facility of the Moross Integrated Cancer Center (MICC).

The bank promotes in-depth study of tumors in all stages of progression. Its resources help scientists identify genes associated with tumor growth, thereby promoting the development of new strategies for cancer treatment. Knowing the genes involved in cancers will support the development of personalized treatments.

The MICC was born out of the Institute's realization that, after decades of losing the "war on cancer," scientists needed to look at the disease in a new way – a more holistic approach that considers cancer in its totality, that incorporates information from the genomics revolution, that harnesses the power of personalized medicine. Under the guidance of talented, experienced scientists such as Prof. Samuels, the MICC will not only produce the finest basic research in cancer, but move its findings from "bench to bedside."

The future of cancer genomics lies in the integration of genetic, functional, and clinical data. To that end, Prof. Samuels collaborates with Institute computational biology, biology, and biochemistry groups to further decipher the genetic and functional landscape of the melanoma genome. One avenue she is pursuing involves sorting the thousands of genes that are mutated in melanoma into "drivers" and "passengers" – that is, those that help the cancer develop and the incidental mutations that are just along for the ride. Another avenue: exploring different experimental approaches and functional models to see which are best for revealing the functions of the various identified genes in their physiological context. While her work involves a deep dive into basic research, Prof. Samuels ultimately wants to move her findings into the clinic, helping cancer patients recover and reclaim their lives.

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