CASE STUDY

Understanding Cancer Processes in Pathway Studio

UNDERSTANDING THE BIOLOGY OF CANCER

There is growing belief that each patient's cancer may be unique. By examining gene expression patterns from cancer patients and mapping that data to biological pathways, researchers can find views into each patient's specific disease.

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DR. ANTON YURYEV
Director of Professional Services, Biology, Elsevier R&D Solutions for Pharma and Life Sciences

Dr. Luminita Castillos had a dream – to offer hope to late stage cancer patients who had exhausted the common standards of care. Combining her years of experience interpreting gene expression data, and her husband's expertise as an oncologist, she looked for a way to identify the molecular processes behind his patient's cancers, looking for potentially alternative treatment approaches. To help her interpret their expression data, Dr. Castillos turned to Elsevier's Pathway Studio, and when she had questions, Dr. Anton Yuryev, a recognized expert in Pathway Studio from Elsevier's technical support team, stepped up to help her find the answers. As a result, she developed a method for modeling disease pathways based on gene expression data from late-stage cancer patients.

Her initial work, which mapped pathways in five patients' tumors, was so successful that Dr. Castillos presented her work at the 2014 International Conference on Predictive, Preventative, and Personalized Medicine & Molecular Diagnostics in Las Vegas. In addition, Dr. Castillos explained how her innovative application of these disease models contributed to extending the lives of several patients who came to her practice after they had been told their cancer was untreatable. Three of her clinic's patients whose overall survival estimate based on standard of care was only a few months, are still alive more than one year later, and MRI screenings indicate that all three patients' tumors have disappeared.

Castillos, a PhD molecular biologist with more than 15 years' experience in industry and academia, is the director of research at Personalized Hematology-Oncology of Wake Forest, a small private clinic in North Carolina run by her husband, Francisco Castillos MD, an oncologist. Her idea was to use Pathway Studio to build models of his patient's cancer pathways.

Dr. Castillos had been measuring the molecular profiles of patients' tumor biopsies for some time. She purchased Pathway Studio to support the next steps in her research: to conduct data analyses to understand each patient's unique cancer process via the molecular pathways in their tumors.

With that knowledge, she hoped to be able to identify approved drugs known to target those pathways, and which had not been previously considered for the treatment of the specific advanced cancers. Ultimately, she hoped the approach would offer therapeutic alternatives for patients who had exhausted standard-of-care options.

"Dr. Castillos takes a biopsy and measures the gene expression profile of a tumor," Dr. Yuryev explains. "She sends me a data file—and the profile is imported into the Pathway Studio system and used to understand what pathways were responsible for that profile, and to find the pathways upstream of the genes that caused the change in the tumor's expression."

Advanced cancers, Dr. Yuryev says, are characterized by at least 10 different hallmarks responsible for the evolution of the tumor—from benign or slow-growing to metastasis to other organs. "We map the molecular profile that Dr. Castillos measures against the published literature for these hallmarks of cancer, and usually we find several pathways, though, often, drugs are not available to target those pathways. We're focused on druggable pathways, and this information is available in Pathway Studio. It is not enough just to find the disease pathways, but you must find the ones that are druggable. This is the same approach used by pharmaceutical companies when looking for new drug targets"

Yuryev says Pathway Studio enables users to identify the most active protein in a given pathway, which might be a candidate for drug targeting. When no drug exists for that target, users can search for drugs that target neighboring or downstream proteins that also impact the pathway.

Dr. Castillos identified 48 cancer-related pathways describing biological processes frequently activated during tumorogenesis: cell cycle, apoptosis, angiogenesis, epithelial-to-mesenchimal transition, macrophage activation and neutrophil infiltration. These pathways contain 3,674 proteins suggesting possible mechanisms for advanced cancer in her patients. Those pathways—validated by the scientific literature, patient microarray data and the efficacy of personalized therapy—correlated with about half of all of the top 100 potential regulatory genes identified in these 5 patients.

"Her approach allows the quick identification of key processes and gene regulators that may be responsible for tumor growth in a given patient," Yuryev says. "We suggest that major expression regulators identified by SNEA in patient tumors can be considered potential targets for therapeutic intervention, or for researchers to potentially identify new therapeutics."

The work has resulted not just in several successes in the Wake Forest clinic, but it has added value to Pathway Studio. Yuryev explains: "The data from Dr. Castillos's patients has helped us gain a better understanding of cancer progression, and that information about cancer pathways can expand the information in Pathway Studio."

For details on how Personalized Hematology-Oncology of Wake Forest leveraged Castillos's research to find and deliver new treatments for "untreatable" patients, see our Customer Story: Pioneering Personalized Options for Cancer Patients

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