

Moffitt *and* FORMA Therapeutics TEAM UP

by Randolph Fillmore

SYNERGISTIC ALLIANCE FORMS PRECISION MEDICINE
APPROACH TO CANCER DRUG DEVELOPMENT



EDUARDO M. SOTOMAYOR, M.D.,
AND EDWARD SETO, PH.D.

Photography: Cliff McBride

You could call it a “dream team” because since Moffitt and FORMA Therapeutics penned an alliance in September, their combined winning efforts against several varieties of cancers have moved onto the “fast track.”

Like all dream teams, this one has synergy — a momentum that occurs when partners working together create a force that is greater than the strengths of the individual members.

Actually, this partnership is a case of synergy times two. **SYNERGY PART ONE:** Moffitt’s researchers and physicians are interested in treating and curing cancer. Scientists at FORMA

Therapeutics, in Watertown, Mass., are interested in developing new drugs to treat cancer. **SYNERGY PART TWO:** Moffitt’s Ralph R. Kaul Endowed Chair scientist and molecular biologist, Edward Seto, Ph.D., provides decades of basic science knowledge and expertise, while Moffitt’s physician-scientist and Susan and John Sykes Endowed Chair in Hematologic Malignancies, Eduardo M. Sotomayor, M.D., provides the team with medical oncology and translational expertise.

“Dr. Sotomayor and I work together extremely well and have a set of complementary expertise,” Dr. Seto says with a smile. “Yes. Working together, we have synergy.”

A decade ago, Dr. Sotomayor’s Moffitt research group was examining how the information in immune cells can be used to make them better at recognizing tumor cells. At the same time, Dr. Seto was beginning to unravel how cancer cells may be influenced by histone deacetylases, or HDACs, pronounced “H-dacs,” a family of proteins composed of 18 known proteins. HDACs play an important role in gene regulation and cell processes, including cell growth, proliferation and repair.

Moffitt and FORMA Therapeutics began exploring their common interests and synergistic potential in late 2013. Groups from both organizations paid visits to each other through the spring and summer of 2014 before penning the agreement on September 23, 2014.

“We found common ground, and we joined our efforts,” says Dr. Sotomayor. “Moffitt’s Office of Technology Management and Commercialization (OTMC), which helps facilitate, launch and



grow faculty startup companies that license Moffitt technologies, was instrumental in leading the business development efforts by driving the partnership opportunity from its concept to a formal, contractual relationship. The OTMC members did a great job.”

HERE’S HOW THE SYNERGISTIC RELATIONSHIP BETWEEN MOFFITT AND FORMA THERAPEUTICS WORKS: FORMA creates new compounds. Moffitt scientists test those new compounds in their laboratories, validating their “molecular signatures” that are the basis for a precision medicine approach to cancer drug development. FORMA makes the compounds into new drugs, and Moffitt matches the drugs to the right patients by conducting clinical trials.

“The focus of our research is to obtain a complete understanding of the functions, mechanisms of action, and regulation of HDACs,” explains Dr. Seto. “Our lab discovered that HDACs regulate important biological processes. These discoveries can be translated into new drugs to treat patients with HDAC-relevant cancers, and that’s why our new partnership with FORMA Therapeutics is so important.”

The discovery of drugs that inhibit some HDAC functions by interrupting the function of the proteins and inhibiting tumor cell growth is an important step toward helping to cure the kinds of cancers related to HDAC activity, such as Hodgkin and non-Hodgkin lymphomas, multiple myeloma, chronic

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and acute leukemias, melanoma, breast cancer and other solid malignancies.

“It was important to FORMA that we could take their drugs from preclinical trials to clinical trials,” Dr. Sotomayor says. “We expect that clinical trials with the new drugs that inhibit various HDACs will start in 2017.”

HOW DRs. SETO AND SOTOMAYOR EACH DEVELOPED THE EXPERTISE THAT CULMINATED IN THE MOFFITT SIDE OF THE PARTNERSHIP WITH FORMA MIGHT BE WORTHY OF A TV MINISERIES.

While a graduate student at the University of California San Francisco, Dr. Seto became fascinated with viruses and the role they play in cancers. He found inspiration for his career after taking a class with two professors — J. Michael Bishop and Harold E. Varmus — who shared the 1989 Nobel Prize in Physiology or Medicine for their discovery of the role viruses play in cancer.

“It was a very exciting time,” recalls Dr. Seto. “I became interested in gene expression, how genes turn on and turn off, and how oncogenes and anti-oncogenes play a role in cancer.”

He has been at Moffitt since 1996 and was named Moffitt’s “Scientist of the Year” in 2003 in recognition of his work in molecular biology and in particular for his pioneering work in the study of the molecular mechanisms by which HDAC inhibitors work against cancer cells.

As a 7-year-old boy in Lima, Peru, Dr. Sotomayor was admitted to the hospital with an infection. The infection was cured, but his interest in medicine and becoming a doctor, the first in his family, grew out of that experience. After completing medical school at Federico Villarreal National University in Lima, he came to the U.S. in the early 1990s and pursued postdoctoral studies at the University of Miami, where he gained an interest in cancer immunology. He then studied cancer immunology in greater depth during another postdoctoral experience at Johns Hopkins University.

“People told me not to pursue a career in immunology as applied to cancer. They told me that it was a field without a future,” recalls Dr. Sotomayor. “That did not discourage me; I saw it as a challenge. Nothing makes me want to do something that interests me more than someone telling me that it can’t be done!”

Not only did he eagerly pursue an area of science he thought had great promise for treating cancer, but it was his expertise in immunology as a potential cancer treatment that brought him to Moffitt in 1999. Now he is on the cutting edge of the convergence of two fields — epigenetics, the study of changes in gene expression that are not based in changes in DNA sequence, combined with immunology, the art and science of “tweaking” or ramping up the immune system to fight disease. The new field is called “immuno-epigenetics.” The promise is that when new and better ways are found to use the body’s immune system to fight the disease, conventional chemotherapy will play an increasingly smaller role in treating many kinds of cancers.

“The goals of this partnership are to combine our resources and expertise not only in HDACs but also in other molecular targets for which FORMA scientists are developing new drugs,” says Dr. Sotomayor. “It is a win-win partnership. But more importantly, when we can bring new treatments to patients, they are the ultimate winners.”

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