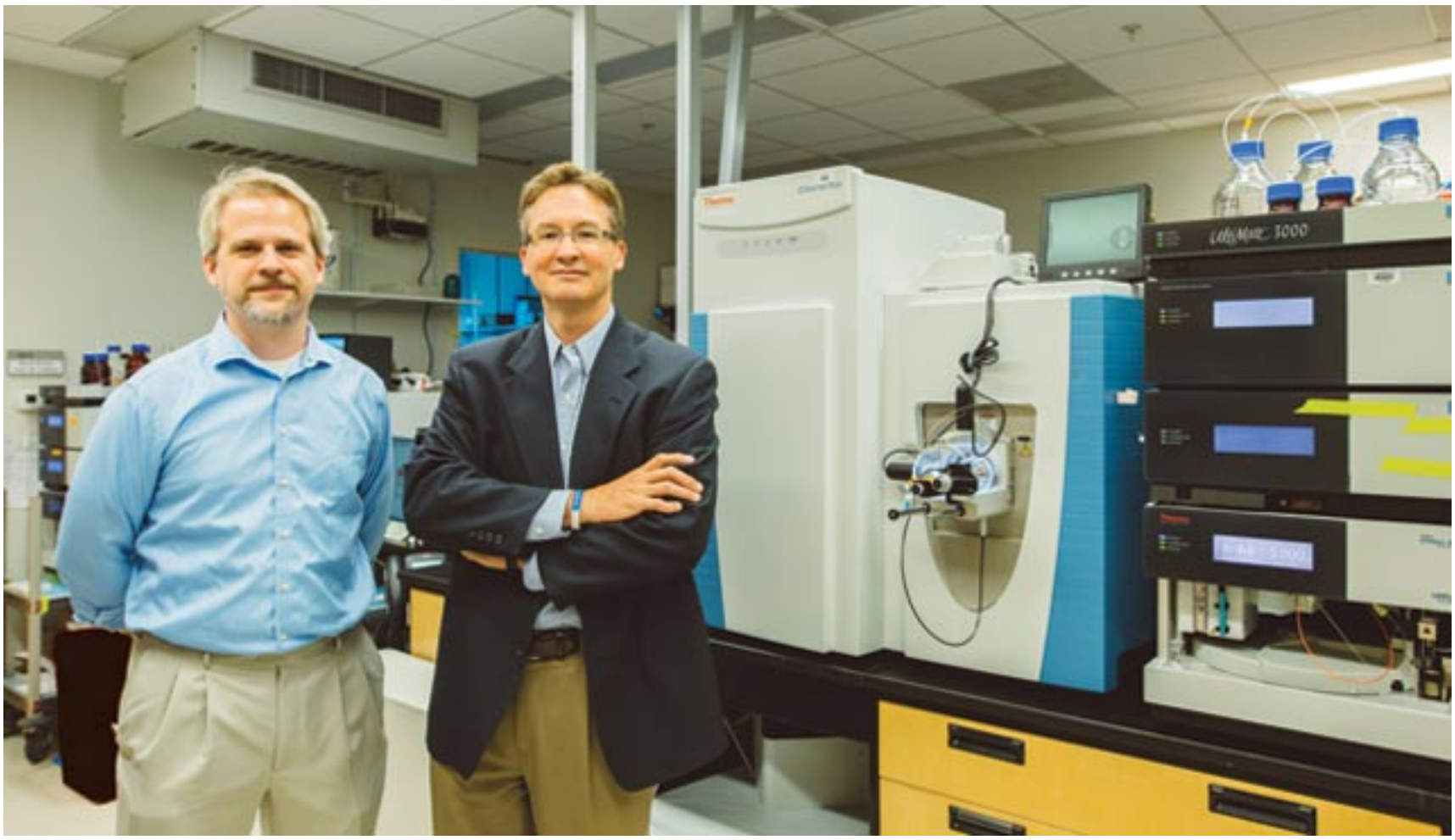
Dr. Eric Haura Studies Proteins To Learn About Immune System



From left, John Koomen, Ph.D., and Eric Haura, M.D., in the proteomics lab.

PHYSICIAN-SCIENTIST COMES FULL CIRCLE

From Biomedical Engineering, To Thoracic Medical Oncology, To Building "Wiring Circuits" For Cancer Cells

By Randolph Fillmore

In every generation, young people are inspired by role models to do important work. After Charles Darwin published the Origin of the Species in 1859, those in the next generation were inspired to find the “missing link.” In the late 19th century, many young people aspired be first to discover the North Pole. In the early 1960s, becoming an astronaut was a popular dream. And, after the breakthroughs in heart transplantation and other heart-related feats of surgical wizardry, the frontiers of cardiology were an inspiration for many aspiring medical students.

“Yes, I was inspired by the likes of Christiaan Barnard, Denton Cooley or Charles DeBakey to be a great heart surgeon,” says Eric Haura, M.D. (/providers/eric-haura/), who leads the Chemical Biology & Molecular Medicine Program (/research-science/research-programs/chemical-biology-and-molecular-medicine/) and directs the Lung Cancer Center of Excellence (/research-science/centers-and-institutes/centers-of-excellence/lung-cancer-center-of-excellence/) at Moffitt. The fascination with being a heart surgeon first led Dr. Haura to get a bachelor’s degree in biomedical engineering from Johns Hopkins University in 1990. Because he wanted to understand the circuitry of the heart, his specialty was electrical engineering. The next step was getting the medical degree. After receiving his M.D. from Duke University in 1994, then serving a residency in internal medicine at Johns Hopkins, followed by subsequent fellowships in genetics, and hematology and oncology at Duke in 2000, Dr. Haura suddenly discovered a new research frontier — cancer.

Although suddenly fascinated by looking for ways to unravel the secrets behind cancer and its cure, he did not know then that his interest and training in electrical engineering would come full circle and help him in his quest “to contribute to the prevention and cure of cancer” — Moffitt’s mission.

The times caught up with Dr. Haura in recent years when cancer researchers recognized the importance of understanding the internal signaling in cancer cells, the connections that transform healthy cells into cancer cells and the circuitry that helps them proliferate. That advancement rang both true and familiar for Dr. Haura, the electrical engineer at heart.

“You could say that we are building ‘wiring circuits’ for cancer cells,” Dr. Haura says. “Protein interactions in cancer cells are not that different from electrical circuits where the connections are critically important. Genetic research has given us a valuable ‘parts list’ for cancer. Now we have to figure out how those parts are connected and interact as well as the interactive functions of proteins.”

It may seem surprising that Dr. Haura, a physician-scientist who has published hundreds of research papers, can readily convey simple, clear analogies for complicated concepts. Beneath the advanced degrees and scientific awards, however, is a sociable guy who enjoys sports and going bowling with his family.

Dr. Haura's current research is in "proteomics" — the large-scale study of protein structure and function. Proteomics aims at evaluating how signaling activity in cancer cells is driven by the proteins in tumors.

"Cellular proteins don't function in isolation," Dr. Haura explains. "They function as parts of larger complexes of proteins, and identifying and measuring these protein complexes in cancer is important. Genes provide the 'blueprint' for cells, while the proteins that are created as the result of genetic 'engineering' are the functional components, or the circuitry, that drives both normal cells and disease cells."

He adds, "Genes can encode proteins, and the proteins are further 'decorated' — these 'decorations' can change the function of proteins, thus offering more fine-tuning in cells."

A few years ago, Dr. Haura went to Austria for several months of training in "mass spectrometry," a complicated and state-of-the-art technology now used for gaining a better understanding of proteins and how they are modified. During that time, the biomedical electrical engineer in him and the researcher/ physician in him shook hands.

"Mass spectrometry is one of our most important discovery engines," Dr. Haura says. "We have to figure out ways to purify different parts of cancer cell protein makeup to better understand how proteins function in cancer. Mass spectrometry does this. It breaks down proteins into their component parts so that we can analyze them and better understand their communication activity. You could say that proteins 'talk' to one another, and unraveling the 'language' they speak will help open doors to developing more effective, personalized therapies for patients."

He compares identifying the characteristics of proteins by mass spectrometry to "fishing" to see what protein ends up on the "hook." For Dr. Haura, discovering the proteins in a tumor and knowing how the proteins are signaling one another is the next giant step for cancer research and developing new personalized therapies.

"For analysis in mass spectrometry, we take a protein, chop it into fine pieces so that we have a long molecule, feed it to the mass spectrometry unit, and out comes a report that helps us build a picture of the protein," Dr. Haura explains. "We can figure out which proteins stick to other proteins, in other words, which proteins are talking to each other."

Dr. Haura says his work in proteomics relies heavily on Moffitt's Proteomics Core (/research-science/shared-resources/proteomics/), a protein investigation shared resource facility headed by John Koomen, Ph.D. (/research-science/researchers/john-koomen/) In the lab, a gathering of mass

spectrometry units hum loudly, and a busy team of laboratory personnel work with purpose. Work aided by mass spectrometry is paying off by providing answers to important research questions. In a research paper featured on the cover of the Jan. 13, 2015, issue of *Science Signaling*, senior author Dr. Haura and colleagues reported a new approach to measure how signaling-associated proteins may have the potential to add to current biomarker tests for drug sensitivity. Prior work with mass spectrometry helped them sort out the characteristics of the proteins involved.

For Dr. Haura, proteomics is the current frontier for cancer research. He is confident that a better understanding of the role of proteins in cancer will empower clinicians to better predict treatment outcomes, overcome drug resistance and identify biomarkers in the proteins that will help personalize treatments. Along with colleagues, he is beginning to think about how proteomics can better decipher the workings of the immune system related to cancer and develop both new diagnostic and therapeutic strategies.

“When I came to Moffitt in 2000, we could only offer patients traditional chemotherapy, in addition to surgery and radiation therapy,” Dr. Haura recalls. “Soon, a patient coming through the doors at Moffitt will have not only their genome sequenced but also have information gathered on their proteome. This opens the door to treatments designed not only for a patient’s genetic individualism but also built on the proteins that are actually at work in their tumors.”

WHAT IS MASS SPECTROMETRY?

Mass spectrometry is an analytical technique and accompanying technology that produces a spectrum of the masses of atoms or molecules in a sample. The spectrum is used to determine the “fingerprint,” or signature of the sample, whether in terms of mass or chemistry. The analysis works by first ionizing — or charging by electron bombardment among other methods — molecules or fragments of molecules and measuring their mass-to-charge ratio. The process is similar for solids, liquids or gasses. The atoms or molecules in the sample can be identified by comparing their determined masses to known masses, or through patterns of fragmentation characteristic of known masses. The mass spectrometer has three components: the ion source, a mass analyzer and a detector. The ions are transported to the mass analyzer via magnetic or electric fields. Data gathered is in the form of a mass spectrum. A pharmacokinetic analysis using mass spectrometry seeks information related to dose and metabolism. The analysis of proteins using mass spectrometry seeks information about the characterization and sequencing of proteins. The two primary methods for analyzing whole proteins are “electrospray ionization” (ESI) and matrix-assisted laser desorption/ionization (MALDI).

To contribute to the prevention and cure of cancer

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