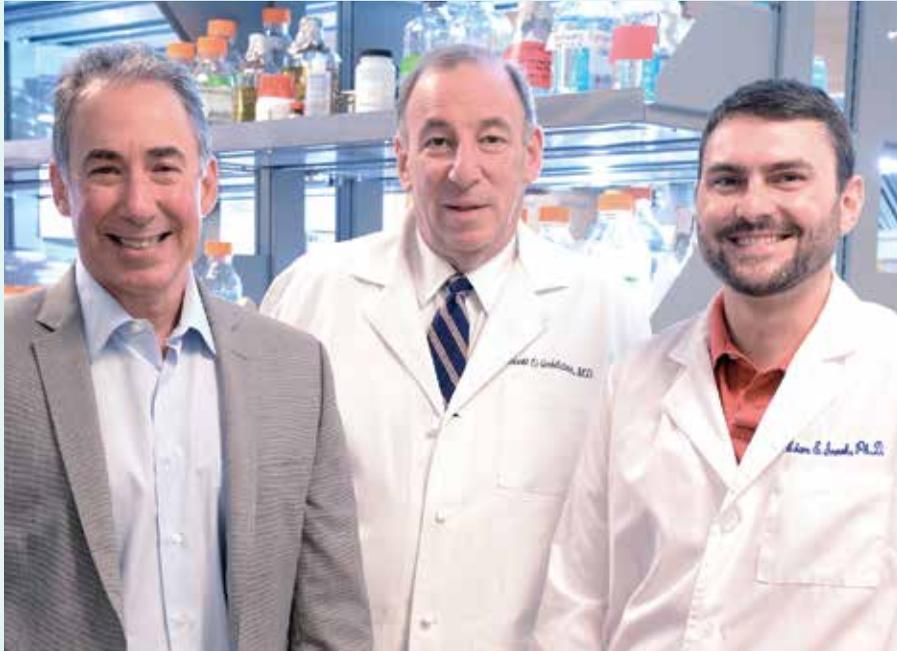


Innovative Colorectal Research Targets Key Tumor-Suppressing Molecule



Researchers Scott Waldman, MD, PhD (left), and immunologist Adam Snook, PhD (right) have made tremendous progress in colorectal research with the help of tissue samples provided by colorectal surgeon Scott Goldstein, MD (center) and his surgical colleagues in colorectal surgery.

If there were a “golden ticket” in the fight against colorectal cancer, it would be guanylyl cyclase C (GCC) – a molecule that plays a critical role in the suppression of colorectal tumors. Most colorectal tumors form or grow larger when GCC is silenced by the hormones that regulate it. Researchers at Jefferson are working to find ways to manipulate these hormones so GCC can get back to work suppressing tumors.

Leading the efforts are clinical pharmacologist Scott A. Waldman, MD, PhD, and immunologist Adam Snook, PhD, of the Waldman-Snook Laboratory. As they study GCC and the associated hormones, Drs. Waldman and Snook collaborate closely with colorectal surgeons Scott D. Goldstein, MD, FACS, Gerald A. Isenberg, MD, FACS, and Benjamin R. Phillips, MD, FACS, FASCRS, as well as physicians from the Division of Gastroenterology.

“The Department of Surgery’s collaboration with the Waldman-Snook Laboratory is helping to improve outcomes and quality of life for those coming to Jefferson for care,” says Dr. Goldstein. “Our team is at the forefront of innovative colorectal cancer research.”

One such project is studying how commercially available gastrointestinal hormones could be deployed to combat colorectal cancer. Funded by the U.S. Department of Defense, the study is using tissue samples gathered by gastroenterologists during colonoscopies and by colorectal surgeons during resections.

“We have mapped the mechanism by which the hormones are lost,” Dr. Waldman explains. “It’s a reflection of the very first mutation in the gene APC, which triggers the cascade of events that leads to tumorigenesis. When APC is mutated, a complicated signaling mechanism shuts off the synthesis of these hormones.” The study’s hypothesis is that dosing patients with commercially available hormone analogs could help turn GCC back on, halting development or progression of colorectal tumors.

In addition to mapping how the hormones are lost, Drs. Waldman and Snook want to understand the precise signaling mechanisms that lead from activation of GCC to the *prevention* of tumor initiation and progression. Another study is supporting that effort, and again, Drs. Goldstein, Isenberg and Phillips are contributing colon and rectal tissue specimens to be studied in the lab. The team is studying these normal and diseased samples both in animals and in test tubes.

“In the mice, we’re letting the tumors grow to see if we can manipulate the GCC and determine what signaling mechanisms are being turned on or off and what proteins are changing,” Dr. Waldman says. “In the test tubes, we’re literally creating ‘mini guts’ so we can get a good read on what downstream molecular pathways are being activated by the tumor-suppressing system. We couldn’t do any of this without our colleagues in Colorectal Surgery.”



Candace Caldwell and Michael Varallo

Last October, Candace Caldwell made a big move—relocating from Portland, Oregon to Philadelphia to join the Department of Surgery. As the Department’s first Operations Analyst, she’s taking on a variety of evolving responsibilities. Among them: data analysis and reporting, expense tracking and process improvement.

With a degree from Oregon State University in Public Health, Health Management and Policy, Caldwell enjoys using data to tell a story about current performance and identify opportunities to improve in the future. She said she also enjoys collaborating with her colleagues.

For Caldwell, exploring a new city has brought some surprises. For example, she’s still adjusting to Philly weather (Portland stays green in winter). Even more surprising: the warmth and friendliness of her co-workers and neighbors.

“People warned me about an abrupt, cold attitude,” she recalls. “But that hasn’t happened at all. Everyone is so nice.”

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In addition to those studies, the Waldman-Snook Laboratory is working with colorectal surgeons on the second phase of a colorectal cancer vaccine study that showed great promise in Phase 1. Patient enrollment will begin in late summer or early fall. Beyond that, Dr. Waldman says the colorectal

One of those friendly co-workers is Michael Varallo, who started as the Department’s Business Manager on Christmas Eve 2018. It’s a role that brought the 34-year-old South Philly native full circle: he started working at Jefferson at age 16 as a runner for the Department of Surgery, a job he held through college.

After graduating from Neumann University with a degree in Finance, Varallo began working in Thomas Jefferson University’s Controller’s Office. Since then, he has moved through progressively responsible positions within the Jefferson enterprise.

As Business Manager, Varallo is responsible for planning and tracking the Department’s budget and managing profit-and-loss statements to ensure revenues and costs are properly accounted for.

Outside work, Varallo and his fiancée are settling in to a new home in the suburbs and planning their October wedding. Looking to this next phase of his life, Varallo jokes, “I’ve put *myself* on a budget!”

surgeons will be highly engaged in an upcoming study involving patients with active metastatic disease.

“With this study, we’ll take ‘killer’ immune cells from the patients’ own bodies and genetically reprogram them outside the body to recognize the specific target – in this case, GCC being expressed on metastatic cancer cells,” Dr. Waldman explains. “We will create billions of those genetically reprogrammed cells, and each one will be a ‘smart bomb’ that ignites when it sees a target on a cancer cell in the lung or liver. In short, these ‘smart bombs’ will home in on the metastatic cancer cells but won’t harm normal lung or liver cells.”