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Two Generations of Surgeons Discover Research

During his first year of medical school at the University of Wisconsin in 2000, Jamie Van Gompel went looking for summer work in the department of surgery, his intended specialty. He found an ideal mentor in Herbert Chen, a newly minted assistant professor with a driving interest in research and an HHMI medical student research fellowship under his belt.

Three years later, that summer job has transformed Van Gompel from a medical student with an interest in surgery into a budding biomedical scientist committed to a career in translational research, seeking ways to translate basic science discoveries into new treatments for patients.

This year, with Chen's encouragement, Van Gompel is taking a break from medical studies to pursue research full time in Chen's lab, on the same kind of HHMI fellowship that sold Chen on research in 1990. The medical student is closing in on a potentially novel protein that may be effective in treating patients with carcinoid tumors and other neuroendocrine cancers.

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want to do."

- Jamie Van Gompel

Van Gompel's initial assignment for Chen was reviewing the charts of several dozen cancer patients to learn how to better treat patients with carcinoid tumors. Often found in the gastrointestinal system, carcinoid tumors produce excessive amounts of hormone-like substances. That work resulted in a paper now in press at *World Journal of Surgery*. He also took on some lab studies, looking at the microscopic structure of carcinoid tumors removed from patients.

Interesting medical students in research comes naturally to Chen. When he was in medical school at Duke University, Chen spent a year researching HIV-1, the virus that causes AIDS, in HHMI's Research Training Fellowships for Medical Students program. That experience "really opened

the door for me [to see] what medical research was like and persuaded me to go into academic surgery," says Chen.

It also helped him land a postdoctoral research position at The Johns Hopkins University School of Medicine. "Most basic scientists don't consider taking surgical residents as postdoctoral fellows," Chen believes, "but my past research experience as an HHMI medical student fellow caught their attention and perhaps gave me some credibility as a serious researcher."

Now, in addition to his teaching and patient practice at the University of Wisconsin, Chen oversees a research lab investigating the cellular mechanisms behind a set of rare cancers known as neuroendocrine tumors. These tumors, which often arise in the gastrointestinal tract, possess a "unique biology," says Chen. They produce hormones that promote the tumor's growth and cause symptoms for patients beyond the pain of the tumor itself, such as flushing and diarrhea. And unlike many other cancers, where abnormal activation of a cell-signaling pathway involving a protein called Raf causes the cancerous growth, Chen and colleagues have found that the opposite may be true for neuroendocrine tumors. That is, abnormal activation of the Raf-1 pathway may inhibit the spread of neuroendocrine cancers.

Furthermore, when the Raf-1 pathway is turned on experimentally in cultured neuroendocrine cancer cells, the cells stop secreting as much of the tumor-promoting hormones. The suppressed hormone production appears to be the work of an unidentified signal downstream in the pathway, Chen and Van Gompel say. Van Gompel now is trying to identify that unknown factor, which might offer a way to reduce the cancerous hormone production in patients and alleviate the debilitating side effects. The protein they're seeking "would really provide a new therapy, and there hasn't been one in a long time for neuroendocrine tumors," says Chen.

Van Gompel estimates he's working more than 60 hours a week, even coming in on weekends to keep the cultures of experimental cells growing. "They're like pets," he says.

Despite the demands of tending cells instead of patients this year, Van Gompel describes the work as "relaxing," compared with the grueling memorization of early medical coursework. "Lab work is a lot more creative too," he says.

Van Gompel is the first "second generation" HHMI medical student fellow working in the lab of a former fellow. And the future physician-scientist may some day mentor a third generation. He's already given a talk to his medical student colleagues about his fellowship experience and "the need for translational research" in medicine. "It's definitely something I want to do," he says.