Harnessing the Power of the Immune System

By Katherine Dvorak

The future of cancer research, in the opinion of Katherine Chiappinelli, PhD, at the George Washington University School of Medicine and Health Sciences (SMHS), centers on combining immunotherapy with other treatments. Pairing immunology with epigenetics, the study of changes in organisms caused by modifications to gene expression, she seeks to better understand the mechanisms behind epigenetic control of immune signaling in cancer cells.

“The body’s own immune system is our most potent weapon against cancer cells,” says Chiappinelli, assistant professor of microbiology, immunology, and tropical medicine at SMHS.

While immunotherapy alone can work to fight cancer, Chiappinelli notes, it is most successful in patients who already have immune cells in their tumors. “Those patients in general respond to immune therapy, but there’s another set of patients [whose] tumor cells are growing very fast and there are few or no immune cells in the tumor to fight it,” she says. “These patients don’t do well with drugs that release the brakes on the host immune system. That’s a big problem in the field.”

And it’s a problem her lab is tackling head-on.

During a postdoctoral fellowship with Stephen Baylin, MD, at Johns Hopkins University, Chiappinelli found that a drug that turns on tumor suppressor genes also has a strong immune effect. She likened it to a changing stoplight — if the gene is turned to green, it means go, but if it’s red, it’s turned off.

“When we treated cancer cells with this drug, they had more immune signaling coming from the tumors and more immune cells in the tumors. But we didn’t know why,” she says. It turned out the answer was in our genomes. “Only about 2–3 percent of [human] DNA codes for proteins. However, about half of our DNA is repetitive sequences, and we don’t really know what they do,” she says. Originally, that was characterized as junk DNA, but it’s not junk, according to Chiappinelli. Those sequences include endogenous retroviruses, or dead viruses in our genetic code. Our cells turn off these viruses on purpose. But epigenetic drugs turn them back on.

We don’t get viral particles that can infect the cell when the retroviruses get a green light, Chiappinelli explains, but the viral RNA is transcribed, and that sets off an alert in the cell. “The alert makes tumor cells think they are infected with a virus, and they die or send out signals to host immune cells to come and kill them,” Chiappinelli says. “So the big effect in human cancer cells and in mouse models of cancer is that you get more immune cells coming in to kill the tumor and a good anti-tumor effect, especially when you combine that with immune therapies.”

Chiappinelli’s interest in medical research dates back to high school AP biology. It was a hands-on class full of lab work that showed her how pursuing science could mean doing something different every day and enjoying the excitement of not knowing what would happen next.

“That can be frustrating sometimes,” she says about the unknowns of scientific research, “but I think it also makes for a really interesting career.” She adds that she gravitated toward epigenetics, a new field during her time in graduate school, because not much was known about it then, and there’s still a lot for researchers to learn.

“I think, for a young person, there’s the opportunity to make important discoveries. It’s a field where there’s still a lot of progress to be made, in terms of both basic science discoveries and impact on patient care,” she adds.

Now a clinical trial Chiappinelli was involved in during her postdoctoral work at Johns Hopkins is underway, combining epigenetics with immune therapy. But even with the discoveries she’s helped make, Chiappinelli has more questions to answer: Which sequences do this? What things are being secreted to bring in the host immune cells? What are the best combinations to fully eradicate tumors?

That’s what Chiappinelli says she likes most about her work, day in and day out: “There’s always something new to discover.”
Funding Both Professional and Personal

Establishing the Marlene and Michael Berman Endowed Fund for Ovarian Cancer Research was both personal and professional for Michael Berman, MD ’67, RESD ’69, a specialist in gynecologic oncology at the University of California, Irvine Medical Center.

On a warm September day in 2017, Berman toured the George Washington University (GW) Cancer Center as part of Reunion Weekend at the GW School of Medicine and Health Sciences (SMHS); it was on that tour he met Katherine Chiappinelli, PhD, assistant professor of microbiology, immunology, and tropical medicine at SMHS, and spoke with her about her research on immunology and epigenetics.

Berman, always interested in discoveries that could benefit the patient population he has been taking care of for nearly 50 years, was intrigued, and not long after speaking with the young researcher, wrote a $100,000 check to help with the growth of the Chiappinelli Lab.

“We’re on the threshold for major advances in immunology and immunological treatments of cancers, and Dr. Chiappinelli’s research is the kind that will lead to positive developments in the care of patients with ovarian cancer,” he said.

That was the professional reason for Berman’s generous donation. His personal reason hit closer to home; Berman’s wife, Marlene, who passed away in 2014, had breast cancer. Later, all four of his daughters tested positive for the BRCA gene, which places them at a higher risk for developing breast or ovarian cancers.

“It’s a strange set of events, when you think about it,” Berman said, “I’m an oncologist with all four daughters at risk for cancer. But I think we’re not too far away from some major breakthroughs that may help patients suffering from this devastating disease.”

He added that the donation also was made to show his appreciation for the alma mater to which he feels greatly indebted.

“GW has permitted me and many others to have an impact on the lives of the people who trust us to make correct decisions and do the right things for them,” he said. “It’s that indebtedness that made me want to give back.”