Undergrad Helps Find Possible West Nile Cure

Dogged research—and long hours in the lab—yields big insights.

"AT FIRST, IT WAS LIKE A WHOLE NEW world to me," says Christopher Doane, 21, of his work in Michael S. Diamond's lab. Awarded an HHMI undergraduate fellowship after his freshman year at Washington University in St. Louis, Doane was assigned to generate monoclonal antibodies against a specific protein of the West Nile virus (WNV).

The goal sounded difficult, and even veteran researchers attest to the complexity of the process. Diamond, who researches infectious diseases at Washington University School of Medicine, taught Doane how to create special antibody-producing cells, called hybridomas, to combat WNV—a mosquito-borne pathogen that can afflict humans with anything from mild flu symptoms to brain swelling and occasionally even death.

The laboratory process involves fusing tumor cells with the spleen cells of lab mice previously inoculated with WNV's E protein. If the fusion is done just right, the two cells create a hybridoma and secrete monoclonal antibodies capable of binding to the E protein, thereby neutralizing the virus. To increase the odds of success, a number of fusions are attempted at once in a multiwell plate; bright fluorescence within a well signals a successful binding.

During his first 5 months, Doane achieved little success. He kept at it into the next school year. Then, one day near Thanksgiving, his luck changed.

"The whole well plate lit up," says Doane. Preliminary results suggested he had generated 30 different hydridomas, each secreting antibody against WNV E protein. Doing further screening, Doane and his colleagues observed that one antibody in particular, named E16, had surprising binding ability—it neutralized 10 different strains of WNV, preventing the virus from infecting cells. Further testing showed that E16 prevented infected mice from dying, even when administered up to 5 days after exposure.

Quite an accomplishment for any scientist, much less an undergraduate. Doane had made an antibody that, as Diamond says, "may be a viable treatment option against WNV in humans."

"Potentially such antibodies could be used in the treatment or prophylaxis of disease caused by a specific virus," says Robert B. Tesh, who studies WNV and other viruses at the University of Texas Medical Branch at Galveston. "Since there is yet no vaccine against or treatment for West Nile virus infection, the Wash. U. antibodies are of special interest, but this technology could be used to produce antibodies against other viral diseases as well."

The research was published in the May issue of *Nature Medicine*, with Doane as the fourth author (among 14). The antibody has been licensed to Rockville, Maryland-based MacroGenics, Inc., which is now trying to bring it to clinical trials. Doane stands to collect royalties if the antibody is commercialized successfully. ■

~Doug Main~

BOB HOWER / QUADRANT PHOTOGRAPHY

Of his great grandfather, who helped found HHMI, Christopher Doane says, "I am just amazed a person could help so many people in his lifetime."

SCIENCE ACROSS GENERATIONS—AND ACROSS HHMI

COURTESY OF THE HHMI ARCHIVE

WEISKOTTEN

Christopher Doane's interest in medicine is due in no small part to the influence of his great grandfather, Herman Weiskotten, a nationally prominent physician and medical school administrator in the early 20th century. As fate would have it, Weiskotten was a consultant to Howard Hughes, and when HHMI was founded in 1953 he was named one of the initial four members of its advisory board. Two years later, Weiskotten followed HHMI to its new headquarters in Miami, where he served on the board of directors for the next 10 years, retiring in 1965. Weiskotten died in 1972, before Doane was born.

Though Doane never met his great grandfather, he keeps Weiskotten's picture in his bedroom and talks glowingly about him. He keeps two leather-bound volumes of thank-you notes Weiskotten received at retirement from the deans of major medical schools and medical leaders around the world.

Doane earned his HHMI fellowship without any special consideration due to his great grandfather. And he plans a career in dentistry rather than medicine. Regardless, he still appreciates the link his research represents with Weiskotten's considerable contributions to HHMI. "I am just amazed a person could do so much and help so many people in his lifetime," says Doane, rightfully pleased that circumstances have enabled him to follow a path that his great grandfather first helped define.—D.M.