

I craned my neck to focus in on the arcades of arteries pulsing in Brandon's\* retina through my handheld 20 diopter lens. Brandon was 23, my age when I started my MD/PhD training. He was fresh out of college and had just been hired as a teacher downtown. He had just bought his first car, and was going to pick it up after the appointment. As I looked around his retina, noting the pigment deposits, I heard Dr. Eller's voice. "Why don't you take a look at this?" He had a map of Brandon's visual field up on the computer. Despite Brandon's excellent visual acuity—20/20, both eyes—he had the narrowest field I had ever seen in someone his age. After a brief conversation, we sent Brandon and his tearful mother home, then called the state and informed them that Brandon could no longer drive. "There's nothing we can do for him," said Dr. Eller. "Sure, we can enroll him in some studies, but his retinitis pigmentosa is going to progress, and eventually he'll lose his central vision too."

This encounter with someone my age, just starting out in life and deprived of his most precious sense, made me realize that I wanted to devote my career to preventing and treating blindness. Similar to Brandon, one in every 28 American adults is visually impaired, and one in 128 is blind.\* The prevalence is only increasing. To address this growing problem, **my long-term goal is to carry out vision research, teach, and care for patients at an academic medical center.** The intersection of chemical biology and vision research is an underdeveloped area that has strong potential for my career. In the short-term, I plan to earn a PhD in chemistry to become an expert in chemical biology, then to complete a residency in ophthalmology and retina fellowship (both with substantial emphasis on and protected time for vision research) after completing medical school. I realized I wanted to pursue this path eight years ago as I was entering my sophomore year of college.

I decided I wanted to become a physician-scientist when I first met a "GM3 Family." This family was struggling with GM3 Synthase Deficiency, an inherited neurological disease affecting the Amish population. The disease causes blindness, deafness, and uncontrollable seizures; it progresses unremittingly and nearly always kills by adolescence. Like most hereditary blindness syndromes, there is no cure. I spent four years working on a new therapeutic approach and corresponding in-house blood test for Ganglioside GM3, the metabolite missing in these children. The project honed my skills as a chemist, but more importantly inspired me to seek further training as a clinician and scientist so I could carry out research and apply it to caring for patients.

To lay the foundation for my long-term goal to become a physician-scientist in ophthalmology, since starting my MD/PhD training through the joint University of Pittsburgh-Carnegie Mellon University Medical Scientist Training Program (Pitt-CMU MSTP), I have completed the preclinical years of medical school (capped off by a clerkship in neurology and psychiatry), passed the United States Medical Licensing Examination (USMLE) Step 1, and completed three graduate school research rotations that have broadened my technical skills and my scientific understanding. My graduate school coursework and preliminary exam is complete, and a longitudinal clerkship in ophthalmology (medical and surgical retina, during which I met Brandon and decided on a career in ophthalmology) is underway, with a second clerkship planned for next fall. In the lab, I am completing several projects involving spatial and temporal control of nucleic acids and proteins using synthetic molecules that interface with biological systems in live cells. This research builds on my background and has helped prepare me to undertake the proposed research under my thesis advisor's (Dr. Alexander Deiters') guidance. By funding my proposed research and ensuring that I can complete my training as a researcher and a clinician, the NDSEG Fellowship will train me to carry out cutting-edge research in chemical biology (specifically, on DNA computation in live mammalian cells).

I have assembled a team of world-class mentors to assist with the project and with my career development via CMU's Center for Nucleic Acid Science and Technology (CNASt, of which Dr. Deiters is a member), including PNA experts Drs. Danith Ly and Bruce Armitage. Outside of the lab, my career advisor (Dr. Donald DeFranco) and a team of clinicians and scientists in ophthalmology (Drs. Jeff Gross, Andrew Eller, and Nils Loewen) will facilitate my development into a vision researcher. In the classroom, the MSTP's curriculum has helped me develop professionally as a physician-scientist through journal clubs; through presentations; and through formal training in biostatistics, grantsmanship, and bioethics. Further, chairing multiple MSTP committees (see CV) has helped me grow as a scientific leader. In my spare time, I lead the medical students on Guerrilla Eye Service missions in which a team of ophthalmologists and students sets up ophthalmology clinics around the area and provides free glasses and vision care to uninsured Americans.

The strong mentorship and rich resources that the NDSEG Fellowship will give me through this team — and, more broadly, through CMU's CNASt and through Pitt's department of chemistry, medical school, and joint MSTP with CMU — will enable me make a fundamental contribution to research on DNA computation in particular and on synthetic biology in general. Further, this fellowship will train me as a physician-scientist at the intersection of chemical biology and vision research who will develop new insights into treating blindness to continue giving back to patients and giving hope to visually-impaired people like the GM3 families and Brandon.

\* Names and identifying details of patients have been altered to protect privacy. Statistics are from The Eye Diseases Prevalence Research Group, *Arch. Ophthalmol.* **122**, 477–485 (2004).