

My Summer

As a child, I loved to wander the labyrinths of my father's university laboratory. I was intrigued by the white lab coats and the incubators. Sometimes, my prayers were answered and my father would allow me into his testing room, where I would sit on a tiny stool in the corner, a silent observer of his practiced agility. My father was a molecular biologist, and his lab, another world—one free of emotions and distractions, where the goal was the pursuit of truth.

by **Rebecca Hu**

Last summer, after years of observing and fantasizing, I was handed my own lab coat. I had been accepted as a medical intern in the Stanford Institutes of Medicine Research Program (SIMR). In this eight-week summer program, high school students from around the country perform research alongside Stanford faculty. I was overjoyed at the prospect of designing and conducting my own research experiment.

Upon acceptance into the program, each of the 58 interns selected a research focus such as cancer, cardiovascular, digital anatomy, immunology, neuroscience, or stem cells. I decided to follow my fascination with brain anatomy and signed up, along with 11 other interns, for the neuroscience institute.

The following week, I received my specific lab assignment: elucidating the role of a common cell-regulating mechanism,

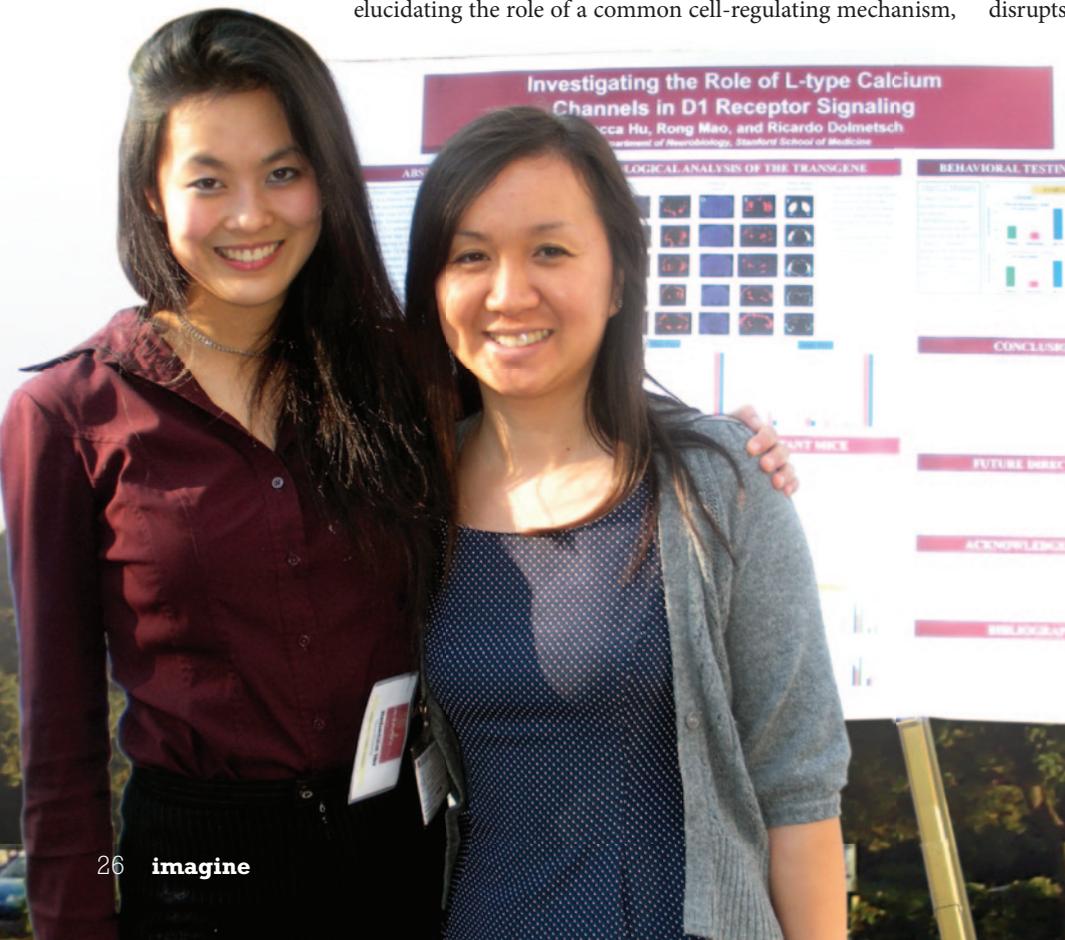
known as L-type calcium signaling, in the dopamine system of the brain. Having studied the dopamine system in my AP Biology class at school, I was eager to bring my conceptual knowledge of neurological systems to the laboratory bench.

A Brainy Journey

Recent evidence had suggested that calcium signaling that occurs in L-type calcium channels (LTCCs) is a critical component of dopamine systems in the brain widely implicated in psychomotor function, reward-based learning, and addictive disorders. To study the role of LTCCs in these pathways, I would focus on a mouse model that expressed a mutant form of $Ca_v1.2$, a subunit of LTCCs. I hypothesized that $Ca_v1.2$ dysfunction disrupts dopamine signaling, resulting in behavioral changes.

During the first week of the program, I attended neuroscience lectures and animal handling training sessions. While I was initially wary of working with mice, after training and practice, I became accustomed to the animal facilities. Over the next eight weeks, I also became well acquainted with the nooks and crannies of the Stanford Department of Neurobiology's Dolmetsch Lab, a place that

Rebecca Hu with her mentor, Dr. Rong Mao.



at SIMR

The Stanford Institutes of Medicine Research Program

reminded me of my father's laboratory so many years before.

Dr. Rong Mao, a research associate, acted as my mentor and oversaw my experiment planning. After a couple of weeks of close supervision and assistance in the lab, I began to acquire a clear sense of direction and independence.

To test my hypothesis, I worked with mouse models that expressed a mutation of Ca_v1.2 in the form of Timothy Syndrome, a developmental disorder characterized by autism, irregular heart rhythm, and the fusion of adjacent fingers and toes. I studied the behavior of the mutant mice to determine the consequences of Ca_v1.2 dysfunction in a subtype of dopamine receptor known as D1 receptor-expressing cells. A SHIRPA test—a basic behavior test that measures autonomic, cerebellar, sensory, muscle, and neuropsychiatric function—showed a decrease in many stress-related functions in the mutant mice compared to mice without the mutation. For example, the mutant mice defecated less, were less responsive to touch, and were less active when transferred from one location to another. In addition, our data from an open field activity test, in which we measured the activity of mice in an enclosed space, suggested the presence of hypoactivity, or reduced motion, in these mutant mice. These observations supported the prediction that the mice with mutant Ca_v1.2 channels exhibited certain behavioral alterations. Future goals could include further specifying these behaviors through behavior tests that target the factors of stress and motor activity.

A Lesson in Safety

As my days in the lab grew longer, sleep became more difficult to come by. My lab table was cluttered with scribbled notes, carefully stacked slide boxes, and half-eaten cups of ramen noodles.

I had grown accustomed to the equipment and procedures that comprised my daily routines: microscopy work, tissue sectioning, genotyping. But as I soon came to learn, even practiced routines aren't always error-proof.

The cryostat machine is used to slice thin sections of tissue specimens for mounting on slides. One day, rushing to complete the seemingly never-ending pile of sectioning work, I sliced my finger on the cryostat blade. An unbelievably large amount of blood gushed from my finger, and I fainted. Luckily, there were people in the lab to help revive me and take me to the emergency room, where I was treated with a skin adhesive

to protect the wound from infection. I returned to the lab bench the next day.

I soon healed from the accident, but realized that if I wanted to pursue my passion for science, I needed to concentrate and focus on my work in order to avoid accidents.

The Home Stretch

As the end of my internship neared, I began compiling the results of my experiments for the required poster and PowerPoint displays that would be presented to the entire Stanford School of Medicine. The last two weeks were especially demanding: in addition to designing and running last-minute experiments to confirm my results, I had to organize my data to summarize the main points of my project. Thankfully, we were given helpful guidelines from SIMR faculty and staff on how best to present our research abstracts and final projects.

My 16-hour workdays and midnight experimental runs paid off. I completed my independent research project, and the results may contribute to a future paper for submission to a scientific journal.

The final poster presentation was a time of mixed feelings: while I had contributed to scientific discovery, I was sorry to see the summer come to an end. My experience at SIMR has given me a profound appreciation for unknowns in the field of medicine and for the immense potential for exploration. Perhaps most importantly to me, my summer at SIMR has given me confidence to pursue my curiosity and taken me one step closer to my aspirations of a career in neurosurgery. **i**



Rebecca Hu is a senior at Aragon High School in San Mateo, CA, where she leads the math, debate, and journalism organizations. When not in the lab, she enjoys playing the piano, Chinese folk dancing, runway modeling, playing volleyball, and relishing good food.



In the Dolmetsch Lab with Stanford med school student Anna Krawisz.

To learn more about SIMR, visit <http://simr.stanford.edu>.