Dr. Jonathan Haines: From picture to person

*Portrait of an Alzheimer's researcher*

By Katie Betzwieser / Intern
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I remember going through the profiles of researchers who were prospective mentors for my upcoming internship for the fall 2001 semester. The brief biographies that had pictures were the most interesting.

One person in particular caught my attention. Not because his research sounded incredibly fascinating, but because he appeared laid back and extremely cool: the exact antithesis of what I was expecting. Grinning like he had just been caught with his hand in the cookie jar, the biophysicist looked like an approachable, everyday Joe who just happened to be doing some sort of research with the brain and genes.

So, it was Jonathan Haines’ affable appearance that influenced my decision to work in his lab for a semester as part of my major in the Communication of Science, Engineering and Technology. But it turned out to be Haines’ research in neurodegenerative disorders, specifically Alzheimer’s disease, that kept me intrigued and eager to learn as much as possible about this devastating illness, its underlying causes and possible treatments.

**Alzheimer’s is not only a disease, but also a story of destruction and debilitation**

Alzheimer’s is not only a disease, but also a story of destruction and debilitation of a human being’s most important organ. According to the National Institute of Aging, four million Americans suffer from Alzheimer’s disease, which progressively destroys the brain leaving a healthy body with no control center. As Alzheimer’s slowly and gradually takes over the brain, those afflicted begin to lose control over daily functions such as memory, time and space orientation and communication skills. Currently, there is no cure, but there is hope for the future.

Haines is a professor of molecular physiology and biophysics at Vanderbilt, where he directs both the program in human genetics and the Center for Research on Human Development at the Kennedy Center. He wants to provide a happy ending to this devastating story. He and his research team are looking at the genetics underlying this affliction. Deciphering the genetic connection is an essential first step toward finding effective treatments or, even better, a cure. Their work is a small but vital part of all the medical research currently being conducted to understand, treat and cure this degenerative disease.

To prepare myself for the internship, I read up on Alzheimer’s via the Internet and the local library. Searching for a humanistic take on the disease, I randomly chose a book, *Hard to Forget: An Alzheimer’s Story*, by Charles Pierce. I was hooked after reading the first few pages and did a double-take when I found that Haines was mentioned in the
Introduction! How often do you get to work with someone who is described in a book as one of the up-and-coming geniuses in his field?

As a result, I was exceedingly excited to begin my work in the lab. In early September, when Haines and I met to discuss the details of my internship, we set up an introduction to the laboratory for the following Tuesday, Sept. 11, 2001.

Lab routine disrupted by 9/11

On that fateful day, I walked to the Haines lab in a state of bewilderment, trying to get a grasp on everything that was happening in New York City after terrorists destroyed the landmark World Trade Center Towers. Despite the horror everyone was feeling, Haines greeted me with a kind smile, much like the one in his photograph. As we walked to the lab, we talked about the events of the day, not once thinking about Alzheimer’s disease or lab work. When we arrived, we found life there revolving around the computer that the lab team was using to find out as much information as they could about the unprecedented terrorist attacks. We made quick introductions and kept watching. Nothing else seemed as important, not even research. After the visit was over, I realized that the experience had been anything but stereotypical.

As I got to know the crew in the Haines lab, I found that they were just as amicable as their boss. Kindness and smiles greeted me every time I arrived. The graduate students, Holli Hutcheson and Shannon Kenealy, were more than willing to help me with anything I requested. The three research assistants – Krista Stanton, Shana Crabtree, and Sarah Zika – were just as enthusiastic and encouraging. And Brent Anderson always provided the bit of male humor needed for a group of gossipy girls. Think of the movie “Office Space” set in a lab, but without the bad boss and monotonous job. They were the “hot-chicks-and-one” lab that the fourth floor of the research building talked about because of their entertaining personalities and happy dispositions. They were the ones who would contribute to one of the most memorable and worthwhile experiences of my lifetime.

Vivid memories of Alzheimer’s effects

When I wanted to know about something, all I had to do was ask. I always got plenty of answers. Not all the questions revolved around Alzheimer’s disease or DNA or research in general. We talked about the things that happened over the weekend and the interesting vendors who sold paraphernalia to the lab. I can state unequivocally that there are no stereotypical science “geeks” in the Haines’ lab.

The lab works on many projects, but I focused my attention on the research being done with Alzheimer’s because the disease affects such a great number of Americans. Currently, Haines and his research team are concentrating on mutations in genes located on chromosomes 10 and 12 as a possible cause for late-onset Alzheimer’s, the most common form of the disease. The researchers begin with blood samples collected from families whose medical histories show an unusually high incidence of the disease. Then they look at the DNA isolated from the samples for anomalies or mutations.

Laboratory divided into three parts

Research in the laboratory is divided into three sections: family ascertainment, core lab and then statistical analysis:
The family ascertainment group gathers family history information and collects blood samples from families that exhibit a high occurrence of Alzheimer’s disease. Researchers in the core lab isolate DNA from the blood and cut it into short pieces so they can look for mutations in specific locations. In the regions of interest, the lab workers compare the base pair sequences in the DNA of normal individuals with that of Alzheimer’s patients and their families.

Data generated in the family ascertainment group and the core lab is sent to the data analysis group. Here, analysts determine the statistical probability that a given gene mutation is implicated in Alzheimer’s.

I spent most of my internship in the core lab where I worked with beginner’s DNA to learn the basic steps of isolating and examining this incredible molecule. Those steps are: PCR, gel electrophoresis, and scanning for the necessary DNA fragments.

PCR, or polymerase chain reaction, is the process used to make large amounts of DNA so that it can be studied and sequenced. The DNA is mixed with primer molecules that attach to specific spots on the DNA strands. A special enzyme, called DNA polymerase, causes the two strands to separate in the region between two primers and makes copies of that portion of the DNA. By repeating this process 30 to 35 times, millions of copies of the desired segment of DNA are produced. This allows the researchers to look at this particular piece of DNA in detail.

The next step is gel electrophoresis that separates replicated DNA strands by size. It is based on the fact that when impelled by an electrical force, shorter DNA fragments can travel more rapidly through a gel than longer ones.

**Learning the basic techniques**

To learn this technique, I began by making the gel, which looks like a glass sandwich with translucent jelly. I treated the marker from the PCR product with dye for easier loading into the gel. Loading a gel with the samples is not easy. Patience, accuracy and precision are a must to prevent mishaps and errors that force one to start all over. With a bit of beginner’s luck, I had few problems, but I saw that even experienced lab workers can have trouble. Next, I hooked the gel mechanism up to a battery that produced the electrical field that pushed the electrically charged DNA fragments down the gel strip.

After the samples ran, I prepared the gel for analysis by adding a nucleic acid stain called SYBERGOLD. The stain causes the DNA to fluoresce under a special scanner known affectionately in the lab as “The Hitachi.” The scanner is hooked to a computer that produces an image of the fluorescence, which can be printed out for analysis. The identity of an unknown fragment is determined by comparing its position on the gel with the positions of known fragments.

During the internship, I met with Haines periodically. In the first interviews, we talked about what the lab was focusing on, what kind of progress the group was making and how he thought his work would contribute to the future. At first, I asked typical questions and got typical answers. I realized that if I wanted to understand what makes Jonathan Haines tick, I needed to delve deeper.

During our interviews that smile – the same one as in the photograph – put me at ease despite the fact I was dealing with a person with so much professional respect. Nevertheless, I had trouble getting beyond his public persona. Despite his genuine interest in helping me, Haines guarded his personal life and this complicated my efforts.
to understand the life of a research scientist. But I would come to find out that the most
difficult questions are the ones that yield the most unique and invaluable answers

As director of the Program in Human Genetics, Haines oversees what goes on in
the lab, writes grant proposals and ensures that the lab is on track. The long hours of
paper work and meetings that characterize his job today is much different from what he
did when he started out as a laboratory statistical analyst, he said.

Haines received his doctorate in genetics from the University of Minnesota and
then did his postdoctoral work at the Indiana University School of Medicine in the
department of medical genetics. He did his first research on Alzheimer’s at Indiana but it
was not his first experience with the disease.

When he was about nine or ten years old, he remembers hearing that his
grandmother had been diagnosed with Alzheimer’s, but he was not aware of the situation
or the implications of the disease until much later. He remembers his mother making
many depressing, stressful trips to visit her mother.

Vivid memories of Alzheimer’s effects

One vivid memory that Haines has of Alzheimer’s effects came from his last visit
with his grandmother when he was a young teenager. Family members sat around the
table discussing how to make the best of an obviously grim situation. His grandmother
did not participate in the conversation. “She seemed clueless about what was going on
around her. She sat obliviously at the table, bringing her thumb and forefinger to her
mouth like she was drinking a cup of tea. There was nothing in her hand, nothing on the
table and nothing was going to her mouth,” he recalled.

As he and his mother left, she turned to him and said, “Don’t ever let me get like
that.”

In 1995, Haines remembers being at another relative’s funeral and watching his
mother. She had difficulty keeping up a conversation and expressing herself. Because of
his sensitization to Alzheimer’s disease and the symptoms, he knew what was coming. In
May 2000, his mother was diagnosed with Alzheimer’s and Haines’ own family became
a candidate for the ascertainment group in his lab.

Having seen the destruction of her own mother, Mrs. Haines has withdrawn from
her normal, active life. Her reaction to her condition has been hard for Haines and his
family to take because they don’t know how to deal with such an emotional and sensitive
situation, he said.

When I asked Haines how this situation affected his work, he replied that he
keeps the perspective of his own risk in the back of his mind and tries to focus on the
bigger picture of his research. Rather than worrying about something he cannot change,
Haines chooses to concentrate on his research; who it will help; when it will make a
difference and how much difference it could make for so many.

Haines smiles as he remarks that his research is important, but it is only the first
piece in the complex puzzle of what causes Alzheimer’s and how to effectively treat and
prevent it. There is a gleam in his eye and enthusiasm in his voice as he talks about his
work and its potential benefits to mankind. His face takes on a look that I immediately
recognize. It is the same look that led me to intern in the Haines’ lab in the first place.

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