I knew almost nothing about the practice of science when I first decided to begin research at UNC-Chapel Hill. Despite my naiveté, I found a lab able to lend structure to an innate curiosity: that of Shawn Ahmed, who investigates germline immortality in the nematode *Caenorhabditis elegans*. My first summer in lab, I was charged with developing a method to measure telomere overhangs. Telomeres are segments of repetitive DNA on chromosome ends that grow shorter with each cell division. When they reach a critical length, they signal cells to stop dividing, acting as a proliferation limit. Germ cells gain immortality by upregulating telomerase, an enzyme that maintains telomere length. Each telomere has a single-stranded overhang that tucks back to form a protective cap called the T-loop. This entire structure helps regulate telomerase's access to chromosome ends, controlling telomere length and thus cell proliferation.

The small size of the Ahmed lab allowed me to work closely with Shawn in creating an assay. I was daunted by the task, but he helped me to unravel the logic behind experimental design. In a way that seemed tedious at the time, but was, in retrospect, instructive, he would allow me to make mistakes and then help me understand what went wrong. By the end of the summer, I had developed a single strand DNA hybridization assay to measure the relative length of telomere overhangs, an indication of T-loop integrity. I realized how much I had grown when I was confident enough to design a new experiment on my own – a set of "yardstick" plasmids that would allow me to quantify overhang length within a few base pairs – before approaching Shawn with my idea. Using this assay, I was the first to characterize *C. elegans* telomere overhang length, demonstrating a similarity to human overhangs not seen in yeast or mice. My work supported the idea that *C. elegans* presents a unique opportunity to study telomere biology in a system similar to humans.

I soon began to address my own questions: How is the T-loop maintained? How does the overhang affect its presence? I was one of fifty undergraduates at UNC-Chapel Hill to receive a Smallwood Foundation Undergraduate Research Fellowship that allowed me to continue my work in the lab. During the next year, I used the overhang assay to further characterize protein activity at the telomere. Although several proteins have been shown to bind the T-loop, their functions remain unknown. Previous work in the Ahmed lab showed that two, CKU-70 and CKU-80, have no effect on telomere length. With my assay, I found that animals depleted for CKU-70, CKU-80, or both, do not have overhangs that differ from wild type, indicating that these proteins have no functional effect on overhang maintenance. While this is the opposite of what is seen for yeast and plant homologs, it is consistent with observations in mammalian systems.

To determine whether certain telomeric proteins stabilize telomere ends, I decided to analyze protein localization in germline nuclei. Although antibody staining is not an obscure technique, members of the lab had little experience with it; as a result, I performed meticulous troubleshooting to develop a protocol. I soon learned that true research, even when done independently, is never done alone. People I had never met were willing to lend me their time and equipment. With the help of others, I was finally able to visualize two proteins – MRT-1 and POT-2 – at the telomere and show the disruption of their localization in telomere-mutant backgrounds. My work implicated these proteins in T-loop formation, which directly affects telomerase regulation and thus, telomere length. My undergraduate research culminated in presentations at several undergraduate symposia and an honors thesis, which I successfully defended in April 2007. Before I left the lab, Shawn asked for my help in developing figures and writing a paper, which has recently been published in *Genetics*.

I had gained depth in one area of biology, and wanted to use graduate school to explore other topics. Last fall, I enrolled in Molecular and Cell Biology at UC Berkeley, a department

renowned for the breadth of its research. I arrived at Berkeley determined to rotate in very diverse fields, which was reflected in my choice to work in labs examining arthropod evolution, neural development, and sex determination. I spent my first year trying to absorb as much as possible through retreats, conferences, seminars, and conversations.

During this time, a formative experience was my rotation with Nipam Patel, whose lab studies the evolution of arthropod development, focusing on the crustacean *Parhyale hawainesis*. Under his guidance, I characterized the expression patterns of several Hox genes, members of a highly-conserved gene family that control body segment identity. I used RNAi to deplete these genes, analyzing phenotypic effects and changes in gene expression. This project appealed to me because it used molecular methods to answer an evolutionary question: How did Hox genes function as a mechanism for the evolution of different body shapes? I demonstrated that *Parhyale* Hox gene regulation differs from the canonical model developed in *Drosophila*, demonstrating that posterior prevalence – in which posterior Hox genes inhibit the expression of more anterior Hox genes – does not affect two *Parhyale* Hox genes. Working with Nipam demonstrated the value of comparative research and an interdisciplinary approach. I left his lab knowing I was most interested by basic research questions with relevance to many systems.

When it came time to choose a thesis lab, I found an ideal project in Barbara Meyer's lab addressing the wide field of meiosis. My rotation in this lab dealt with the effect of a chromatin-remodeling protein on meiotic crossovers. Preliminary data suggested that animals depleted for this protein might have a higher incidence of double strand breaks, some of which are resolved as crossovers. Although my project showed that there are no discernable effects on crossover frequency, it was a wonderful introduction to the field of recombination and chromosome biology. I am intrigued by how little is known about recombination, despite the fact that it has been studied for over a century, as well as the putative role of recombination in genome evolution, which I discuss further in my research proposal.

My undergraduate experience illustrated how science depends entirely upon the open communication and diligent work of its practitioners. Coming to Berkeley has shown me how much can be accomplished by taking an interdisciplinary approach. This is why I believe that the Meyer lab is an ideal place to conduct a study of crossover regulation. Using a combination of genetic, cytological, molecular, and biochemical techniques, the lab is able to address all sides of a question. I believe that research relies on an environment that encourages support as well as constructive dissent; members of the Meyer lab have the expertise I hope to gain and the patience to help me. An NSF Fellowship would allow me to continue my education even as I contribute to the education of others, a goal I discuss in my personal statement. I strongly believe that a scientific researcher can have a significant impact on the world, especially when one can temper a love for discovery with a dedication to teaching

Publications & Presentations

Lowden MR, Meier B, **Lee TW,** Hall J, Ahmed S. (2008) End-Joining at *Caenorhabditis elegans* telomeres. *Genetics* 180: 741-54.

Lee TW. "The effects of *cku-70, cku-80, mrt-1* and *pot-2* on *C. elegans* telomeres." (2007) Koeppe Undergraduate Research Symposium. UNC-CH, Chapel Hill NC.

Lee TW. "Consequences of Unprotected Chromosome Ends." (2006) Celebration of Undergraduate Research. UNC-CH, Chapel Hill NC.