THE LUMEN PRIZE: APPLICATION

PART I: PRELIMINARY INFORMATION

Title:

Understanding the role of the body's immune system in atherosclerosis through analysis of TLR4 and HSP interactions

Names:

(Mentor: Dr. Kathryn Matera)

Abstract:

Recent research has identified the body’s inflammatory response as a major contributor to the build-up of arterial plaques. Cellular receptors within the body, in particular toll-like receptors (TLRs), may hold the key to combating plaque formation. TLRs interact with heat-shock proteins (HSPs), small biomolecules regulated by the immune system, in response to the body’s stresses. This interaction fuels the formation and progression of plaques through initiating an inflammatory response. The mechanism by which TLRs and HSPs interact could hold the key to eradicating much of the body's inflammatory response related to plaque build-up. Previous experiments have been performed within the body and do not allow for in-depth exploration of these interactions. Using a variety of methods, TLRs and HSPs will be analyzed in vitro to determine their role in the formation of arterial plaques. Once determined, inhibitors can be synthesized to prevent such interactions and dampen the immune system’s contributions to heart disease.

Background Statement:

I have often been described as “too serious,” “intimidating,” and “a perfectionist.” These words have been hurtful to me, but when I look at the bigger picture, I realize that they are exactly the right adjectives to describe me as I become engrossed in my dream of becoming a doctor.
I wasn’t always that way. In middle school, I loved hanging out with friends and watching movies like any other preteen. But in high school, I became fascinated with learning how things worked. What is the make-up of an atom? How does the heart pump blood through the body? It didn’t matter- I wanted to know how and why. In my tenth grade biology class, I had the opportunity to dissect a fetal pig. While many girls opted to write papers to avoid the dissection, I stood, scalpel in hand, peering inside, utterly amazed at how all the systems of the pig’s body worked together to sustain the whole. It was then that I realized that I wanted to enter the field of medicine. I wanted to learn all about how the human body worked!

But it isn’t just studying the way the human body works that intrigues me. I genuinely have a desire to contribute to the welfare of those around me. This desire led me to spearhead the “blankie project.” In high school, I purchased fabric which the honor society tied into blankets and distributed to the children on the oncology floor at Upstate Medical Center in New York. Since my first semester at Elon, I have been working to establish a chapter of Global Medical Brigades on campus. This spring, I will lead fourteen other students and four health professionals to Honduras for our inaugural trip where we will provide much-needed healthcare to local inhabitants.

Now, under the tutelage of Dr. Kathryn Matera in the Chemistry Department, I have conducted two years of research, including as part of the SURE program, studying the effect of oxidized lipids on the composition of atherosclerotic plaques. In addition, I have conducted research reviews for my application to the Goldwater Scholarship examining the body’s inflammatory response and its contribution to heart disease. I have found these research experiences particularly gratifying as my own family history involves the untimely deaths of my grandfather and uncle due to heart disease. It would be rewarding if the research I conducted could
someday lead to a better understanding of this prevalent disease. By doing so, I accomplish my dream of working towards an M.D./Ph.D. and contributing to the well-being of others.

So, I am “too serious” because I am always in the laboratory; I am “intimidating” because I don’t settle for just getting it done; I am a “perfectionist” because I strive for the very best in me. That is me. I have come to realize that I can’t be anything less than what I am – a student whose goal is to be the very best doctor and medical researcher that she can be.

**PART II: NARRATIVE**

**Focus:**

Over the years, scientific research has allowed for greater understanding and better treatment of a variety of diseases. However, there is still no cure for heart disease, despite it being the most common cause of death in developed nations.¹ Recent research has identified the body's inflammatory response as a major contributor to the build-up of arterial plaques. Specifically, the function of cellular receptors within the body, in particular toll-like receptors (TLRs), may hold the key to combating such plaque formation, also known as atherosclerosis. It has been shown that when lipids are oxidized, the body initiates an inflammatory response to clear the oxidized lipids. By doing so, it increases the release of heat shock proteins (HSPs) which then aggregate to the site. When HSPs are recognized by TLRs on nearby cell membranes, they interact and extend the inflammatory response by causing the release of other small biomolecules. Once all these molecules reach the site, the oxidized lipid is surrounded and cannot be cleared, forming a core at which additional molecules of oxidized lipid bind.

Research into the relationship between TLRs and heart disease is particularly interesting to me, as it offers a means to combine my passion for biochemistry with my aspirations to matriculate into an M.D./Ph.D. program. Through nuclear magnetic resonance (NMR) experiments, I will
examine the interactions between TLR4 and heat shock proteins. If the binding site of TLR4 and HSPs is known, inhibitors can be synthesized to prevent binding in the hopes of decreasing the aggregation of inflammatory molecules at the site of plaque formation. The effect of varying concentrations of inhibitors will be examined to see how they affect binding through ultraviolet light spectroscopy and gel electrophoresis. While research has already been performed on HSPs and TLRs in relation to atherosclerosis, the majority of these studies have been in vivo studies. This research has provided information regarding the results of the inflammatory response, but large gaps still exist within the research.\textsuperscript{2} Studies have also shown that high amounts of TLR4 are present within atherosclerotic lesions and are associated with a pro-inflammatory response.\textsuperscript{4} But while in vivo research provides a necessary baseline of information, we need to know how changes in various conditions affect these interactions. Further information regarding the chemical processes by which TLR4 and HSPs bind will provide enhanced knowledge through which the causes of the disease can be avoided.

**Proposed Experiences:**

**Summer 2009**

In preparation for beginning my research on toll-like receptors and their role in atherosclerosis, I will be participating in the Amgen Scholars Program at the University of California at San Francisco during the summer after my sophomore year. I will participate in a selective eight week biomedical research internship focused on biochemical reactions within the body. My participation in this program will allow me to gain invaluable lab experience, teach me how to think more like a scientist and how to work independently in a lab. I will also be presenting my research at a conference in Los Angeles, as well as in San Francisco, which will allow me to network with other biomedical researchers. In addition, I will be leading fourteen other Elon students and four health professionals to Honduras in May as part of Global Medical Brigades to
provide much needed medical care to those in need. Finally, I have applied to present my previous research findings at the National American Chemical Society conference in Washington, D.C. this August.

Fall 2009

Beginning the fall of my junior year, the Lumen Prize will provide me with the necessary resources to begin experimentation to determine exactly how TLRs and HSPs bind and what other factors are important in these interactions. In addition, I will be enrolled in Human Gross Anatomy and Biochemistry I, which will allow me to learn more background information on the human body and the reactions within it to apply to my research.

Spring 2010

In addition to continuing my research, the Lumen Prize will allow me to apply to either the “Membrane Transport Proteins” seminar at the University of New England, or the “Immunoochemistry and Immunobiology” conference in Switzerland. As both of these conventions are part of the Gordon Research Conferences, a selective set of seminars for experts in a specific scientific field, my attendance at either conference would provide me with the opportunity to speak with researchers familiar with my field of research. This would allow me to exchange information, learn about cutting-edge research and speak with leaders in the field. In addition, I would like to present my research at SURF and at the biological section of an American Chemistry Society research conference. While conducting research and presenting at conferences, I will also be enrolled in Biochemistry II and Molecular and Cellular Division, two courses that will again provide me with valuable background information that I can apply to my research.
Summer 2010

During the summer after my junior year, I hope to participate in a medically related internship. I would like to intern with either a medical doctor or an M.D./Ph.D. in order to learn more about the medicine behind heart disease and the in-depth workings of the heart. As I will already have completed two semesters worth of initial data regarding TLRs and HSPs, a summer medical internship will allow me to apply my findings to the human body and discuss with doctors how these interactions take place within the body, as well as possible ways to prevent it. I will also be leading a group of students and medical professionals to Honduras for our second Global Medical Brigades trip in May. In addition, I will be applying for M.D./Ph.D. programs.

Fall 2010

During the fall of my senior year, I will continue my research into TLRs and heat shock proteins. In addition, I will most likely be interviewing at a variety of M.D./Ph.D. programs and discussing my research with other respected individuals in the field of biomedical research.

Winter 2011

I will finalize my assays and collect the final data on my research project. I will also enroll in a General Studies course related to healthcare to understand what nationwide factors affect the implementation of scientific discoveries.

Spring 2011

During the spring, I will analyze the data and write a research paper of publishable quality that I can submit to the journal of Biochemistry as well as to the Elon College Fellows program. In addition, I will be enrolled in Medicinal Chemistry which will bring together all of my previous courses regarding the human body and biochemical reactions. Finally, with the resources provided by the Lumen Prize, I will present my final findings at SURF and the National Conference of Undergraduate Research.
**Proposed Products:**

The culmination of my work and experiences over my four years at Elon University will result in a variety of products, both tangible and intangible. I will write an extensive research paper that will be submitted to the journal of *Biochemistry* for publication. This final report on the interactions between TLRs and HSPs will also be used for my final paper for my Fellows research. The findings discussed in my report will be presented at the previously mentioned conferences, as well as provide me with a springboard off of which to begin my research in graduate school. My receipt of the Lumen Prize will allow me to combine my passions for both medicine and research, by allowing me to participate in a variety of research conferences and a medical internship. These will allow me to develop a strong network of doctors and researchers to which I can refer when applying for M.D./Ph.D. programs. Obtaining my Ph.D. will give me both the accreditation and knowledge to perform in-depth biochemical studies. Obtaining my M.D. will provide me with the thorough knowledge of the human body needed to better apply my experimental findings to alleviating the causes of atherosclerosis. This combination of degrees will provide me with the background needed to continue my dream of becoming a biomedical researcher.

**PART III: FEASIBILITY**

**Feasibility Statement:**

My proposed project is feasible due to my personal drive to advance the knowledge of modern science, the manageable amount of time that will be dedicated to research, and the ability of the project to remain within the allotted budget.
**Budget:**

The following proposed budget is an estimate of the expenses necessary for the completion of my proposal. If granted, the Lumen Prize money will provide financial assistance for a summer medical internship, various chemicals and enzymes needed to perform research and travel to research conferences. The remainder of the funds would be used to supplement the cost of tuition.

- $2,500- A supplemental stipend for an un-paid summer medical internship focused on researching the mechanisms of the heart and how TLRs function within them.
- $1,000- Travel expenses to the National American Chemistry Society conferences in California in the spring of 2010 and to the National Conference of Undergraduate Research in the spring of 2011.
- $1,000- Travel to the Gordon research conference in the spring of 2010.
- $2,500- Chemical expenses for various reagents and proteins needed to perform laboratory research.
  - Heat Shock Protein 70 (800µg)- $1,000.00
  - Toll-like Receptor 4 (600µg)- $1,320.00
  - Shipping and Handling- $180.00
- $8,000- Tuition
## Timeline:

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<tr>
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<th>Proposed Experiences</th>
<th>Proposed Product(s)</th>
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<tbody>
<tr>
<td><strong>Summer 2009</strong></td>
<td><strong>Biomedical Research Program at the University of California at San Francisco; Present at the National American Chemistry Society conference in Washington, D.C.; Global Medical Brigades trip to Honduras</strong></td>
<td>Network with other researchers, learn more background information on immunology, atherosclerosis, and/or enzymatic reactions, and learn about other experiments possible to monitor protein-protein interactions; Network with other researchers at the National American Chemical Society conference; Learn about healthcare in Honduras</td>
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<td><strong>Fall 2009</strong></td>
<td><strong>Begin research with 1 credit of CHM 499; Take Human Gross Anatomy and Biochemistry I</strong></td>
<td>Preliminary data regarding how TLRs interact with other biomolecules; Learn more about the body and the biochemical processes within through coursework</td>
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<td><strong>Winter 2010</strong></td>
<td><strong>Study Abroad in Europe</strong></td>
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<tr>
<td><strong>Spring 2010</strong></td>
<td><strong>Continue research with 1 credit hour of CHM 499; Take Biochemistry II and Molecular and Cellular Division; Present at SURF, a National American Chemical Society conference and attend a Gordon Research Conference</strong></td>
<td>Collect more data on TLR interactions and begin to hypothesize conclusions to present at the two research conferences; Learn about additional cellular processes in the body through coursework; Network and learn more about the cutting-edge research occurring by attending the Gordon conference</td>
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<td><strong>Summer 2010</strong></td>
<td><strong>Medical Internship; Global Medical Brigades trip to Honduras</strong></td>
<td>Learn more about the workings of the heart while discussing applications of the initial conclusions drawn from my research with various medical doctors; Learn about healthcare in Honduras</td>
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<td><strong>Fall 2010</strong></td>
<td><strong>Continue research with 1 credit hour of CHM 499; Conduct interviews for M.D./Ph.D. programs</strong></td>
<td>Collect more data on TLR interactions and specify a hypothesis; Discuss my research with other medical doctors and researchers at prestigious graduate programs</td>
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<td><strong>Winter 2011</strong></td>
<td><strong>Continue research; Take a GST course related to healthcare</strong></td>
<td>Begin finalizing experimental assays; Apply my findings to healthcare and the global economy through coursework</td>
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<tr>
<td><strong>Spring 2011</strong></td>
<td><strong>Continue research with 1 credit hour of CHM 499; Take Medicinal Chemistry; Present findings at SURF and the National Conference for Undergraduate Research</strong></td>
<td>Finalize all experimental assays and gather presentable data and graphs; Write a research paper of publishable quality and submit it to the journal of <em>Biochemistry</em>; Learn about chemical reactions and their influence on medicine through coursework; Present my findings at research conferences</td>
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Reference List:

1. Centers for Disease Control and Prevention, Heart Disease Facts and Statistics. 


Personal Information and Signatures:

Name: Datatel ID #:

Major(s): Biochemistry Minor(s): Mathematics

Local Address (include city, state, zip):

Campus Box
Elon, NC 27244

Primary Telephone: Elon email:

Started at Elon [mm/yyyy]: 08/2007 Expected Graduation [mm/yyyy]: 05/2011

The student’s typed name below serves as his/her electronic signature and indicates that the information contained in the application is accurate, and reflects his or her best faith plans for scholarly activities during the remaining two years at Elon. Applicant hereby gives the Selection Committee permission to obtain a copy of current transcript and to verify that student is in good standing at the university. Recipients of the Lumen Prize will be asked to sign a Letter of Agreement indicating their commitment to uphold the standards associated with being a Lumen Scholar.

________________________________________(Applicant’s “signature”) Date 03/16/2009

The faculty/staff mentor’s typed name below serves as his/her electronic signature and indicated support of the proposal described herein and willingness to serve as an ongoing mentor to the applicant.

______ Kathryn Mansfield Matera ________ (Mentor’s “signature”) Date 3/16/2009