My name is Daria Amiad Pavlov and I am a senior student at the bioengineering department, University of Washington. I was born in Russia and migrated with my family to Israel when I was 8 years old. I arrived to Seattle after completing high school and army service in Israel and with the assistance of an athletic scholarship that I was offered here. My choice of UW was not an accident; I was looking for the highest level of academic education, especially in natural sciences. My undergrad experience at University of Washington and specifically at the bioengineering department reinforced my interest and motivation to complete a PhD program in this field and pursue career as a scientist.

My parents always encouraged me for excellence in school but also allowed me to be physically active. As I was discovering my inclination towards math, physics and the natural world from the educational stand point, I was also growing as an athlete. After high school I served in a technological unit in the army, focused on development of optical equipment, and in parallel completed two year coaching courses in track and weight lifting. Naturally, I was trying to find a connection between science and sports, and now being familiar with the basic physiology and anatomy that makes our body works, but most importantly realizing how much remains unknown, I made up my mind to continue my education in the field of biomedical engineering, researching human body mechanism, specifically muscles, to design and develop new diagnosis, prevention and treatment methods.

At the end of my sophomore year, after I was accepted to the bioengineering department I felt ready to start practically applying my knowledge by being involved in a research. Since muscle was the area I was so interested in, and after finding out about Heart and Muscle Mechanics (HAMM) lab in the bioengineering department I decided that it's the best fit for me. I joined lab HAMM, directed by Dr. Mike Regnier, in summer 2006, where at first I assisted a research scientist

in the lab, Dr. Galina Flint, with the goal of familiarization with the different projects and research techniques available in the lab. HAMM lab uses various research techniques and approaches to study the molecular and cellular level mechanisms responsible for regulation of muscle contraction. The primary goal is to use the gained knowledge to develop therapeutics for damaged or diseased cardiac and skeletal muscle.

During the summer I was introduced to a variety of experimental techniques and research projects in the lab. The first project I became involved in was to perform a solution ATPase essay to study the effect of EMD 57033 on skeletal and cardiac muscle contractile proteins. After some practice, I was able to perform these measurements independently and my experiments showed interesting results, opening me a door for further individual investigation. As a result, last year I worked on a project investigating the mechanism by which EMD positively affects muscle contraction. To achieve this goal I learned to handle and manipulate skeletal and cardiac muscle cells and performed various mechanical and kinetic measurements that also helped better understanding of general molecular mechanisms of cardiac and skeletal muscle activity, and their differences. I received a two quarter Mary Gates award for this project that, in addition to giving me confidence in my work, also made it possible to spend more time in the lab and establish me as student-researcher. The most important skill I believe I acquired through this project, that couldn't be taught in a classroom, is using the experimental data to propose possible explanations to questions and mechanisms not completely known yet, and to modify the experiments to further that understanding.

Being part of HAMM lab gives me the privilege to work with outstanding researchers and people that are providing me knowledge and assistance each in their field of expertise but in the same time allowing independent thought and work. The HAMM lab also collaborates with several laboratories in and outside of University of Washington, providing the students in the lab unique

opportunities for research projects. Therefore, mainly due to Dr. Mike Regnier's knowledge of my personal interest in skeletal muscle repair, and with the help of my experience in mechanical testing of muscle fibers, I was offered to be involved in a skeletal muscle tissue engineering project, in collaboration with Dr. Margaret Allen's lab from Benaroya research institute.

Skeletal muscle tissue engineering is a new, promising approach to replace and repair lost muscle, and although no clinical solutions has been developed yet, other engineered tissues such as skin are undergoing clinical trials and some are even commercially available[1]. The main goal is developing tissue engineered constructs composed of muscle-derived stem cells (MDSC's) and natural matrix components to regenerate muscle and bridge areas of extensive muscle loss caused by explosives, combat injuries, accidents and tissue wasting in cancer patients. My specific part in the project aims in optimizing method for *in vitro* MDSC's seeding on a collagen scaffold, to produce best survivability, proliferation and differentiation of cells, with emphasis on proper alignment that is characteristics of native tissue and crucial for functionality of the muscle. MDSC's are very rarely occurring myogenic cells that in contrast to previously discovered satellite cells show true stem cells characteristics[3]; they are pluripotent, can survive transplantation, and can be distinguished from regular myoblasts [2,3]. Studies have shown that MDSC's can differentiate into muscle, neural, and endothelial lineages [2], outperform satellite cells in terms of survivability and proliferation rate [4] and preserve myogenic potential after differentiation into other lineages [5]. Therefore we hypothesize that MDSC's are preferable over satellite cells as method for rapid *in vitro* muscle growth. Although satellite cells are more abundant in skeletal muscle, 1-5% in contrast to only $1:10^6$ MDSC's, satellite cell concentration in skeletal muscle decrease with age [2, 6]. MDSC's on the other hand were found in human body up to 76 years of age [5], providing potential method of tissue engineering for very wide range of population.

The skills of cells handling and mechanical testing I acquired on my previous project will be used in this project to assess the functionality of the muscle constructs. Mechanical and kinetic test will include 1) electrical stimulation tests to observe contraction and z-disk pattern, 2) force generation in various Ca^{2+} concentrations, to generate force-pCa curves, fitted with Hill equation, widely used for muscle function assessment, and finally 3) kinetic studies measuring the rate of force redevelopment (k_{tr}), that can also be linked to degree of activation found by pCa curves.

This project is the first step in an attempt to provide active repair and reconstruction of skeletal muscle following injury and trauma. Tissue engineering can potentially solve problems associated with currently available treatments such as autologous tissue transfer and patient autoimmune rejection of donor tissue. The field of skeletal muscle injury and repair was always my biggest interest, and it was made possible for me thanks to the opportunity I was given by Dr. Mike Regnier when I first asked to join the HAMM lab and because I was able to demonstrate the skills and motivation for this field on the individual project from my junior year that was also made possible by the Mary Gates award I received for it. The current project allows me to explore the fields of stem cells and tissue engineering in biomedical research, that I wasn't familiar with before, but also combine my previous experience in muscle mechanics and apply theoretical knowledge of science and engineering I gained during my college education. As this project is much more involved and challenging than what I previously performed, I already experience the higher time demand and responsibilities, but I am thrilled to take on that challenge. Since my goal is continuing my bioengineering education I will be applying this winter for PhD programs, and hope to find a good program with a focus on muscle tissue engineering. Being able to work on such innovative skeletal muscle tissue engineering project and be recognized for it with a Mary Gates award will extremely help me to strengthen my graduate school application and achieve my goal.

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