Determining the Role of 3’ Untranslated Region Somatic Mutations in Prostate Cancer Pathogenesis
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Mentor: Andrew Hsieh, Human Biology, Fred Hutchinson Cancer Research Center
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Prostate cancer (PCA) is the most commonly diagnosed and second most deadly cancer in men. Almost all of these deaths are the result of a very progressed form called metastatic, castration-resistant prostate cancer (mCRPC), which currently has no cure and is incompletely understood. Cancer-related mutations in the untranslated regions (UTRs) of mRNA transcripts have been found to contain various sequence or structural motifs that contribute to the regulation of these cancer-causing genes. These regions are extremely dynamic in their control over gene expression affecting mRNA stability and translation efficiency which have both previously implicated in prostate cancer. However, the degree to which these mutations in the UTRs functionally contribute to prostate cancer remains poorly understood – especially in the 3’ untranslated region (3’UTR). A candidate gene list to investigate was constructed from an analysis of patient tumor sequencing data from a broad cohort of 230 localized and metastatic prostate cancer patients. I Gibson cloned wild type (WT) and mutant 3’UTRs from the candidate genes into luciferase plasmid constructs. Subsequent dual luciferase assay data revealed significant changes in protein expression between WT and mutant constructs most notably in the genes NCL and CLEC18B. Nucleolin (NCL) is a protein involved in the synthesis and maturation of ribosomes and is oncogenic in many cancers when overexpressed, while CLEC18B is largely unstudied. Given this existing functional evidence and my preliminary data, further investigation into the differential expression of NCL and the cellular mechanism through which it is achieved is warranted. My project focuses on elucidating the effects of 3’UTR somatic mutations on translational regulatory regions of the human genome, so that we may uncover new patterns in the progression of prostate cancer and subsequently elicit possible novel therapeutic targets with which to better treat these patients.

Wireless, Low Cost, Semi-Autonomous Cage-side Training Reward System for Nonhuman Primates
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Training a nonhuman primate (NHP) for research experiments generally requires the NHP to spend large quantities of time learning experimental tasks outside their home environment, and this requires a human researcher to be present at all times during training sessions. The purpose of this project is to create a wireless, semi-autonomous, low cost, cage-side training reward system allowing NHPs to train on experimental tasks for extended periods of time without the presence of a human researcher. An ideal device would allow for wireless data collection and provide both real-time and post-training information on the NHP’s training progress. Exposing NHPs to tasks first in the low-stress environment of their home cage before exposing them to the same task in an experimental booth can potentially speed up training processes. This lets research laboratories maximize researcher time and efficiently use equipment. Our cage-side training reward system consists of an iPad displaying touchscreen tasks, a speaker supplying audial cues for the tasks, an automatic feeder administering treats to the NHP for correct performance, and a computer to control the touchscreen tasks and collect data with custom MATLAB code. The iPad and computer communicate via a Wi-Fi router and this router also communicates with a Wi-Fi receiver which runs the feeder and speaker. The connection methods give the ability for wireless communication through walls, allowing the researcher to run tasks semi-autonomously from a computer outside the animal.
room. Excluding the costs of the iPad, computer, and MATLAB license, the system is estimated to cost under $300. Two rhesus macaques have undergone cage-side training with this device and have subsequently transitioned smoothly to learning tasks in a traditional experimental booth. In conclusion, this device serves as a low-cost method to enhance the training process for non-human primates while saving time and resources of the research laboratory.

Engineering a Multilayered Perfusionable Tissue Construct that Integrates Two Different Vascularization Techniques.
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Mentor: Ying Zheng, Bioengineering
Mentor: Nicole Zeinstra, Bioengineering

In a given year, a combined surplus of 20,000 transplants are performed in the US for patients requiring a new kidney, liver, or heart, and the need for these organs continues to increase rapidly with changes in societal and cultural outlooks on personal behavior. Recent regenerative medicine techniques have been implemented in attempts to create engineered tissues that support solutions to these problems, yet they are limited to thin or avascular tissues. In order to create thicker tissue constructs for implantation, vascular networks must be introduced to supply nutrients and oxygen to highly metabolic tissues. Yet, current methods can be expensive or require high-tech equipment. To address this issue, this project aims to design a construct that integrates two vascularization techniques into a multilayered tissue. This new design of a thicker tissue will benefit from the advantages of both independent systems, endothelial cords and perfusable, patterned microvessels, advancing the tissue engineering field.

Case Study of Social Networks in Ottoman Iraq
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Mentor: Walter Andrews, Near Eastern Languages and Civilization

Secondary scholarship on life in Iraq during the period of direct rule by the Ottoman Empire from the mid-19th century to World War I is minimal. A few primary historical texts have survived—these “forgotten texts” are largely individual accounts of daily life and business, which illuminate the events of a period of which little has been written. A study of such texts can prove valuable, allowing us to get to know individuals dwelling in Iraq and their lives. In this project, I explore the social networks of Joseph Mathia Svoboda, a British steamship purser living in Baghdad, through a collection of his diaries written between 1865-1908. Due to his family ties, profession, and vibrant social life, Joseph interacts with a wide variety of groups, from family, friends, religious and political leaders, to individuals of diverse backgrounds who he encounters throughout his travels; thus, his writings provide a fascinating viewpoint from which to study the Ottoman Empire. I conduct text and social network analyses of Joseph’s diaries, which involve visually mapping ties between people and analyzing the dynamics of the resulting structures. In my presentation, I will review the use of network analysis and entity detection methods in various contexts, such as literature, history, and the social sciences, and explore how these techniques can be applied to automate the extraction of persons mentioned from the diaries, and then subsequently visualize this information. In particular, I focus on Diary 47 of Joseph Svoboda’s diaries as a case study. In the future, the insights gained from this could be applied to the rest of the collection. As the diaries were written from Joseph’s young adulthood to old age, his narratives provide a unique opportunity to study societal relations in Ottoman Iraq.

Porous Degradable Biomaterial Designed to Improve Vascularization and Reduce Inflammation Around Implanted Medical Devices
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Implanted medical devices may be rejected by the body because of various physical and material properties such as the size and shape of the implant, the tissue-implant mechanical mismatch, or micro-motion caused by the implant. These properties can elicit an inflammatory immune response during the post-implantation healing process which ultimately leads to encapsulation of the device by fibrous scar tissue. This process, known as the foreign body response (FBR), is directed by immune cells called macrophages and can significantly impede the functionality of the implant. Prior research from the Ratner lab has demonstrated that porous biomaterials can be designed to induce a pro-healing response to improve healthy tissue growth by modulating macrophage phenotype to limit scarring and stimulate vascularization. The aim of this project is to design such an immunomodulatory gelatin biomaterial that increases the pro-healing polarization of macrophages, guides the process of vascularization throughout the porous architecture, and degrades at a controlled rate while maintaining the vasculature. Gelatin is a natural extracellular matrix component derived from collagen which has demonstrated utility as a biomaterial because of its anti-immunogenic properties and ability to match the mechanical properties of various tissues by tuning chemical crosslinking density. Currently, an in vitro degradation as-
say is being used to study the relationship between crosslinking density and degradation rate, targeting rates relevant to native tissue regeneration. Future in vivo studies will investigate the impact our gelatin biomaterial has on vascularization, macrophage polarization, and regeneration of healthy tissues as it degrades at an optimized rate. Ultimately, this biomaterial has the potential to benefit patients in need of implanted medical devices by promoting healthy integration of the device into surrounding tissue with a minimized inflammatory response.

Investigating Form and Function of Engineered Vascular Smooth Muscle Tunica Media

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Mentor: Nisa Williams, Bioengineering
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Cardiovascular diseases are the dominant killer worldwide. Many of these pathologies result in myocardial infarctions or heart failure, but they often originate in the vasculature. Understanding the vascular component of this system is critical to intervene early and prevent the onset of heart disease. In the native micro-environments of blood vessels, contractile smooth-muscle tissue is aligned circumferentially around a vessel’s lumen to modulate blood pressure throughout the body. Tissue engineering seeks to recapitulate tissues for the study of disease. A three-dimensional in vitro approach can aid in the study of arterial pathology, but current tissue-engineered arterial models lack physiologically relevant form and function. Here we seek to engineer tubular vascular tissues that mimic the circumferential architecture of the smooth muscle cell layers using nanopatterning techniques and fibrin hydrogels. Fabrication of biomimetic models of the arterial tunica media has enabled our investigation into circumferentially aligned tissues, and we conduct burst pressure measurements to study the mechanical properties of this tissue model.