Student Research Day
May 9, 2018
Project Abstract Descriptions

Name: Jaclyn Alois, MS Biotechnology Management **Graduating Date: May 2018**
Mentor: Joseph Crisco, PhD
Future Plans: Senior Marketing Associate, US Metabolics at Alexion in Boston, MA
Project Title: Play Mechanisms Associated with Intentional High-Magnitude Impacts in Youth Football

Creating the safest possible playing environment for football athletes has been at the forefront of researchers and governing bodies alike. While most of the research has focused primarily on high school and collegiate football players, this study aimed to identify the circumstances of which high-risk impacts occur in the youth population ages 8 to 14. To our knowledge, no study has examined the mechanisms of intentional high-magnitude impacts that occur in this athlete population. High-magnitude impacts were of focus because these are the impacts that are associated with a greater risk of concussion. The specific aims of this study were to examine the (1) primary impact mechanism as well as the impact mechanism distribution across (2) session type, (3) player position, (4) and ball possession of intentional high-magnitude impacts. Focusing on characterizing intentional high-magnitude impacts is believed to guide future prevention strategies.

Name: Douglas Barber, AB Health and Human Biology **Graduating Date: May 2018**
Mentor: Christopher Born, MD **Co-Mentor:** Dioscaris Garcia, PhD
Future Plans: I will be conducting clinical research on the interface between substance use and HIV/AIDS with Dr. Frederick Altice. I will also be an Emergency Department Technician at Yale New Haven Hospital.
Project Title: Developing an *in vitro* Model for Visualizing and Classifying Bacterial Biofilms on Orthopaedic Materials

Open fractures pose significant therapeutic challenges for orthopedic trauma surgeons. Infection rates as high as 30% lead to high morbidity and mortality among affected patients. Bacteria that have adhered to orthopedic devices produce a matrix of proteins, exopolysaccharides, and extracellular DNA that encapsulate the microbes. Once mature, these biofilms are virtually impossible to eradicate due to horizontal gene transfer, low metabolism “persister” cells, and low permeability of the extracellular matrix. Because antibiotics are largely ineffective for treating biofilms, the field of orthopedic trauma would benefit from novel methods of biofilm prevention and removal. This project aims to create an in vitro model of biofilm development and visualization on orthopedic materials using confocal laser scanning microscopy (CLSM) and scanning electron microscopy (SEM). By fluorescently staining different matrix components, the structure and composition of the biofilm can be identified at each stage of development. Scanning electron microscopy allows for structural and topographical analysis of the biofilms. This model will serve to advance our understanding of how biofilms develop on orthopedic materials, and to test novel prevention and removal methodologies.

Name: Sean Flannery, PhD Biomedical Engineering **Graduating Date: May 2021**
Mentor: Braden Fleming, PhD
Future Plans: Continuing BME PhD program
Project Title: Assessing Meniscus Health Post-ACL Repair with MRI T_2^* Relaxometry

Patients with an ACL tear are at an increased risk for the development of post-traumatic osteoarthritis[1]. The injury results in numerous systemic effects to the knee that include degradation of the meniscus. Because meniscal trauma is often seen concomitantly with ACL injury, the effects of ACL injury and surgical ACL repair (ACLR) on meniscal health have been difficult to isolate. Quantitative MRI T_2* relaxometry has previously been validated as a method to non-invasively map soft tissue quality and quantity *in vivo*[2]. With this method, we examined whether ACL transection followed by ACLR induced meniscal alterations (i.e. changes in meniscal volume and median T_2* relaxation time) independent of acute ACL injury. We hypothesized that ACLR does not affect the medial meniscus T_2* relaxation time or volume within the first 24 weeks post-surgery

Name: Yun Gao, MD, PhD candidate
Graduating Date:
Mentor: Qian Chen, PhD
Co-Mentor:
Future Plans: Residency program in Shanghai, China
Project Title: MechanomiR-365 Promotes Pro-Inflammatory Cytokine IL-6 Expression Through Inhibiting A Transcriptional Repressor Nr1d2 During Osteoarthritis in Mice and Human

MiR-365 can be induced by both mechanical loading and inflammatory cytokine, and is up-regulated in OA tissues. To study the role of miR-365 in cartilage, we created Col2-Cre;miR-365 Tg mice and observed early OA onset since 6-month-old. Our project is to dissect the mechanism behind the miR-365 cartilage specific over-expression driven OA development

Name: Mursal Gardezi, ScB Biology- Immunology
Graduating Date: Mat 2018
Mentor: Christopher Born, MD
Co-Mentor: Dioscaris Garcia, PhD
Future Plans: Clinical Research at Yale University
Project Title: Fluorescent-Conjugated Antibodies as Ex Vivo Markers of Bacterial Infection on Surgical Sites

Infection is the biggest problem facing orthopedic surgeons. Preventing these infections from being introduced is a big topic of interest to researchers, however the method of detecting these infections has not received nearly as much attention. The methods currently used to diagnose these infections are unreliable, slow, and expensive. We have been working on a rapid visualization assay to detect bacterial infection on hardware, tissue, and synovial fluid using fluorescent conjugated antibodies. Samples were obtained through IRB approval from six Rhode Island Hospital faculty orthopedic surgeons and clinical data was compared to results from our assay. Thus far, this assay has reliably labeled gram-negative and gram-positive bacteria on 75 clinical samples of screws, tissue, and synovial fluid. Further, it allows us to visualize morphology and localize bacterial presence. This potentially allows surgeons to offer more precise treatment plans quicker than ever before, saving money, as well as sparing patients some of the pain and suffering that comes with dealing with these infections.

Name: Brianna Irons, AB Health and Human Biology
Graduating Date: May 2018
Mentor: Christopher Born, MD
Co-Mentor: Dioscaris Garcia, PhD
Future Plans: Undecided, gap year while applying to medical school
Project Title: Elucidation and Purification of Secondary Bioactive Metabolites with Antimicrobial Activity from the Rhode Island Coastline.

In April of 2014, the World Health Organization (WHO) released its first report warning of the post-antibiotic era. This report brought back the prospect of a pre- World War II medical crises, where a small infection could be potentially life threatening. This prospect is highlighted by the rise of antibiotic-resistant pathogens and a concurrent decrease in the discovery of antibiotics over the last 30 years. In order to combat this new threat, a return to previous methods of antibiotic discovery is of upmost importance. Historically, compounds produced by soil bacteria, particularly *Actinomycetes Sp.* and Streptomycetes *Sp.*, have accounted for the discovery of many new antibiotics. The historical success of antibiotics derived from natural sources and the unique environment of the Rhode Island coastline provide a significant opportunity for the discovery of novel antimicrobial compounds. This project is aimed at identifying, isolating, and purifying secondary bioactive metabolites with antimicrobial activity from marine soil bacteria found in the Rhode Island coastline.

Name: Justin Lee, ScB Biomedical Engineering **Graduating Date: May 2018**
Mentor: Braden Fleming, PhD
Future Plans: Undecided
Project Title: Comparing histological predictors of ACL healing to MRI derived T2* relaxometry data in repaired ligaments at early stages of healing.

The Ligament Maturity Index (LMI) is the current gold standard for histological assessment of a healing ACL. My project was to learn this scoring method and then see if it could be used to predict the variation in healing response indicated by MRI derived variables that have been shown to be predictive of the structural organization of the ligament. For my project I learned how to score ligaments by looking at histology slides of surgically repaired ligaments and assessing various characteristics. The scoring system I used focused mostly on the cell, collagen and blood vessel organization and orientation in the ligament. Through this process I found that changes seen through histology aren't quite reflected in the same way as in MRI at early stages of healing (6-24weeks) but I propose that a more macroscopic perspective could provide more insight into these trends.

Name Wenguang Liu, PhD Molecular Cell Biology and Biochemistry **Graduating Date: December 2018**
Mentor: Qian Chen, PhD
Future Plans: Lecturer or Postdoc in University
Project Title: TGFβ is necessary and sufficient to induce hypertrophy, mineralization and catabolism in human osteoarthritis stem cells.

Osteoarthritis stem cell (OASC), a type of novel stem cell in OA cartilage, harbored high osteogenic potential. TGFβ, a key factor in chondrogenesis in chondrocyte, could induce OASC hypertrophy, mineralization, and catabolism. TGFβ1 could induce Psamd1 in OASC which normally are induced by BMP. TGFβ has different role in OASC, OAC and bMSC. Secreted TGFβ from OAC could induce OASC hypertrophy, mineralization, and catabolism. Secreted MMP13 from OASC could induce OAC degeneration. Furthermore, the worse and worse loop may contribute OA pathogenesis. Therefore, targeted inhibition of TGFβ signaling in OASC may be a powerful therapeutics for OA treatment.

Name: Matthew Lo, ScB Biomedical Engineering **Graduating Date: May 2018**
Mentor: Braden Fleming, PhD
Future Plans: Brown University BME Master's Program
Project Title: The Functional Role of Lubricin in Preventing Fibrosis of the Knee Joint

Synovial fluid provides lubrication for the knee joint, allowing the tibia to slide passed the femur with little friction. In healthy joints, lubricin (PRG4) molecules provide surface lubrication and prevents any cell adhesion. Lubricin has been found to prevent damage to tissues in the superficial joint. Studies have shown that lubricin downregulation is correlated to knee joint injuries. Downregulation of Lubricin leads to chondrocyte death and promotes an environment for osteoarthritis. We investigated the relationship between lubricin downregulation and synovial fibrosis on the mechanical properties of synovial tissue. We believed that Young's modulus and Yield strength would be lower in mice knee joints without lubricin (PRG4 -/-) than wildtype mice (PRG4 +/+). The hindered mechanical properties would be a factor for increased osteoarthritis. Twenty murine C57BL wildtype mice knee joints (PRG4 +/+) were compared to twelve knockout mice knee joints (PRG4 -/-). Knee joints were dissected, and posterior synovial tissue was isolated by a method we developed that peeled away the knee cap and cut through all ligaments in the superficial zone. The specimens were then run through controlled mechanical failure testing and stress strain curves were found by measuring actuator displacement and force. In addition, immunohistochemistry was run on both groups to look at the presence of Smooth Actin muscle molecules, which is a hallmark for fibrosis. Our results showed a trend to significance, as Young's modulus of the PRG4+/+ was greater than that of PRG4-/-. However, large variations in readings and small specimen groups led to our data to be insignificant. Future studies would look at mechanical properties, but with larger study groups.

Name: Anthony Minnah, ScB Biomedical Engineering **Graduating Date: May 2018**
Mentor: Christopher Born, MD **Co-Mentor:** Dioscaris Garcia, PhD
Future Plans: Working at Travera, LLC as a Research Engineer
Project Title: An Analysis of the Antimicrobial Effects of a Silver doped Titanium-dioxide Polydimethylsiloxane (PDMS)coating on Multi Drug Resistant Acinetobacter baumannii and Vancomycin Resistant Enterococcus faecalis on Orthopaedic Biomaterials

Infections are one of the most prevalent complications associated with orthopedic implant surgeries. In the United States, surgical site infections (SSIs) account for approximately 20% [1] of total health associated infections leading to over 8,000 [1] deaths annually. The rise of multidrug resistant bacteria negates traditional antibiotic-dependent methods and can form protective biofilms that further prevent eradication. Multi- Drug Resistant Acinetobacterium baumannii and Vancomycin-Resistant Enterococcus faecalis species account for about 40% [2] of organisms responsible for orthopedic SSIs. In order to eliminate infections caused by these pathogens, this study explores the effects of an alternative, antibiotic-independent approach to fighting these infections. The objective of this study is to assess the antimicrobial properties of a silver-doped titanium dioxide-polydimethylsiloxane (PDMS) hybrid coating on the adherence and proliferation of these pathogens. This coating is an important tool with which to combat multidrug resistant bacteria.

Name: Daniel Louis Roque, AB Health and Human Biology **Graduating Date: May 2018**
Mentor: Christopher Born, MD **Co-Mentor:** Dioscaris Garcia, PhD
Future Plans: Working as a tech in a hospital in NJ while applying to medical school.
Project Title: Imparting Antibiotic-Independent Antimicrobial Properties to Surgical Sutures and Prosthetic Liners With a Silver-doped Coating.

As it is our primary defense from external microbes, any disruptions in the skin, such as surgical wounds, greatly increases the chance of infection. Despite proper wound closure by sutures, all surgical patients face a risk post-operatively because the transcutaneous fixation of sutures provides pathogens a direct route of entry into the wound. Whether braided or monofilament, sutures have been found to be sites for bacterial adhesion and biofilm formation. Once their wounds have healed, amputees face an additional challenge for the remainder of their lives due to the enclosed design of prosthetic socket. Use of a prosthetic liner leads to friction of the residual stump tissue, and accumulation of debris and sweat. These factors promote irritation, breaks in the skin, microbial growth, and eventual infection. There are approximately 185,000 patients who undergo amputations yearly, with a projected 50% increase in the amputee population within the next 35 years. Viewed in light of increasingly prevalent antibiotic-resistant pathogens, there is a call for improved infection prevention, care and, treatment in this large patient population. The objective of this study was to validate the biocompatible chemistry formulations of a silver-doped titanium dioxide- polydimethylsiloxane (PDMS) coating, to change its formulation to utilize heptane as an alternative component, and to test its antimicrobial efficacy on selected sutures and prosthetic liners.

Name: Claire Sise, ScB Biomedical Engineering **Graduating Date: May 2018**
Mentor: Joseph Crisco, PhD **Co-Mentor:** Rohit Badida, MS
Future Plans: Columbia University Biomedical Engineering MS/PhD Program
Project Title: Effects of Musculoskeletal Simulation and Coordinate System Definition on Determining Intact Wrist Mechanical Properties

Clinically, mobility of the wrist is described in terms of four anatomical directions of motion: flexion, extension, radial deviation and ulnar deviation. Most activities of daily movement involve coupled motions that are combination of these directions. We sought to assess the biomechanical properties of the wrist in all directions of physiological motion to characterize the mechanical properties of the wrist joint. We completed range-of-motion tests on 12 intact specimens using a six axis industrial robot which allowed for 6 degrees of freedom in the

Cartesian directions of rotation. The specimen were tested with and without a musculoskeletal loading system. Additionally, the data collected was converted to three different coordinate systems, ISB, Styloid, and Scapho-Lunate. ROM envelopes were generated for the specimen

Name: Yasmine Suliman, AB Health and Human Biology **Graduating Date: May 2018**
Mentor: Christopher Born, MD **Co-Mentor:** Dioscaris Garcia, PhD
Future Plans: Working as a clinical research coordinator in the orthopedics department at the Children's Hospital Los Angeles
Project Title: Comparative Analysis of a Novel Microbial Detection System and Gram Staining Utilizing Synovial Fluid.

In the world of orthopedics, post-surgical site infections are a pressing problem, where up to 2% of all post-surgical sites become infected, with the rate climbing up to 28% in open fractures. This leads to longer healing times, extended hospital stays, higher healthcare costs, and ultimately a lower quality of life for patients. Hospitals continue to use traditional culturing, PCR, and gram staining methods to diagnose these issues, however, these methods continue to encounter issues with their speed, accuracy, and reliability. Our study aims to tackle this problem by exploring a new microbial detection system that utilizes fluorescently-conjugated antibodies and confocal laser scanning microscopy. We aim to make a new diagnostic tool available that can visualize bacterial infections in a more accurate and reliable way, all in 35 minutes.

Name: Franklin Tarke, ScB Mechanical Engineering **Graduating Date: May 2018**
Mentor: Braden Fleming, PhD **Co-Mentor:** Jillian Beveridge, PhD
Future Plans: Attending Stanford for Mechanical Engineering MS
Project Title: Sensitivity of knee joint motion calculated from CT- and MRI- derived bone models.

The kinematics of the human knee joint are altered after ACL injury. One way to measure the effectiveness of ACL repair is to measure the knee kinematics of the repaired knee and compare them to the healthy knee. Bi-planar video radiography (BVR) is an imaging technique that uses two calibrated xray video cameras oriented at different angles to record two different xray radiographs. 3D bone models, generated from either CT or MRI, can then be simultaneously matched to both xray images by aligning the edges and contours of the model to the radiographs. Currently, there are no known studies that compare the differences between CT and MRI models when used to track kinematics using high speed BVR. This study looks to fill the literature gap by looking at the kinematic differences when using the two models when tracking a frozen cadaver knee using BVR, and to determine if there is a consistent bias in these kinematics. Additionally, by comparing data obtained from multiple individuals (trackers) operating the motion tracking software, it can be determined if there is a bias created by different trackers when performing the tracking, or if the differences in kinematics originate from the bone models themselves.

Name: **Daniel Yang, ScB Biomedical Engineering and Public Health, AB**
Graduating Date: May 2019
Mentor: Braden Fleming, PhD **Co-Mentor:** Dr. Ata Kiapour
Future Plans: Finishing my final undergraduate year before matriculating to Alpert Medical School
Project Title: Anatomical Determinants of Outcomes after ACL Reconstructive Surgery

Background: Tibiofemoral articulation, as modulated by osseous anatomy such as the medial femoral condyle and medial tibial plateau with menisci, functions to dynamically stabilize the femur in an internal rotation mechanism as the knee approaches extension (Flandry et. al, 2011). Given this complex interplay between osseous and soft tissue components, certain anatomical characteristics have been identified as risk factors for anterior cruciate ligament (ACL) injury. Decreased femoral notch width, increased posterior-inferior lateral tibial slope, and increased middle cartilage slope have been associated with increased ACL injury risk (Sturnick et. al 2015, Whitney et al., 2014, Bojicic et, al, 2017). Despite the evidence linking knee anatomy to ACL injury

risk, the effect of knee anatomy on ACL reconstruction (ACLR) outcomes and graft loading remains unclear. A recent study provides initial evidence for an association, investigating patellofemoral alignment and trochlear morphology as associated with patellofemoral osteoarthritis following ACLR (Macri, 2017). **Objective:** The objective of this study was to determine of role of the knee osseous and soft tissue anatomy on the clinical and functional outcomes as well as patient-oriented and OA-related outcomes of ACLR in both short- and long-term. **Methods:** Medial and lateral posterior slopes of the tibial plateau, medial tibial depth, femoral notch size as well as medial and lateral, anterior and posterior meniscus height, cross-sectional area, and bone angle were measured at 3, 5, and 7 years. These anatomical measures were correlated to clinical (anterior-posterior [AP] knee laxity), functional (1-legged hop for distance), and patient-oriented outcome measures (Knee Injury and Osteoarthritis Outcome Score [KOOS]) at 3, 5, and 7 years after ACL reconstruction. **Results:** Univariate linear regression of KOOS subscores on coronal tibial slope (CTS), lateral tibial slope (LTS), and medial tibial slope (MTS) revealed a significant negative relationship at some time points. CTS and LTS were significant positive predictors of OARSI score. Medial tibial depth (MTD) was a negative predictor of OARSI score as well as AP laxity. MTD was a positive predictor of hop distance as well as KOOS subscores. A significant negative relationship was found between notch width and AP laxity. LTS was a significant positive predictor of AP laxity at 7 years only. **Conclusions:** Further analysis is needed in this project to control for possible covariates. Influence of anatomy on how outcomes change longitudinally across time should be more rigorously analyzed. This study gives preliminary evidence as to the predictive role of patient osseous anatomy on outcomes after ACLR. Modifying high-risk anatomy may facilitate more favorable kinematics and reduce osteoarthritis in the years following ACLR (Yamaguchi et. al, 2018).