Student Research Day
May 20th, 2020
Project Abstract Descriptions

Name: Leah Peipert **Graduating Date: May 2020**
Mentor: Joseph Crisco, Ph.D., Arnold-Peter Weiss, M.D.
Future Plans: Working as a Medical Assistant at South Shore Dermatology in Brockton, MA and will be applying to medical schools.
Project Title: Morphological Changes of the Carpometacarpal Joint Associated with Early Progression of Carpometacarpal Osteoarthritis

This project utilizes CT imaging data from a 6-year follow-up longitudinal study to identify and quantify two prominent morphological changes of the carpometacarpal (CMC) joint during early progression of thumb CMC osteoarthritis (OA): volar recession of the first metacarpal (MC1) and Thumb Osteoarthritis (ThOA) Index measurements of the trapezium (TPM). The analysis included 86 patients with early thumb OA and 22 healthy controls. We hypothesized greater volar beak recession and larger ThOA index measurements in the OA population and sought to compare these measurements to the progression of CMC OA as measured by osteophyte growth. We observed MC1 volar beak recession in the OA cohort, strongly correlated with MC1 osteophyte growth ($P<0.0001$). Increasing ThOA index was also strongly correlated with TPM osteophyte growth ($P<0.0001$). Both rates of MC1 volar beak recession and increasing ThOA index were significantly greater in the early OA cohort compared to the control group. Sex had no statistically significant effect on either measure. Quantitative measurement of MC1 volar beak recession and ThOA index may be useful markers to evaluate early CMC OA progression. This analysis draws attention to the volar region of the CMC joint as a location of potent physical stresses and biological changes. Further analyses should be performed to better understand the stressors in this area as well as the temporal sequence of morphological changes on the MC1 and TPM to guide future prevention and treatment of CMC OA.

Name: Kathleen Turajane **Graduating Date: May 2021**
Mentor: Wentian Yang, M.D., Ph.D.
Future Plans: Completing my second year of graduate school in Brown's Biotechnology Masters' program.
Project Title: Novel Insights into the SHP2's Regulation of Osteoclastogenesis

Src-homology-2 domain containing protein tyrosine phosphatase 2 (Shp2), a widely expressed protein tyrosine phosphatase, plays a critical role in osteoclast (OC) development and skeletal remodeling. Through a tissue-specific gene knockout model, mice with deletion of Shp2 in OCs exhibit osteopetrotic phenotype, a marked increase of bone density. Additional analyses revealed that Shp2 specifically regulates the fusion of pre-OCs during osteoclastogenesis [1]. However, the mechanism by which Shp2 regulates the osteoclastogenic program is not fully understood. Therefore, this project aims to identify SHP2 interacting proteins in OCs using BioID2 system, a proximity dependent biotin ligase labeling technique [2]. Briefly, macrophage (BAC1.2F5) stably expressing SHP2-BioID fusion protein will be constructed. Subsequently, the cells will be cultured in the presence of biotin and stimulated with macrophage colony-stimulating factor (M-CSF), and/or receptor activator of nuclear factor kappa-B ligand (RANKL). In combination with the use of mass spectrometry, the biotinylated proteins through which SHP2 modifies M-CSF and/or RANKL signaling and osteoclast biology will be investigated.

Name: Christian Maldonado-Rodas **Graduating Date: May 2020**
Mentor: Braden Fleming, Ph.D.
Future Plans: I will be working as a Research Assistant at UCSF Carol Franc Buck Breast Care Center.
Project Title: Understanding Cartilage Contributions to Chronic Knee Joint Kinematics

X-ray Reconstruction of Moving Morphology (XROMM) is a 3D imaging pipeline developed at Brown University for quantifying and visualizing skeletal movement in vivo. It combines 3D models of bones with movement data from bi-planar x-ray video to create accurate reanimations of 3D bone moving in 3D space. In Dr. Fleming's lab, we have used XROMM to determine whether tibial internal rotation, anterior positioning and rotational and translational excursions would differ greatly among ACL-R patients than in healthy controls. We have learned that anterior positioning varied greatly among ACL-R patients and healthy controls, however, there is not a sufficient amount of data to conclude any cause-effect relationship. In order to further delve into this subject, we are focusing on how medial and lateral cartilage contribute to the differences seen in knee joint kinematics among ACL-R patients and healthy controls.

Name: **Andrea Gilmore** **Graduating Date: May 2020**
Mentor: Christopher Born, M.D. **Co-Mentor:** Dioscaris Garcia, Ph.D.
Future Plans: Working in a research position while taking a gap year to apply to medical school
Project Title: An Analysis of the Antimicrobial Effects of a Silver Carboxylate Titanium-dioxide Polydimethylsiloxane Coating on Multi-Drug Resistant *Serratia marcescens* on Orthopedic Biomaterials

My independent research project investigates the capabilities of a silver carboxylate antimicrobial coating comprised of titanium dioxide (TiO_2), polydimethylsiloxane (PDMS) with silver carboxylate dopage at preventing adherence of antibiotic resistant bacterium, *Serratia marcescens*, on orthopedic biomaterials. This project tested various concentrations of the coating in order to find the ultimate preparation at preventing growth on Polyetheretherketone (PEEK), titanium, and stainless steel.

Name: Joseph Harrington Jr.
Mentor: Roy Aaron, M.D.
Future Plans: Attending graduate school at the University of Nebraska Omaha.
Project Title: Estimation of MCID for KOOS Pain and VR12 PCS in Total Knee Replacement Patients

Patient-reported outcomes (PROs) are important tools for assessing health care quality and outcomes. Interpreting PROs utilizes the minimum clinically important difference (MCID) or other metrics of change. However, we, and others, are finding that the MCID is not as stable a metric as has been believed and needs to be calculated for each individual study. The MCID is defined as the smallest difference in score, within the domain of interest, which patients perceive as beneficial. Traditionally, three methods have been applied to calculated MCID: (1) distribution-based methods; (2) anchor-based methods; and (3) the Delphi method, each with its own set of advantages and disadvantages. We are using, and will describe, the anchor-based method, believing it to most accurately reflect patients' perceptions of benefit. Our analysis adds to the quantitative rigor of the method by utilizing the ROC cut-off point method, which identifies the most precise score for the MCID. Using validated patient reported outcome measures (PROMs) from KOOS and VR-12 within the Function and Outcomes Research in Comparative Effectiveness Research in Total Joint Replacement (FORCE-TJR) registry used at the Miriam Hospital TJC, our analysis divides outcomes of total knee replacement into binary or categorical criteria of successful and unsuccessful outcomes by defining the MCID for pain and function outcome domains.

Name: Lori Sahakian **Graduating Date: May 2020**
Mentor: Christopher Born, M.D. **Co-Mentor:** Dioscaris Garcia, Ph.D.
Future Plans: Clinical Research at Boston Children's Hospital
Project Title: "Visual and Quantitative Biofilm Evaluation Platform for the Development of Surgical Debridement Irrigation Agents"

This project is based on an in vitro model of biofilm development, growth, and quantification on three commonly utilized orthopedic implant materials: Titanium Alloy, Poly-ether-ether-ketone (PEEK), and Cobalt Chromium. Titanium has previously shown some degree of antimicrobial properties and PEEK is a commonly used polymer with an elastic modulus similar to that of human bone. An assessment of biofilm development on implant

materials with different chemical properties will allow for the development of an irrigation solution that targets specific components of the biofilm. The study aims to identify the composition and dynamics of biofilm development on implant materials using Confocal Laser Scanning Microscopy and Scanning Electron Microscopy. This platform allows for identification of bacterial biofilm at distinct stages of formation, allowing for specific targeting of macromolecules essential to bacterial viability and biofilm growth. This quantitative biofilm visualization platform of *Pseudomonas aeruginosa* and *Staphylococcus epidermidis* was then used to test the efficacy of several novel irrigation formulations on several orthopaedic implant materials and on glass.

Name: Edgar Garcia-Lopez **Graduating Date: May 2020 (Master's)**
Mentor: Joseph Crisco, Ph.D.
Future Plans: Finish fourth year of medical school at Brown
Project Title: Evaluating Dorsal Subluxation on Radiography and Computed-Tomography in Patients with Early Thumb Carpometacarpal Osteoarthritis

First metacarpal (MC1) subluxation is a postulated cause of abnormal biomechanical loading that leads to thumb carpometacarpal osteoarthritis (CMC OA). The oblique orientation and saddle shape of the carpometacarpal joint make it challenging to radiographically measure subluxation. In this study we sought to determine how dorsal subluxation measured from radiograph and CT scans of the CMC joint changed as OA progressed. We additionally assessed the agreement between CT and radiographic dorsal subluxation measurements.

Name: Troy Li **Graduating Date: May 2019**
Mentor: Christopher Born, M.D. **Co-Mentor:** Dioscaris Garcia, Ph.D.
Future Plans: Searching for a position in Boston.
Project Title: Characterization and Optimization of a Silver Carboxylate Eluting Antimicrobial against Cutibacterium acnes and Methicillin-resistant Staphylococcus aureus

It is estimated that there are over 150 thousand cases of surgical site infections (SSIs) that occur each year. These infections not only increase the morbidity and mortality of patients, but also the length of stay and cost of hospitalization. For every SSI, it is estimated that 11 extra days are spent in the hospital and cost the U.S. healthcare system over $3 billion annually. Particularly, post-operative *Cutibacterium acnes* (C. acnes) and Methicillin-resistant *Staphylococcus aureus* (MRSA) SSIs continuously prove to be hard to prevent and treat. Some of these SSIs can be attributed to ineffective to inadequate skin prep techniques that fail to eradicate bacteria at the site of injury. The current methods of sterilizing a patient's body include the application of an antiseptic compound that can include Chloraprep/chlorhexidine, Duraprep, or Betadine. However, it has been shown that C. acnes and MRSA may be resistant to preparations using these compounds as strains of Chlorhexidine-resistant pathogens have been emerging in hospital environments. The over-reliance on these conventional methods fuels the need to develop novel methods of dealing with infections. This is the basis of my project as we hypothesize that our silver-carboxylate eluting antimicrobial will be an effective tool that healthcare providers can utilize to prevent SSIs due to the inherent antiseptic behavior of silver. In addition, silver has many mechanisms of action that allow it to kill and inhibit bacterial growth in numerous ways which reduces the chance of bacteria developing resistance against silver.