Research Day, April 18, 2023

PhD Poster Presentations

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PG1	9:45-10:45	Uyen Cao	Three-dimensional plant-based hydrogel culture system in the application for salivary gland regeneration
PG2	9:45-10:45	Neha Dinesh	Pathomechanisms of fibronectin mutations causing spondylometaphyseal dysplasia
PG3	9:45-10:45	Mahdokht Mahmoodi	Plasma fibronectin regulates trabecular bone mass and bone remodeling
PG4	9:45-10:45	Mahmoud Moussa	Adverse Effects of Botulinum Toxin-A Injection on Mandibular Bone Structures: A Systematic Review and Meta-Analysis
PG5	9:45-10:45	Wen Bo Sam Zhou	Age related changes of systemic immune profile in nerve injured male and female mice
PG6	9:45-10:45	Elnaz Alikarami	Neural correlates of trigeminal nerve morphogenesis in chronic painful temporomandibular disorders (TMD)
PG7	9:45-10:45	Taylor Devet	Short and long terms changes in murine hindlimb vasculature are initiated by mechanical loading
PG8	9:45-10:45	Josephine Tauer	Embryonic bone development: Structure of the ossifying bone collar
PG9	9:45-10:45	Priyesh Patel	Overview of rare disease meta-analysis, a method to aggregate n =1 data
PG10	9:45-10:45	Isabela Vitienes	Effect of genetic strain and loading history on bone mechanical and structural properties
PG11	9:45-10:45	Olawale Dudubo	The oral health of refugeed children: A discourse analysis of Canadian health policy
PG12	9:45-10:45	Nona Attaran kakhki	Understanding oral health-related well-being of children experiencing cancer: A participatory hermeneutic ethnography
PG13	9:45-10:45	Mattias Neset	Citizen science approach for searching and curating literature of the effects of spaceflight on cardiovascular outcomes in rodents and humans
PG14	9:45-10:45	Rachita Seth	Assessing validity of the COVID-19 Anxiety Syndrome Scale in Canadian dentists
PG15	9:45-10:45	Aseel Alzaghoul	Characteristics of self-rated oral health among Syrian refugee parents in Ontario
PG16	9:45-10:45	Haitham Shoman	Improving quality of life of the elderly through innovative oral hygiene tools to prevent infections and poor oral health?
PG17	9:45-10:45	Marie Vigouroux	Applied philosophical hermeneutics research: The Hermeneutic Wager
PG18	9:45-10:45	Heba Madi	Characterizing the inflammation around dental implants: Bacterial infection, hypersensitivity, or both?
PG19	9:45-10:45	Jan Kwan	PEEK as an alternative non-metallic restorative material for implant-supported fixed partial dentures
PG20	9:45-10:45	Hossein Poorhemathi	Analyzing the physicochemical aspects of biological hydroxyapatite precipitation Using mathematical modeling

PhD Poster Presentations

PG1: Three-dimensional plant-based hydrogel culture system in the application for salivary gland regeneration

Uyen Cao

Supervisor(s)/Collaborator(s): Simon Tran

Cluster: Biomaterials, Nanobiotechnology and Tissue Engineering.

Introduction: Nowadays, millions of patients worldwide are reported to have dry mouth symptoms or xerostomia. Craniofacial radiotherapy and Sjogren's syndrome are the two most common causes of xerostomia. These patients suffer from oral infections, dental caries, gum diseases, and swallowing discomforts which lead to a decrease in nutrition intake and quality of life. The current treatments for these disorders are mostly palliative care that only relieves the pain or reduces the symptoms for the patients. Such treatments fail to restore properly salivary secretion and often associate with numerous adverse effects. Recently, salivary gland engineering has been an innovative approach to the treatment of dysfunction. Particularly, researchers try to develop different biomaterials to build scaffolds for salivary gland regeneration. Animal-derived product such as Matrigel is one of the most widespread materials used in the 3D culture system. However, due to its origin from mice tumor cell lineages, its inconsistencies and cost-ineffectiveness, Matrigel has hardly been tested in clinical settings. Recently, the soy-derived product has been considered a potential plant-based source of biomaterials, owing to its environmental sustainability and abundance of proteins and antioxidants. Interestingly, recent findings have reported that soy protein isolate (SPI)/alginate hydrogel has been successfully used for biomedical applications such as wound healing or bone formation. The authors demonstrated that soy-based hydrogel can provide a promising microenvironment for cell proliferation, differentiation, and transplantation. Hence, my research attempts to build optimal plant-based scaffolds on which the salivary gland cells can grow, which later can restore the function of the cells and the tissue. Aim: My research attempts to build optimal soy-based scaffolds on which the salivary gland cells can grow, which later can regenerate the function of the damaged glands.

Objectives: 1. Determine the physicochemical properties of the soy scaffolds. 2. Evaluate the biocompatibility of the soy scaffolds in vitro. 3. Evaluate the biocompatibility of the scaffolds in vivo. Methods: For objective 1, I combine the new soy-based with alginate and gelatine at different concentrations (1%, 1,5%, 2%, 2.5%), crosslink them with CaCl2 to form microcapsules and then evaluate their degradation rate, swelling behavior, weight loss, surface roughness, material stiffness, and porosity. Regarding objective 2, I will perform in vitro 3D cell cultures using different cell lines such as the normal salivary simian virus 40-immortalized acinar cells (NS-SV-AC), mesenchymal stem cells (MSCs) on my soy-bean scaffold and measure their metabolic activity, perform IF staining, Live/Dead cell staining then analyze cell viability and proliferation. Finally, I will perform in vivo studies by implanting the soy-scaffolds in mice to see how they will behave inside living body.

Expected outcomes: We expect to construct an optimal 3D salivary gland scaffold after this project. This potential hydrogel can be an alternative approach for drug screening, cell transplantation and migration for future salivary gland regeneration.

PG2: Pathomechanisms of fibronectin mutations causing spondylometaphyseal dysplasia

Neha Danish

Collaborator(s)/Supervisor(s): Justine Rousseau, Philippe Campeau, Dieter Reinhardt

Cluster: Mineralized Tissue and Extracellular Matrix Biology Cluster

Fibronectin (FN) is a ubiquitous matrix glycoprotein essential for physiological development. The role of FN in cartilage development and function is not known. We and others have previously identified heterozygous dominant mutations in the fibronectin gene (FN1) as a cause for corner fracture type spondylometaphyseal dysplasia (SMD) with short stature and growth plate defects. The current study addresses the functional importance of FN in physiological skeletal development and pathomechanisms underpinning SMD. The physiological role of FN in skeletal development was analyzed by conditional knockout mouse models for i) cellular FN in cartilage (cFNKO), ii) plasma FN in hepatocytes (pFN KO), and both FN isoforms (dKO). The single FN knockout mice had no obvious alterations in cartilage and skeletal growth. However, the dKO mice showed defective skeletal development postnatally, including reduced body weight and length, shortening of long bones, reduced bone volume and significant changes in the bone microarchitecture. The dKO mice also displayed reduced growth plate length with shortening of distinct chondrocyte zones and altered deposition/assembly of collagen II and X. To determine the consequence of FN mutations in SMD, induced pluripotent stem cells were generated using fibroblasts donated by SMD patients with FN mutations (p.Cys123Arg, p.Cys231Trp) that were subsequently differentiated into mesenchymal stem cells and chondrocytes. FN mutant cells displayed intracellular protein retention, co-localization of FN with ER-Golgi markers and consequently initiation of the unfolded protein response. Reduced FN secretion from mutant cells was associated with a deficiency of FN and collagen II assembly. FN mutant cells exhibited mitochondrial dysfunction with alterations in structure and membrane potential. Mutant cells when subjected to chondrogenic differentiation displayed impaired mesenchymal condensation, increased cellular apoptosis and reduction in expression level of over 25 key chondrogenic markers. We demonstrate that FN is essential for proper chondrogenesis and skeletal development. Mutations in or the absence of FN in the developing cartilage leads to critical alterations in cell function, differentiation, and ECM assembly resulting in skeletal defects.

PG3: Plasma fibronectin regulates trabecular bone mass and bone remodeling

Mahdokht Mahmoodi

Supervisor(s)/Collaborator(s): Mari T. Kaartinen

Cluster: Mineralized Tissue and Extracellular Matrix Biology Cluster

Introduction: Osteoporosis is a bone disease characterized by loss of bone mass (osteopenia) and an increased prevalence of bone fractures. The causes of osteoporosis are linked to genetics, nutrition, and medication. While osteoporosis is more prevalent in ageing women, it can also affect men and occur at any time of life. At the cellular level, osteoporosis results from imbalanced activity between bone-eliminating and bone-forming cells, which form the *bone multicellular unit (BMU)* that is responsible for the bone renewal process throughout life. The liver regulates bone health through different pathways, including vitamin D, which affects calcium metabolism, and via the secretion of *hepatokines* and growth factors that can regulate bone remodeling. Bone remodelling involves bone resorption by osteoclasts and bone formation by osteoblasts. Both cell types' differentiation and activity can be regulated by extracellular matrix (ECM) components. *Fibronectin* (FN) is a multifunctional glycoprotein of extracellular matrix (ECM) which can regulate cellular adhesion, proliferation, migration, and differentiation as well as assembly of other ECM components. Two protein forms of FN exist; cellular FN and plasma FN (pFN) based on its origin of production. pFN is synthesized by hepatocytes in the liver, which circulates in the blood at a high concentration, from where it can accumulate in tissues to contribute to ECMs. It is estimated that 90% of bone FN is plasma-derived. pFN knockout mice have been reported to have altered mineral-to-matrix ratio and decreased biomechanical strength *in vivo* in mice, but osteopenia/osteoporosis, i.e., bone mass or bone remodeling status, was not assessed or reported. Changes in this can be hypothesized because cell culture studies have demonstrated that osteoblasts and bone marrow mesenchymal stem cells assemble pFN matrix, which affects their differentiation. Osteoclastogenesis has also been reported to be regulated by FN, where it upregulates osteoclast activity but inhibits osteoclast formation *in vitro*.

Hypothesis: We hypothesized that pFN is an important regulator of bone remodeling and maintenance of bone mass in adult mice *in vivo*.

Aims and approaches: The aim was to investigate the skeletal phenotype of liver-specific conditional FN knockout that lacks pFN in circulation. *pFN knockout mice* (pFN KO) (Fn-/-^{ALB}) and its control ($Fn^{flx/flx}$), mice (male and female) (n=8-11) were subjected to skeletal phenotyping at five months of age. Analyses included the assessment of bone microarchitecture parameters via CT, and femur biomechanical strength via 3-point bending test. This data was complemented with blood parameter analysis of bone turnover markers using CTX-1 ELISA kit that measures C-terminal telopeptide of type I collagen for bone resorption and procollagen type I N-propeptide (P1NP) ELISA for bone formation.

Results: CT data on the bone microarchitecture of adult, 5-month-old mice show a significant reduction of trabecular parameters in *male* pFN KO mice (n=5), including decreased trabecular number (p=0.0001), and the bone volume/tissue volume ratio (BV/TV; p=0.0004), and an increase of osteoporotic values such as trabecular separation (p=0.0072) Measurement of bone resorption and formation markers, CTX-1 and PINP, respectively, showed a significant reduction of *bone formation* in *male* pFN KO mice (p=0.0008) compared to their control group (n=8-11). Female pFN KO mice showed no change in serum PINP levels ($p<0.05$). Surprisingly, bone resorption (CTX-1) marker showed *a decrease* in both female and male pFN mice compared to their controls; this was significant *in female* (p=0.0077), but not in male pFN KO mice (p=0.07), perhaps due to small sample size (n=2 vs 5).

Conclusion: Our study suggests that pFN may be an important *hepatokine*-type regulator of bone mass and BMU activity. The results need to be substantiated with increased sample size, CT analysis of female mice and histomorphometry to assess BMU quantities in trabecular bone.

PG4: Adverse Effects of Botulinum Toxin-A Injection on Mandibular Bone Structures: A Systematic Review and Meta-Analysis

Mahmoud S. Moussa

Supervisor(s)/Collaborator(s): Dona Bachour, and Svetlana Komarova

Cluster: Mineralized Tissue and Extracellular Matrix Biology

Background: Botulinum Toxin-A (BTX), one of the most potent toxins known to man, is used in dental practice to temporarily paralyze muscles and reduce hyperfunction implicated in temporo-mandibular disorders (TMDs). BTX use in TMDs remains off-label and potential adverse effects are understudied. In animal models of paralysis, BTX is known to induce significant bone loss.

Objective: The objective of this study is to systematically review the literature for articles investigating changes in mandibular bone structure following BTX injections and meta-analyze available data on reported bone outcomes. Methods: Comprehensive search of 3 databases retrieved 934 articles. Following screening, 20 articles quantitatively describing changes in mandibular bone structure after BTX injection in masseter and/or temporalis muscles in humans (6 articles), rabbits, rats or mice (14 articles) were included. Study characteristics and covariates were identified and tabulated. Means and variance of meta-analyzable parameters were collected and effect sizes calculated. Meta-analysis was conducted using random effects model and heterogeneity was assessed.

Results: For humans, 86% of participants received BTX for myofascial TMDs, with 96% of all participants being females 27 – 55 years of age. For animals, injections in young to skeletally mature mice, rats and rabbits were reported, with balanced male/female ratio. BTX doses varied from 0.2-10 BTX units in animal studies, and 50-240 BTX units for human participants. Meta-analysis of human participant data revealed decreased cortical thickness of mandibular regions following BTX injection, with percent difference compared to baseline being -9.0% [Confidence Interval (CI);-15.3; -2.7], while bone volume was not significantly affected (-2.5%[-13.0; 7.9]). Subgroup analysis by mandibular regions suggested higher cortical bone loss in condyle. In animals, significant loss of mandibular cortical thickness (-12.3%[-18.9; -5.6]) and trabecular density (-40.9%[-50.0;-31.8]) in BTX-injected compared to contralateral site.

Conclusion: We demonstrated that BTX injection in the masticatory muscles induced mandibular bone loss in human participants and in animal models. Data scarcity was evident for all species. Meta-analytic estimates of the effect size and variance produced in this study will help in designing future trials.

PG5: Age related changes of systemic immune profile in nerve injured male and female mice

Wen Bo Sam Zhou

Supervisor(s)/Collaborator(s): Xiang Qun Shi, Magali Millecamps, Jeffrey Mogill, Younan Liu, Simon Tran, Ji Zhang

Cluster: Pain and Neuroscience

Introduction: Aging is associated with a higher prevalence of many chronic non-communicable diseases including chronic pain, and there is a higher prevalence of chronic pain in women than in men. Aging is also associated with low grade systemic chronic inflammation (inflammaging). However, the relationships between inflammaging, chronic pain, and sex difference have not been fully understood.

Methods: We performed the spare nerve injury (SNI) and sham surgery on 3-month-old male and female mice, and longitudinally monitored them for 2 years. We used the von Frey and acetone tests to measure mechanical and cold sensitivities, flow cytometry to determine immune cell compartments, and the Luminex multiplex assay to evaluate changes in serum cytokines and chemokines. We also treated 23-month-old SNI mice with mesenchymal stem cell extracts (MSCE), as our previous data showed its effectiveness in alleviating neuropathic pain in young nerve injured mice.

Results: Both male and female SNI mice exhibited persistent, stable mechanical and cold allodynia over the 2 years following surgery. Flow cytometry results showed age and sex dependent changes in circulating immune cell numbers, where the impact of nerve injury is minor. We found that as the sham and SNI mice aged, there is an increase of monocytes, more significantly in male mice, and a decrease of NK and CD4 T cells, both of which are more significant in female mice. Neutrophil numbers remain mostly unchanged in both male and female mice. CD8 T cells and B cells slightly increase with age in male but dramatically decrease in female mice. Proportionally, the monocyte and neutrophil compartments expand in aging female mice but do not change considerably in aging male mice. Unexpectedly, MSCE treatment was not able to alleviate either mechanical or cold allodynia in both male and female aging SNI mice.

Conclusion: We characterized age and sex dependent changes of systemic immune profile in mice, which is barely affected by nerve injury. Further investigation into inflammaging will help us to better understand mechanisms of chronic pain in aging population and to develop effective pain management strategy.

PG6: Neural correlates of Trigeminal nerve morphogenesis in chronic painful temporomandibular disorders (TMD)

Elnaz Alikarami

Supervisor(s)/Collaborator(s): Carolina B. Meloto

Cluster: Pain and Neuroscience

Introduction: Painful temporomandibular disorders (pTMD) involve the orofacial area innervated by the trigeminal nerve (the fifth cranial nerve pair, CNV). Genome-wide based pathway analysis has revealed the highest correlation between 'trigeminal nerve morphogenesis' and pTMD among all the other pathways. Genes in these pathways have principal roles in the morphogenesis of neural tissues. Here, we hypothesize that morpho-structural abnormalities along the CNV nociceptive pathways may facilitate pTMDs. To investigate this, we will test if there are differences in the CNV trajectory and/or connectivity between individuals with and without pTMD.

Methods: There will be 25 pTMD patients (myalgia > 3 months) and 25 pain-free controls participating in this study, undergoing neuroimaging (diffusion tensor imaging, DTI). We will use tractography to delineate the CNV trajectory and a Sholl-based analysis to quantify the neural connectivity. Both indexes will be compared between groups. Participants will take surveys assessing pain-related and psychological symptoms and the relationship between the DTI-based CNV measures and pain severity and psychological symptoms will be explored.

Results: Data collection is ongoing, and our study presently counts with a pool of 12 potential pTMD participants. DTI data collected from the first participants indicate that CNV tracts can be tracked and quantified both toward the periphery and the brain.

Conclusion: These pilot findings demonstrate the feasibility of our study. Of note, secondary analyses of DTI data available to us (PMID23685183) using our methods has revealed group differences that were not previously identified. Thus, we have putatively developed a more sensitive metric of nerve abnormalities in pTMD.

PG7: Short and long terms changes in murine hindlimb vasculature are initiated by mechanical loading

Taylor deVet

Supervisor(s)/Collaborator(s): Mahmoud Moussa, Svetlana Komarova, Bettina M. Willie

Cluster: Mineralized Tissue and Extracellular Matrix Biology Cluster

Introduction: In humans acute load-bearing exercise is known to increase blood flow to the bone through vasodilatation of the bone blood vessels. Chronic exercise causes changes in bone blood flow by altering properties of existing blood vessels and angiogenesis. In mice, in vivo compressive tibial loading has been shown to increase overall limb perfusion acutely, with similar changes occurring after each loading event over a two week period. However, active adaptation of vessels and vascular network topology in response to loading are still unknown. The present work aims to identify correlations between acute and chronic changes in vascular structure and function and adaptive bone (re)modelling during 2 weeks of in-vivo tibial loading in mice.

Methods: We applied in vivo cyclic tibia to the left tibia of 26-week-old female C57BL6/J mice (n=9), with the right limb used as a non-loaded control. Loading was applied 5 days a week for 2 weeks. Vascular ultrasound was conducted on days 0 and 15 and directly before and after loading events on days 1,3,7, and 9. The effect of loading on vasculature was analyzed using a two-way ANOVA and pairwise Student's t-tests. In vivo microCT scans were performed on days -2 and 15. Cortical bone at 50% of the bone length was analyzed. Pairwise Student's t-tests were used to test for statistical significance. For all reported parameters, significance was set at $p < 0.05$.

Results: Loading events led to significant increases in blood flow in the tibial and saphenous arteries. The femoral artery feeds these two vessels, but we did not observe a significant change in this vessel during loading until day 7 and onwards. Chronic effects of loading were seen as changes in both tibial and femoral artery flow from day 0 to 15, with no significant change to the saphenous artery. As expected, microCT analysis demonstrated that this 2-week in vivo tibial loading protocol led to significantly increased cortical bone formation, specifically an in thickness (CtTh), medullary area as well as cortical bone area/total bone area (CtAr/TtAr).

Discussion: This work demonstrates that compressive limb loading results in both significant adaptation to the bone, as well as the local vasculature. Loading of the limb increases blood flow to the entire hindlimb acutely, while in the longer-term, loading led to more targeted vascular adaptations. Acutely, after each loading episode, blood flow to the limb increased, likely in response to the induced bone and surrounding tissue strain. Vascular adaptation to mechanical loading is an important component that is often overlooked when studying bone (re)modeling.

Conclusion: Although it is known that blood flow increases in a loaded limb, the present study demonstrates that some of the vessels adapt to longer term loading, while some only change acutely after a single loading episode. These findings suggest that vascular adaptation plays a significant active role in loading induced bone (re)modeling.

PG8: Swim training induces differential osseous gene expression in anosteocytic and osteocytic teleost fish

Josephine T. Tauer

Supervisor(s)/Collaborator(s): Tobias Thiele, Catherine Julien, Lior Ofer, Paul Zaslansky, Ron Shahar, Bettina M. Willie

Cluster: Mineralized Tissue and Extracellular Matrix Biology Cluster

Introduction: Osteocytes are the mechanosensory cells of the bone, regulating bone (re)modelling in response to mechanical stimuli. Surprisingly, evolutionarily advanced fish lack osteocytes but are still able to response to mechanical loading via bone modeling. Thus, we aimed to determine underlying molecular mechanisms in anosteocytic bones in advanced (medaka) and osteocytic bones in basal (zebrafish) teleosts after swim training.

Methods: Anosteocytic medaka and osteocytic zebrafish were submitted to a single 5-minute swimming bout against a current. After 1h, 8h or 24h after the swim session, vertebrae were isolated and cleaned off any muscle or nerve tissue. RNA was extracted from the vertebrae and subjected to RNAseq analysis and compared to control not swim-trained fish.

Results: RNAseq analysis resulted in a total of 26,976 gene reads for zebrafish and 19,480 gene reads for medaka at each time point investigated. After cleaning off previously identified nonskeletal genes (Ayturk et al. JBMR, 2013:28(10)), 14 differentially expressed genes (DEGs) were identified at 1h, 54 DEGs at 8h, and 977 DEGs after 24h in zebrafish, while medaka demonstrated 65 DEGs at 1h, 61 DEGs at 8h, and 545 DEGs at 24h. Gene ontology analysis focussing on osseous adaptation revealed increased expression of genes associated with 'osteoblast differentiation' at 8- and 24h in zebrafish, respectively. In contrast, medaka demonstrated significant downregulation of DEGs belonging to 'skeletal system development' at 8h post-training. Analysis of shared DEGs between zebrafish and medaka revealed one overlapping DEG at 1h, six at 8h, and 67 DEGs at 24h post-training. Narrowing these overlapping DEGs down to bone-related genes, identified myocilin, a stimulator of osteogenic differentiation, to be positively expressed in both species, but more predominantly in zebrafish. However, evaluation of DEGs for canonical Wnt pathway, the main mechano-induced signaling cascade, demonstrated 5 upregulated DEGs in zebrafish and 2 upregulated in medaka at 24h, respectively. Sclerostin, main regulator of Wnt pathway, was not significantly expressed at any timepoint in both species.

Conclusion: These results clearly demonstrate that zebrafish benefits from numerous boneembedded osteocytes and their capacity to induce bone formation in response to mechanical stimuli. Contrary, as medaka is lacking osteocytes, swim-training resulted in downregulation of skeletal modeling. Previously, it was concluded that in medaka nonosteocytic cells, such as bone lining osteoblasts, chrondrocytes, and chordoblasts, sense and response to mechanical load but in a different time-dependent manner (Ofer et al. PLoS Biol, 2019:17(2)). Our results challenge the current paradigm of osteocytes' exclusivity in bone-modeling regulation, suggesting the existence of multivariate feedback networks in bone modeling.

PG9: Overview of rare disease meta-analysis, a method to aggregate n =1 data

Priyesh Patel

Supervisor(s)/Collaborator(s): Svetlana Komarova

Cluster: Mineralized Tissue and Extracellular Matrix Biology Cluster

Introduction: Meta-analysis is a tool that uses strict methods and rigorous statistical analysis to generate high-quality and low-bias information for knowledge synthesis and clinical decision-making. Rare disease literature cannot be used in the traditional meta-analysis because it primarily comprises single patient case studies, and even individual patient meta-analysis tools rely on multiple patients reported in a single study. There is currently no methods to aggregate n=1 data from multiple sources. In the field of rare disease, a method to aggregate n=1 data becomes necessary for knowledge consolidation in this area. Objective: My goal is to create a new method for meta-analysis, called rare-disease meta-analysis (RDMA), which aims to aggregate n=1 data. The protocol will have outlined concrete steps and guidelines for data interpretation.

Methods: The development of the framework for rare disease meta-analysis (RDMA) will include an assessment of biases and a quality checklist. A method to estimate the standard deviation when most studies have n=1 patients will be developed, and methods to quantify the heterogeneity will be amended. The data analysis protocol of RDMA will be updated to reflect the comparison between the disease group and the healthy control. The performance of the new method will be validated using synthetic data.

PG10: Effect of genetic strain and loading history on bone mechanical and structural properties

Isabela Vitienes

Supervisor(s)/Collaborator(s): Nicholas Mikolajewicz, Seyedmahdi Hosseinitabatabaei, Alice Bouchard, Catherine Julien, Gabrielle Graceffa, Ana Rentsch, Tina Widowski, Russell Main, Bettina Willie

Cluster: Mineralized Tissue and Extracellular Matrix Biology Cluster

Introduction: Egg-laying hens are an interesting model to study the mechanical behaviour and adaptation of bone since they suffer from disuse osteoporosis and often experience bone fractures. We aimed to investigate how genetics and loading history influence bone mechanical and structural properties, and hypothesized that 1) genetic strain would affect *in vivo* strains and bone curvature, and 2) increased opportunity for physical activity during youth would coincide with a decrease in *in vivo* strains and bone curvature in a dose-dependent fashion.

Methods: White feathered (*W*) and brown-feathered (*B*) chickens were raised in either conventional cages (no physical activity, *Conv*) or two styles of rearing aviaries (offering opportunities for *Low* or *High* activity levels) until 14 weeks. We sampled 42 birds (n=7/genetic strain/rearing environment), surgically instrumented the right tibiotarsi with strain gauges at the anterior, medial, and posterior midshaft surfaces and measured strains while the chickens performed a variety of steady and non-steady activities. Longitudinal strains were measured at each anatomical site, principal (tensile and compressive) and shear strain at the anterior surface, and peak axial and bending strains were derived from anterior and posterior longitudinal strains. The effects of genetic strain and rearing housing on *in vivo* mechanical strains were determined by two-way ANOVA and Benjamini-Hochberg adjusted pairwise Student's t-tests. After euthanasia, tibiotarsi were μCT-imaged and radii of curvature (C_R) along the bone length was calculated as the distance between the bone's longitudinal axis and the cross-sectional centroid. C_R was also decomposed into anterior-posterior (C_{AP}) and medial-lateral (C_{ML}) components. The effects of genetic strain and rearing environment on curvature were determined by two-way ANOVA and Tukey's post-hoc testing. Significance was set at $p<0.05$ and reported effects are significant unless otherwise indicated.

Results: The tibiotarsus of young egg-laying hens experiences a complex loading environment dominated by torsion-induced shear. *W* birds had greater anterior and medial longitudinal and anterior principal tensile strain, and lower posterior longitudinal and anterior principal compressive strains, compared to *B*. The effect of genetic strain on shear strain was activity type-dependent, while peak axial and bending strains were consistently higher in *B* compared to *W*. Rearing housing influenced all parameters except for medial longitudinal strain. Although pairwise comparisons were nonsignificant, we saw a consistent pattern where during steady activities, *Conv* birds had higher strains than *Low* and *High*, whereas during non-steady activities, *Conv* strains were lower. We also saw that genetic strain and rearing housing affected bone curvature, and therefore the effects of genetic strain and housing on *in vivo* mechanical strains may occur through these effects on bone curvature. Genetic strain influenced C_R at the proximal midshaft, where among birds reared in *Conv*, *B* had 51% lower C_R than *W*. Housing influenced C_{AP} at the distal midshaft, while C_{ML} was nearly unaffected by both genetic strain and rearing housing. Peak C_R was in the posterior convex direction and was achieved at 84% bone length (proximal-to-distal), with an 88% contribution from the AP component.

Significance: Our results suggest that the effects of loading history on *in vivo* strains are activity-style dependent, and that bone curvature is an important factor mediating the effects of genetics and loading history on long bone mechanical properties. *In vivo* strain data of the pullet tibiotarsus will

inform future loading studies examining the bone's mechanoresponse, and we identify the 84% region at the distal tibiotarsus as a region of interest to measure the tibiotarsal mechanoresponse, since the observed peak curvature likely causes peak *in vivo* strains to occur at this location.

PG11: The oral health of refugeed children: A discourse analysis of Canadian health policy.

Olawale Dudubo

Supervisor(s)/Collaborator(s): Beatriz Ferraz Dos Santos, Belinda Nicolau, Mary Ellen Macdonald

Cluster: Population Oral Health

Introduction: Humanitarian migrant children (child refugees and asylum seekers) have worse health experiences and outcomes than children in their host countries. One of these poor health domains is oral health: Humanitarian migrant children's oral health is shaped by their countries of origin, migration journeys, and multiple factors once in host countries, including public health policies.
In Canada, the Interim Federal Health Program (IFHP) includes dental services for a maximum of $1,000 per person. The dental coverage provides emergency dental services and restorative treatments for humanitarian migrant children. This care covers treatments such as emergency examinations, amalgam and composite restoration, tooth extractions, incisions and drainage of dental abscesses, life-threatening complications of dental origin. It does not cover child-focused preventive treatments (e.g., annual examinations, fluoride application, sealants) prefabricated pediatric crowns, or endodontic treatments (e.g., pulpotomies) . This dental coverage is minimal when compared to provincial standards for Canadian children. Objectives: The aim of this project is to examine the IFHP for its impacts on the oral health disparities between humanitarian migrant children and citizen children. We will discursively examine the IFHP, as well as the accompanying history of this policy, exploring how humanitarian migrant children are recognized – or not - as children with unique needs and rights. We will compare this federal response to humanitarian migrant children's oral health with both national and provincial standards for Canadian children (e.g., Canadian Dental Association; provincial standards). In forcing this comparison, this project aims to understand the rhetorical and actual commitments of Canada to humanitarian migrant children.

Methodology: We will use discourse analysis methodology to explore how humanitarian migrant children's oral health is framed and addressed in Canadian policy documents. We will apply Bacchi's "What's the Problem Represented to Be" analytical framework to critically examine the way humanitarian migrant children's oral health is represented. This framework builds on a body of post-structural scholarship highlighting how policies are not merely tools of governance but also key sites to produce meanings around social problems. Significance and knowledge translation: This is the first study to critically examine how humanitarian migrant children are constructed by, and then attended to, via Canadian policy. Our overall goal is to build a foundation from which to better understand current empirical data regarding humanitarian migrant children's oral health and oral healthcare experiences, as well as directions for future research and policy creation. This project will advance the Migrant Oral Health Program (MOHP) research on humanitarian migrant children's oral health, building on the UN's Sustainable Development Goals. Further, by integrating this study with previous work done by MOHP, we anticipate three modes of knowledge translation: 1) a doctoral thesis, 2) manuscripts and 3) a plan for future work with oral health policy stakeholders.

PG12: Understanding oral health-related well-being of children experiencing cancer: A participatory hermeneutic ethnography

Nona Attaran

Supervisor(s)/Collaborator(s): F.A Carnevale, Beatriz Ferraz Dos Santos, Mary Ellen Macdonald

Cluster: Population Oral Health

Each year, approximately 400,000 children and adolescents are diagnosed with cancer globally. Whereas childhood cancer mortality used to be dire, today upwards of 80% of childhood cancers can be cured with treatments such as chemotherapy, radiotherapy, and surgery. Notwithstanding these vast improvements, cancer and its treatments can leave devastating impacts on cancer survivors. These effects can be especially difficult for children who experience higher rates of radiotherapy and chemotherapy-induced complications than adults. Many systemic sequelae manifest in the oral cavity of children surviving cancer; that is, they cause oral and dental complications. Treatment-related oral side effects can occur during or soon after treatment, or months – even years – later. They are classified as early/acute effects and late effects. Early oral effects include oral mucositis, xerostomia (dry mouth), oral infections (e.g., candidiasis and herpes virus infections), and taste disturbances. Late effects include caries, and abnormalities in dental and jaw development. These oral health complications can lead to cognitive, psychological, and social impairments which can have a profound impact on children's well-being. To date, our knowledge of these effects of cancer treatment comes from clinical research, and research involving caregivers' perspectives. While this research is clearly important, childhood scholars have suggested that children's perspectives are not always consistent with adults. Therefore, it is essential to also engage children directly in research to better understand their experience first-hand. Article 12 of 'The United Nations Convention on the Rights of the Child' stipulates that children's experiences must be rendered through their own voices, that they have a right to express their own views with respect to their age and maturity. In addition, affording children who have survived cancer this opportunity, by designing research that actively solicits their experiences from their perspectives, ultimately ensures a fuller, more accurate picture of the impacts that cancer therapy has on children's day-to-day life. Therefore, the aim of this project is to better understand how oral health effects of cancer treatments impact the well-being of children surviving cancer. Participants will be recruited from a tertiary care pediatric hospital. We will use a participatory hermeneutic ethnographic methodology, with a Childhood Ethics theoretical framework to center children's perspectives in our data and analysis. Data will be generated with participant observation and semi-structured interview. We will observe discussions among children, families/friends, and healthcare providers, paying particular attention to information about the child's well-being. We will interview 10-15 children surviving cancer, as well as their parents, siblings, friends, and their healthcare providers. Through this research, we will be able to identify how the oral health effects of cancer treatment affect children's well-being and understand how the impacts of cancer and its treatment influence their experience. Findings will focus on what is important to the well-being of children surviving cancer; together with our clinical and patient partners, we will translate these results into clinical and policy recommendations and develop future research activities.

PG13: Citizen Science Approach For Searching And Curating Literature Of The Effects Of Spaceflight On Cardiovascular Outcomes In Rodents And Humans

Mattias Neset

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Cluster: Population Oral Health

Background: The spaceflight environment causes significant changes to the structure and function of the cardiovascular system, including fluid redistribution, alterations in blood pressure, and changes in cardiac output. Objective: The goal of this project is to quantitatively summarize the data on the effects of actual or simulated microgravity and radiation exposure resulting from spaceflight on the cardiovascular system in humans and rodents.

Methods: Based on a list of relevant cardiovascular search terms developed by a group of investigators approached through a collaboration of the Ames Life Science Data Archive (ALSDA) Analysis Working Group, medical librarians generated and executed the search strategy in Medline, CINAHL, Embase and NASA repositories. In parallel, we recruited students and young professionals (~100) from various space industry-affiliated organizations. These individuals completed a virtual training course on the nature and methodologies of the project. Participants were then structured into teams, screening 18,837 studies using the systematic review tool, Covidence.

Results: Teams initially screened at a rate of 5000 articles/month, however individualized training from project supervisors increased this rate to 60000 articles/month. Our team of recruits is continuing to work on dividing the remaining articles into subgroups for full-text analysis.

Conclusion: Our approach reduces the length of time to complete title/abstract screening time from 1-2 years needed for this volume of studies, to several weeks. This effort will also result in collaborative publications based upon the literature meta-analyses, and several publicly accessible datasets for reuse, modeling, and machine learning.

PG14: Assessing validity of the COVID-19 Anxiety Syndrome Scale in Canadian dentists

Rachita Seth

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Cluster: Population Oral Health

Background: The COVID-19 pandemic has resulted in a high level of mental health problems for the populations worldwide including healthcare workers. Given that, a number of instruments have been developed and validated. There is a need to understand the long-term mental health effects on dentists in Canada. The COVID-19 Anxiety Syndrome Scale (C-19ASS) was developed to reliably assess the presence of anxiety syndrome features associated with COVID-19 in general adult population in the US. The Generalised Anxiety Disorder-7 (GAD-7) tool is one of the most frequently used, validated self-reported questionnaires that is used to screen for, diagnose and assess the severity of Generalised Anxiety Disorder. Hence, the objective of this study was to evaluate the divergent validity of the C-19ASS questionnaire against the GAD-7 tool in a sample of dentists in Canada.

Methods: To address this objective, we used data from a prospective cohort study aiming to estimate COVID-19 incidence rates among licensed dentists from across Canada during August 2020 to October 2021. Dentists were recruited through e-mail invitations sent by collaborating provincial dental associations and licensing bodies. As part of this study, the C-19ASS was added to the monthly follow-up questionnaire in January 2021 and repeated monthly until the end of the study in October 2021. The GAD-7 instrument was added to the online questionnaire in October 2021. Analyses for convergent and divergent validity of C-19ASS were performed comparing the scores with those of GAD-7. Exploratory Factor Analysis (EFA), Confirmatory Factor Analysis (CFA) and Pearson correlation analyses were performed on the data from the October 2021 follow-up.

Results: The EFA and CFA revealed a 2-factor structure of the C-19ASS in our sample as the original validation of C-19ASS. The Pearson correlation analyses revealed that the total C-19ASS, as well as the avoidance and perseveration scores were positively correlated with the total GAD-7 score. The EFA showed a 3-factor solution: the perseveration and avoidance items of C-19ASS loaded on two separate factors, while the GAD-7 items tightly loaded onto a third factor.

Conclusion: The study results support the convergent validity of C-19ASS with the GAD-7. In terms of divergent validity, the EFA revealed that the C-19ASS is not identical with the GAD-7, with the C-19ASS evaluating specifically COVID-19 related anxiety, which is separate from GAD. Practical Implications: This validated measure will contribute to the understanding of the mental health impact of the pandemic on Canadian dentists and enable dental regulatory authorities and organizations to intervene to improve the mental health of dentists.

PG15: Characteristics of Self-Rated Oral Health Among Syrian Refugee Parents in Ontario.

Aseel Alzaghoul

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Cluster: Population Oral Health

Background: Canada has been hosting Syrian refugees since early 2015. Almost half of the Syrian refugee population lives in Ontario, with dental health being at the top of the list of important immediate needs. The objective of the study was to evaluate self-rated oral health and its associated factors among Syrian refugee parents residing in Ontario.

Methods: This was a cross-sectional study where 540 Syrian refugee parents, residing in Ontario and with at least one child less than 18 years of age were interviewed. Information about self-rated oral health was collected based on the question “In general, how would you rate the health of your teeth and mouth?” with answers ranging from 1 representing “Excellent” and 5 representing “Very Poor”. Multiple linear regression analysis was performed to assess the independent relationship between each of the sociodemographic-, migration-, health-, dental-related factors and self-rated oral health.

Results: The overall prevalence of poor and very poor self-rated oral health was 43.5%. The results showed that the presence of dental health insurance, private sponsorship, improved physical and mental health, and regular visits to the dentist were factors related to improved oral health. Discussion: To achieve better oral health outcomes among refugee populations, including Syrian refugees, efforts should be focused on improving dental care and dental insurance for vulnerable populations. Keywords: Syrian refugees, oral health, dental insurance, self-rated.

PG16: Improving quality of life of the elderly through innovative oral hygiene tools to prevent infections and poor oral health?

Haitham Shoman

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Cluster: Population Oral Health

Introduction: About seven million of the population over 65 years are categorised under special needs or disabilities. In 13-48% of the cases, premature death is attributed to lung infection from bad oral hygiene, specifically in nursing homes resulting from aspiration pneumonia. The leading cause of poor oral hygiene is dental neglect which can occur to old residents while under professional care. An estimated 40% reduction in aspiration pneumonia is due to more effective oral hygiene. The aim of this project is to estimate the reduced incidence of aspiration pneumonia and improved quality of life through effective oral hygiene program including the Ora-3D with its behavioural intervention. Ora-3D is a new innovative semi-autonomous brush that utilizes the bite and glide motion for better cleaning of the teeth.

Methods: A clinical trial will be registered under clinicaltrials.gov and conducted in a senior residence in Montreal following the CONSORT statement guidance. The eligibility criteria include people aged 65-75 years of both genders regardless of race and ethnicity. Participants should be free of background lung infections and have no underlying disease causing weak immunity. A sample of 50 participants will be randomized after meeting the eligibility criteria and will be divided into two arms where one receives the intervention program and the second is the control arm. The project will run for 12 months and will estimate aspiration pneumonia cases averted and dental caries everted. It will also estimate the percentage of compliance with the program. Results (provisional) Provisionally it is estimated that the intervention program would help reduce the cases of aspiration pneumonia due to better oral health by 90%, dental caries cases averted of 85%, and compliance of 95%. It is also estimated that 80% of the participants will complete the entire project and a dropout of about 20%. Finally, it is estimated that there would be a reduction in labor hours by healthcare workers spending time on oral hygiene practices of about 30% giving them more time to focus on more pressing health matters for other residents.

Conclusion: The innovative OraBrush and its awareness programs have the potential of being a province-spread measure in long-term care residences to help the elderly population improve their quality of life through better oral hygiene practices. This will help reduce the incidence of aspiration pneumonia, dental caries and reduce nursing labor hours spent on oral hygiene practices with the elderly.

PG17: Applied Philosophical Hermeneutics Research: The Hermeneutic Wager

Marie Vigouroux

Supervisor(s)/Collaborator(s): Angela Morck, Richard Hovey

Cluster: Population Oral Health

In 2021, the research team facilitated a series of meeting for a working group bringing together a diverse group of people with different expertise regarding obstacles and opportunities in innovations in pediatric oncology. Through a series of virtual meetings, the research team based their facilitation on the conversations of the hermeneutic wager (imagination, humility, commitment, discernment, and hospitality) to build a strong and efficient research community. The informal consensus from the working group was that the hermeneutic wager was highly efficacious in achieving the depth and significance of community to begin their important work together. However, there is a paucity of literature in this area and little is known about how the hermeneutic wager works on a day-to-day functional level. We examined the working group's experiences with the hermeneutic wager to gain further understanding of how this powerful innovative approach operates at a personal, interpersonal, and research level. Our overarching objective is to develop a comprehensive, useable, accessible research methodology that is grounded in evidence-based best practices and remains responsive to the ever-changing landscape of research. We interviewed members of the working group who have experienced the hermeneutic wager and are able to speak to how it influenced their work individually, as a team, and as a research methodology. The collected data will be analyzed alongside the working group interviews, following the practices of applied philosophical hermeneutics. The data is first read over carefully by the team members who generate an interpretative memo, representing their initial analyses of the data. These are brought together in meetings to discuss the most relevant findings and begin the process of writing for dissemination of the new knowledge. Thus, applied philosophical hermeneutics will allow a means to uncover the deep meanings and understandings of how the hermeneutic wager influences and operates at a personal, interpersonal, and research level. The significance of this understanding will allow the hermeneutic wager to be utilized across diverse groups of researchers, working groups, and topics as an effective new qualitative research approach.

PG18: Characterizing the inflammation around dental implants: Bacterial infection, hypersensitivity, or both?

Heba Madi

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Cluster: Population Oral Health

Introduction: Titanium dental implants are widely used due to their high success rates and predictability. However, peri-implant inflammatory diseases including peri-implant mucositis and peri-implantitis still occur in frequencies ranging between 1% and 22%. These conditions can lead to progressive bone loss and eventual loss of the functional implant. Although bacterial plaque accumulation is the main cause of inflammation around dental implants, emerging evidence suggests that inflammation could also be the result of hypersensitivity reaction to titanium implant surface corrosion by-products.

Objective: This study aims to investigate the cytokine and matrix metalloproteinase (MMP) levels in peri-implant crevicular fluid (PICF) associated with bacterial infection and hypersensitivity reaction in healthy and inflamed dental implants.

Methods: A cross-sectional study is conducted at the Montreal General Hospital Oral and Maxillofacial clinic, involving 177 individuals with at least one functional dental implant placed between 2010 and 2016. Clinical and radiological examinations are performed to classify implants as healthy or inflamed. PICF samples are collected from each implant and analyzed using the Human Luminex Assay to establish cytokine levels associated with bacterial infection (Type 1 and 3) and hypersensitivity (Type 2), as well as MMP levels. Comparisons between healthy and inflamed implants will be made, and the relationship between cytokine/MMP levels and clinical diagnosis will be investigated.

Results: The levels of cytokines and MMPs associated with bacterial infection and hypersensitivity reaction will be quantified in healthy and inflamed implants. Statistical analysis will be performed to determine if there are significant differences in the levels of cytokines and MMPs between healthy and inflamed implants. Additionally, correlations between the levels of cytokines and MMPs and clinical parameters such as probing depth, bleeding on probing, and radiographic bone loss will be examined.

Conclusion: By analyzing cytokine and MMP levels in PICF, this study seeks to further our understanding of the inflammatory processes associated with peri-implant diseases and potentially identify the role of biomarkers (bacterial and hypersensitivity reaction) for diagnosis and treatment of peri-mucositis and peri-implantitis. The findings of this study could help to develop more targeted and effective treatment strategies for peri-implant diseases, leading to better outcomes for patients with dental implants.

The study is registered on ClinicalTrials.gov: NCT05675241

PG19: PEEK as an alternative non-metallic restorative material for implant-supported fixed partial dentures

Jan Kwan

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Cluster: Biomaterials, Nanobiotechnology and Tissue Engineering.

Purpose: The aim of this study is to evaluate a high-performance thermoplastic polymer of the polyacryl family, polyether ether ketone (PEEK), as a suitable material for the fabrication of implant-supported fixed partial denture frameworks.
Materials and

Methods: Patients requiring teeth replacement with dental implants were included for partial and edentulous cases in the maxilla and mandible. Using the lost wax technique, the interim fixed partial denture (FPD) was fabricated with hex castable copings and PEEK granules. The common path of insertion was established by reducing the coping that is in obstruction to the healing abutment. Retention was provided by the reciprocated guide surfaces of multiple hexagonal-shaped healing abutments.

Results: 23 custom interim PEEK FDPs supported by 166 implants in 20 partial and edentulous patients were provided during the treatment period. The average functional period of the interim PEEK FDP for maxillary and mandibular cases was 7.43 (months) ± 0.95 and 4.54 (months) ± 2.92, respectively. All interim PEEK FDPs functioned as intended for the entire treatment period. There were a total of 10 complications, 4 cases had resin and denture veneers debond from the PEEK framework. 3 partial edentulous cases required supplementary screw retention. 3 implants in separate cases did not osseointegrate requiring extended use of the interim prosthesis. No fracture of the PEEK framework was observed.

Conclusion: PEEK can be a suitable non-metallic restorative material used in provisional and permanent fixed partial dentures with additional biomechanical studies that relate to the distances between implants. The reciprocated guide surfaces of hexagonal-shaped healing or final abutments can provide sufficient mechanical retention and resistance in edentulous FPDs. Selective reduction of obstructing PEEK copings or hexagonal healing abutments can create a path of insertion for provisional and permanent FPDs, respectively.

PG20: Analyzing the Physicochemical Aspects of Biological Hydroxyapatite Precipitation Using Mathematical Modeling

Hossein Poorhemathi

Supervisor(s)/Collaborator(s): Svetlana Komarova

Cluster: Mineralized Tissues and Extracellular Matrix Biology

Formation of hydroxyapatite in bone, dentin and enamel occurs at restricted molecular sites that are provided by specific extracellular matrix proteins and is controlled by multiple mineralization inhibitors. However, the role of physicochemical factors such as the availability of required ions and the saturation status of the aqueous environment in biological mineralization is not fully understood. The goal of this study was to use mathematical modelling to describe the complex physicochemical environment permissive to the precipitation of biological hydroxyapatite. We simulated the processes occurring in the interstitial fluid (ISF) in the bone vicinity. The ISF was defined as an aqueous environment containing seven commonly reported chemical components (calcium, phosphate, carbonate, sodium, potassium, magnesium, and chloride) that form 30 chemical species. We simulated reversible equilibrium reactions among these chemical species, and calculated supersaturation for hydroxyapatite as well as precipitation rate using kinetic theory. The simulated ISF was of correct ionic strength and predicted the equilibrium component concentrations that were consistent with the experimental findings. Supersaturation of physiological ISF was ~5-10 depending on the initial total concentration of components and pH, which is supported by prior findings that mineralization inhibitors are required to prevent spontaneous mineral precipitation. The initial hydroxyapatite precipitation rate was faster than observed experimentally suggesting a strong influence of biological regulators. Examining how the total amounts of all the chemical components affect the precipitation process demonstrated that calcium and phosphate had the highest effect, followed by carbonate, which also had the strongest influence on system pH. After combining with the previously developed model of biological regulation of bone mineralization, this model will allow in silico studies of complex clinical scenarios associated with alterations in ISF ion composition, such as rickets, hypophosphatemia and chronic kidney disease. Moreover, with minor adaptations, it could be used to understand other mineralized tissues, such as dentin and enamel.