Faculty of Dentistry Summer Research Positions 2016

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   Supervisor: Dr. J Michael Lee

Details of each project are provided below.
Project 1: Ecological Modulation of Streptococcus mutans in Biofilms by Pheromone-guided Antimicrobial Peptides.

Supervisor: Dr. Yung-Hua Li

Background:
A major challenge using antimicrobial agents to treat infectious diseases in a natural ecosystem, such as in the oral cavity that contains the normal microflora, is that these therapies may result in ecological disruption and negative clinical consequences. The problems resulting from broad-spectrum antimicrobial agents combined with the emergence of antibiotic resistance highlight the urgent need for new antimicrobials that selectively target specific pathogens. Recent studies have developed a new class of antimicrobials, called pheromone-guided antimicrobial peptides (PG-AMPs), which are capable of selective inhibition or killing. Such pheromone-guided antimicrobial peptides have been found to be effective against several bacterial pathogens, including MRSA S. aureus, vancomycin-resistant E. faecalis, Pseudomonas spp, and cariogenic pathogen Streptococcus mutans.

In our laboratory, we have successfully identified several PG-AMPs that selectively target S. mutans. We have found that these PG-AMPs function in different ways and show at least three types of action mechanisms against S. mutans. In this study, we aim to expand our investigation into these peptides to explore their potential application in modulating the ecology and pathogenesis of S. mutans in an *in vitro* biofilm model system.

Research Objective/Question:
1. To determine how effectively PG-AMPs kill S. mutans or interfere with S. mutans quorum sensing-mediated activities in mixed culture biofilms;
2. To determine whether PG-AMPs compromise quorum sensing-mediated activities and growth advantage of S. mutans in mixed culture biofilms.

Methods:
These questions will be investigated by several methods available in our laboratory. The student will work together with a technician to perform the experiments. Full training will be provided. Viable cell counts combined with a Live/Dead BacLight bacterial viability assay are used to determine cell death of S. mutans following exposure to PG-AMPs in mixed cultures. An *in vitro* biofilm model system will be used to culture saliva-derived biofilms, with addition of S. mutans strain, to establish a mixed biofilm, and determine how PG-AMPs modulate S. mutans ecology in mixed cultures, in terms of quorum sensing activity, bacteriocin production and population shifts in the community. Bacterial species in saliva-derived biofilms can be determined by phylogenetic analysis of 16S rRNA genes of bacteria using PCR-DGGE analysis, which include sample collection, DNA preparation, PCR, electrophoresis and DGGE profile image analysis. Lux reporter assays are used to monitor gene expression profiles related to quorum sensing activities in S. mutans.

Role of the Student: The student will be engaged in: laboratory experiments and data analysis.
Project 2: Effect of Universal Adhesives' Etching Mode on Their Bonding Strength When Used As Self-Etching or Etch-and-Rinse Agents.

Project Supervisor: Dr. Pierre-Luc Michaud

**Background:** A very extensive array of resin products is available on the market. As a result, it is getting increasingly difficult for clinician-dentists to decide which material to use and to know of potential incompatibility between products. We have shown in previous research that a product dependency exists between some light and dual curable adhesive systems and light and dual curable composite resins – not all adhesive agents performed as well with all the composite resins used. Also, some incompatibilities were discovered and it was concluded that mixing and matching different adhesive agents with different composite systems should be avoided until the combination is tested in-vitro. In this study we will extend our studies on 'universal' adhesive systems with dual-curable composite resins and investigate the effect of etching protocol on bonding strength.

**Research Objective/Question:**
To assess whether or not bonding strength will be different when using the etch-and-rinse vs the self-etch protocol to bond dual-curable core build-up composite resins on dentin with ‘universal’ adhesive systems.

**Methods**
This project is an in-vitro study where bonding strength will be compared between different groups. Three ‘universal’ bonding agents (3M Scotchbond Universal, Ivoclar Adhese and Bisco Allbond universal) and 2 dual-curable core build-up materials (Premier CompCore and Bisco CoreFlo DC Lite) will be used. The bonding agents will all be tested using an etch-and-rinse and a self-etch protocol. After bonding these samples, the bonding obtained will be assessed with a micro-tensile bond strength test by using an Instron universal testing machine. Training will be provided.

**Role of the Student:** The student will be engaged in searching the literature, laboratory experiments, data entry, manuscript preparation and possibly poster preparation.

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Project 3: A real-time assay to measure barrier function in epithelial acini model.

Supervisors: Dr. Brendan Leung

Background: The epithelium is a major class of tissue with very specific functions. It typically lines surfaces that form the interface between stromal tissue and the external environment, serving as a barrier for material transport and defense against pathogens. Its dysfunction is implicated in the pathology of a wide range of diseases, including cancers, infectious diseases and metabolic syndromes. In the lab, we study epithelium function using models like the transwell culture, where epithelial cells are grown over a flat semi-permeable membrane. However, this model is not ideal and ultimately loses barrier function. There is a need to develop 3 dimensional culture systems that can mimic human epithelium for future pathophysiology studies and drug discovery. One solution is 3-D acini culture, where epithelial cells self-organize into hollow spheres. In this study, we will test the barrier function of epithelial acini models using a series of assays. The student will acquire hands-on experience in cell culture, microscopy and image analysis techniques. Training will be provided.

Research Objective/Question: The project seeks to determine if 1) real-time, nondestructive assays based on dye permeation and image analysis can provide quantitative measurement of barrier function in acini culture, and 2) can these measurements predict sub-lethal injury of acini. The successful development of such assays will expand our ability to understand the mechanism of cell disorganization in acini culture and to better model diseases in vitro.

Methods: We will use Madin-Darby Canine Kidney (MDCK) acini culture as a testing platform for developing barrier function assays. Acini exposed to known agents that disrupt epithelium integrity, including digestive enzyme (trypsin) and cytokines (TNFa) will be compared to untreated MDCK acini (baseline). Degree of injury can be tuned by changing dose and time of treatment. Initially we will test a modified version of fluorescent dye flux assay used in 2-D culture to measure barrier function.

Role of the Student: The student will be engaged in: searching the literature, laboratory work and data analysis. 

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Project 4: Resistance to fracture of teeth undergoing chemical or thermal sterilization processes for educational use.

Supervisors: Drs. Isabel Mello and Pierre-Luc Michaud

Background:
During preclinical training, dental students perform treatment in simulation facilities in order to gain technical proficiency so they can then move to the next level and treat patients in the clinic. Extracted teeth must be sterilized before being used for training purposes. Effective methods for tooth sterilization include immersion in formaldehyde, and steam sterilization procedures. The literature reports that sterilization procedures may affect the tooth structures, making the tooth brittle and more prone to fracture, however, it is unknown whether these changes may affect the student’s learning experience. Student frustration is remarkable when a tooth breaks in the middle of a procedure and they are forced to start their assignments all over again. It is important to identify a method for sterilization of teeth that does not make the tooth more prone to fracture.

Research Objective/Question: Are sterilized teeth more prone to fracture during preclinical training? Does one method of sterilization make teeth more prone to fracture than another?

Methods: Extracted third molars of similar dimension will be selected. All teeth will be checked for the presence of cracks under a microscope and cracked teeth will be discarded. Teeth will be stored in saline at 37°C until use. Teeth will be assigned to one of the 4 groups: G1 - teeth will be autoclaved for 40 min at 240°F at 20 psi; G2 - teeth will be immersed in 10% formalin for one week; G3: teeth will be immersed in 10% formalin for 2 weeks; CG: teeth will not be submitted to a sterilization protocol. After sterilization is complete, teeth will be stored in 1% sodium hypochlorite solution for 24 hours. Teeth will have access opening done, working length established and cleaning and shaping completed with rotary files. The presence of fracture, location, tissues involved (dentin/enamel) will be recorded.

Role of the Student: The student will be engaged in: searching the literature, laboratory work, data entry, manuscript preparation and poster preparation.
Project 5: Investigating the efficiency and efficacy of a wireless blood pressure device (Qardioarm) in dental education.

Supervisors: Drs. Cynthia Andrews and Chris Lee

Background:
Blood pressure (BP) monitoring is an important component in dental care. Twenty to twenty-five percent of Canadians have hypertension. Forty percent of those are unaware of it, and another 40% are aware but poorly controlled (>140/90). Therefore, only 20% of Canadians with hypertension are aware and well controlled.

All new patients should have their BP taken for baseline data. Patients with a history of hypertension, cardiovascular disease, stroke, kidney disease, diabetes and obesity should have their blood pressure recorded at every dental visit. Dental procedures can cause an intrinsic increase in blood pressure due to their painful or fear-provoking nature. Dental procedures can also cause an extrinsic increase in blood pressure due to vasoconstrictors in local anesthetics.

Dentistry students are currently trained using their own stethoscope and manual blood pressure cuff.

Research Objective/Question: How does a wireless blood pressure device (Qardioarm) compare with traditional methods (stethoscope and blood pressure cuff) in efficiency, efficacy and cost, when tested in a group of dentistry students?

Methods: Voluntary participants will include students from the DDS2, DDS3 & DDS4 classes. Participants will attend a refresher lecture on traditional methods for recording blood pressure, and will be introduced to the wireless device (Qardioarm) and its use. A Simulation Mannequin (SM) whose BP can be regulated by the researcher, will be utilized for the study. Participants will record blood pressure on a SM using a stethoscope and BP cuff, and again using the Qardioarm device. The BP settings will be changed each time a measurement is taken. Participants will be timed for each procedure, and each procedure’s measurements will be compared to the accurate BP of the SM for that iteration. At the end of the measurement session, participants will complete an online feedback survey about the two different methods.

The research student will become familiar with the Qardioarm by using it on patients in Dr. Lee's GPR and ER clinics to determine its user- and patient-friendliness.

Role of the Student: The student will be engaged in: searching the literature, developing questionnaire, assistance in clinic, data entry, data analysis, recruiting participants, coordinating testing sessions, manuscript preparation and poster preparation.
**Project 6: Impact of Maxillomandibular Advancement (MMA) on Health-Related and Functional Outcomes - A Prospective Multicenter MMA Study.**

**Supervisors: Dr. Reginald Goodday and Dr. Karim Al-Khatib**

**Background:** Obstructive sleep apnea (OSA) is a common disorder affecting at least 2-4% of the adult population and is associated with a diminished quality of life, hypertension, diabetes, and cardiovascular disease, thereby making it a significant public health concern. Positive airway pressure (PAP) is the accepted first-line therapy for patients with OSA. PAP is highly efficacious, virtually eliminating OSA. The major barrier to translating this efficacy into clinical effectiveness is non-adherence with PAP therapy; which leaves the patient inadequately treated and at increased risk for cardiovascular events and diminished quality of life. Currently, it is unclear what alternative therapy should be used to treat patients with moderate to severe OSA who are inadequately treated by PAP. Several observational studies indicate that maxillomandibular advancement surgery (MMA) may be a clinically effective alternative therapy for patients with moderate to severe OSA who are unable to adhere to PAP therapy. However, little is known about changes in important outcomes such as levels of inflammatory biomarkers indicative of cardiovascular disease, quality of life, and neurocognitive function following MMA. This study is designed to determine if MMA results in significant improvement in several important health-related and functional outcomes.

**Research Question:**
We hypothesize that treatment of moderate to severe OSA by MMA will result in significant improvement in the levels of inflammatory biomarkers indicative of cardiovascular disease, quality of life, sleepiness and neurocognitive function.

Aim 1: Determine the changes in the levels of inflammatory biomarkers indicative of cardiovascular disease (high sensitivity C-reactive protein, interleukin-6, tumor necrosis factor alpha), following management of moderate to severe OSA by MMA.

Aim 2: Determine the changes in quality of life, sleepiness and neurocognitive function as measured by changes in health related-quality of life surveys (Functional Outcomes of Sleep Questionnaire, SF-36), the Epworth Sleepiness Scale, and neurocognitive testing (Psychomotor Vigilance Task, N-back task) following management of moderate to severe OSA by MMA.

**Methods:** We are conducting a prospective multicenter cohort study and plan to recruit 36 adults who have been diagnosed with moderate to severe OSA (AHI > 15) and have elected to undergo MMA for treatment of OSA. Patients who enroll in the trial will undergo baseline/pre-MMA and 6 month post-MMA evaluation for several primary and secondary outcome measures.

**Role of the Student:** The student will be engaged in: literature search/review, conducting interviews, chart review, assistance in clinic, data entry/manipulation, data analysis, manuscript and poster preparation.
Project 7: Infant Oral Health: Age of Initial Screening and the Prevention of Severe Early Childhood Caries Within the North Preston Dental Clinic

Supervisor: Drs. Jennifer MacLellan and Ferne Kraglund

Background: Early childhood caries is a serious disease that can negatively affect the health and well-being of young children, and yet it is preventable. In order to prevent early childhood caries, the Canadian Dental Association recommends that infants be assessed within six months of the eruption of the first tooth and no later than one year of age. The first dental visit provides an opportunity for early diagnosis and prevention of dental disease, and the provision of anticipatory guidance to caregivers around topics such as diet and oral hygiene. Despite the recommendation by the Canadian Dental Association, many children have already developed early childhood caries by the time they are assessed by a dentist. For some children, their first dental visit may occur at a school based clinic.

Research Question: The research question being addressed by this study is whether there is a relationship between age at first dental visit and caries incidence at the first visit among pediatric patients of the North Preston dental clinic.

Methods: The student will develop a narrative of the history of the North Preston dental clinic. S/he will speak to leaders in the North Preston community, as well as leaders in Dalhousie's Faculty of Dentistry responsible for the development and implementation of the dental clinic located at Nelson Whynder Elementary School in North Preston. The student will also complete a chart audit of all dental charts of new pediatric patients seen in the last 15 years at the North Preston dental clinic. Data to be collected from the chart review will include age at first dental visit and dmft (decayed, missing, filled primary teeth) scores.

Role of the Student: The student will be engaged in: literature review, chart review, interviews, data entry, data analysis, manuscript and poster preparation.
Project 8: Does soft tissue overload injury reveal integrin binding sites via local denaturation in nano-scaled collagen fibrils?

Supervisor: Dr. J. Michael Lee

Background: Injury-induced damage in soft tissues has been the subject of much interest due to the tremendous societal and economic consequences. In looking at the structural changes associated with injury, most work has looked at tissue or fibre-level damage via light microscopy, alteration in cell function, or whole-tissue mechanics. We have long suspected and have found evidence that structural features of “failed” or “damaged” collagen—that is, motifs at the fibrillar or subfibrillar level—signal inflammatory or synthetic cells that this collagen is damaged and requires attention. We have evidence that discrete plasticity kink structures serve as cell-recognizable markers of damage. We have tested this idea with inflammatory macrophages and found the first evidence that a structural motif for collagen damage—in and of itself—cues cellular activity. This research will address the question of what *exactly* the macrophages are recognizing at damaged sites? This is an important question since its answer may carry key information for understanding the inflammatory response and the subsequent healing response in traumatic injury.

Research Question: Since discrete plasticity damage in collagen fibrils is characterized by local denaturation of collagen, it is likely that unfolding of the triple-helical structure reveals otherwise-cryptic polypeptide zones on collagen that are important to cellular binding to matrix. So, the research question is: Is nano-scaled unfolding of collagen fibrils co-localized with integrin binding sites for inflammatory or synthetic cells?

Methods:
To get at this question, we plan to employ a novel polypeptide probe that will provide a label for where, in injured tissue, the fibrillar collagen is denaturing. We will use bovine tail tendon collagen as a test substrate. Tail tendons will be harvested and cut into two segments: (i) control, and (ii) overloaded. The overloaded segments will be subjected to 5 cycles of controlled plastic overload. Both segments will then be subject to decellularization to remove all cellular debris, leaving behind a matrix of nearly-pure collagen: both native and overloaded. We will then label both segments with the polypeptide probe, labelled in this case with a fluorophore emitting at a known wavelength suitable for scanning laser confocal microscopy. Since we know that the overload damage produced in this tendon model is heterogeneous, we expect to see (with appropriate titration of the probe), patchy fluorescence from the overload samples where tissue damage is most intense— and virtually no fluorescence from control (undamaged) tissues. We will then counter-label these samples with monoclonal antibody probes for epitopes of identified integrin binding sites for macrophages and/or fibroblasts. These antibodies will be labelled with a different fluorophore which emits at a second wavelength. Under confocal microscopy, we will co-map injury-induced collagen denaturation and exposure of integrin binding sites.

Role of the Student: The student will be engaged in: laboratory work, data analysis, manuscript and poster preparation.