Index-Description

The Material Interactions with Biological Systems Laboratory focuses on improving the biocompatibility of biomaterials and biomedical devices, specifically in the ocular and circulatory systems. With the increasing utilization and invention of biomedical devices, the lives of countless individuals have been improved significantly. To maintain and maximize this improvement, the potentially life-threatening side-effects of such innovations, including infection, thrombosis, and fibrosis must be understood, and through this understanding, prevented, to ensure each patient’s safety and satisfaction. Hence, this laboratory studies the interactions which occur between biomaterials and biological systems to understand the mechanisms behind these negative outcomes along with those that could theoretically arise from a biomedical device or therapeutic measure. To do so, our laboratory studies biological systems’ responses to biomedical devices and therapies on a cellular level to comprehend and identify these mechanisms and to quantitatively evaluate their biocompatibility. By understanding these mechanisms, and recognizing needs for improvement in the industry, our laboratory innovates to develop materials, therapeutics and devices with improved biocompatibility. To justify the value of our conceptions, we often develop in-vitro models to closely represent the biological systems we study to negate the necessity of testing on humans and animals. Overall, MIBS is dedicated to the improvement of therapeutics, and biomedical devices for the sake of innumerable patients worldwide.

CPB Model Description

Cardiopulmonary bypasses (CPB) frequently result in excessive bleeding, and consequently this surgery contributes to 10-15% of the national blood demand. This is caused by complex mechanisms, and is patient-variable, making for convoluted prediction methods. However, the main causes are believed to be platelet dysfunction, hyperfibrinolysis and coagulopathy. Coagulopathy specifically, is associated with the duration and complexity of the surgery, hemodilution, anti-platelet therapies, shear stress induced by the CPB flow conditions, blood-air and biomaterial interfaces, comorbidities, heparin and protamine doses, and genetics. The prediction of this phenomena is essential as it could potentially be utilized to inform treatment decisions, signal the need for prophylactic and preventative measures, ensure the necessary blood for transfusion is prepared, and overall improve the patient’s care. Currently, platelet function testing (PFT) is the technique used to coordinate surgeries for patients on antiplatelet therapy, and to improve transfusion algorithms since CPB-induced coagulopathy is not observed by other assays. Unfortunately, this test only has a predictive sensitivity of 70%, generating a high rate of false positives, diminishing its clinical value. This is a consequence of the fact that these tests are conducted under resting conditions and the fact that platelets experience changes during surgery which preoperative testing does not account for. Consequently, a prototype was designed to mimic the stresses that blood experiences during CPBs in vitro and in the future will be used on the blood of volunteers. After comparing these results with post-operative CPB results the device will be modified to more accurately predict patient-based outcomes. If this is successful, a point-of-care testing device will be designed.

Investigation of Latanoprost Release from Contact Lens Material

In this study research was conducted to evaluate the ability of contact lenses to uptake and release glaucoma drugs in vitro. This experiment was conducted by allowing different contact lenses to soak in solutions of glaucoma drugs for 24 hours. Afterwards, the lenses were placed on one of three models, a monolayer with human corneal epithelial cells (HCECs), a multilayer with HCECs, and a PET insert without any cells. Over 48 hours, the drug diffusion was calculated periodically for each of the contact lens types, in different mediums. Previous literature has demonstrated that this method has a low potential for drug administration, and that hydrophobic interactions between the drug and the contact lens material is the determining factor for adsorption. However, most of these studies have only been conducted on deionized water, phosphate buffered saline, and artificial tear solutions. Sources also state that the amount of drug released is also significantly greater in vivo than in vitro. In total, the results demonstrated that in cell-based in vitro models, the drug release is significantly higher than models without cells even when using different media in the no-cells model, as well as a dead-cell model. Regardless, only 2-3% of the drug adsorbed by the contact lens was released after 24 hours. Nonetheless, more drug may possibly be released from silicon hydrogels making them potentially useful for an ocular drug delivery system. Overall, this research exemplifies the importance of using cell models for studying drug release in instances where the drug must be metabolized before being diffused within the tissue. In the future, a Tear Replenishment System will be deployed to more accurately simulate the dynamic environment characteristic to the front of the eye.

Untangling the Mysteries of the Tear Fil Neutrophil

Polymorphonuclear neutrophils (PMNs) invade the cornea while the eye is closed. A closed-eye environment is also known to induce hypoxia, tear components, and interactions with corneal epithelial cells, which could be responsible for the difference between tear PMNs and blood-isolated PMNs. This study was conducted to determine if, by exposing blood-isolated neutrophils to this environment that they could mimic the tear-film neutrophils to develop improved in vitro models to more accurately study ocular inflammation. In this experiment, tear PMNs were collected from donors via washing the PMNs off the cornea immediately after waking up. Meanwhile, blood was also collected, and the neutrophils were isolated from these samples. The tear PMNs were immediately stimulated with LPS, PMA, and fMLP and analyzed with flow cytometry. Afterwards, the isolated neutrophils were exposed to FBS and ATS, followed by half of these neutrophils being exposed to hypoxia normoxia and were allowed to interact with human corneal epithelial cells for 6 hours. The first half was immediately tested in the same manner as the tear PMNs, and the second half was tested immediately after the hypoxia and cell exposure. Once the cellular data was observed, it was clear that the experiment did not cause the isolated neutrophils to mimic the tear film neutrophils, however it was observed that the exposure to human corneal epithelial cells, incubation time, and different media do induce significant changes. Regardless of these results, future experiments will be conducted as the development of tear film neutrophil models are essential to study material interactions in the cornea in vitro.

The Effect of Substrate Elastic Modulus on CECs

It is known that chemical signals can induce cellular proliferation, differentiation, and directional migration, as well as mechanical signals such as stress and the properties of the substrate that the cells interact with. These mechanical signals are especially interesting in the study of keratoconus, a corneal condition which involves mechanical changes such as corneal thinning and consequently decreased mechanical stability and elastic modulus. Hence, this study was conducted to determine if these mechanical alterations elicit changes in the cellular environment, specifically changes to the elastic modulus. To do so, human corneal epithelial cells were cultured on substrates with differing elastic moduli, and were subsequently studied regarding their viability, cytoskeletal structure, adhesion molecule expressions, apoptosis, and inflammatory responses. The variant elastic moduli were constructing via using differing concentrations of polyacrylamide. Afterwards, it was determined through analysis that this biomaterial was not toxic by conducting a cell viability test, while the differing elastic moduli affected the cytoskeletal structure. Specifically, the compliant substrate resulted in the crumbling of actin fibers and a disrupted overall structure, while the cells cultured on a stiff substrate expressed stretched and well-organized actin fibers. Through the video above, it was observed that the lack of organization and deteriorated actin fibers directly affected the migratory behavior of the cells in the softer substrate. Meanwhile, the apoptosis assay revealed that substrates with decreased mechanical properties had an increased rate of apoptosis, while the differing substrates did not change the levels of adhesion molecules or the ability of the cellular inflammatory response. Overall, this study determined that substrates with a relatively low stiffness induce apoptosis and disrupted actin fibers and as a result disrupted migration, which prompts further research involving the context of keratoconus.

Infrared Therapy for Healthy and Diabetic Conditions

While corneal epithelial and other epithelial tissues are similar, they are certainly not identical. Unfortunately, corneal epithelial tissue heals significantly slower, leading to seemingly everlasting visual complications. To make things worse, 2% of successful natural wound healing processes lead to corneal abnormalities. While there are technologies currently available, many patients are reluctant to utilize them as they are invasive, expensive, and inconvenient. This is especially regrettable for diabetics as they experience even slower corneal wound healing, and an increased rate of post-surgical complications. Thus, one of our current projects has been to study an alternative method of wound healing therapy, infrared radiation. In the past, studies have demonstrated that certain wavelengths of infrared radiation can stimulate the mitochondria of different tissues, leading to an increase in ATP production, reactive oxygen species, nitric oxides, and calcium ions, which overall lead to an increase in cellular proliferation, and consequently wound healing. Therefore, we are determining whether or not these effects can be observed in the corneal epithelium as well to improve the wound healing rate of diabetic and otherwise healthy patients alike. Through our experiments we have been studying the physical and chemical properties of scraped human corneal epithelial cells that have either been exposed to a standard growth environment, or an environment with increased glucose to reflect diabetic conditions, along with different fluencies and wavelengths of infrared radiation. In total, we hope our results, using a more complex corneal model will be successful in vitro, and eventually in vivo to improve the corneal wound healing process for everyone, including diabetics.

Maud Gorbet

As the Material Interaction with Biological Systems laboratory director, Doctor Gorbet is dedicated to aiding millions of people by solving biocompatibility complications between biomaterials and biomedical devices, as well as therapeutics. Through her research, she has published a series of papers which have benefitted the biomedical community by providing the information and insight necessary to develop novel biomaterials, biomedical devices, and therapeutics, and has provided them with improved in vitro models, which more accurately mimic biological systems to ensure that innovations are successful when implemented in the industry. Meanwhile, as biomedical engineering department director and associate professor at the University of Waterloo, Doctor Gorbet is dedicated to ensuring that the future of biomedical engineering is optimistic, and that her legacy of biocompatibility will be maintained for years to come.