SPEAKERS ABSTRACTS

Industry Key Note Address

Scott Sidwell, PhD
Vice-President of Research and Development at Biomet

Abstract
We will begin with a brief introduction of Biomet including the types of products that are offered as well as the company history. We will present our portfolio of cranioplasty solutions and will discuss the use of poly-ether-ketone-ketone (PEKK) as a novel material for cranioplasty

Academia Key Note Address: "Bottom-Up Engineering of the Extracellular Matrix"

Adam W. Feinberg, PhD.
Department of Materials Science and Engineering
Department of Biomedical Engineering
Carnegie Mellon University, Pittsburg, PA

Abstract
The extracellular matrix (ECM) is a nanofibrillar network of proteins such as collagen, fibronectin and other molecules that physically integrates cells into tissues and acts as an insoluble, mechanosensitive signaling network. Recent work has demonstrated that the ECM in decellularized organs can serve as a scaffold to regrow tissues by providing instructive cues for cells. However, this is a top-down approach requiring an existing organ to be decellularized first. We asked, why not build the ECM from the bottom-up just like cells do during embryogenesis or wound healing? To do this, we have developed a biomimetic, surface-initiated assembly process that recapitulates how cells naturally build the ECM in tissues. This provides a reductionist system where complexity can be engineered back into the matrix system, which we are exploiting as a tissue engineering platform and basic science tool. Using this technology we are (i) studying basic ECM mechanobiology, (ii) developing strategies to build 3-D protein scaffolds and (iii) applying these scaffolds in cardiac and ophthalmic tissue engineering. In preliminary results, fibronectin nanofibers can undergo strains >8-fold, with complete elastic recovery. Similar studies are ongoing to elucidate the biomechanical properties of laminin and collagen type IV nanofibers. We are also using these ECM nanofibers to engineer scaffolds for cardiac tissue engineering that mimic the ECM structure and composition in the embryonic heart, using developmental biology as a design template. Thus, we are putting the ECM back together from the bottom-up and building ever more complex ECM structures from nanofibers, to basement membranes to 3-D matrices.

Lenny Terry, PhD

Licensing Officer Office of Technology Licensing
University of Florida

Abstract
The University of Florida Office of Technology Licensing has earned a reputation as a leader in commercializing discoveries that make the world a better place. This reputation is the result of a collaborative working relationship between faculty generating new discoveries, Office of Technology

Licensing staff, and our commercial partners. UF OTL was established in 1985 to work with inventors to facilitate the transfer of technologies created at UF to the commercial sector for public benefit. We are dedicated to assisting employees who feel they have something new and useful that is potentially able to be patented or copyrighted. The first step is to report a new discovery on our new web-based disclosure form. Upon receipt, we will contact you to schedule an appointment to discuss your new discovery and determine the next steps. OTL is here to ensure your rights are protected.

Session 2: "The Journey of a Biomaterials Scientist"
Iris V. Schumacher, PhD
Customer Solutions Associate Marketing Manager
Kimberly-Clark Corporation

Abstract
Iris V. Schumacher, Ph.D. is a Customer Solutions Associate Marketing Manager for the Kimberly-Clark Corporation. Dr. Schumacher is currently the marketing leader for Kimberly-Clark's largest retailer, Wal-Mart, Inc. within the Kimberly-Clark Professional (KCP) business division. Iris has been with Kimberly-Clark for six years where she has held positions in commercialization, process development, and front-end concept and technology development. Iris has most recently embarked upon the KCP Leadership Development Program (LDP), which makes her one of four candidates to assume this position since the program began in 2009. The KCP LDP is a two year rotational program where candidates obtain cross-functional business experience in six month increments in preparation of assuming a leadership position upon program completion. Through this program, Iris will complete rotational assignments in Sales, Marketing, Product Management, and Strategy.
The purpose of this presentation is intended to broaden the view of potential careers awaiting a biomedical or biomaterials engineer after graduation. An overview of careers at the Kimberly-Clark Corporation will be shared along with details regarding recent innovations in the biomedical/biomaterials space. The presentation will end reflecting on the three most important lessons Dr. Schumacher received at the University of Florida: 1) Authenticity; 2) Ethics; and 3) Accountability.

Session 3: "Bone as a Versatile Biomaterial"
Ron Cobb, PhD
Vice-President of Biologics Nanotherapeutics

Abstract
Bone has been used in a variety of orthopedic applications. Currently, autograft bone is the gold standard for use in most orthopedic and dental applications due to its inherent osteoinductive, osteoconductive and osteogenic potential. One current market substitute to autograft is bone graft substitutes. Bone graft substitutes come in a variety of materials, structures and delivery systems to be used in bone grafting procedures. These materials are useful in augmenting the healing of bony defects caused by traumatic injury, tumor removal, abnormal skeletal development, cyst removal and prosthetic loosening. Bone graft substitutes may also be used as a drug delivery device. Human and bovine bone loaded with antibiotics such as gentamicin release clinically relevant levels of drug for up to 14 days. No adverse effects on new bone growth were observed. Bone can also be loaded with growth factors. The growth factor loaded devices have been shown to be superior to autograft materials in several different animal studies. Additional studies were performed investigating the ability of bone as a scaffold to deliver mesenchymal stem cells. Taken together, bone is a very versatile biomaterial with numerous applications in the orthopedic and dental market.

Session 1: "Magnetic Nanoparticles as Nanoscale Probes and Actuators in Complex Fluids and Biological Systems"

Carlos Rinaldi, PhD
Professor J. Crayton Pruitt Family Department of Biomedical Engineering
Department of Chemical Engineering
University of Florida

Abstract
Magnetic nanoparticles are of interest in a variety of applications which take advantage of their manipulation using externally applied magnetic fields. Depending on the material used, these nanoparticles may possess either a freely rotating magnetic dipole or a dipole pointing in a fixed particle-locked direction. Their response to magnetic fields depends on the nature of the magnetic material, their coating, and the viscous properties of the suspending medium. In this talk I will briefly summarize our recent work on the response of magnetic nanoparticles in suspension and subjected to time-varying magnetic fields through two topics. First, the dynamic response of magnetic nanoparticles with particle-locked dipoles in oscillating magnetic fields can be used to obtain information of the mechanical properties of the surrounding fluid. This is demonstrated through experiments in which properly functionalized nanoparticles are used to determine the liquid-solid transition temperature in a physical gel and to quantitatively determine the viscosity “felt” by nanoparticles suspended in simple and complex fluids. In the latter case deviations are seen between the nanoscale and macroscale viscosities. Second, application of high frequency and moderate to high amplitude magnetic fields to suspensions of magnetic nanoparticles results in conversion of magnetic energy to thermal energy, resulting in a localized increase in temperature. Such an effect can be applied to the treatment of certain diseases such as cancer. I will present part of our work on developing targeted magnetic nanoparticles which are biocompatible and colloidally stable in biological fluids and *in vitro* evaluation of the applicability of this novel form of treatment in destroying cancer cells.

Session 2: " Advances in Nanocomposite Design: Towards Electronic and Biomedical Applications"

Jennifer S. Andrew, PhD
Assistant Professor Department of Materials Science and Engineering
University of Florida

Abstract
In many single-phase materials certain properties are mutually exclusive. Examples of this property dichotomy include strength and toughness, high electric permittivity and high magnetic permeability,
and soft and hard magnetic properties. Nanostructured composite materials have the potential to overcome some of these limitation of single-phase materials. From these new materials a number of novel applications ranging from electronics to biomedical devices can be developed and realized. For example, magnetic and ferrolectric materials can be combined on a single particle or fiber, yielding new nanostructured building blocks for multiferroic composites with enhanced properties. By fabricating composites on a single particle or fiber in an anisotropic manner (e.g. Janus-type) the surface and bulk properties of each phase remain accessible, providing additional degrees of freedom in composite design. For biomedical applications, nanocomposites provide a means to combine therapeutic and diagnostics. By taking advantage of how materials with specific size, shape, and chemistry respond and behave in the body new minimally invasive diagnostic platforms that detect diseases at their earliest stages can be realized.

Session 3: "Engineering Bioactive Materials for Islet Transplantation"

Cherie Stabler, PhD
Associate Professor Biomedical Engineering
Diabetes Research Institute
University of Miami

Abstract
Clinical islet transplantation (CIT), the intraportal infusion of allogeneic pancreatic islets into a diabetic recipient, is a promising treatment for type 1 diabetes; however, the success of clinical islet transplantation is hindered by the location of the implant site, which is prone to mechanical stresses and exposure to high drug and toxin loads, as well as the strong inflammatory and immunological response to the transplant in spite of systemic immunosuppression. To address these challenges, we have focused on three primary strategies: the development of scaffolds to house islets at alternative transplant sites; the fabrication of ultrathin encapsulation protocols for the immuno-camouflage of the transplant; and the production of bioactive biomaterials for the local delivery of oxygen and immunomodulatory drugs and/or cells. Three-dimensional scaffolds serve to create a more favorable islet engraftment site, by ensuring optimal distribution of the transplanted cells, creating a desirable niche for the islets, and promoting vascularization. Ultrathin encapsulation decrease immune recognition via masking cell surfaces, thereby reducing/eliminating the need for systemic immunosuppression. Finally, engineering materials for local oxygen or drug release serves to enhance potency at the transplant site, while minimizing side effects. While these biomaterial approaches serve to enhance the efficacy of islet transplantation for the treatment of Type 1 Diabetes, these platforms have broad applicability to the field of tissue engineering.

STUDENTS ABSTRACTS

Clayton Argenbright
Title: Hierarchical Patterning Using self-assembled block copolymers

Adwoa Baah-Dwomoh
Title: Using Irreversible Electroporation to Introduce Pores in Bacterial Cellulose Scaffolds for Tissue Engineering

Abstract: Tissue engineering holds great promise for treating some of the most devastating diseases of our time. The process involves the seeding and attachment of human cells onto a scaffold. The major challenge thus far is attributed to the inability to create functional 3 dimensional tissue structures in vitro, which is the case for complex organs such as the liver or kidney. The improper exchange of nutrients and gases between the cells of these complex organs and the surrounding environment leads to increased stress on the cells causing them to starve and eventually die. Different mechanisms have been hypothesized will increase cell viability, (1) manufacturing scaffolds that mimic the extracellular matrix and (2) creating pores on the scaffold material to allow cells to migrate through it and proliferate. The work proposed here utilizes biofabrication, in which 3D networks of cellulose will be custom fabricated through precise control of bacterial motion.[1] Bacterial cellulose, a natural polymer, is an ideal scaffolding material for tissue engineering due to its proven biocompatibility, mechanical integrity, hydroexpansivity, and its stability under a wide range of conditions[2]. Our approach to incorporate porosity into the cellulose scaffold will be through the use of irreversible electroporation (IRE). IRE is a process in which the delivery of electrical pulses gives rise to an increase in membrane permeability by altering transmembrane potential which in turn results in cell death through the creation of irrecoverable defects in the membrane [3] [4]. We hypothesize that by using IRE to kill the bacteria in

specific locations, and at particular times during cellulose production, we can introduce conduits in the overall scaffold by preventing cellulose deposition at these sites. Through mathematical modeling and experimental techniques, the electrical effects will be investigated and the parameters for IRE of bacteria will be determined. Some constraints to be considered while developing the IRE protocol include cell shape and size, and whether cellulose production will affect the electric field distribution.

Jordan Ball

Title: Advanced Nanocomposites for Bone Regeneration

Authors: Jordan P. Ball, Josephine B.

Abstract: With the mean age of the population rising, it increasingly important to identify more successful treatment options in regenerative medicine. Interest in utilizing synthetic biomaterials has increased in past decades to circumvent limitations in the availability of autografts. While allografts can also alleviate problems associated with autograft usage, the risk of immunological rejection and pathological concerns are still present. Orthopedic tissue regeneration is a major topic of interest as the annual occurrence of bone grafting procedures performed in the United States is estimated to be near 500,000. One method for the regeneration of bone tissue defects is the introduction of either an osteoinductive scaffold material or a growth factor to achieve a similar result. Here, we present findings from an investigation to characterize a material system for orthopedic tissue engineering. Poly(octane-1,8-diol co citrate) combined with β-tricalcium phosphate (TCP), containing immobilized bone morphogenetic protein-2 (BMP-2), has been designed to accomplish the goal of having an osteoconductive scaffold as well as an osteoinductive growth factor for improved bone tissue growth. Results were obtained through measuring osteogenic gene expression in human mesenchymal stem cells (hMSCs) as they differentiate via real-time quantitative polymerase chain reaction (RT-qPCR). Alkaline phosphatase, runt-related transcription factor 2, and osteocalcin gene expression results showed a 9, 5, and 20-fold increase, respectively, in stem cells cultured on POC/TCP scaffolds loaded with BMP-2 after 6 weeks. Our findings indicate that POC/TCP composites have great potential for use in orthopedic tissue engineering applications.

Ana Carolina Bohorquez

Title: Studying nanoparticle-protein interactions in situ

Authors: Ana C. Bohorquez1, and Carlos Rinaldi*1,2,3 1J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida 2Department of Chemical Engineering, University of Florida 3Department of Chemical Engineering, University of Puerto Rico, Mayagüez

Abstract: A technique to study protein-nanoparticle interactions in situ is proposed. The technique consists of magnetic measurements of the rotational diffusion of thermally blocked cobalt ferrite nanoparticles in protein solutions. To illustrate the technique we studied the effect of degree of carboxylic acid substitution in carboxymethyl dextran coated magnetic nanoparticles on their interaction with model proteins such as albumin (BSA), lysozyme (LYZ), immonuglobulin G (IgG), fibrinogen (FIBR), apo-transferrin (TRANS), and histone (HIS) in a wide range of protein concentrations. Experiments indicated that interactions between negatively charged particles and negatively charged proteins BSA, IgG, FIBR, and TRANS were negligible. On the other hand, positively charged proteins LYZ and HIS seemed to readily absorb on the particle surfaces, as evidence by an increase in size and eventual aggregation of the particles. Onset of this effect seemed to happen at lower concentration of HIS, compared to LYZ. The technique can be easily applied to the other particle surface coatings and to particles in complex protein mixtures such as serum, allowing systematic in situ studies of protein-nanoparticle interactions.

Evelyn Bracho

Title: Delivery of Indoleamine 2,3-Dioxygenase to Dendritic Cells for the Induction of Tolerance

Abstract: Indoleamine 2,3-dioxygenase (IDO), an enzyme that catalyzes the rate limiting step of tryptophan catabolism into N-formyl-kynurenine, has been shown to play critical role for the promotion of tolerance. IDO-related depletion of tryptophan increases susceptibility of T cells to apoptosis while some of the resulting metabolites have a direct cytoxic effect on T cells resulting in reduced immune activation. In addition, IDO-expressing cells preferentially induce proliferation of regulatory T cells that inhibit T cell response and promote tolerance. Therefore, identifying methods to manipulate IDO expression and induce regulatory T-cells for the prevention and reversal of autoimmune diseases will provide crucial information for future therapeutic interventions. Dendritic cells are the most efficient antigen presenting cells in the body and express IDO on their surface. The goal of this project is to harvest dendritic cells and use poly(d lactide-co-glycolide) microparticles to deliver indoleamine 2,3 dioxygenase in order to induce regulatory T-cell proliferation and prevent specifically type 1 diabetes. Several delivery methods will be assessed including surface tether of IDO and encapsulation. The efficiency of these methods will be assessed using a mixed lymphocyte reaction (MLR) in vitro. The proposed study will allow the investigation of IDO micro-particle delivery impact on promoting tolerance and controlling type 1 diabetes and for the optimization of its effects with minimal side effects.

Matthew Carstens

Introduction: The ability to fabricate an ex vivo device capable of accurately mimicking the in vivo microenvironment responsible for signaling which modulates cellular function would possess enormous potential in the study of cell biology. Microarrays can be utilized to delineate the various interactions of molecular signaling that affect cellular responses in vivo as well as embody a device that mimics a particular class of cell's microenvironment. Microarray technology has emerged as a valuable tool in biological sciences, particularly for high-throughput applications. While small molecule microarrays have demonstrated their capacity to screen a variety of drugs on a small cell population, a microarray consisting of discreet islands of cells, thereby mitigating potential cross talk and diffusion concerns, has yet to be shown. An application for such technology would be to screen drug efficacy on rare cell populations. Patient-derived colon cancer stem cells are one such population, having only recently been recognized as a potential cause of colon cancer with several cell markers identified. As such, this cell population has been targeted for future therapeutics. One approach to therapy lies in manipulating signaling pathways, which govern self-renewal. Toward this aim, here we report a method for performing such analyses on HCT116 cells, a well characterized epithelial colon cancer cell line, with future studies directed at colon cancer stem cells isolated from human patients. Development of such a method alongside a clinical collaboration allows for a personalized medicine approach to colon cancer. Methods: Arrays consisting of amine islands with a PEG-based non-fouling background were manufactured as described previously from our lab. Biocompatible ethylene vinyl acetate (EVA) (Sigma) was dissolved in cyclohexanol (Acros, Geel, Belgium). Small, hydrophilic molecules were loaded into water while hydrophobic molecules were loaded in cyclohexanol. Drug-loaded polymer was then printed over the amine islands. HCT116 cells were seeded over the array and allowed to incubate until cell attachment on the EVA islands occurred. The arrays were then gently washed and placed in an incubator for 24 or 72 hrs. Arrays were then stained for Annexin V and BrdU, fixed in paraformaldehyde with Hoechst, and mounted with Fluoro-Gel (Electron Microscope Sciences, Hatfield, PA). The arrays were then imaged using an Axiovert 200M microscope and analyzed. Analysis was performed by quantifying the area of fluorescence and reported as RFI. Results and Conclusions: Cellular arrays can be manufactured with tightly controlled specificity of cell attachment allowing for co-localization of cells with drug releasing polymer while eliminating cross-talk between islands as shown in Figure 1. Proliferation of HCT116 cells was characterized via cell populations on the drug-eluting islands in a dose-

dependent manner as shown in Figures 2 and 5. Apoptosis was quantified via Annexin V [Fig 3]. Proliferation was quantified via BrdU [Fig 4]. Ongoing studies are testing the efficacy of drug release and cellular uptake of a library of small molecules on drug-loaded cellular arrays by quantifying apoptosis and proliferation. Additionally, colon cancer stem cells are being seeded on arrays loaded with multiple signaling pathway inhibitors in a randomized fashion. Proliferation and differentiation will be quantified providing critical information about these rare cell populations and providing a platform for future treatment.

Kelsey Crannell

Title: Polymer-based Nanocomposite for the Early Detection of Lung Cancer

Authors: Kelsey Crannell, Stefan Kelly, and Dr. Jennifer Andrew

Abstract: Lung cancer is the leading cause of cancer deaths worldwide; however, if lung cancer is detected at an early stage, prior to metastasis, it is a treatable, if not curable disease. Current methods for the diagnosis of lung cancer are highly invasive and unreliable. This project proposes a non-invasive, rapid and early detection method for lung cancer. A hydrogel-based nanocomposite, made of polymer with an incorporated peptide, will encapsulate luminescent silicon nanoparticles. In the presence of MMP-9, a protease that is overexpressed by cancerous cells, the peptide will cleave and release the nanoparticles, which can be detected when released from the body. Concentrations of the polymer with DI water are varied to obtain initial degradation profiles without the presence of MMP-9 to ensure the nanoparticles remain encapsulated in the hydrogel. These profiles are correlated with physical properties of the hydrogel, including crosslink density and mesh size. In addition, these properties and degradation profiles are compared to hydrogels with incorporated peptide. Understanding the comparison between the hydrogel's physical properties and degradation rates will allow the fabrication of gels with desired properties.

Joe Decker

TITLE: A Thermodynamic Approach to Engineering Antifouling Surfaces

ABSTRACT: Unintended colonization of biomaterial surfaces remains one of the most significant problems in our world today. The accumulation of biological material on a surface is pervasive in every aspect of our lives. Fouling by bacteria remains a significant factor in the implantation of biomaterials. Nosocomial infection is the single largest contributor to patient time in hospitals [1, 2, 3]. Our severe limitations of potable water have lead to the development of desalination and water treatment plants which are limited by fouling issues [4,5]. In the marine industry, biofouling reduces fuel efficiency, speed, operational readiness for navies and increases the transportation of invasive species [6,7]. is severely limited by biofouling in each of these areas. Yet, after thousands of years research and development, we do not have a fundamental relationship between fouling and surface properties. It is absolutely essential that we develop models that relate the observed attachment behavior of biological organisms with the physics and chemistry of the surfaces to which they attach. Ideally, this model would be insensitive to the systems biology, and would instead focus on the surface aspects that the engineer can control. This presentation will describe a novel, thermodynamics-based method for predicting microbe-biomaterial interactions, and demonstrate the method's effectiveness at predicting attachment for both human pathogens and marine fouling organisms.

Maria Di BonaVentura

Title: Thermal and Mechanical Properties of PET and PC for Potential Food Packaging Applications

Authors: Maria C. Di Bonaventura, Anthony Brennan

Abstract: The purpose of this research project is to define the variables needed to design the proper polymer film for food packaging. The selected polymers suitable for the specific polymer films

requirements in this project include polycarbonate (PC), and polyethylene terephthalate (PET). The first experiments conducted include thermal analysis, and dynamic mechanical analysis. After the polymer film has been tested and proved to meet the IFAS requirements for food packaging, an innovative perforated film will be designed while studying the permeability effects of different environments (water, nitrogen, and oxygen) and increasing linear thermal expansion coefficient by a factor of 2.

Maria Di BonaVentura

Title: Study of an Mg-2Y-1Sc alloy for biodegradable implant applications

Authors: Maria C. Di Bonaventura, Ida S. Berglund, Michele V. Manuel

Abstract: There is an increasing interest in biodegradable Mg alloys for biomedical applications. The different mechanisms controlling the dissolution behavior, such as microstructure and surface characteristics, need to be considered in the design of these materials in order to achieve an optimized degradation behavior. In the current study, a ternary Mg-Sc-Y alloy was designed and is being characterized and investigated. The alloy's degradation behavior and mechanical properties are assessed through hydrogen evolution measurements in Hanks' solution, and Vickers microhardness testing, respectively. The observed behavior is discussed in regard to the microstructure and surface characteristic of the alloy.

Rohan Dhavalikar

Title: Simulation of Magnetic Particle Imaging

Authors: Rohan Dhavalikar1 and Carlos Rinaldi*1,2 1Department of Chemical Engineering, University of Florida 2J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida

Abstract: Magnetic Particle imaging (MPI) is a new tomographic imaging technique which utilizes static and oscillating magnetic fields to map the spatial distribution of super paramagnetic iron oxide (SPIO) nanoparticles used as tracers. This technique overcomes the disadvantage of host tissue background signal encountered in MRI as it directly images the tracer particles and is a safer imaging alternative especially for Chronic Kidney Disease (CKD) patients for whom the iodine contrast agents are toxic. The non-linear magnetization of SPIO nanoparticles is the principle by which Frequency domain and X-space MPI obtain millimeter scale resolution images. The imaging process uses a strong field gradient creating a Field Free Point (FFP) where the magnetic field magnitude is weaker than the saturation field of SPIOs. The change in the magnetization of the SPIO is detected by an induction receiver coil as a change in voltage, which on further signal processing leads to images. Models have been developed to describe this imaging process, however, they make approximations that may not depict the actual behavior, limiting their use in predicting the MPI signal of magnetic nanoparticle tracers. The relaxation effect and net magnetization of particles, which play a significant role in determining the resolution of the acquired image, need to be incorporated in these models. With the help of simulations, we will incorporate the effects of finite relaxation dynamics and non-linear magnetization into models for the MPI contrast signal of magnetic nanoparticle tracers. The theory of quaternions plays a vital role in these simulations and we have been successful in obtaining the magnetization curve and AC susceptibility curve using simulations which serve as a strong foundation for developing our magnetic particle imaging model.

Melanie Dufva

Title: Determination of the Phosphate Binding Affinity of Lanthanum Carbonate for Pharmaceutical Applications

Authors: Melanie J. Dufva, Christopher Batich

Luke Gibson

Title: PolyUrethane Testing for Tough, Durable Antifouling Topographies

Brittany Hicks
Title: Effect of Substrate Stiffness on Collective Cell Migration

Cassie Ilano
Title: Engineering Mucin-Polyelectrolyte Multilayers
Authors: Cassandra Llano, Thomas Crouzier, Katharina Ribbeck, and Michael Rubner
Abstract: Mucus has become a topic of exploration in biomedical research because it has exquisite hydrogel properties that can be utilized as anti-biofilm coatings, immune aid and biological filters within the human body. The aim of this study is to engineer multilayers that maintain mucins' biological functions. Amongst these functions are inhibition of bacterial and mammalian cell binding and inactivation of viruses. To approach this task we combined mucins (building blocks of mucus) with selected polyelectrolytes and investigated the resulting function of the mucin-containing multilayers. In this study, a method of screening polyelectrolyte multilayers was established and different biological test were successfully completed such as biofilm formation.

Stefan Kelly
Title: The title for my poster/abstract is: Polymer Nanocomposites for Early
Diagnosis of Lung Cancer
Abstract: Lung cancer is the most frequent cancer worldwide for men, and second only to breast cancer for women. However, lung cancer is the leading cause of cancer death worldwide. Yet, if cancer is detected at its earliest stages it is a treatable, if not curable disease. In this study enzymatically degradable hydrogels loaded with Si quantum dots will be utilized for lung cancer detection. An enzymatically cleavable peptide linker will be incorporated into the polymer backbone and will break down in the presence of matrix metalloproteinase-9 (MMP-9) enzymes, which are overexpressed in lung cancer. The release of Si quantum dots from the gel will indicate a positive diagnosis. Shallow degradation profiles of the polymer-peptide hydrogels in the presence of a PBS solution indicate a slow breakdown of the hydrogels in the body with the absence of the MMP-9 enzyme, which will prevent the release of quantum dots in the case of a negative diagnosis. Current research shows the peptide has been fully incorporated into the hydrogel, confirmed by FTIR. Hydrogel swelling experiments reveal that crosslink density, mesh size and swelling ratios can be tuned by varying the concentration of peptide linkers in the hydrogel matrix. Degradation profiles of the hydrogel nanocomposite in a MMP-9 concentrated solution will be presented.

Cary Kuliasha
Title: Random Acrylate Oligomer Surface Grafting to Poly(dimethyl siloxane) Elastomer Surfaces for Improved Anti-Biofouling
Authors: Cary Kuliasha, Canan Kizilkaya, and Anthony Brennan

David Lovett
Title: "Modulation of nuclear shape by substrate rigidity"
Authors: David B. Lovett, Nandini Shekhar, Jeffrey A. Nickerson, Kyle J. Roux, and Tanmay P. Lele.
Abstract: The nucleus is mechanically coupled to the three cytoskeletal elements in the cell via linkages maintained by the LINC complex (for Linker of Nucleoskeleton to Cytoskeleton). It has been shown that mechanical forces from the extracellular matrix (ECM) can be transmitted through the cytoskeleton to the nuclear surface. We asked if substrate rigidity can control nuclear shape. We found that the nucleus

in NIH 3T3 fibroblasts undergoes significant changes in shape as the substrate rigidity is varied. On soft substrates (0.4 kPa), the nucleus appears rounded in its vertical cross-section, while on stiff substrates (308 kPa), the nucleus appears more flattened. Over-expression of dominant negative Klarsicht ANC-1 Syne Homology (KASH) domains, which disrupt the LINC complex, caused cell rounding and eliminated the sensitivity of nuclear shape to substrate rigidity; myosin inhibition had similar effects. GFP-KASH4 over-expression altered the rigidity dependence of cell motility and cell spreading. Cells seeded on very thin gels exhibited large spreading area and flattened nuclei, suggesting they sense a composite stiffness of the gel and the underlying glass. Taken together, our results suggest that nuclear shape is modulated by substrate rigidity, and that a mechanically integrated nucleus-cytoskeleton is required for rigidity sensing. These results are significant because they suggest that substrate rigidity can potentially direct nuclear function and hence cell function.

Lorena Maldonado Camargo

Title: Viscosity of Synovial Fluid using Rotational Dynamics Theory of Magnetic Nanoparticles

Authors: Edwin De La Cruz-Montoya, Lorena Maldonado-Camargob, Liliana Polo-Corrales, Kyle D. Allenc and Carlos Rinaldi a, b, c* aDepartment of Chemical Engineering, University of Puerto Rico, Mayagüez. bDepartment of Chemical Engineering, University of Florida. cJ Crayton Pruitt .Family Department of Biomedical Engineering, University of Florida.

Abstract: Synovial fluid (SF) is an essential part of the functioning of joints, allowing bones to freely articulate. SF consists primarily of hyaluronic acid (HA) and blood plasma proteins (albumin and globulin). Prior studies have established a correlation between changes in SF rheology and joint diseases. Most commonly, a decrease in viscosity is observed, which has been related to changes in the molecular weight of the HA component. These observations suggest that routine analysis of the physicochemical properties of synovial fluid could be a valuable tool for diagnosis of joint disease. However, the large volumes of fluid needed for rheological characterization limit this application. Here, we report a novel technique to obtain information on the physicochemical properties of SF through measurement of the rotational diffusivity of magnetic nano- and sub-micron particles. Our measurements demonstrate the technique can distinguish between normal SF and SF treated with an enzyme that digests HA as a mimic of degradation SF in joint diseases. Keywords: Nanotechnology, Biosensor, Synovial fluid, Hyaluronidase, Rotational diffusion

Adam Monsalve

Title: Magneto-mechanical actuation of cell surface receptors using iron oxide particles.

Abstract: In the fields of cell engineering and regenerative medicine, chemical agonists are often utilized to control cell and tissue growth; however mechanical cues can also play a role in cell signaling. These processes span the entire spectrum of cellular pathways including apoptosis, proliferation, differentiation, and migration. On the macroscopic scale, muscular atrophy occurs when use of the muscle is lost or hindered and the muscle cells no longer receive vital mechanical cues. This demonstrates the crucial role that mechanical forces play in the maintenance and development of healthy tissue. Current strategies aiming to exploit or control mechanical forces for cell engineering tend to use elastomeric substrates which apply a mechanical load to the cell upon deformation of the substrate upon which the cells are growing. One of the drawbacks of this method is that the applied forces cannot be targeted to specific cell surface receptors, making the elucidation of mechanically transduced pathways difficult. We have developed novel technology for targeted mechanical actuation of cell surface receptors using magnetic nanoparticles with applied magnetic fields as a “remote control” switch. Using this technique, we can target and activate specific receptors or apply general mechanical

deformation to the cell by targeting the particles to integrin receptors. The nanoparticles are composed of superparmagnetic iron oxides coated with biocompatible polymers and are functionalized with targeting ligands. In this case, the particles were functionalized with the peptide Arginine-Glycine-Aspartic Acid (RGD) in order to target integrin receptors on the membrane of NIH 3T3 cells and prostate myofibroblasts. With particles bound to the membrane, a NdFeB magnetic needle with a diameter of ~200 µm was positioned to within 100 and 200 µm of cells using an electronic micromanipulator. The needle tip generates a strong magnetic field gradient which "pulls" on the particles bound to the receptors. The cells were loaded with a Ca++ reactive dye, which increases its fluorescence when bound to Ca++. Magneto-mechanical activation of the integrin receptors with the magnetic needle was shown to result in calcium influx into the cell, presumably via activation of mechanosensitive Ca++ channels. This method of targeted cellular actuation provides researchers the opportunity to study biochemical pathways at the scale of surface proteins in order to help discover the mechanisms governing mechanotransduction.

Jolin Rodrigues

Title: A perfused flow phantom of a biological tumor for magnetic nanoparticle-mediated hyperthermia studies

Authors: Authors: Jolin P.Rodrigues, Jon Dobson

Abstract : Targeted magnetic fluid hyperthermia is an interesting and promising concept for cancer therapy. When used in conjunction with other cancer therapies like radiotherapy and chemotherapy, it has the potential to achieve localized tumor heating, due to strong coupling of the fields to the particles and the fact that tumor cells are more heat-sensitive than surrounding healthy cells in the tumor environment. Through this technique, elevation of the tumor tissue temperature to above 43°C has the potential to destroy tumor cells while limiting side effects. The technique consists of targeting magnetic nanoparticles to tumor tissue followed by application of an external alternating magnetic field (AMF) that induces heat through relaxation losses in the magnetic nanoparticles. Here, a perfused flow phantom for MNP- mediated hyperthermia on tumor tissue is studied in vitro, using a superporous hydrogel of poly(acrylamide-co-acrylic acid)/polyethyleneimine interpenetrating polymer network(P(AM-co-AA)/PEI IPN)to mimic tumor tissue. This flow phantom system uses a water-jacketed tissue bath system that fits in the chamber of a magneTherm radiofrequency coil system that induces an AMF in the chamber. Iron oxide MNP's are bound to the polymer in varying concentrations to mimic targeted binding to tumor tissue. The AMF generated causes the MNP's to heat up to high temperatures. Water is then passed through the polymer matrix to replicate blood-tissue perfusion. The temperature changes are monitored with the help of a fiber-optic temperature probe. The concentrations of the MNP's are varied and optimum concentration is determined for hyperthermia applications. The IPN used in this reactor comprises of two polymer networks ((p(AM-co-AA) and PEI)which are partially interlaced but not covalently bonded to each other. It provides considerableadvantages over single polymers, in mechanical strength, thermal stability and high hydrophilicity, besides others. This model holds considerable promise to determine the best parameters for the treatment of tumors with hyperthermia.

Michael Springer

Title: Differentiation of Adipose Derived Stem Cells on Nanofibrous Collagen and Elastin Matrices

Abstract: Electrospun collagen and elastin matrices have gained widespread interest in the scientific community as a promising option for vascular tissue engineering. It is well known that adult stem cells

have a role in vascular remodeling in vivo and are a promising cell source for tissue engineering applications. The differentiation of adult stem cells is influenced by the multiple factors such as extracellular matrix proteins, soluble growth factors, and cytoskeletal arrangement. The focus of this project is to investigate a strategy to differentiate adipose derived stem cells (ADSCs) on three dimensional protein scaffolds to create a functional medial layer for tissue engineered small diameter arteries. Gene expression of both ACTA2 and MYH11 was significantly upregulated for ADSCs when supplemented with 1ng/mL TGF-β on TCP (Figure 1). Furthermore, there was a significant increase of α-actin expression of all samples of ADSCs on electrospun fibers regardless of protein composition (Figure 2). The additional supplementation of TGF-β to ADSCs cultured on fibers did not significantly impact ACTA2 expression compared to fibers without TGF-β (data not shown). Conclusions: Our results suggest that a 14 day culture of ADSCs supplemented with 1ng/mL TGF-β is sufficient to induce smooth muscle cell differentiation. The increase in smooth muscle myosin heavy chain expression that was observed indicates that the ADSCs are differentiating into smooth muscle cells as myosin heavy chain is specific to mature smooth muscle cells and is only expressed in the later stages of differentiation1. These results agree with what has been previously found when culturing mesenchymal stem cells with TGF-β2. ADSCs cultured on protein fibers all show significant increases in smooth muscle cell gene expression. Under all conditions (with and without TGF-β), smooth muscle α-actin expression showed significant upregulation. Stimulation with TGF-β did show small increases in α-actin expression when compared to non-supplemented samples; though this difference was not significant. Expression of α-actin was increased with the increasing concentration of elastin in the electrospun scaffolds. This suggests that the contribution of elastin toward the differentiation of ADSCs into SMCs is more significant than that of collagen.

Melanie Suaris

Title: Nucleation and Growth of Epithelial Cell Clusters

Authors: Jolie Breaux, Steven Zehnder, Dr. Thomas E. Angelini

Abstract : Cells move in condensed groups during major steps of development, re-epithelialization during later stages of wound healing, and cancer. However, cell populations are sparse in many biological contexts and processes. In an injury, for example, during the proliferation phase of wound healing, granulation tissue is produced by fibroblasts and is sparsely populated by many cell types. To comprehend these processes, an understanding of the transition between sparse populations and dense populations is necessary. Current understanding comes from confluent sheets or “scratch tests.” Little information is available on the transition between the gas-like free space state to the fluid-like continuum state. This understanding would help engineer tissues and understand cancer and fibroblasts. Here we study the density dependent motion of cells on a surface. We start with a sub-confluent population and observe collective cell motion as the layer transitions from a dispersed distribution to a highly condensed monolayer. We find that this transition is similar to the gas to fluid phase transition process where density rises, velocity drops and slow cells form clusters. We also observe a critical cluster size, a growing correlation length that diverges with increasing cell density, and a migration velocity that appears to diverge negatively with increasing cell density.

David C. Sullivan

Title: Immunogenicity of Decellularized Porcine Liver for Bioengineered Hepatic Tissue

Authors: David C. Sullivan1,2*, Sayed-Hadi Mirmalek-Sani3*, Cynthia Zimmerman3, Thomas D. Shupe3, Bryon E. Petersen2,3 1J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida 2Child Health Research Institute, Department of Pediatrics, College of Medicine, University of Florida 3Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine *Equal contribution

Abstract: Liver disease affects millions of patients each year. The field of regenerative medicine promises alternative therapeutic approaches, including the potential to bioengineer replacement hepatic tissue. One approach combines cells with acellular scaffolds derived from animal tissue. The goal of this study was to scale-up our rodent liver decellularization method to livers of a clinically relevant size. Porcine livers were cannulated via the hepatic artery then perfused with phosphate-buffered saline, followed by successive Triton X-100 and sodium dodecyl sulfate solutions in saline buffer. After several days of rinsing, decellularized liver samples were histologically analyzed. In addition, biopsies of decellularized scaffolds were seeded with hepatic cells or implanted subcutaneously into rodents to investigate scaffold immunogenicity. Histological staining confirmed cellular clearance from pig livers with removal of nuclei and cytoskeletal components as well as widespread preservation of structural extracellular molecules. Scanning electron microscopy confirmed preservation of an intact liver capsule, porous acellular lattice structure with intact vessels and striated basement membrane. Liver scaffolds supported hepatic cell growth over 7 days, and no increased immune response was seen with either allogeneic (rat-into-rat) or xenogeneic (pig-into-rat) transplants over 28 days as compared to sham-operated controls. These studies demonstrate that successful decellularization of the porcine liver could be achieved with protocols developed for rat livers, yielding non-immunogenic scaffolds for future hepatic bioengineering studies.

Richelle Thomas

Abstract: The necessity for scaffolds with pro-regenerative internal architectures and chemically advantageous components is conserved across many facets of tissue engineering. Constructs able to leverage long-range order that is biocompatible and architecturally similar to native tissue may yield significant benefit. Hyaluronic acid is a natural polymer associated with the body's wound healing process and is commonly employed for neural regenerative therapies. Hydrogels of this polymer, however, are traditionally amorphous and therefore only provide chemical regenerative support to the area of interest. We hypothesize that by exploiting the ability to stabilize colloidal-crystal-derived voids within hyaluronic acid gels, the resulting bulk material properties will allow a framework wherein many applications such as nerve regeneration, stem cell expansion and wound healing may be explored. Long range internal templating via crystalline self-assembly is expected to provide an environment where cells cultured within the hydrogel matrix present results closer to in vitro cellular behavior. CryoSEM images confirm hydrogel polymer restricted to the interstitial crystalline space and more ordered surface morphology as compared to amorphous hydrogel. Confocal images show crystalline organization throughout 2mm depth of hydrogel sample and 3D geometry. Cytotoxicity experiments determined that any residual porogen material remaining in the hydrogels have non-significant effect on fibroblast cell viability as compared to the control group. Thus, the method of imparting strategic organization within hydrogel lumen is a promising and novel method to manipulate cell-material interaction.

Laura Villada

Title: Porosity effect on anti-fouling efficiency of HEMA-Siloxane based hydrogels
Authors: Laura Villada, Dr. Angel Ejiasi, Dr. Anthony Brennan

Jessica Weaver

Title: Drug-Releasing Constructs Mediate Localized Inflammation in an Islet Transplant Site
Authors: Jessica D. Weaver1,2, Eric Y Song2-3, Antonello Pileggi1-2;4, Peter Buchwald2-3, and Cherie Stabler1-2;4 1Department of Biomedical Engineering, 2Diabetes Research Institute, 3Department of Molecular and Cellular Pharmacology, and 4DeWitt-Daughtry Department of Surgery, Miller School of Medicine, University of Miami, Miami, FL

Abstract: Clinical islet transplantation has demonstrated promise for the reversal of Type I Diabetes Mellitus; however, inflammation at the transplant site contributes to significant graft loss post transplantation. Administration of systemic anti-inflammatory drugs has improved this outcome, but typically contributes to adverse effects on patient health. Alternatively, the localized, sustained delivery of anti-inflammatory agents at the transplant site has the potential to reduce detrimental inflammation while eliminating potential systemic complications. Previous studies on the incorporation of hydrophobic drugs within hydrophobic materials have demonstrated the potential of this strategy for controlled, long-term release. Critical design parameters in the development of sustained drug delivery platforms include material surface area, volume, geometry and drug loading. In our model system, we evaluate the local delivery of the anti-inflammatory corticosteroid Dexamethasone from a polydimethylsiloxane (PDMS) implantation device in an islet transplant site, and the capacity of this platform to reduce inflammatory cell infiltration within the islet graft. Methods: PDMS-Dexamethasone construct fabrication: PDMS-Dexamethasone was fabricated by mixing PDMS (part A), platinum catalyst (part B)(4:1, GE Silicones), and Dexamethasone (Alexis Biochemicals), and curing at 40^{o}C for at least four hours. Constructs were formed by extruding PDMS rods from 2.8mm diameter tygon tubing. Drug release was measured over 30 days. Il-6 Suppression in Macrophages by PDMS-Dex disks: THP-1 Monocytes (ATCC) were activated by PMA (Sigma) in RPMI (CellGro) for 48hrs, and cultured to macrophage differentiation for 8 days. Two PDMS-Dex disks or PDMS disks alone were added and cells stimulated for 6 hrs with LPS (Sigma). Inflammatory cell suppression by PDMS-Dex rods in a syngeneic mouse transplant model: Blank PDMS or Dex-loaded (1 or 2, 10%) PDMS rods were transplanted with syngeneic islets housed in a PDMS scaffold in the epididymal fat pad (EFP) of diabetic B6 mice. Blood glucose levels were observed to determine time of diabetes reversal. Mice were sacrificed at days 3 and 6 for fluorescence-activated cell sorting (FACS) analysis of inflammatory cell populations present at the transplant site (CD45, CD11b, F4/80, CD86). Mice were also sacrificed at day 90 for histological evaluation. Results: PDMS-Dex rod design parameters (surface area, volume, drug load) were optimized to achieve sustained drug release within a targeted therapeutic range (0.05-0.5μg/day), demonstrating release within this range for a minimum of 30 days. PDMS-Dex constructs (5, 10, 20% load) co-incubated with activated THP-1 macrophages suppressed overall levels of IL-6 release upon stimulation with LPS. FACS assessment of early (acute) inflammation at days 3 and 6 revealed suppression of monocyte and macrophage migration and activation in PDMS-Dex rod groups. Specifically, overall CD45 expression and CD86 activation was lower ($p < 0.005$) in both rod groups on day 3 compared to blank controls, indicating infiltration of fewer leukocytes due to the presence of dexamethasone. Further, a significant ($p < 0.05$) decrease in the percentage of monocytes (CD11b+F4/80-) present, as well as percentage of overall CD11b expression in both the one and two PDMS-Dex rod groups was found at both days 3 and 6. A significant ($p < 0.05$) decrease in macrophage (CD11b+F4/80+) populations, as well as overall F4/80 expression, was observed on day 3 for the 2 PDMS-Dex rod group only. Immunofluorescence staining of sections exhibit reduced presence of infiltrating leukocytes (CD45) in PDMS-Dex rod groups compared with controls. Islet function was evident by stabilization of blood glucose levels, as well as positive insulin staining in engrafted islets. Conclusions: Herein, we demonstrate the fabrication of controlled and sustained drug releasing PDMS-Dex constructs through optimization of key design parameters. These drug-releasing constructs exhibit the capacity to suppress inflammatory cell activation in vitro and in vivo, without demonstrable adverse effects on islet engraftment or function. This model platform provides an effective tool for localized delivery of anti-inflammatory drugs to an islet transplant site, whereby reduced inflammatory cell infiltration may improve islet engraftment in more complex models. Future studies will investigate the effectiveness of this strategy in allogeneic rodent models. Acknowledgements This research is supported by the Juvenile Diabetes Research Foundation and the Diabetes Research Institute Foundation

Steven Zehnder

Title: The cytoskeleton drives intercellular fluid flow

Authors: Steven M. Zehnder, Alison C. Dunn, Juan Manuel Urueña, W. Gregory Sawyer, Thomas E. Angelini

Abstract: Cells in tissues possess the two essential components of a pump: pressure generating machinery and fluid permeable conduits. When a cell contracts its cytoskeleton, it stresses neighboring cells, the surrounding extracellular matrix, and intracellular materials like microtubules. In most tissues, cells are not sealed off from one another but are interconnected by fluid channels, known as connexons, grouped into plaques, called gap junctions. The role of gap junctions in intercellular chemical communication and the cytoskeleton in migration have been studied extensively, however, the role of both structures in pressure driven intercellular flow is unexplored. Here we show, in Madin Darby canine kindey (MDCK) epithelial monolayers, that the cytoskeleton drives multi-cellular pressure fluctuations, forcing fluid from cell-to-cell. We observe that cell volumes spontaneously fluctuate and that volume fluctuations directly correlate with intercellular fluid motion. We measure the hydraulic permeability of cells with a micro-indentation system, and we measure the pressurization of cells forced to take in fluid. The observed permeability and pressurization levels suggest that intercellular fluid transport in large cell assemblies is controlled by a multi-cellular balance of cell-generated stress.

Wenbo Zhang

Title: “Nutrient uptake of Bacillus subtilis induced by extracellular matrix”

Authors: Wenbo Zhang, Thomas Angelini

Abstract: The formation of biofilms is always accompanied by the production of an extracellular matrix. The polymer exopolysaccaride (EPS), which makes up the matrix, has been known to dictate the architecture of the biofilm. EPS has the potential to produce an osmotic pressure due a difference of EPS concentration between the biofilm and the surrounding environment. The presence of such a suction force would help the biofilm grow and proliferate by driving the nutrient from the surrounding environment into the biofilm. This function the extracellular matrix, however, has remained largely unexplored. We investigated the forces produced by the EPS by comparing the propagation rate of a nutrient front in two different strains of Bacillus subtilis. We observed that the wild type strain, which produced EPS, produced a suction force on its growth medium. Under the same conditions, we observed that the EPS knockout strain, which lacked the extracellular matrix, did not produce a suction force. The results of these experiments suggest the extracellular matrix exerts an osmotic pressure on the nutrient source and is a driving force in the up take of nutrients by bacteria biofilm.