Abstracts submitted to the 2014 University of Washington Biomaterials Day poster session

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Abstract Title: Charge transport through methylated DNA strand
Abstract (between the dashed lines):

Cytosine methylation has been found to play a crucial role in various biological processes, including a number of human diseases. The detection of this small modification remains challenging. In this work, we computationally explore the possibility of detecting methylated DNA strands through direct electrical conductance measurements. We study the electronic properties and charge transport through an eight base pair methylated DNA strand and its native counterpart using ab initio calculations and the Landauer-Buttiker method. We first analyze the effect of cytosine methylation on the highest occupied molecular orbital (HOMO) and tight-binding parameters of the DNA strands. We find that while for both strands the charge density at the HOMO levels is on average larger on the guanine bases, the difference is more pronounced in the native strand. The origin of this difference is understood more clearly by studying the tight-binding parameters at the HOMO level of the two strands.

We then model the transmission of electrons through the DNA strand both with and without decoherence. Our results show that in the phase-coherent limit, the transmission of the methylated strand is smaller in the bandgap at energies close to the HOMO, while inside the HOMO band, the transmission is oscillatory and the methylated DNA may have a larger transmission in certain energy windows. The trend in transmission also holds in the presence of the decoherence though there is a crossover in the transmission of the native and methylated strands away from the HOMO level. Our calculations confirm that the methylated DNA strand can be identified by direct conductance measurements.

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Abstract Title: Engineering Peptides towards Infection-Free Dental Implants
Abstract (between the dashed lines):

Medical implants ranging from artificial hips to pacemakers profoundly impact millions of Americans by replacing malfunctioning body parts, restoring normalcy to patients' everyday life. However, microbial infection related issues have been a cause of frequent implant failure. Preventative measures against implant infections in patients are vitally important to patient health as well as the efficiency of the healthcare system nationwide. The Tamerler Lab research focuses on antimicrobial craniofacial implants that are comprised of Ti and Ti-Alloys as well as zirconia. Zirconia based implants are commonly employed on dental applications due to its mechanical strength, fatigue resistance, antimicrobial properties, and aesthetic similarity to teeth, as compared to other ceramics such as alumina, or medical grade titanium. Our group's focus has been on engineering peptides that may reduce zirconia implant failure due to bacterial infection. Our group has been generating
sets of peptides which are identified as strong peptide binders to zirconia powder using fluorescent microscopy. In conjunction with our experiments, antimicrobial peptides (AMPs) were computationally designed, synthesized, and tested against bacteria that are common to general dental implant infections. The AMPs' minimum inhibition concentrations (MICs) were determined to prevent bacterial growth. We are currently coupling both functionalities in the same peptide constructs and testing if reduction or loss in the desired properties will be observed. The MIC values and zirconia-binding affinities of the bi-functional peptides will be determined and compared with those of the individual peptides. Finally, they will be tested on the implant surfaces as self-organized coatings.

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Abstract Title: Role of Microarchitecture in Co-delivery of Drug Combinations from Electrospun Fabrics
Abstract (between the dashed lines):

Combination drug delivery has several advantages compared to single-drug therapy in applications including cancer and HIV-1 therapy and antibiotic treatment. However, there are many challenges associated with co-delivery of multiple drugs, including delivery of physicochemically diverse drugs and independently controlling the temporal release of the drugs. Electrospun fibers are an elegant delivery vehicle for co-delivery as they are able to encapsulate a wide range of drugs and can be and can be independently tuned to realize a wide range of release kinetics. We have developed a topical delivery system using electrospun fibers for multipurpose prevention of HIV-1 acquisition and unintended pregnancy using a combination of levonorgestrel (LNG), a hydrophobic contraceptive, and tenofovir (TFV), a hydrophilic antiretroviral. We aimed to investigate how the microarchitecture of the electrospun medical fabrics affected the fiber properties, in vitro release profiles, crystallinit

y of the drugs, and activity of encapsulated drugs.

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Abstract Title: Modulation of Dendritic Cells by Engineered Biomaterial Porous Scaffolds
Abstract (between the dashed lines):

Background: Dendritic cells (DCs) are a type of unique antigen-presenting cells that can initiate T cell response. Many immune therapy applications have been developed to modulate DCs phenotypes. These applications will often contain biomaterials that can interact with DCs and affect their phenotypes. In this study, we investigated how DCs respond to 3D polymeric structures. It is hypothesized that 3D structures with specific pore sizes provide unique mechanical stresses and microenvironments for cell infiltration and signaling. The goals for this project are: 1) Construct porous constructs with uniform and controllable pore sizes; 2) Use in vitro and in vivo models to study how scaffold materials and pore sizes may affect DCs maturation and infiltration.

Results: A series of polyHEMA and silicone scaffolds were constructed with 3 controlled pore sizes (20, 40, 80µm). JAWsII dendritic cells were cultured with the scaffolds in vitro for 24 hours and a number of cell maturation cytokines, chemokines, and surface markers (TNF-alpha, MIP-1alpha, CD86, etc) were measured. Results showed that silicone scaffolds induced almost 1.5 times higher DCs maturation than polyHEMA scaffolds. Among three pore sizes, 40µm scaffolds induced minimal DCs maturation. These observations were followed by in vivo study with C57BL/6J mice models. Similarly, more immune cells were detected around and within silicone scaffolds than pHEMA scaffolds after 48 hours implantation. When immunized with model antigen ovalbumin, mice with scaffold implantations had higher serum anti-ova IgG production. And 40µm silicone scaffolds induced higher serum anti-ova IgG production than 40µm pHEMA scaffolds.

Conclusions: These experiments suggested that 3D porous scaffolds made with different materials and pore sizes can promote or minimize dendritic cells maturation. In vivo, they also demonstrated similar adjuvant effect. Additionally, scaffolds provide unique environment for immune cell recruitment as well as programing. 3D porous scaffolds can be used as carriers to deliver therapeutic agents to modulate immune response.

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Abstract Title: In vitro Co-Culture of Human Skin Cells on Natural Polymer-Based Scaffold as Skin Graft
Abstract (between the dashed lines):

Tissue engineered skin is a candidate for skin therapies since detrimental wounds require replacement of both the epidermal and dermal layers. For successful replacements, it is important to mimic the skin structure consisting of two layers: a top epidermis layer with a dermis layer beneath, which is made up of keratinocytes and fibroblasts respectively. In the present study, we developed the skin graft by seeding the two types of skin cells, keratinocytes (HeCat) and fibroblasts (hFF), on opposite sides of a porous, biodegradable, and biocompatible 3D natural polymer-based scaffold. The skin graft was investigated by using Alamar Blue Assay, Histology, and SEM. The results showed that (1) the HeCat and hFF proliferated better in co-culture on the scaffold, (2) HeCat forms differentiate into 5 layers, compared with control. This infers that the 3D structure of the scaffold not only acts as a mechanically sufficient substrate for cells to grow and receive nutrients, but also c
reates a good environment for signaling between the two types of skin cells. These findings indicate that the integration of a natural polymer-based scaffold with co-cultured HeCat and hFF in vitro can be used for a living skin graft in vivo.

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Abstract Title: Photoswitchable DNA-modified nanoparticles: controlling DNA hybridization stringency with light
Abstract (between the dashed lines):

We describe stimulus-responsive DNA-functionalized gold nanoparticles that incorporate azobenzene-modified oligonucleotides. Beyond the classic self-assembly and sensing behaviors associated with oligonucleotide-modified nanoparticles, these particles also exhibit reversible photoswitching of their assembly. We show that perfectly complementary and partially mismatched strands exhibit clearly distinguishable photoinduced disaggregation properties, and we demonstrate that photon dose can thus be used in place of temperature or ionic strength to control hybridization stringency with the ability to discriminate single-base mismatches in sensing applications. We further study the influence of DNA complementarity on the photoswitching of gold nanoparticles by measuring the azobenzene photoisomerization quantum yield in different local environments. When inserted at different positions with respect to that of mismatched base, we find that the azobenzene demonstrates differently. We propose that this sequence dependent quantum yield underpins different photoinduced nanoparticle disaggregation rates, and underpins the ability to use photostringency to discriminate perfectly

complementary and partially mismatched sequences using these materials.

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Abstract Title: Peptides as Stealth Biomaterials: Biomimetic, Rational, and Combinatorial Design
Abstract (between the dashed lines):

Stealth properties are relevant to many biomedical applications including drug delivery, surface coatings, and biosensing. Natural materials such as peptides can offer several advantages as biomaterials: they are biocompatible, well-defined, multifunctional, and offer nearly infinite sequence combinations to explore. Recently, we have identified several stealth peptide sequences including glutamic acid/lysine (EK) and asparagine (N) through rational and biomimetic design [1,2]. The versatility of the EK peptide sequence has been demonstrated as a self-assembled monolayer coating on surfaces [2] and on gold nanoparticles [3]. In both these systems one peptide possesses biomolecular recognition, stealth properties, and surface anchoring, achieving multiple functions in one material while avoiding complex bioconjugation chemistries. In addition to rational and biomimetic design, combinatorial techniques have also been developed to identify novel peptide sequences containing low nonspecific binding properties [4]. A combinatorial library was created on a controlled pore glass substrate and screened for protein adsorption using fluorescently tagged fibrinogen. Stealth sequences were identified and peptide sequences were recovered via partial Edman degradation. The development of stealth peptide sequences via rational, biomimetic, and combinatorial techniques can provide access to novel biomaterials that can be used in an array of applications.

References:
(1) White A. D. Chem. Sci. 2012 3, 3488-3494
(2) Nowinski A. K. J. Am. Chem. Soc. 2012, 134, 6000-6005
(3) Nowinski A. K. Langmuir 2014, 30, 1864-1870
(4) Keefe A. J. Biomaterials 2013, 34, 1871-1877

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Abstract Title: Ultra-low Fouling Zwitterionic Biomaterials for Biomedical Applications
Abstract (between the dashed lines):

Poly(carboxybetaine) (PCB) is a zwitterionic material with multifunctional and ultra-low-fouling characteristics. Nonspecific protein adsorption, or fouling, is the first step of many undesirable effects a host can mount against biomaterials, and PCB can resist this fouling from complex biological media [1]. Zwitterionic polymers show improvement over poly(ethylene glycol) (PEG) [2], which has been universally used as a highly protein-resistant, non-fouling material in many applications.

Our group has reported many unique properties and applications of zwitterionic polymers such as PCB. For example, we recently demonstrated for the first time that PCB is able to maintain both the stability and bioactivity of a conjugated enzyme due to its superhydrophilic nature, while PEG conjugation greatly reduces bioactivity due to its amphiphilicity [3]. We have also shown that a PCB hydrogel is able to avoid collagenous capsule formation due to the foreign-body reaction for at least three months in vivo, and promote angiogenesis in the surrounding tissue [4]. PCB hydrogels are additionally capable of time-independent self-healing through a ‘zwitterionic fusion’ process [5]. Nanoparticles coated with PCB exhibit a blood circulation half-life many times longer than those coated with PEG, and do not promote polymer-specific antibody production [6]. Finally, antibody-functionalized PCB can enable highly sensitive biomarker detection with very low background noise, which
has recently been applied to paper-based sensing platforms [7]. Overall, poly(zwitterion)-based materials have great potential in a wide variety of biomedical applications, ranging from drug and gene delivery and diagnostics to the generation of biocompatible implantable medical devices and tissue scaffolds.

References:
1. Jiang S, et al. Advanced Materials 2010, 22:920-932.
2. Jiang S, et al. Biomacromolecules 2008, 9:1357-1361.
3. Keefe AJ, et al. Nature Chemistry 2012, 4:60-64.
4. Zhang L, et al. Nature Biotechnology 2013, 31:553-556.
5. Bai T, et al. Biomaterials 2014, DOI:10.1016/j.biomaterials.2014.01.077
6. Yang W, et al. Nano Today 2014, DOI: 10.1016/j.nantod.2014.02.004
7. Zhu Y, et al. Analytical Chemistry 2014, DOI: 10.1021/ac500467c

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Abstract Title: Fabrication of poly(ethylene glycol): gelatin methacrylate composite nanostructures with tunable stiffness and degradation for vascular tissue engineering
Abstract (between the dashed lines):

Although synthetic polymers are desirable in tissue engineering applications for the reproducibility and tunability of their properties, synthetic small diameter vascular grafts lack the capability to endothelialize in vivo. Thus, synthetically fabricated biodegradable tissue scaffolds that reproduce important aspects of the extracellular environment are required to meet the urgent need for improved vascular grafting materials. In this study, we have successfully fabricated well-defined nanopatterned cell culture substrates made of a biodegradable composite hydrogel consisting of poly(ethylene glycol) dimethacrylate (PEGDMA) and gelatin methacrylate (GelMA) by using UV-assisted capillary force lithography. The elasticity and degradation rate of the composite PEG-GelMA nanostructures were tuned by varying the ratios of PEGDMA and GelMA. Human umbilical vein endothelial cells (HUVECs) cultured on nanopatterned PEG-GelMA substrates adhered more than those cultured on unpatterned PEG-GelMA substrates. Additionally, HUVECs cultured on nanopatterned PEG-GelMA substrates displayed well-aligned, elongated morphologies similar to those of native vascular endothelial cells and demonstrated rapid and directionally persistent migration. The ability to alter both substrate stiffness and degradation rate as well as culture endothelial cells with increased elongation and alignment is a promising next step in recapitulating the properties of native human vascular tissue for tissue engineering applications.

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Abstract Title: Nanotopographically Guided Maturation of Human Pluripotent Stem Cell Derived Cardiomyocytes

Abstract (between the dashed lines):

Cardiac tissue engineering holds an immense amount of promise to deliver groundbreaking discoveries to medical science. With the advent of pluripotent stem cell technologies, human pluripotent stem cell-derived cardiomyocytes (hPSC-CMs) can be utilized to build more realistic and translationally applicable models of the heart. Currently, hPSC-CMs exhibit rather immature structural and functional properties and do not assemble into anything resembling adult human myocardium in vitro. Our previous studies have shown that bio-inspired anisotropically nanofabricated substrata (ANFS) enhance the alignment and functional properties of neonatal rat ventricular myocytes. It is unknown, however, whether the same nanotopographic cues will have a similar positive influence on the maturation of hPSC-CMs. In this study we tested the hypothesis that ANFS will enhance the maturation of hPSC-CMs, resulting in cardiomyocytes more suitable for in vitro cardiac tissue engineering applicatio
ns. We seeded hPSC-CMs on ANFS of variously sized dimensions and compare their maturation with hPSC-CMs cultured on traditional flat substrates. To characterize maturation, the structural and functional phenotypes of hPSC-CMs were analyzed from their morphology, calcium handling properties, and gene expression. We found that, similar to neonatal rat ventricular myocytes, hPSC-CMs exhibit a size-dependent change in their structure and function, with dimensions sizes >200nm having the most profound effect. hPSC-CMs on ANFS with dimensions >200nm had increased sarcomere length, cell size, and alignment compared to hPSC-CMs cultured on traditional flat substrates. As ever more robust protocols are developed to generate hPSC-CMs, methods for enhancing the structural and functional maturity of these cells must also keep pace. ANFS provide a cost-effective tissue culture platform that can enhance the maturation of hESC-CMs in vitro.

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Abstract Title: Nanopatterned muscle cell patches for enhanced myogenesis and dystrophin expression in a mouse model of muscular dystrophy

Abstract (between the dashed lines):

Skeletal muscle is a highly organized tissue in which the extracellular matrix (ECM) is composed of highly-aligned cables of collagen with nanoscale feature sizes, and provides structural and functional support to muscle fibers. As such, the transplantation of disorganized tissues or the direct injection of cells into muscles for regenerative therapy often results in suboptimal functional improvement due to a failure to integrate with native tissue properly. Here, we present a simple method in which biodegradable, biomimetic substrates with precisely controlled nanotopography were fabricated using solvent-assisted capillary force lithography (CFL) and were able to induce the proper development and differentiation of primary mononucleated cells to form mature muscle patches. Cells cultured on these nanopatterned substrates were highly-aligned and elongated, and formed more mature myotubes as evidenced by up-regulated expression of the myogenic regulatory factors Myf5, MyoD and myogenin(MyoG). When transplanted into mdx mice models for Duchenne muscular dystrophy (DMD), the proposed muscle patches led to the formation of a significantly greater number of dystrophin-positive muscle fibers, indicating that dystrophin replacement and myogenesis is achievable in vivo with this approach. These results demonstrate the feasibility of utilizing biomimetic substrates not only as platforms for studying the influences of the ECM on skeletal muscle function and maturation, but also to create transplantable muscle cell patches for the treatment of chronic and acute muscle diseases or injuries.

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Abstract Title: A thermoresponsive nanofabricated substratum for the engineering of three-dimensional tissues with layer-by-layer architectural control
Abstract (between the dashed lines):

Current tissue engineering methods lack the ability to properly recreate scaffold-free, cell dense tissues with physiological structures. Recent studies have shown that the use of nanoscale cues allows for precise control over large area 2D tissue structures without restricting cell growth or cell density. In this study, we developed a simple and versatile platform combining a thermoresponsive nanofabricated substratum (TNFS) incorporating nanotopographical cues and the gel casting method for the fabrication of scaffold-free 3D tissues. Our TNFS allows for the structural control of aligned cell monolayers, which can be spontaneously detached via a change in culture temperature. Utilizing our gel casting method, viable, aligned cell sheets can be transferred without loss of anisotropy or stacked with control over

individual layer orientations. Transferred cell sheets and individual cell layers within multilayered tissues robustly retain structural anisotropy, allowing for th
 e fabrication of scaffold-free, 3D tissues with hierarchal control of overall tissue structure.

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Abstract Title: Characterizing an Inducible Osteoclast System as Cell Therapy for the Treatment of Ectopic Calcification
Abstract (between the dashed lines):

Osteoclasts are bone-resorbing cells that are critical for the normal formation and maintenance of teeth and skeleton. Osteoclast deficiency can contribute to heterotopic ossification (HO), a pathology that is particularly detrimental to the mechanical functions of joints, valves and blood vessels. On the other hand, osteoclast over-activity is a major cause of osteoporosis. A reliable method for controlled generation of osteoclasts would be useful as a potential autologous cell therapy for HO, as well as high-throughput drug screening for anti-osteoporotic drugs. In this report, we describe the development of a cell engineering approach to control monocytic precursor cell differentiation to osteoclasts. Oligomerization of receptor activator of nuclear factor κB (RANK) is known to be essential for osteoclast differentiation from monocyte/macrophage precursors. We engineered a murine monocytic cell line, RAW264.7 to express a fusion protein comprising the intracellular RANK s
 ignaling domain and FK506-derived dimerization domains that bind to a small molecule chemical inducer of dimerization (CID). Virally infected cells expressing this fusion protein were treated with CID and dose-dependent induction of tartrate-resistant acid phosphatase activity, as well as multinucleated osteoclast formation were observed. Furthermore, NF-κB signaling was upregulated in a CID-dependent fashion, demonstrating effective RANK intracellular signaling. Functionally CID-induced osteoclasts had robust mineral resorptive activity in both two-dimensional and three-dimensional in vitro resorption assays. In addition, the CID-induced osteoclasts have the same life span as native RANKL-induced osteoclasts. Most importantly and crucially, the engineered cells differentiated into osteoclasts that were resistant to

the potent osteoclast inhibitor, osteoprotegerin. Taken together, these studies are the first to describe a method for inducible control of monocytic precursor
differentiation to osteoclasts that may be useful for future development of an engineered autologous cell therapy as well as high-throughput drug testing systems to treat diseases of osteoclast over-activity that are independent of osteoprotegerin.

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