



Welcome to Biomaterials Day 2015!

On behalf of the planning board at Vanderbilt University, the University of Memphis, and the University of Kentucky, we would like to extend a warm welcome to all attendees of Biomaterials Day at Vanderbilt University! We have worked hard to organize a conference bringing together regional representatives from academia, industry, and the scientific community. We hope to promote dialogue between these groups in the biomaterials field in order to initiate and support collaborative research and discuss recent developments in the field of biomaterials.

The Biomaterials Day 2015 program exemplifies the quality and diversity of the biomaterials field in the region. Students and faculty from 8 institutions will be presenting their work across a wide range of topics in synthetic biology and biomaterials research. We are honored to have two keynote speakers, Dr. Joshua Leonard from Northwestern University and Dr. Junghae Suh from Rice University. Following today's program, all attendees are invited to attend a closing awards ceremony and reception.

We would like to thank our sponsors from the Society for Biomaterials and Vanderbilt School of Engineering. Finally, we'd like to thank all attendees for your interest and participation in the Biomaterials Day 2015!

Once again, welcome to Vanderbilt University. We hope you enjoy the meeting!

Sincerely,

The 2015 Biomaterials Day Planning Board

Table of Contents

<u>Welcome</u>	<u>1</u>
<u>Table of Contents</u>	<u>2</u>
<u>General Information</u>	<u>3</u>
<u>Keynote Speakers</u>	<u>4-5</u>
<u>Schedule</u>	<u>6</u>
<u>Oral Presentations</u>	<u>7-23</u>
<u>Poster presentations</u>	<u>24-26</u>
<u>Faculty/Industry Panel Session</u>	<u>27</u>
<u>Event Map</u>	<u>28</u>

General Information

Location

Vanderbilt Student Life Center, Ballrooms B and C

310 25th Avenue South, Nashville, TN 37240

Interactive campus map: <http://www.vanderbilt.edu/map/>

Wireless Internet Access

Find “Other Network” in available networks; enter “vumniv” when prompted for the SSID.

Networking Luncheon

Lunch will be provided in the Student Life Center, Ballroom B.

Poster Presentations

Poster presentations will be in Ballroom C and its adjacent hallway in the Student Life Center. Poster boards and push-pins will be provided. Posters can be set up during registration on Friday morning (8–9 AM).

Panel Sessions

A faculty/industry panel discussion on career paths will be held from 4:15–5:15 pm in Ballroom B of the Student Life Center.

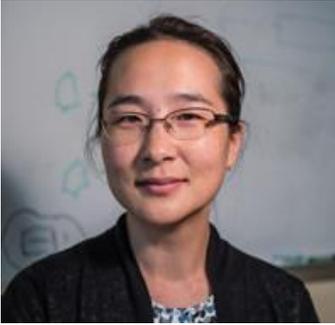
Closing Reception

The closing reception will be held at 5:30 pm in the atrium of Featheringhill Hall (directions provided on event map, pg. 26).

Parking

Parking for Nashville Biomaterials Day is offered on campus at Vanderbilt University 25th Avenue garage, within walking distance of the Student Life Center.

Keynote Speakers



Junghae Suh, Ph.D.

Assistant Professor in Bioengineering

Rice University, Huston, TX

9:00 – 10:00 am Ballroom B

Dr. Suh received her Ph.D. in Biomedical Engineering at Johns Hopkins School of Medicine, where she investigated the paradigms that govern the performance of nanoparticles designed for biomedicine. Before joining the Rice University Department of Bioengineering as an assistant professor in 2007, she completed a two-year postdoctoral fellowship in the Laboratory of Genetics at the Salk Institute for Biological Studies. There she studied how natural viruses interface with cellular machinery to uncover insights into how synthetic nanoparticle systems can be designed to perform as efficiently as natural viruses.

Currently, Dr. Suh's research group works at the interface of virology, biophysics, molecular biology, and protein engineering to investigate and create novel virus-based materials for various biomedical applications. By manipulating the "inputs" and "outputs" of virus nanoparticles (VNP), she endeavors to develop platform technologies that can be used as therapeutics for a broad range of human diseases. She was awarded the NSF CAREER Award and the MDACC Ovarian Cancer SPORE Career Development Program Award for her innovative work on reprogramming viruses as therapeutic platforms. Additionally, Dr. Suh was part of the multi-institutional team of investigators that was awarded an NIH Grand Opportunities grant aimed at investigating the intracellular transport of a variety of engineered nanomaterials used for biomedical applications.



Joshua N. Leonard, PhD

*Assistant Professor of Chemical and
Biological Engineering*

Northwestern University, Evanston, IL

1:30 – 2:30 pm Ballroom C

Dr. Leonard received his Ph.D. in chemical engineering from the University of California, Berkeley in 2006, where he developed novel gene therapies for treating HIV infections. From 2006–2008, Leonard trained in immunology as a postdoctoral fellow at the Experimental Immunology Branch of the National Cancer Institute, where he elucidated a central aspect of the antiviral immune response and developed novel targeted vaccine adjuvants. In 2008, Leonard joined the faculty of Northwestern University. He also co-directs a graduate cluster in Biotechnology, Systems, and Synthetic Biology and mentors Northwestern’s international Genetically Engineered Machines team.

Dr. Leonard’s research group engineers novel biological systems that perform customized, sophisticated functions for applications in biotechnology and medicine. Using the tools of synthetic biology, biomolecular engineering, systems biology, and gene therapy, they develop technologies such as programmable cell-based “devices” that make it possible to probe and modulate immune responses in a patient- and disease-specific fashion. They are applying this approach to develop new treatments for cancer, programmable smart vaccines, and inexpensive diagnostics for applications in global health. By bringing an engineering approach to the analysis, design, and construction of biological systems, the Leonard group is advancing the frontiers of design-based medicine to address unmet medical needs and create safe, effective, and long-lasting treatment options that improve both quantity and quality of life.

Starting Time	Biomaterials Day Schedule	
	Ballroom B	Ballroom C
8:00 AM	Registration/ Poster Setup	
9:00 AM	Keynote Address Junghae Suh	
9:15 AM		
9:30 AM		
9:45 AM		
10:00 AM		
10:15 AM	Thomas Werfel - VU	Dan Balikov - VU
10:30 AM	Madhu Dhar- UT Knoxville	Andrew Harmata - VU
10:45 AM	Sue Lee - VU	Hongsik Cho - UTHSC
11:00 AM	Thomas Dziubla - University of Kentucky	David Wright - Vanderbilt University
11:15 AM		
11:30 AM	Poster Session	
11:45 AM		
12:00 PM		
12:15 PM		
12:30 PM		
12:45 PM		
1:00 PM		
1:15 PM		
1:30 PM	Keynote Address Joshua Leonard	
1:45 PM		
2:00 PM		
2:15 PM		
2:30 PM		
2:45 PM	Russell Pagano - Wright Medical	Murali Yallapu - UTHSC
3:00 PM	Patrick Aldinger - Smith & Nephew	Sichang Lu - VU
3:15 PM	Break	
3:30 PM	Subhash Chauhan - UTHSC	Kameron Kilchrist - VU
3:45 PM	Lucas Hofmeister - VU	Richard Boyer - VU
4:00 PM	Kristin Poole - VU	Prachi Gupta - UK
4:15 PM	Faculty/Industry Panel Discussion: Career Paths	
4:30 PM		
4:45 PM		
5:00 PM		
5:15 PM		
Closing Reception in Featheringhill Atrium		

Oral Presentations

10:15–10:30 am, Ballroom B:

Combinatorial library of ternary polyplexes enables identification of improved siRNA nanocarriers for rapid in vivo translation

Thomas A. Werfel, Martina Miteva, Taylor Kavanaugh, Kellye Kirkbride, Meredith Jackson, Rebecca Cook, Todd Giorgio, Craig Duvall

Many previous non-viral siRNA vector development efforts have yielded reagents effective for in vitro transfection but that have poor in vivo pharmacokinetics and bioactivity. The current work focuses on development of a siRNA nanocarrier optimized to overcome both cell-level barriers (uptake/endosomal escape) and systemic barriers following intravenous delivery (stability for long circulation time and small size for effective tissue penetration). To this end, a combinatorial library of ternary polyplexes was herein investigated to optimize formulations for siRNA delivery. The compositions tested build from our previous finding that balancing cationic and hydrophobic content in binary polyplexes can enhance both particle stability and endosome escape. Through this ternary complex/combinatorial approach, we were able to systematically study important structure–function characteristics such as polyplex surface PEGylation density, size, stability, and endosomolysis. Ternary polyplexes which were optimized to overcome multiple barriers to siRNA delivery achieved highest gene silencing and endosomolysis was identified as a crucial parameter for achieving siRNA silencing in vitro. Lead polyplexes were able to localize to tumors after intravenous administration and achieved target gene silencing of the model gene luciferase in vivo.

10:15–10:30 am, Ballroom C:

Copolymers induce increased stemness and pericyte phenotype in human mesenchymal stem cells

Dan Balikov, Boire TC, Crowder SW, Lee JB, Kirkbride KC, Gupta MK, Murthy S, and Sung HJ

The current state of culturing stem cells for regenerative medicine has inherent limitations in maintaining the potency of autologous and allogenic stem cells for human subjects. For mesenchymal stem cells (hMSCs), a core issue is maintaining a high stemness state as well as addressing the issue of how to make these cells behave as 'younger' cells when the primary donor is of advanced age. In this study, we have created a library of copolymers comprised of hydrophobic/protein-adsorbant PCL and hydrophilic/protein-repellent PEG where increase in stemness properties of hMSCs was observed. Specifically, pluripotency factor expression levels (SOX2 and Nanog) and phenotypic properties (low proliferation rates and decreased reactive oxygen species) exhibited by the hMSC on the copolymers relative to TCPS approached levels normally seen in in vivo stem cell niches. Moreover, hMSCs cultured on the copolymer substrates display pericyte-associated properties including an increased capacity to maintain endothelial cell tubulogenesis. Finally, we have begun interrogating the nanoscale properties of the copolymer films to identify a structure-function relationship that drives the phenotype alteration via surface repellency and nanoscale surface features of the copolymers and potential protein mediators integrin- α 2 and PECAM.

10:30–10:45 am, Ballroom B:

Animal models in cell-based therapies – Importance of cells and biomaterials

Madhu S. Dhar, Ph.D.

Combining stem cells with biomaterial scaffolds provides a promising strategy for engineering tissues and cellular delivery. The prospective clinical use of adult mesenchymal stem cells holds enormous promise for improved treatment of a large number of diseases in humans and companion animals. Although the use of bone-marrow-derived mesenchymal stem cells appears to be a popular therapy; the therapy suffers from the donor-to-donor variation in the quality and quantity of harvested cells. One critical biological factor that researchers and clinicians must take into account is this variability and how it may affect the clinical outcome in regenerative therapy. The focus of research in the Laboratory of Regenerative Medicine at the College of Veterinary Medicine is to understand this variation in adult mesenchymal stem cells, and to test various combinations of biomaterials and cells in animal models of bone and cartilage damage. We have optimized in vitro molecular and cellular assays to isolate, characterize, and differentiate rat, horse and goat adult mesenchymal stem cells; we can generate an ex vivo model of a specific disease, and finally we can design a controlled animal (in vivo) study to test their biological function in regeneration. The goal of this three-step process is to improve clinical outcomes as well as increase our basic knowledge of stem cell function. Currently, we are carrying out experiments to test the efficiency of constructs generated by combining adult mesenchymal stem cells and novel biomaterials. We are investigating their potential in wound healing, treatment of corneal ulcers, bone and cartilage tissue engineering.

10:30–10:45 am, Ballroom C:

45S5 Bioactive Glass/Polyurethane Biocomposites for Repairing Weight-bearing Bone Defects

Andrew J Harmata, S Uppuganti, M Granke, CL Ward, K Zienkiewicz, JS Nyman, JC Wenke, SA Guelcher

Of the nearly 1.6 million bone graft procedures conducted annually to treat bone fractures in the U.S., ~25% of these fracture patients require rehospitalization due to graft failure. Injectable and settable synthetic bone grafts that possess initial quasi-static mechanical strength and dynamic fatigue resistance exceeding that of host bone and maintain properties comparable to bone while remodeling could improve the clinical management of a number of orthopaedic conditions. Ceramic/polymer composites have been investigated as weight-bearing bone grafts, but they are typically weaker than trabecular bone due to poor interfacial bonding. We hypothesized that entrapment of surface-initiated poly(ϵ -caprolactone) (PCL) chains on 45S5 bioactive glass (BG) particles within an in situ-formed polymer network would enhance the mechanical properties of reactive BG/polymer composites. The designed polyurethane (PUR) synthetic graft composite comprising PCL-modified 45S5 bioactive glass particles exhibited quasi-static compression and torsion, as well dynamic compressive fatigue, mechanical properties equal to or greater than those of native human trabecular bone and commercially available calcium phosphate cements. When injected into femoral condyle defects in rats and sheep, the composites supported new bone formation. The initial bone-like strength of BG/polymer composites and their ability to remodel in vivo highlight their potential for development as injectable grafts for repair of weight-bearing bone defects.

10:45–11:00 am, Ballroom B:

In situ cross-linkable gelatin hydrogels for vasculogenic delivery of mesenchymal stem cells

Sue H. Lee, YunKi Lee, Pampee Young, Ki D. Park, Hak-Joon Sung.

Directing robust differentiation of mesenchymal stem cells (MSCs) to endothelial cells for regenerative medicine remains challenging, although not impossible. Gelatin is highly biocompatible, biodegradable, adhesive and non-immuno/antigenic, thus possessing desirable characteristics for tissue engineering. However, its application has been limited due to low melting temperature < 37°C. We recently developed injectable gelatin-based hydrogels by conjugating hydroxyphenyl propionic acid to gelatin (GHPA) that crosslinks *in situ* via a horseradish peroxidase (HRP)-mediated reaction. Interestingly, when encapsulated in GHPA, MSCs began to undergo extensive tubulogenesis and express distinctive endothelial cell markers without biological molecules supplementation in *in vitro* 3D culture and an *in vivo* murine subcutaneous implantation model. The pro-vasculogenic effects of GHPA on MSCs were demonstrated *in vitro* and *in vivo*. In particular, *in vivo* results showed that vasculogenesis was significantly enhanced with crosslinked GHPA gels, suggesting a causative role of the gelatin stability in retention and material-guided endothelial differentiation of delivered MSCs. The results are highly significant as these desirable effects were achieved without addition of any bioactive molecules. Studies to identify and elucidate a mechanism involved in this purely material-driven MSC differentiation to endothelial cells are currently under way. The preliminary results indicate a mechanistic role of integrin expression in the vasculogenic effect and necessitate further investigation into potential interplay of integrins with VEGF signaling, and downstream integrin signaling.

10:45–11:00 am, Ballroom C:

Targeted nanosomes for osteoarthritis in PTOA mouse model

Hongsik Cho, Karen A. Hasty

Osteoarthritis (OA) is one of the most prevalent causes of pain and disability in older individuals for which there are few therapies. OA is a complex process that develops over a long period of time. Post Traumatic Osteoarthritis (PTOA) is a prevalent form of OA commonly developing from joint injury. One complication with PTOA treatment is that it is difficult to detect cartilage damage before symptoms present and irreversible damage has already occurred. If a method of early cartilage degradation was available, then there might be great benefit in prompt treatment with pharmacologic intervention. In order to create cartilage degradation, we use a mouse model of mechanical loading. In this PTOA mouse model we use non-invasive and physiologically relevant loading to induce joint injury. Mechanically loaded models of PTOA have been shown to correlate with histological progression of OA in mice. This provides a valuable tool to researchers in establishing the degree of arthritic progression in a joint but requires the sacrifice of the specimen. A reliable method of quantifying articular cartilage damage without tissue removal could benefit both research and diagnosis of the condition. Antibody targeted to type II collagen(CII) has been shown to bind selectively to damaged tissue. Targeted nanosomes with encapsulated fluorescent tags can be readily detected in anesthetized mice using IVIS imaging. By correlating IVIS measurements of fluorescence intensity to histological damage in mechanically loaded mouse knees, we provide a non-invasive method of diagnosing PTOA in affected joints. Also, the CII targeted nanosomes will be provided as a vehicle for the delivery of drugs to the site of damaged cartilage.

11:00–11:30 am, Ballroom B:



Invited Talk – Thomas Dziubla, Ph.D.

Gill Associate Professor, University of Kentucky
Chemical and Materials Engineering Department

11:00–11:30 am, Ballroom C:



Invited Talk – David Wright, Ph.D.

Stevenson Professor & Department Chairman, Vanderbilt University
Department of Chemistry and Biochemistry

2:30-2:45 pm, Ballroom B:



Invited Talk-Eric Rodenberg, Ph.D.

Biomaterials research scientist at Cook Biotech

2:30-2:45 pm, Ballroom C:

Cell protective, ABC triblock polymer-based thermoresponsive hydrogels with ROS-triggered degradation and drug release

Mukesh K Gupta, JR Martin, TA Werfel , T Shen, JM Page, and CL Duvall

A novel ABC triblock polymer poly[(propylenesulfide)-block-(N,N-dimethylacrylamide)-block-(N-isopropylacrylamide)] (PPS-b-PDMA-b-PNIPAAM) was synthesized to form injectable, biodegradable hydrogels. At ambient temperature, PPS-b-PDMA-b-PNIPAAM assembled into 66 nm micelles comprising a hydrophobic PPS core that can be loaded with therapeutic cargo. Upon heating to 37 °C, micelle solutions (at ≥ 2.5 wt%) sharply transitioned into stable, hydrated gels with concentration-dependent mechanical properties. These hydrogels demonstrated reactive oxygen species (ROS) triggered degradation and drug release based on the oxidation-dependent phase change behavior of PPS from hydrophobic to hydrophilic. The hydrogels were proven to have utility for cell encapsulation in vitro and to provide sustained, local drug release in vivo. These collective data support the broad potential biomedical use of dual thermo- and ROS-responsive PPS-b-PDMA-b-PNIPAAM hydrogels.

2:45–3:00 pm, Ballroom B:



Invited Talk–**Russell Pagano, Ph.D.**

Vice President, Clinical and Regulatory Affairs, Wright Medical
Technology, Inc.

2:45–3:00 pm, Ballroom C:

*Implications of protein corona on physico–chemical and biological
properties of magnetic nanoparticles*

**Muralli M. Yallapu, N Chauhana, SF Othmanb, V Khalilzad-Sharghib, MC
Ebeling, S Khana, M Jaggia, SC Chauhana**

Interaction of serum proteins and nanoparticles leads to a nanoparticleeprotein complex formation that defines the rational strategy for a clinically relevant formulation for drug delivery, hyperthermia, and magnetic resonance imaging (MRI) applications in cancer nanomedicine. Given this perspective, we have examined the pattern of human serum protein corona formation with our recently engineered magnetic nanoparticles (MNPs). The alteration in particle size, zeta potential, hemotoxicity, cellular uptake/cancer cells targeting potential, and MRI properties of the MNPs after formation of human serum (HS) protein corona were studied. Our results indicated no significant change in particle size of our MNPs upon incubation with 0.5e50 wt/v% human serum, while zeta potential of MNPs turned

negative due to human serum adsorption. When incubated with an increased serum and particle concentration, apolipoprotein E was adsorbed on the surface of MNPs apart from serum albumin and transferrin. However, there was no significant primary or secondary structural alterations observed in serum proteins through Fourier transform infrared spectroscopy, X-ray diffraction, and circular dichroism. Hemolysis assay suggests almost no hemolysis at the tested concentrations (up to 1 mg/mL) for MNPs compared to the sodium dodecyl sulfate (positive control). Additionally, improved internalization and uptake of MNPs by C4-2B and Panc-1 cancer cells were observed upon incubation with human serum (HS). After serum protein adsorption to the surface of MNPs, the close vicinity within T1 (~1.33–1.73 s) and T2 (~12.35–13.43 ms) relaxation times suggest our MNPs retained inherent MRI potential even after biomolecular protein adsorption. All these superior clinical parameters potentially enable clinical translation and use of this formulation for next generation nanomedicine for drug delivery, cancer-targeting, imaging and theranostic applications.

3:00–3:15 pm, Ballroom B:



Invited Talk—Patrick Aldinger, BSME & MBA

Research Engineer in Advanced Surgical Devices, Smith & Nephew

3:00–3:15 pm, Ballroom C:*Substrate Modulus and Pore Size of 3D Scaffolds Fabricated by Templated Fused Deposition Modeling Regulate Osteogenic Differentiation*R Guo, **Sichang Lu**, JM Page, AM Merkel, JA Sterling, S Basu, SA Guelcher

The properties of the extracellular matrix, including elastic modulus, porosity, pore size, and curvature, are known to regulate cell fate in a number of physiological processes. Biomimetic 3D systems are needed for investigating interactions between cell populations and the microenvironment. Three dimensional polyurethane (PUR) scaffolds with tunable rigidity (10-900 MPa) and pore size (423-557 μm) were fabricated by a new template-Fused Deposition Modeling (t-FDM) process to investigate the effects of substrate modulus and pore size on osteogenic differentiation of rat bone marrow-derived mesenchymal stem cells (BMSCs). Total protein assay indicated that modulus and pore size had minimal effects on cell proliferation. In contrast, BMSCs were more metabolically active and migrated faster on rigid substrates. Gene expression of osteogenic markers, including Runx2, Collagen-1, Fibronectin, and Osteopontin was up-regulated on rigid scaffolds. Mineralization of BMSCs on D21 was significantly up-regulated on rigid scaffolds with decreasing pore size, suggested by Alizarin Red S staining and SEM. These findings would guide the rational design of cell-responsive scaffolds that recapitulate the bone microenvironment for restoration and repair of bone damaged by trauma or disease.

3:30–3:45 pm, Ballroom B:*Ormeloxifene nanoparticle formulation for pancreatic cancer***Subhash C Chauhana, Ph.D.**

Pancreatic cancer is the fourth most prevalent cancer with about 85% mortality rate; thus, an utmost need exists to discover new therapeutic modalities that would enhance therapy outcomes of this disease with minimal or no side effects. Ormeloxifene (ORM), a synthetic molecule, has exhibited potent anti-cancer effects through inhibition of important oncogenic and proliferation signaling pathways. However, the anti-cancer efficacy of ORM can be further improved by developing its nanoformulation, which will also offer tumor specific targeted delivery. Therefore, we have developed a novel ORM encapsulated poly(lactic-co-glycolic acid) nanoparticle (NP) formulation (PLGA-ORM NP). This formulation was characterized for particle size, chemical composition, and drug loading efficiency, using various physico-chemical methods (TEM, FT-IR, DSC, TGA, and HPLC). Because of its facile composition, this novel formulation is compatible with antibody/aptamer conjugation to achieve tumor specific targeting. The particle size analysis of this PLGA-ORM formulation (~ 100 nm) indicates that this formulation can preferentially reach and accumulate in tumors by Enhanced Permeation and Retention (EPR) effect. Cellular uptake and internalization studies demonstrate that PLGA-ORM NPs escape lysosomal degradation, providing efficient endosomal release to cytosol. PLGA-ORM NPs showed remarkable anti-cancer potential in various pancreatic cancer cells (HPAF-II, BxPC-3, Panc-1, MiaPaca) and BxPC-3 xenograft mice model resulting in an improved animal survival. PLGA-ORM NPs suppressed pancreatic tumor growth via suppression of Akt phosphorylation and expression of MUC1, HER2, PCNA, CK19 and CD31. This study suggests that the PLGA-ORM formulation is highly efficient for the inhibition of pancreatic tumor growth and thus can be valuable for the treatment of pancreatic cancer in the future.

3:30–3:45 pm, Ballroom C:

Cellular uptake and intracellular trafficking of MAPKAP kinase 2 inhibitor peptide delivered via endosomolytic nano–polyplexes

Kameron V. Kilchrist, Brian C. Evans, Kyle M. Hocking, Colleen M. Brophy, Craig L. Duvall

Coronary artery bypass grafting with autologous saphenous vein is the gold standard treatment for multivessel coronary artery disease. However, almost half of saphenous vein grafts fail within 18 months due to intimal hyperplasia (IH) and ultimately graft occlusion. The stress activated p38/MAPK signaling pathway is implicated as a key factor in IH: MAPK Activated Protein Kinase 2 (MK2) is a downstream effector of p38/MAPK and directly modulates inflammation, fibrosis, and cell migration in IH. We have previously demonstrated the ability of a cell penetrant MK2 inhibitory peptide (MK2i) that binds to MK2 and inhibits its ability to phosphorylate its downstream effectors. However, free MK2i suffers from entrapment in the endolysosomal pathway, causing poor cytosolic bioavailability. Electrostatic complexation of MK2i with poly(propylacrylic acid) triggers self-assembly into ~120 nm nanopolyplexes (MK2i–NP) that demonstrate enhanced uptake and retention relative to free peptide, facilitate endosomal escape and cytosolic delivery, and abrogate IH in human saphenous vein *ex vivo*. Understanding the mechanisms of MK2i–NP internalization into vascular smooth muscle cells is necessary to characterize the biological response to this drug delivery platform and enable its clinical translation. We have characterized MK2i peptide and NP uptake in the presence of various uptake inhibitors by flow cytometry and fluorescence microscopy. Our data suggest MK2i–NP binds to cell membrane via hydrophobic interactions and is internalized alongside membrane recycling through mechanisms representative of micropinocytosis. Interestingly, scanning electron microscopy and fluorescence microscopy demonstrate a lack of ultrastructural differences indicative of macropinocytotic upregulation in MK2i–NP treated cells. Future ultrastructural studies by TEM are required to fully confirm the mechanism(s) of MK2i–NP internalization.

3:45-4:00 pm, Ballroom B:*Phage display-mediated nanocarrier targeting to atheroprone vasculature***Lucas Hofmeister, Lee SH, Harrison DG, Sung HJ**

In regions of the circulation where vessels are straight and unbranched, blood flow is laminar and unidirectional. In contrast, at sites of curvature, branch points and regions distal to stenoses blood flow becomes disturbed. Atherosclerosis preferentially develops in these regions of disturbed blood flow. Current therapies for atherosclerosis are systemic, and may not sufficiently target these atheroprone regions. In this study, we sought to leverage the alterations on the luminal surface of endothelial cells caused by this atheroprone flow for nanocarrier targeting. In vivo phage display was used to discover unique peptides that selectively bind to atheroprone regions in the mouse partial carotid artery ligation model. The peptide GSPREYTSYMPH (PREY) was found to bind 4.5-fold more avidly to the region of disturbed flow, and was used to form targeted liposomes. When administered intravenously, PREY-targeted liposomes preferentially accumulated in endothelial cells in the partially occluded carotid artery and other areas of disturbed flow. Proteomic analysis and immunoblotting indicated that Filamin A was preferentially bound by PREY-nanocarriers in vessels with disturbed flow. In additional experiments, PREY-nanocarriers were used therapeutically to deliver the nitric oxide synthase co-factor tetrahydrobiopterin (BH4), which we have previously shown to be deficient in regions of disturbed flow. This intervention increased vascular BH4 and reduced vascular superoxide in the partially ligated artery in wild-type mice, and reduced plaque burden in the partially ligated left carotid artery of fat fed atheroprone mice (ApoE^{-/-}). Targeting atheroprone sites of the circulation with functionalized nanocarriers provides a new approach for prevention of early atherosclerotic lesion formation.

3:45-4:00 pm, Ballroom C:

Affinity-based delivery of neurotrophins in decellularized nerve allografts

Richard B. Boyer, David C. Riley, Alonda C. Pollins, R. Bruce Shack,
Wesley P. Thayer

The gold standard therapy for nerve gap repair is autologous nerve grafting. In addition to significant donor site morbidity, donor nerve harvesting requires increased operative time and post-operative rehabilitation. Transplants of fresh cadaveric nerve allografts are precluded by the need for cytotoxic immunosuppressive drugs, such as tacrolimus and cyclosporine. Recently, acellular nerve allografts have become clinically available with reduced antigenicity and without the requirement for immunosuppression. Similar to other decellularized organs, acellular nerve allografts are processed with specific detergents to remove the membranous and cytoplasmic components of the neuronal and non-neuronal cells present in peripheral nerve while preserving extracellular matrix proteins and microstructure of the basal lamina and endoneurium. Loss of pro-regenerative factors, such as Schwann cells and neurotrophic factors, during nerve decellularization limits the performance of acellular nerve allografts, particularly in proximal nerve injuries where target reinnervation may not occur prior to complete denervation muscle atrophy. In this study, we leveraged the preserved extracellular matrix proteins in acellular nerve allografts for affinity-based delivery of nerve growth factor (NGF) to regenerating axons following nerve injury. Under infinite sink conditions, Sondell detergent-decellularized nerve allografts were found to retain NGF over 21 days in vitro while maintaining bioactivity. In vivo rodent sciatic nerve injuries repaired with NGF-loaded acellular nerve allografts were found to increase mid-graft neurite regeneration. Immunohistochemistry and high-resolution diffusion tensor imaging indicated improved axon regeneration at early and late time points in NGF-loaded acellular nerve allografts. Affinity-based delivery of neurotrophic factors in acellular nerve allografts may provide a new tool for enhanced axon regeneration in proximal nerve gap injuries.

4:00-4:15 pm, Ballroom B:

Preclinical evaluation of ROS-responsive, antioxidant therapies for diabetic peripheral arterial disease

Kristin M Poole, Kavanaugh TE, Nelson CE, Joshi RV, Madonna MC, Lee J, Skala MC, Duvall CL

A microparticle-based delivery system was synthesized from reactive oxygen species (ROS)-responsive poly(propylene sulfide) (PPS) and tested for "on demand" antioxidant therapy. PPS is hydrophobic but undergoes a phase change to become hydrophilic upon oxidation and thus provides a useful platform for ROS-demanded drug release. This platform was first tested for delivery of the promising anti-inflammatory and antioxidant therapeutic molecule curcumin, which is currently limited in use in its free form due to poor pharmacokinetic properties. PPS microspheres efficiently encapsulated curcumin through oil-in-water emulsion and provided sustained, on demand release that was modulated in vitro by hydrogen peroxide concentration. The cytocompatible, curcumin-loaded microspheres preferentially targeted and scavenged intracellular ROS in activated macrophages, reduced in vitro cell death in the presence of cytotoxic levels of ROS, and decreased tissue-level ROS in vivo in the diabetic mouse hind limb ischemia model of peripheral arterial disease. Due to the inherent ROS scavenging behavior of PPS, blank microparticles also showed therapeutic properties that were synergistic with the effects of curcumin in these assays. Functionally, local delivery of curcumin-PPS microspheres accelerated recovery from hind limb ischemia in diabetic mice, as demonstrated using non-invasive, quantitative optical imaging techniques. Ongoing work includes evaluating the functional response to delivery of a superoxide dismutase mimetic, TEMPO-benzoate, from PPS microspheres for more specific targeting of excessive superoxide levels associated with hyperglycemia. Overall, this work demonstrates the potential for PPS microspheres as a generalizable vehicle for ROS-demanded drug release and establishes the utility of this platform for improving local bioavailability of antioxidant molecules for treatment of chronic inflammatory diseases.

4:00–4:15 pm, Ballroom C:

Prolonged protection against mitochondrial oxidative stress using Curcumin conjugated poly (β - amino esters) nanogels.

Prachi Gupta, Dr. Mihail Mitov, Dr. D. Allan Butterfield, Dr. J. Zach Hilt,
Dr. Thomas Dziubla

Mitochondria are considered to be the energy power plants of the cell, but can also initiate and execute cell death, stimulated by oxidative stress (OS). OS induced mitochondrial dysfunction is characterized by a loss in oxygen consumption and reduced ATP production, and it has been linked to a wide variety of diabetic, cardiovascular, and neurodegenerative disorders. Curcumin is considered to be a potential drug to suppress mitochondrial oxidative stress, but rapid metabolism and aqueous insolubility prevent it from being an effective therapeutic. A lot of work has been done to incorporate curcumin into liposomal/micellar nanocarriers for improving the delivery of its active form. However, most formulations have limited net drug loading and exhibit significant burst release of curcumin. To resolve the problem of unhealthy curcumin bolus dosage due to burst effect and deliver the antioxidant at therapeutic levels, self-precipitated curcumin conjugated poly (β -amino ester) (C-PBAE) nanogels in dilute reaction conditions were synthesized utilizing the Michael addition chemistry. Easy control over the nanogel size by varying the reactant concentrations and drug loading of 62% w/w was achieved employing this one-pot synthesis process. Upon hydrolytic degradation of the ester bond, these curcumin PBAE pro-drug nanogels showed uniform release of active curcumin over 30 hours under physiological conditions, enhancing the release rates with control over the initial burst release effect as well as structurally stabilizing the labile drugs for an extended period of time. Real time response analysis of mitochondrion bioenergetics like basal respiration, mitochondrial ATP production using Seahorse Bioscience XF96 analyzer, showed continuous prolonged protection against H₂O₂ mitochondrial oxidative stress confirming the uniform sustained release of active curcumin from pro-drug C-PBAE nanogel.

Poster Presentations

Graduate Students and Postdoctoral Researchers:

1. **Asafo–Adjei, Theodora**– University of Kentucky, *Synthesis and Characterization of a Simvastatin Polyprodrug*
2. **Bailey, Mark** – University of Kentucky, *Curcumin Poly(β -amino ester) as a Targeted Radioprotectant for Lung Cancer Treatment*
3. **Chun, Young Wook** –Vanderbilt University, *Combinatorial Tailored Polymers to Enhance Maturation of Human Cardiomyocytes*
4. **Cook, Andrew** –Fisk University, *Developing a Raman–Based Biosensor to Identify Circulating Tumor Cells Using Functionalized Zinc Oxide Nanowires*
5. **Elkhenany, Hoda** –University of Tennessee, *Graphene based scaffold for stem cell delivery in cortical bone defect: A preliminary study*
6. **Evans, Brian**– Vanderbilt University, *A Novel Platform Technology for Cytosolic Peptide Delivery with Endosomolytic Nanopolyplexes Applied to Vascular Graft Intimal Hyperplasia*
7. **Faley, Shannon**– Vanderbilt University, *Development and Validation of Microfluidic, Free–standing Gelatin Hydrogel Cell Scaffolds as 3D Vascular Model Systems*
8. **Gordon, Andrew**–Vanderbilt University, *Gold Nanorods as Optical Coherence Tomography Contrast Agents*
9. **Jackson, Meredith**–Vanderbilt University, *Facile preparation of a hydroxyl–functionalized RAFT copolymer of DMAEMA and BMA for branched polyglycidol chemistry*
10. **Jayaram, Rohith**–University of Kentucky, *Development of a Local, Sustained Delivery Vehicle for Zoledronic Acid to Treat Tumor–Mediated Bone Resorption*

11. **Kavanaugh, Taylor**–Vanderbilt University, *Targeted Microparticles for Sustained, On–Demand Delivery of Anti–inflammatory Agents for Prevention of Post–traumatic Osteoarthritis*
12. **Kendall, Peggy**–Vanderbilt University, *Antigen Specific Targeting of Autoreactive B Lymphocytes by siRNA Nanoparticles to Prevent T1D*
13. **Martin, Timothy**– University of Memphis, *Changes Of MSC Proliferation On Chitosan Coatings Due To DDA And Protein Addition.*
14. **Miller, Sinead**–Vanderbilt University, *A Nanoparticle–Based Model to Guide Therapeutic Design for Bacterial Sepsis*
15. **Najarzadeh, Amir**–University of Kentucky, *Fabrication and characterization of functionally graded hybrid scaffolds*
16. **Nelson, Christopher**–Duke University, *CRISPR/Cas9-Targeted Gene Correction of Duchenne Muscular Dystrophy in Mice*
17. **Pasek, Raymond**–Vanderbilt University, *Therapeutic Delivery of CTGF with PLGA Microspheres to Induce Beta Cell Proliferation*
18. **Rhodes, Cheyenne**–University of Memphis, *Extended Degradation and Biocompatibility Evaluation of Sodium Acetate Buffered Chitosan Sponges*
19. **Sarett, Samantha**–Vanderbilt University, *Conjugation of trivalent, cyclic RGD to siRNA for improvement in gene silencing*
20. **Schreyack, Gretchen**–University of Memphis, *Development of an Air–Impedance Electrospinning Technique for Cartilage Regeneration*
21. **Song, Min**–University of Kentucky, *Ongoing study to characterize the dependence endothelial sprout formation rates on hydrostatic pressure*
22. **Tarhan, Ozugur**–Purdue University, *Use of Enzyme–Induced WPI Gels for Biomedical Applications*

23. **Unlu, Gokhan**—Vanderbilt University, *Mechanism Regulating Synchronous Collagen Expression and Trafficking during Stem Cell to Chondrocyte Differentiation*
24. **Zayed, Mohammed**—University of Tennessee, *Synovial fluid-derived mesenchymal stem cells as a cell source for cartilage tissue engineering*

Undergraduate Students:

1. **Black, Maggie**—University of Memphis, *Effects of size on release of molecules from phosphatidylcholine coatings*
2. **Chandra, Irene**—Vanderbilt University, *Palmitic Acid–siRNA Conjugates for Increased Stability and siRNA Packaging Efficiency of PEGylated Polyplexes*
3. **Duncan, Elizabeth**—University of Memphis, *Proliferative and Migratory Responses of Mesenchymal Stem Cells Exposed to Adenosine*
4. **Shen, Tianwei**—Vanderbilt University, *Environmentally-responsive Composite Porous Silicon Nanoparticles for Improved Delivery of PNA Therapeutics*
5. **Wells, Carlos**—University of Memphis, *Release of Tobramycin and Vancomycin from dual-loaded local delivery systems*

Faculty/Industry Panel Session:

“Career Paths: Perspectives from Industry and Academia”

4:15–5:15 pm, Ballroom B

Moderator: John Martin, Biomedical Engineering graduate student,
Vanderbilt University

Panelists from Industry:

Russell Pagano – Wright Medical

Patrick Aldinger – Smith & Nephew

Eric Rodenberg – Cook Biotech

Panelists from Academia:

Craig Duvall–Vanderbilt University

Thomas Dziubla–University of Kentucky

Event Map:

