PARTICIPANTS

Sara C. Arenas De Leon, B.S. (California State University Los Angeles)
Mentor: Thomas Hollis, PhD
Biochemistry, Redox Biology & Medicine Center
" The Intracellular Binding Partners of the SAM Domain of SAMHD1"

Pascaline E. Ezouah, B.S. (Virginia Commonwealth University)
Mentor: Kristina Henderson-Lewis, MD, MPH, SM
Epidemiology & Prevention, Division of Public Health Sciences
"Development of a Video Intervention to Reduce Sugar-Sweetened Beverage (SSB) Consumption in Children"

Yismeilin R. Feliz-Mosquea, B.S. (Inter American University of Puerto Rico)
Mentors: David Soto-Pantoja, PhD, Surgery/Hypertension, Comprehensive Cancer Center, Maya Angelou Center for Health Equity
Katherine L. Cook, PhD, Surgery/Hypertension, Comprehensive Cancer Center, Redox Biology & Medicine Center
"Anti-CD47 Immunotherapy Regulates T Cell Metabolism and Hypoxia in the Tumor Microenvironment"

Victoria D. Giammattei, B.A. (University of North Carolina at Chapel Hill)
Mentor: Andrew M. South, MD, MS
Section of Nephrology, Department of Pediatrics
"Preliminary Results of the PHREG Pediatric Hypertension Registry"

Kalan J. Leaks, B.S. (University of Southern California)
Mentor: Aleksander Skardal, PhD
Wake Forest Institute for Regenerative Medicine
"Engineering a Novel Bioink for Functional 3D Cardiac Constructs"

Mildred D. Perez, B.S. (Wake Forest University)
Mentor: Jason Grayson, PhD
Microbiology & Immunology
"Using Unsupervised Machine Learning to Predict Patient Outcome After HSCT"

Pedro L. Sanchez, B.S. (Barry University)
Mentor: Nicole H. Levi-Polyachenko, PhD
Plastic & Reconstructive Surgery
"Evaluation of a Hyperthermic Nanocomposite Against Staphylococcus Aureus Biofilms"

We wish to extend our sincere appreciation to the mentors for their outstanding contributions to the success of the program.

Wake Forest School of Medicine

Wake Forest University
Graduate School of Arts & Sciences

2018 POST-BACCALAUREATE RESEARCH EDUCATION PROGRAM (PREP) SCHOLARS RESEARCH SYMPOSIUM

Keynote Speaker

David McIntosh, PhD

Vice President & Chief Inclusion and Diversity Officer

"Understanding the Climate and Navigating the Path: Perspectives on Diversity"

Tuesday, June 12th, 2018
10:00 am – 1:30 pm
Biotech Place, Atrium and Conference Rooms 155 A & B

WFSM PREP

The WFSM Post-baccalaureate Research Education Program (PREP) Scholars opportunity is funded by the NIGMS and commenced in August of 2001 to provide 1-2 years of research, coursework and GRE preparation to students under-represented in seeking the PhD for careers in biomedical sciences research. Drs. Debra Diz and TanYa Gwathmey are the directors of the program. Trainees accepted into the program select research mentors from a wide range of topic areas for their research-intensive experience. Enrichment activities include journal club and research seminars, technical skills and professional development activities provided throughout the year.

Summary of Our Success

Since 2001, 86 trainees have been supported by the PREP, with 96% of participants in research-intensive or research-related careers. Fifty-seven (68%) trainees have entered PhD programs; 9 (11%) entered Professional Schools. PREP Scholars have ~90% retention rate in post-PREP programs. The majority of the participants are African American (~75%) and Hispanic (~20%). The PREP pipeline contributes ~25% of the minority students in WFUGS Biomedical Sciences PhD programs and the percentage of under-represented minority students in PhD programs rose from less than 5% to 16-20% during the period that PREP has been active. Twenty-four past PREP Scholars already hold academic (assistant or associate professors), government or industry leadership positions.

This educational series is partially supported by Farley-Hudson Foundation, Inc.

Evaluation of a Hyperthermic Nanocomposite against *Staphylococcus aureus* Biofilms

Pedro L. Sanchez, *Nicole H. Levi-Polyachenko,* Anila R. Pullagura, Kenneth Vogel

Biofilms are polysaccharide extracellular matrices containing bacteria attached onto surfaces. Biofilm is a common cause of infection on silicone-based implants. Because silicone does not generate heat, Poly[4,4-bis(2-ethylhexyl)-cyclopenta[2,1-b;3,4-b']dithiophene-2,6-diyl-alt22,1,3-benzoselenadiazole-4,7-diyl] (PCPDTBSe) nanoparticles (BSE N.P.) were incorporated into silicone and stimulated with 800nm laser light. It was hypothesized that the reduction or elimination of biofilms could be achieved by hyperthermic therapy via application of laser treatment and possibly enhancing this hyperthermia effect against the engineered strain of *Staphylococcus aureus*, Xen29, by augmenting antibiotics using heat. Xen29 biofilm were grown on nanocomposites followed by laser treatment to induced mild-hyperthermic temperatures of 48°C. As a result of inducing hyperthermia by laser treatment, biofilms cultivated on nanocomposites decreased microbial biofilms by 90%. These experiments are the first confirmation that nanoparticle doped silicone can induce hyperthermia and decrease bacterial burden on silicone implants.

Using Unsupervised Machine Learning to Predict Patient Outcome After HSCT

Mildred Perez, *Jason Grayson*, Zachariah McIver, Lauren Blaha, Camille David, Arsh Patel, Yolanda Shaw

Hematopoietic stem cell transplantation (HSCT) is a therapy for diseases such as lymphoma, leukemia, immunodeficiency illnesses, and congenital metabolic defects. However, a major problem is the risk of severe graft-versus-host disease (GVHD), which is derived from complications of allogeneic bone marrow or peripheral blood stem cell transplantation. GVHD often leads to significant morbidity and mortality, therefore it is important to understand and further research the factors that control patient outcome. We hypothesize that using high dimensional flow cytometry data of the immune system, and sampling combined with supervised and unsupervised machine learning will allow us to understand mechanisms controlling GVHD. To address this hypothesis, we have isolated peripheral blood mononuclear cells (PBMCs) of 10 healthy control patients and 118 patients of different outcomes that have undergone allogeneic HSCT. Each patient has multiple frozen aliquots of PBMCs before and 30, 45, 60, 90 and 180 days post-transplant. Using an 18-antibody panel to generate a high dimensional profile of the patient immune system by flow cytometry, t-SNE analysis revealed heterogeneity among acute GVHD Scores. Additionally, we found higher CD38 and CD16 correlates with severe acute GVHD. Thus, the results suggest that NK cell populations may play an important biological role. Recent evidence in mice suggests increased expression in CD38 causes metabolic disturbances. Because we have unused aliquots, we can further examine with other panels focused on all subtypes of a given population potentially leading to new biomarkers.

SCHEDULE

10:00–10:05a	Welcome and Introductions
10:05-11:00a	David McIntosh, PhD Vice President & Chief Inclusion and Diversity Officer *"Understanding the Climate and Navigating the Path: Perspectives on Diversity"*
11:00-11:10a	Coffee Break Refreshments Provided
11:10-11:45a	PREP Scholar Oral Presentations
11:45a-12:00p	Presentation of Certificates
12:00-1:30p	Poster Presentations

David McIntosh, PhD,
Vice President & Chief Inclusion and Diversity Officer
Wake Forest School of Medicine

David McIntosh, PhD, Vice President & Chief Inclusion and Diversity Officer, provides strategic leadership for all diversity and inclusion across the Medical Center, including Wake Forest Baptist Health, Wake Forest School of Medicine and Wake Forest Innovations. Along with key divisions and other executive leaders, he provides vision, leadership, coordination, alignment and strategic planning for the design and implementation of an institutional-wide platform to ensure diversity, inclusion, equity and respect for all staff, faculty, students, trainees, patients, families and vendors throughout Wake Forest Baptist. Dave brings diverse leadership experience across many academic institutions. Most recently, he served as Associate Dean for Urban Health Innovation and Chief Diversity Officer for the University of Louisville School of Medicine, where he designed and led the implementation and assessment of a comprehensive diversity strategic plan to foster a culture supporting inclusion at all levels, including faculty, students, staff and clinicians. Previous positions include service at Texas A & M University, Michigan State University and the University of Missouri. Throughout his career, Dave has served on numerous boards and committees and has been a noted speaker and presenter on diversity matters at the American Association of Medical Colleges and health care conferences. His work has focused on creating equitable workplaces for all people by evaluating the climate, measuring the presence of diversity in the environment and assessing the policies, programs, procedures and structures of organizations to ensure equitable outcomes from systems. Dave earned a degree in Economics from Ripon College, a Masters in Educational Leadership and Policy Analysis from the University of Missouri, and a Doctorate in Higher Education Administration from Texas A & M University, where he graduated with distinguished honors.

Engineering a Novel Bioink for Functional 3D Cardiac Constructs

Kalan J Leaks, *Aleksandar Skardal*

Currently, cell therapies are unsuccessful in regenerating the scar tissue formed following myocardial infarction There have been attempts to make bioengineered cardiac patches that restore the infarcted tissue, but most existing approaches are simplistic in design and do not mimic the extracellular matrix (ECM) of human tissues. We hypothesize that a successful patch should consist of a combination of the most prevalent polysaccharides and proteins found in tissue, such as collagen, hyaluronic acid, fibronectin, and laminin. In this study, 3D cardiac constructs made from multiple hydrogel bioink compositions were tested for viability and function. The cardiomyocytes were encapsulated in 3D in multiple hydrogel bioink compositions and were visually assessed for a 14-day period. At the end of the period, cell activity was measured with an ATP assay and viability was determined with LIVE/DEAD imaging. Our studies found that cardiac constructs formed by collagen, HA and fibronectin offered the highest ATP activity compared to other compositions, but failed to exhibit beating. Fibrin constructs failed to keep intact, but exhibited beating during the period. These findings suggest that fibrin cardiac organoids infused with fibronectin offer greater potential for spontaneous beating when grown with media infused with the antifibrinolytic Aprotinin.

Preliminary Results of the PHREG Pediatric Hypertension Registry

Victoria Giammattei, *Andrew M. South*

Adult hypertension (HTN) is the leading cause of death among all cardiovascular risk factors and originates in childhood. Pediatric HTN is common, but robust data on patient characteristics are lacking. PHREG is a Pediatric Hypertension Registry of all HTN patients seen at Brenner Children's Hospital Pediatric Nephrology Hypertension Clinic created to improve our understanding of HTN. Phase 1 is a retrospective cohort of patients diagnosed before their 18th birthday since January 1st, 2013. Medical records were reviewed and relevant data collected, including race, sex, blood pressure (BP), obesity status (BMI ≥85% for age/sex), and target organ damage (proteinuria or left ventricular hypertrophy). We used frequencies and means to summarize the data and *t*-test for between-group comparisons. 32 patient records were analyzed. 63% were male, 41% were black, and 16% were Hispanic. Black subjects tended to have higher baseline SBP compared to non-blacks (136.5 vs. 127.1 mmHg, p=0.15), while Hispanics tended to have lower baseline SBP compared to non-Hispanics (119.8 vs. 132.9 mmHg, p=0.14). At baseline, 25% had Stage 1 HTN and 19% had Stage 2. Baseline target organ damage was detected in 42%. This data indicates HTN varies by race. In addition, HTN is often severe at baseline with target organ damage in the kidneys and heart. Further analysis will enable us to fully characterize these relationships.

ABSTRACTS

The intracellular binding partners of the SAM domain of SAMHD1

Sara Arenas, Ryan Davis, LeAnn Rogers, *Thomas Hollis*

The sterile alpha motif histidine aspartate domain-1 (SAMHD1) protein is a viral restriction factor in non-dividing hematopoietic cells and resting T cells. It accomplishes this by hydrolyzing deoxynucleotide triphosphosphate (dNTP) compounds and preventing viral DNA replication. Mutations in SAMHD1 are linked to diseases like Lupus systemic erythematosus, Aicardi Goutieres syndrome, and cancer. Despite multiple research studies conducted on the SAMHD1 protein, it is not known whether intracellular proteins or DNA interact with the SAM domain of SAMHD1. To address this question, we purified the human SAM domain and conducted pull down and cross-linking procedures with whole cell lysate to determine whether soluble proteins and single stranded DNA interacted with the SAM domain. The results from this study provide further insight into the interactions that occur in vivo with the SAM domain of SAMHD1. They also provide a platform for developing novel treatments for autoimmune diseases like Aicardi Goutieres syndrome, Lupus systemic erythematosus, and cancer as well as developing mechanisms to restrict infection with Human Immunodeficiency virus in dividing hematopoietic cells.

Development of a Video Intervention to Reduce Sugar-Sweetened Beverage (SSB) Consumption in Children

Pascaline Ezouah, Fang-Chi Hsu, Beatriz Ospino-Sanchez, Elsie M. Taveras, Joseph Skelton , Jason P. Block, *Kristina H. Lewis*

SSBs are linked to child obesity. Electronic health records (EHRs) offer a novel platform by which to address this behavior. Since March 2017, we have used the EHR to screen for child SSB consumption and enter an educational paragraph about SSBs in the after-visit summary (AVS) document. Parents reported low viewing rates of the AVS, so we sought to create a more effective way to educate families about SSBs. To create an educational video for parents, we conducted three 90-minute focus groups with 11 caregivers of children 3-10y. We explored preferred methods of demonstrating: sugar content/health consequences of SSBs, and strategies to promote water intake. Participants watched and reacted to 3 example video styles: an informational/didactic video (purely factual), a narrative/story-telling video (actors demonstrating information in an entertaining fashion), and a reality television video (with real families portraying health behavior change). Participants were interested in messages that: highlighted health consequences of SSB consumption, compared sugar in SSBs to candy, and provided fun strategies to gradually reduce SSB intake/increase water intake. There was a strong interest in a relatable, reality TV-style video. Educational videos to address SSB consumption should be relatable, with a style not typical of most healthcare-produced videos.

Anti-CD47 immunotherapy regulates T cell metabolism and hypoxia in the tumor microenvironment

Yismelin R. Feliz-Mosquea, Elizabeth Stirling, *Katherine L. Cook*, Adam Wilson, Manish Bharadwaj, Anthony J. Molina, Liliya Yamaleyeva, Pierre L. Triozzi, *David R. Soto-Pantoja*

Dysfunction of infiltrating CD8+ effector T cells can be induced by hypoxia and aberrant tumor metabolite uptake in the microenvironment causing an exhausted T cell phenotype that limits anti-tumor immunosurveillance. Hence-therapeutic strategies aimed at improving T cell bioenergetics have the potential to reinvigorate T cell responses to reduce tumor burden. CD47 is a widely expressed receptor that controls phagocytic activity by engaging its counter receptor, SIRPα, in macrophages. Our prior work shows that targeting CD47 on CD8+ T cells enhanced cytotoxicity against cancer cells. Our new data shows that targeting CD47 reduced the growth of B16 melanoma tumors by approximately 50%. Further examination of tumors by live photoacoustic imaging showed that tumors of animals treated with anti-CD47 had reduction in oxygen tension when compared to control. Cell respirometry measurements showed increased levels of mitochondrial metabolism and glycolytic flux in CD47 null T cells when compared to WT. Moreover, these cells showed increased mitochondrial density and increased levels of the mitochondrial biogenesis regulator, PGC1-a. Treatment with CD47 antibody enhanced Pmel-1 CD8+ T cell effector function by reducing B16 melanoma target cell viability by over 60%. Anti-CD47 treatment of these T cells also resulted in upregulation of cell bioenergetics, suggesting that targeting CD47 may impact T cell metabolism to enhance cytotoxic activity against cancer cells. Our studies show a new role of CD47 immunotherapy regulating immuno-metabolism of T cells to enhance effector function which may lead to improvement of clinical outcomes in Melanoma patients.