The Center for Clinical and Translational Science

Annual Spring Meeting

&

Team Science Event

Thursday, April 19, 2018
Lebanese Taverna,
2642 Connecticut Ave. NW

CCTS

Ines Alamo
Tulane University School of Medicine- LA CaTS, Faculty/Scientist
ialamo@tulane.edu

Carla Ammons
UAB, Pre-Doc Trainee
cjammons@uab.edu
Poster Session A**:** A325

Neural Correlates of Face Processing in Autism Spectrum Disorder: A Quantitative Meta-analysis of Current Literature & Future Directions: Autism Spectrum Disorder (ASD) affects 1 in 68 people and includes restricted, repetitive behavior and social communication deficits. Aspects of face processing (i.e. identity, emotion perception) are impaired in some with ASD. Neuroimaging studies have shown aberrant patterns of brain activation and connectivity of face processing regions. However, small sample sizes and inconsistent results have hindered clinical utility of these findings. Object is to establish consistent patterns of brain responses to faces in ASD and provide directions for future research. Neuroimaging studies were identified through a multi-database search according to PRISMA guidelines. 23 studies were retained for a sample size of 383 healthy controls (HC) and 345 ASD. Peak coordinates were extracted for activation likelihood estimation (ALE) in *GingerALE v2.3.6*. Follow-up ALE analyses investigated directed vs undirected gaze, static vs dynamic, emotional vs neutral, and familiar vs unfamiliar faces.

Andria Cimino
UAB, Administrative Staff
ciminoa@uab.edu

Josh Clark
Mississippi Center for Clinical and Translational Research, Administrative Staff
jtclark2@umc.edu

Jennifer Croker
UAB, Administrative Staff
jcroker@uab.edu

Amanda Dumas
Louisiana State University Health Sciences Center, Faculty/Scientist
sdumas@lsuhsc.edu
Poster Session B**:** B150

Mind the Gaps: The Contraceptive Experiences of Parenting Adolescents: Despite significant declines over the past 25 years, the US continues to outpace other industrialized nations in teen pregnancy and birth rates. The US experiences 57 pregnancies per 1000 15-19 year old girls, compared to an average of 28 for all other countries with complete data.[1] Additionally, 17% of births to 15-19 year olds were to mothers who already had one or more children, indicating a rapid repeat pregnancy rate in this population and compounding the well-known health and social risks associated with teen parenting.[2-7] Nationally, significant geographic and racial disparities persist. Overall declines have been slower to impact minority youth and the southern US, thus the rates of teen pregnancy and birth remain significantly elevated in Black teens in Louisiana. Louisiana spent an estimated $152 million on teen childbearing in 2010, however is lacking clear data on pregnancy risks and outcomes.[8] The national Pregnancy Risk Assessment Monitoring System does not contain data for Louisiana prior to 2004, and Louisiana opts out of the reproductive health questions posed in the Center for Disease Control and Prevention's Youth Risk Behavior Survey. Due to this lack of coherent data we have a limited understanding of the risk factors and barriers that may contribute to Louisiana's high teen birth rate. For example, nationally, 86% of the decline in teen birth rates is attributable to increased contraceptive use, and the

majority of teens report some form of contraceptive use at first intercourse.[9,10] However, contraceptive type and prescribing patterns have not been described for teens in this region and it is unknown if neighborhood services and pharmacy availability support or hinder contraceptive options for Louisiana youth. It is difficult to direct policy and healthcare priorities to fill indicated gaps if those gaps cannot be described, as is the current landscape in the state. The long-term goal of this research is to prevent repeat adolescent pregnancies and reduce disparities in adolescent reproductive healthcare. Through this proposal, we will describe the contraceptive use, access barriers, and geographic landscape that influences pregnancy risk among New Orleans teens. This data will inform the larger community around interventions and supports for parenting and at-risk teens.

Jeffrey Engler
NRMN
engler@uab.edu
Friday, April 20, 1:00 pm
Novel Approaches to Successful Grant Writing
This session will introduce a novel way for teaching and learning the skill of writing NIH-style research proposals. It will draw on a method developed and used over the past decade, focusing on learning and writing to rhetorical patterns. It will also demonstrate in real time the use of oral feedback processes with mentors and peers to replicate how reviewers read and evaluate proposals. Attention will also be given to key elements of transitioning from K to R funding.

Vivian Fonseca
Tulane University School of Medicine- LA CaTS, Faculty/Scientist
vfonseca@tulane.edu

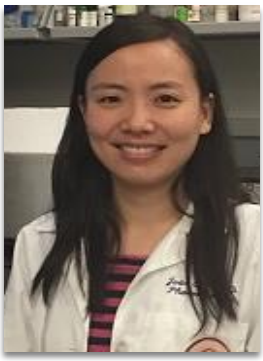
Naveed Farrukh
UAB, Pre-Doc Trainee
nfarrukh@uab.edu

Poster Session A**:** Thursday, April 19, 6:30 pm -8:00 pm and Friday, April 20, 7:00 - 7:45 am
Chronic Pain in Older Survivors of Hematopoietic Cell Transplantation (HCT) – a report from BMTSS-2 : We sought to understand the prevalence of moderate-to-severe pain and use of prescription pain medication (including opioids) among long-term HCT survivors when compared with a frequency-matched sibling cohort. The study population was drawn from BMTSS-2, a retrospective cohort of patients who underwent HCT at City of Hope, University of Minnesota or University of Alabama at Birmingham between 1974 and 2014 at age ≥60y and survived at least 2y after HCT. HCT survivors and siblings completed a comprehensive survey detailing demographics, health conditions, presence of moderate-to-severe pain and use of prescription pain medications, including opioids. Survey participation rate among HCT survivors was 59% and 60% for siblings. Median age at study participation was 71y (63-82) for the 438 HCT recipients and 69y (65-86) for the 210 siblings. Median time from HCT was 5y (2-13). Compared to their siblings, the HCT recipients were 1.6 times more likely to report pain (95%CI, 1.4-2.3; p=0.006); 2.8 times more likely to report prescription pain medication use (95%CI, 1.5-5.0; p<0.0001); and 3.9 times more likely to report opioid pain medication use (95%CI, 1.4-11.3; p<0.0001). Over 67% of the HCT recipients followed >5y reported moderate-to-severe pain. Use of prescription pain medications among HCT recipients remained elevated at 19.5% >10y. Targeted specialized pain management needs to be directed to the vulnerable sub-populations of HCT survivors to improve quality of life.

Abby Gamble
University of Mississippi Medical Center
agamble2@umc.edu

Exploring Exercise Behavior in Pregnant and Postpartum Adolescents in Mississippi: The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) is a long-standing federal program that is ideally suited to stem the tide of early pediatric obesity in low-income populations through the provision of ancillary healthy foods and nutritional education and counseling. Prevention of pediatric obesity in high-risk populations using behavioral interventions that target parents and parent behavior through preventive health services like WIC have potential long-term implications for individual, familial, and population obesity across the lifespan. A robust body of scientific literature supports an energy balance approach to the prevention of obesity; however, an extant gap in obesity prevention research excludes low-income pregnant and postpartum adolescents, and to date WIC intervention studies have predominately focused on improving dietary behaviors with a minimal focus on exercise education and counseling. *Thus, the goal of this two-year pilot study is to identify modifiable psychosocial, cultural, and environmental factors related to exercise behavior in pregnant and postpartum adolescent WIC participants in Mississippi.*

Juan Gao
LSUHSC School of Medicine- LA CaTS, Faculty/Scientist
jgao1@lsuhsc.edu



Saturday, April 21, Roosevelt 3

Radiofrequency Renal Denervation Attenuates Kidney Fibrosis in Spontaneously Hypertensive Rats: Hypertension is a leading cause of end stage renal disease and elevated blood pressure serves as an independent risk factor contributing to further decline of glomerular filtration rate.[1, 2] Renal fibrosis, characterized by glomerulosclerosis and tubulointerstitial fibrosis, is a common outcome of a wide variety of renal diseases such as chronic kidney disease (CKD).[3] Unfortunately, there is not yet an effective therapeutic approach to prevent renal fibrosis. A major mechanism recognized to contribute to the development of renal fibrosis is chronic renal inflammation.[4] Further, heightened renal sympathetic nerve activity contributes to renal inflammation in hypertension.[5] Related to these observations, spontaneously hypertensive rats (SHR) have increased sympathetic nerve activity, and develop chronic inflammation and renal fibrosis as their hypertension progresses.[6] We have observed significant renal fibrosis in both glomerular and tubulointerstitium in 25 weeks old hypertensive SHR. Also, we have shown that radio-frequency ablation of the renal arteries (RF-ABL) decreases sympathetic nerve activity and renal inflammation.[7] However, whether RF-ABL can slow or halt the progression of renal fibrosis remains unknown. Recent reports have suggested that bone marrow-derived fibroblast (BMF) precursors migrate into the kidneys in response to renal injury. BMF then proliferate and differentiate into myofibroblasts, which drive extracellular matrix production, collagen deposition and lead to consequent fibrosis.[8, 9] Infiltration of BMF is activated by several chemokines. Interestingly, our findings show that the expression of chemokine (C-C motif) ligand 5 (CCL5) is decreased by RF-ABL in SHR, thus supporting a role of increased sympathetic activity in this pro-fibrotic pathway.

Elena Gibson
UAB, Pre-Doc Trainee
egibson1@uab.edu

Poster Session A**:** A140

Perceived Susceptibility to Cervical Cancer among African American Women in the Mississippi Delta: Does Adherence to Screening Matter?

Although preventative measures have greatly reduced the national burden of cervical cancer, racial/ethnic and geographic disparities remain, including the disproportionate incidence and mortality among African American women in the Mississippi Delta. Along with structural barriers, health perceptions and cultural beliefs influence participation in cervical screening. This study examined perceived susceptibility to cervical cancer among African-American women in the Delta across three groups:

(1) women attending screening appointments (screened) (2) women attending colposcopy clinic (colposcopy), and (3) women without screening in ≥3 years (un/under-screened).**Methods:** Data were collected during a study assessing the feasibility/acceptability of self-collected sampling for human papillomavirus (HPV) testing as a cervical screening modality. A questionnaire assessed demographics, health care access, and cervical cancer knowledge and beliefs (including perceived susceptibility). We asked, "Do you think you are at risk for cervical cancer", and responses included "yes, "no", and "I don't know". Multinomial logistic regression models compared variables associated with answers among each group. **Findings:** Out of 524 participants, one-half did not know if they were at risk of cervical cancer (50%) or HPV exposure (53%). Between the un/under-screened (n=160), screened (n=198) and colposcopy (n=166) groups, age (p<.001), education (p=.02), and perceived risk of HPV exposure (p<.01) differed. Older age and younger age at first intercourse (un/under-screened), family history and screening recommendations (screened), and family history and perceived risk of HPV exposure (colposcopy) were associated with perceived risk for cervical cancer. **Conclusions:** Differences in perceived susceptibility to cervical cancer exist between African-American women in the Delta. Understanding these variations can help in developing strategies to promote screening.

Gregg Gilbert
UAB, Faculty/Scientist
ghg@uab.edu

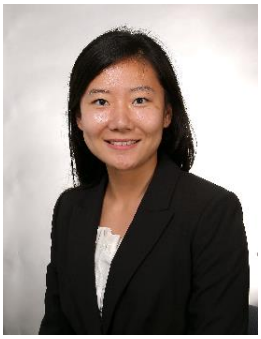
Anne Gilmore
Pennington Biomedical Research Center- LA CaTS, Faculty/Scientist
anne.gilmore@pbrc.edu
Poster Session B: B198
Attitudes toward physical activity and nutrition intervention during cancer treatment: Including those who are currently receiving treatment, there are more than 2.8 million women who have a history of breast cancer in the United States. The likelihood a woman will die from her breast cancer diagnosis has been steadily decreasing since 1993 which allows for cardiovascular disease to be the leading cause of death among cancer survivors. Thus, the metabolic and behavioral alterations that may occur during adjuvant therapy such as weight gain, decrease in diet quality, and decreased physical activity can no longer be ignored, nor continued to simply be viewed as a secondary consequence of the intense pharmaceutical intervention. In addition, there is growing evidence that physical activity and proper nutrition during neoplastic treatment may improve quality of life, increase treatment tolerance and response, attenuate weight gain, and decrease risk of cancer reoccurrence and development of comorbid conditions. However, there are mixed attitudes and perceived barriers to participating in a lifestyle intervention during treatment from patients and clinicians. This study aims to further investigate these barriers and attitudes toward physical activity and nutrition intervention during and after neoplastic treatment in women with breast cancer. With a greater understanding of the desires, attitudes, and potential barriers to participation, lifestyle interventions may be better tailored to the specific needs of this population. In this observational study, 25 women will be followed through their adjuvant therapy for stage I-III breast cancer. The women will be asked to provide their opinions and desires for lifestyle intervention at different times throughout and after treatment. In addition to qualitative data, basic clinical data will be collected (anthropometrics, vital signs, dietary intake, and physical activity). The primary goal of this pilot study is to investigate the anthropometric and behavioral changes that occur in patients undergoing adjuvant therapy for breast cancer.

Paula Gregory
LSUHSC School of Medicine- LA CaTS, Faculty/Scientist
pgrego@lsuhsc.edu

William "Tom" Harris
UAB, Faculty/Scientist
tharris@peds.uab.edu

Poster Session B: Friday, April 20, 2:15 - 3:15 pm and Friday, April 20, 6 -7:30 pm
miRNA manipulation to improve CFTR correction in pediatric cystic fibrosis
In vitro, we have identified a miRNA that impairs utility of CFTR directed therapies. miR-145 is upregulated by TGF-β (a genetic modifier of CF lung disease) with a direct binding site on the 3'-untranslated region of CFTR mRNA. Binding of miR-145 to CFTR destabilizes mRNA transcript and impedes protein translation. Overexpression of miR-145 abolishes benefit of F508del CFTR correction. Antagonists to miR-145 block TGF-β suppression of CFTR function and augment response to CFTR correction.
This project evaluates in vivo impact of TGF-beta and miRNA manipulation on CFTR functional readouts including nasal potential difference (NPD) and short circuit current (Isc) across tracheal explants in addition to standard biochemical measures.

Muhan Hu
UAB, Pre-Doc Trainee
mhu1@uab.edu



Poster Session A: A256
Novel PGF_{2a} synthesis pathway in epithelial ovarian cancer
Ovarian cancer is the fifth leading cause of cancer related deaths in women. Epithelial ovarian carcinomas account for 90% of ovarian cancer related deaths. This high mortality rate is due to a combination of ineffective early detection and development of chemoresistance to standard chemotherapeutic agents (taxanes and platinum compounds). Current efforts are invested in identifying novel adjuvant therapeutic options. Prostaglandins are lipid signaling molecules involved in many biological processes, including tumorigenesis. Increased levels of PGE2, PGF2a, and PGI2 have been associated with many epithelial cancers. To date, the bulk of studies on prostaglandin and epithelial ovarian cancer have focused on PGE2. These studies have found that PGE2 is elevated in ovarian cancer tissue, and is involved in malignant transformation and increased proliferation of epithelial ovarian cancer cells. However, little is known about the effects of PGF2a on ovarian cancer progression. Prostaglandins are classically synthesized via cyclooxygenase (COX) enzymes. However, recent studies using *C. elegans*, mice and human follicular fluid suggest PGF2a may be synthesized by an alternate, COX-independent mechanism. Understanding the role and mechanism of PGF2a in ovarian cancer may unveil a novel target pathway for epithelial ovarian cancer therapy. In this study, we used mass spectrometry to measure the levels of PGF2a in high grade epithelial ovarian cancer and test whether PGF2a is dependent on COX function. We treated OVCAR3 high grade epithelial ovarian cancer cells with indomethacin, a COX-1 and COX-2 inhibitor. While PGF2a levels decreased with indomethacin treatment, significant levels of PGF2a are still detected. These preliminary results suggest PGF2a may play a role in epithelial ovarian cancer and may be regulated through a novel, cox-independent pathway. Future work will focus on understanding the mechanism of this novel PGF2a metabolic pathway and its role in epithelial ovarian cancer progression.

Aditi Jani
UAB, Pre-Doc Trainee
ajani@uab.edu

Poster Session A
The Role of Interleukin-23 In Human Melanoma
Interleukin-23 (IL-23) promotes differentiation of naïve T-cells into Th17 cells, which drive the pathogenesis of autoinflammatory conditions such as psoriasis. IL-23-neutralizing antibody therapies are now in use for treatment of psoriasis, with promising results. Studies in mice have shown that IL-23 plays a role in inhibiting the growth, progression, and metastasis of melanomas. Thus, therapeutic neutralization of IL-23 in patients may inadvertently increase their susceptibility to development of melanoma. We aim to characterize expression of IL-23 receptors (IL-23R) in human melanocytes and melanoma cells and tissue and to study the effect of IL-23 on growth, proliferation, and tumorigenicity of these cells.

IL-23R expression was characterized using immunofluorescence staining, Western Blot, and Flow Cytometric analysis. Response of melanoma and melanocytes to recombinant IL-23 treatment will be studied through similar methods and with assays of cell proliferation.
Preliminary results indicate that both human melanoma and primary melanocytes express IL-23 receptors. Western Blot analysis showed that melanoma cell line A375, expressed nearly twice the amount of IL-23R versus normal melanocytes ($p < 0.05$). We anticipate that addition of recombinant IL-23 to cultures of melanoma will reduce proliferative potential. We expect similar addition to normal melanocytes will increase DNA repair.
In showing that human melanocytes and melanoma cells express IL-23 receptors, and potentially showing the inhibitory effect of IL-23 in the development of melanocytic neoplasms, our findings imply that using IL-23 neutralizing therapies may increase risk of developing melanoma, especially in patients who are already susceptible.

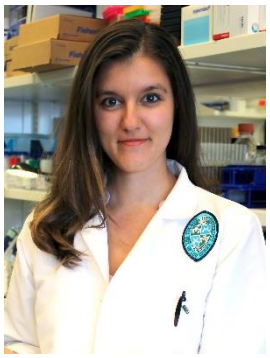
Renata Jaskula-Sztul
UAB, Faculty/Scientist
sztul@uab.edu
Friday, April 20, 2:15-3:15 pm and Friday, April 20, 6-7:30 pm, Exhibit Halls A and B South, Lower Level

Synaptic vesicle 2 receptors as a novel targets for neuroendocrine cancer therapy
Neuroendocrine (NE) malignancies are hormone secreting neoplasms which include carcinoid, islet cell tumors, and medullary thyroid cancers. Patients with NE cancer often present with liver metastasis, which can cause debilitating symptoms, such as uncontrollable diarrhea, flushing, skin rashes, and heart failure due to the excessive hormone secretion that characterizes these tumors. Despite the recent development of targeted therapies such as sunitinib and everolimus, these compounds have marginal clinical benefits and they may promote NE cancer metastasis with prolonged treatment. Thus, discovering alternative targets and therapies are critical for patients with metastatic NE cancers.
Synaptic vesicle 2 (SV2) proteins gained attention as a new biomarker abundantly expressed in NE cells; nevertheless, not much progress has been made since their discovery. Botulinum neurotoxin type A (BoNT/A) binds to SV2 as co-receptors to enter cholinergic neurons. The non- toxic 50 kDa heavy-chain receptor binding domain of BoNT/A (HCR) is responsible for recognizing SV2, thus making it a good candidate for drug delivery vehicle to target NE tumors (NETs). In our preliminary data, we have shown that recombinant HCR (rHCR) specifically targets NETs with no BoNT/A related toxicity in vitro. More importantly, treatment of human NE cancers cells with rHCR leads to a marked reduction in NE markers and hormones, suggesting that HCR may potential be a therapeutic benefit for NE cancers.

Carolyn Jones
jones.5342@osu.edu
Friday, April 20 10:30am

Development of New Tools for Evaluation of Training
Two perspectives: one project aims to enable indexing, classifying, and discovery of tools in practice across the CTSA; another demonstrates leveraging LMS collaboration tools for skill assessment and knowledge checks

Tiffany Kaul
Tulane University School of Medicine- LA CaTS, Pre-Doc Trainee
tkaul@tulane.edu
Poster Session B: B231



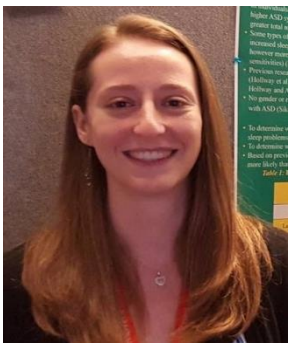
L1 EXPRESSION ANALYSIS IN ADIPOCYTE DERIVED STEM CELLS

Long interspersed element-1s (L1s) are autonomous, mobile elements that are able to copy and insert itself throughout the genome with its own reverse transcriptase and endonuclease. These elements make up 17% of the human genome with over 500,000 copies, though the vast majority of these elements are defective and only a few dozen are potentially responsible for L1 activity. Full-length L1s have the potential to contribute to mutagenesis through random insertion and increased genetic instability. Here we set out to study L1 expression at the specific loci level in bone marrow derived stem cells (bmSCs) and adipocyte stem cells (ASCs) and compare the levels of expression from ASCs from donor patients who are young and lean, obese, and old. Adipocyte stem cells and bone marrow derived stem cells were isolated from patient donors. The following samples were collected: ASCs from 3 young and lean patients, ASCs from 3 patients over the age of 59, ASCs from 3 patients with BMI>30, and bmSCs from 4 young and lean patients. Cytoplasmic RNA from the cell populations were isolated and sequenced from the cell populations. Using our recently developed bioinformatics pipeline, we set out to quantify L1 expression and identify the few culprit L1s at specific loci that are actively transcribing to RNA in the ASC and bmSC samples.

Robert Kimberly
UAB, Faculty/Scientist
AI and Machine Learning in Clinical Research: Experience in Implementation, AI and Machine Learning in Clinical Research: Experience in Implementation
Friday, April 20; 9:15 AM - 10:15 AM, Roosevelt 1
Moderator: Robert Kimberly, MD, University of Alabama at Birmingham
Speaker: Michael Liebman, PhD, IPQ Analytics & Beth DiGiullian, MS, Booze Allen Hamilton

Marie Krousel-Wood
Tulane University, Faculty/Scientist
mawood@tulane.edu

Jenna Lebersfeld
UAB, Pre-Doc Trainee
jbl1@uab.edu
Poster Session: A



The SAM Robot: A Social Skills Intervention for Children with Autism Spectrum Disorder

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that affects one in 68 children. Children with ASD have two core areas of difficulty: social communication skills and restricted and repetitive interests and patterns of behavior. Children with social skills deficits are at higher risk of developing mental health problems, and underdeveloped social skills predict poorer quality of life in adulthood. Therapies have been developed to help people with ASD improve social abilities in childhood, often involving a clinician directly teaching social skills lessons, either one-on-one or in a group setting. However, children with ASD can become anxious when interacting with other people and have an intrinsic motivation to interact with technology. To capitalize on this interest, this research team developed a robot, the Socially Animated Machine (SAM) to teach social skills to children with ASD. Previous research found that this intervention was feasible and enjoyable for children with ASD and average cognitive ability, and participants improved in complex emotion recognition following intervention. The purpose of this study was to determine whether participants of all IQ levels were motivated by the SAM intervention, and whether they improved on emotion identification, facial recognition, social skills, and adaptive behavior.

Kim Littlefield
Universtiy of South Alabama, Faculty/Scientist
kplittlefield@southalabama.edu

Robinna Lorenz
UAB, Faculty/Scientist
rlorenz@uabmc.edu

Margarite Matossian
Tulane University School of Medicine- LA CaTS, Pre-Doc Trainee
mmatossi@tulane.edu

Poster Session A: A246

Patient-derived xenografts as translational models for targeted therapeutic research in triple negative breast cancer

Triple negative breast cancers (TNBCs) constitute approximately 12% of all breast cancers and are approximately twice more prevalent in African-American populations. Louisiana has a high proportion of African-American residents (32.5% in 2015), and among the highest incidences of TNBC in the country. TNBCs have an aggressive clinical presentation due to high rates of metastasis, recurrence and chemoresistance, and targeted therapy remains elusive. Discovery of novel therapeutic targets, especially within the subset of previously uncharacterized kinases in TNBC could provide important insights into future targeted therapies. However, current models utilized in target discovery research are limited by the inability to accurately recapitulate the complex architecture and heterogenous genetic and molecular composition of breast cancer. Recently our laboratory has successfully established four TNBC patient-derived xenograft (PDX) models representing different patient ethnicities, responsiveness to chemotherapies, and different TNBC molecular subtypes and metastatic behavior. Our primary objective was to dissect and evaluate the various individual components (tumor cell biology, stroma, immune, extracellular matrix) that drive complex interactions within TNBC tumors. We utilize these models *in vivo, ex vivo* and *in vitro* to examine how unique kinases and small molecule inhibitors affect the distinct tumor characteristics. In addition to *in vivo* treatment studies, we generated cell lines and mammospheres (TU-BcX-2K1, TU-BcX-2O0, TU-BcX-49S, TU-BcX-4IC, TU-BcX-4EALNb, TU-BcX-4M4) and we utilize novel techniques such as tissue decellularization to examine extracellular matrix components. We also analyze mechanistically relevant transcript (qRT-PCR) and protein (Western Blot, immunohistochemistry) expression patterns that are unique to each PDX model to evaluate the effect of small molecule inhibitors on these transcripts and proteins. Our aim is to leverage novel patient-derived models from under-studied patients with a range of clinical presentations to guide the selection of therapeutically targetable pathways and molecules in specific molecular subtypes of TNBC.

Jeanne Merchant
UAB, Administrative Staff
jsmerchant@uabmc.edu

Matt Might
UAB, Faculty/Scientist
might@uab.edu

Friday, April 20 10:30am

Precision Medicine: challenges and opportunities to advance personalized medicine

This session will explore genomics, deep clinical phenotyping and drug discovery/repurposing in advancing individualized clinical therapeutics and advancing these insights through ultimate approval and adoption in clinical care.

Mercedes Morales-Aleman
UA - Tuscaloosa, Faculty/Scientist
mmmoralesaleman@ua.edu
Saturday, April 21, 9:00 am Roosevelt 4

Developing a Conceptual Model of Healthcare Access for Adolescent Latinas in the US South
Adolescent Latinas in the US and in AL are disproportionately affected by sexual health disparities as evidenced by the disproportionate burden of HIV, STIs and early pregnancy compared to their non-Hispanic, white counterparts. Empirical data with adult Latinas in the Southeast suggest significant barriers to sexual healthcare access. However, to our knowledge, no other researchers have examined barriers and facilitators to sexual healthcare access for this subpopulation. The goal of this 3-phase study is to (a) better understand the factors underlying sexual health disparities and gaps in healthcare access among adolescent Latinas; (b) develop a conceptual model based on these data and the extant literature summarizing the theorized pathways through which factors at differing levels of the socioecological model of health (SEMH) impact sexual healthcare access for this group and (c) develop community-driven, theory-based, culturally-relevant, multilevel intervention strategies to reduce sexual health disparities and increase sexual healthcare access for this group through a community-engaged, intervention mapping process. This presentation will summarize our conceptual model (see draft attached). For ease of interpretation, we have created two sub-models which summarize theorized pathways through which policy, community, organizational and family-level factors influence young Latina women's access to sexual healthcare services with regard to: gender and immigration. Alabama (AL) experienced a 145% increase in its Latino population between 2000 and 2010; making it the state with the second fastest growing Latino population in the United States (US) during that time. Adolescent Latinas in the US and in AL are disproportionately affected by sexual health disparities as evidenced by the disproportionate burden of HIV, STIs and early pregnancy compared to their non-Hispanic, white counterparts. In 2011, Alabama passed one of the harshest anti-immigration laws in the nation. Following the passing of this law, county health department visits among Latino adults decreased by 25% for STIs and 13% for family planning. Empirical data with adult Latinas in the Southeast suggest significant barriers to sexual healthcare access. However, to our knowledge, no other researchers have examined barriers and facilitators to sexual healthcare access for this subpopulation. Therefore, the goal of this 3-phase study is to (a) better understand the factors underlying sexual health disparities and gaps in healthcare access among adolescent Latinas; (b) develop a conceptual model based on these data and the extant literature summarizing the theorized pathways through which factors at differing levels of the socioecological model of health (SEMH) impact sexual healthcare access for this group and (c) develop community-driven, theory-based, culturally-relevant, multilevel intervention strategies to reduce sexual health disparities and increase sexual healthcare access for this group through a community-engaged, intervention mapping process. Community based participatory research (CBPR), which ensures equitable participation of stakeholder groups through partnerships, and the SEMH, which conceptualizes the individual as nested within a set of social structures, provide the philosophical and theoretical frameworks for the work.

Christina Muzny
UAB, Faculty/Scientist
cmuzny@uabmc.edu
Thursday, April 19, Exhibit Halls A/B

Genital Microbiomes of Women with Recurrent BV and their Regular Male Sexual Partner
Epidemiologic data suggest that BV is sexually transmitted with male partners colonized or infected with the responsible organism(s). Our objective was to compare the genital microbiota of women with recurrent BV and their regular male sexual partner using 16S rRNA gene sequencing and quantitative PCR targeting BV-candidate bacteria (*Gardnerella vaginalis*, *Atopobium vaginae*, BVAB1-3, *Sneathia*, *Leptotrichia*, and *Megasphaera* type I).
Women with recurrent BV (≥3 prior episodes, including a current episode) and their regular male partner participating in a BV treatment trial and providing genital specimens (women: vaginal; men: urethral, coronal sulcus, urine) at enrollment were included. Male specimens for each participant were pooled. 250bp 16S rRNA V4 region PCR amplicons were sequenced and analyzed using the QIIME pipeline. Taxonomy was assigned using the RDP Classifier against a modified Greengenes database with additional vaginal taxonomies added. An average relative abundance cutoff

of 0.5% was used for analysis. qPCR was also performed for specific BV-candidate bacteria. Spearman correlation coefficients were used to investigate associations between all genital bacteria in addition to BV-candidate bacteria between partnerships. To determine positive associations between partnerships, the Wilcoxon signed rank test was used.

Candice Myers
Pennington Biomedical Research Center- LA CaTS, Faculty/Scientist
candice.myers@pbrc.edu

Poster Session A: A115

Psychological Mechanisms Linking Food Insecurity and Obesity

The current study is investigating an emergent risk factor for obesity: food insecurity, which is defined as the limited or uncertain availability of nutritionally adequate and safe foods. While paradoxically linked, numerous studies have shown a significant association between food insecurity and obesity. Moreover, recent narrative works have developed new, untested hypotheses linking food insecurity and obesity positing the causal role of certain psychological mechanisms. These psychological mechanisms, delay discounting (delayed versus immediate gratification), grit (long-term goal perseverance), future time perspective (prospective thinking), and subjective social status (psychosocial stress) specifically, are cognitive indicators of decision-making in individuals. Given this, this study is collecting new psychological data in a sample of food secure and food insecure adults with and without obesity to examine the connections between food insecurity, body weight, and psychological mechanisms. Specifically, via multiple, validated questionnaires we are assessing four key psychological constructs: delay discounting, grit, future time perspective, and subjective social status, as well as assessing a number of additional measures, including health literacy, sociodemographics, food assistance use, and dietary quality. This objective is being achieved via a cross-sectional, mixed method study collecting both quantitative and qualitative data. This study is also community-based, with all screening and study assessments conducted in designated community

Matthew Neu
UAB, Pre-Doc Trainee
neumb@uab.edu

Poster Session B: Friday, April 20, 2:15 - 3:15 pm and Friday, April 20, 6 -7:30 pm (B155)

Attitudes and Preferences for Return of Results from Next-Generation Sequencing

Decreasing costs and increasing evidence for clinical utility have contributed to whole genome sequencing (WGS) becoming a clinical reality. While previous studies have surveyed the attitudes of patients and community members towards specific gene tests, an emerging literature has begun to describe the preferences of diverse recipients for WGS results. In this study, we sought to identify and synthesize the quantitative evidence on preferences for results from WGS using a systematic review of the literature. We conducted a search of articles on PubMed including subject index terms whole genome sequencing, whole exome sequencing, genome sequencing, secondary findings, incidental findings, attitudes, preferences, choices, utilities, stated-preferences, discrete choice experiment, and willingness-to-pay. We conducted 11 formal searches to refine the strategy and conducted a final search in December 2017. Duplicates were eliminated and a title and abstract review was conducted to select articles meeting inclusion criteria. Our search strategy identified 79 publications meeting initial search criteria with 30 manuscripts meeting inclusion criteria. Of these, most studies were conducted with patient-participants enrolled in existing sequencing studies, while few engaged members of the general public. Of the studies conducted on patients, most were on the medical setting of cancer and related syndromes. The earliest publication date of a manuscript meeting our inclusion criteria was in 2012, yet the majority were published in 2015 or later. Between 2012 and 2015, we saw an increasing focus in the medical literature on understanding public and patient preferences for return of results from WGS and WES. Both public and patient populations participating in surveys expressed -preferences for receiving results from nextgeneration sequencing, even if the results are secondary or incidental findings unrelated to the primary indication for sequencing. A primary factor related to patient interest in incidental or secondary findings is the extent to which these results can inform medical intervention. Few studies surveyed representative population-based samples, and this may be an area for future investigation.

Milza Opper
UAB, Pre-Doc Trainee
milza@uab.edu

Poster Session A: A181

Identification of Herpes Simplex Virus (HSV) Shedding In The Female Genital Tract Of Pregnant Women By The Xpert HSV 1/2 Assay and Routine PCR

Despite advances in treating neonatal HSV, many babies continue to die or develop long-term neurologic sequelae as a result of intrapartum transmission. Screening of women at delivery to detect those who are shedding HSV in their genital tract has the potential to provide targeted preemptive therapy to their exposed neonates, thereby preventing neonatal HSV disease before devastating infection and disease can occur. Currently, real time PCR is the standard for diagnosis of HSV; however this method consists of many steps and requires technical training to perform the test correctly. The Xpert HSV 1/2 is a new self-contained PCR assay that requires little training, runs in a much shorter time than standard PCR, and may allow large scale screening of pregnant women in the labor and delivery suite. To estimate the positive percent agreement and negative percent agreement of the Xpert HSV 1/2 PCR Assay relative to routine PCR for detecting HSV DNA in the genital tract of pregnant women admitted with the intent of delivery. Vaginal swabs were obtained from 12,500 asymptomatic pregnant women with the intent to deliver and no evidence of HSV lesions. Approximately half of the samples are being assessed by Xpert HSV1/2 PCR and routine PCR, while the other half are being stored for possible future testing. Xpert and routine PCR results from samples tested will be compared, and positive and negative percent agreements will be calculated.

Robert Oster
UAB, Research Methods
roster@uabmc.edu

Becky Reamey
UAB, Faculty/Scientist
reamey@uab.edu

David Redden
UAB, Faculty/Scientist
dredden@uab.edu

Erica Rosemond
NIH Program Officer

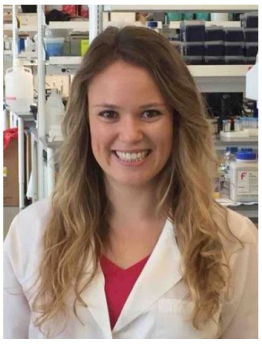
Erica K. Rosemond joined NCATS as a program director in the Division of Clinical Innovation in October 2015. She provides programmatic direction for multiple Clinical and Translational Science Awards (CTSA) Program hubs and contributes to the program's Workforce Development Domain Task Force and Informatics Domain Task Force. Rosemond earned her Ph.D. in pharmaceutical sciences at the University of Toronto in Canada, where she specialized in the neurosciences. She joined NIH in 2005 and trained in the National Institute of Diabetes and Digestive and Kidney Diseases as a fellow in the Intramural Research Program. Prior to joining NCATS, Rosemond managed grant portfolios at the National Cancer Institute and the National Institute of Mental Health, supporting research education, career development and training. She has provided support to the NIH Advisory Committee to the Director Working Group on the Biomedical Workforce and led education and training efforts for the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative(link is external). Currently she is leading efforts in the NIH Big Data to Knowledge (BD2K)(link is external) initiative in the areas of education and training.

Ibolya Rutkai
Tulane University School of Medicine- LA CaTS, Faculty/Scientist
irutkai@tulane.edu

The role of mitochondria in the cerebral circulation

Ischemic stroke is responsible for approximately 87% of all strokes and is the fifth leading cause of morbidity and mortality in USA. Women are protected during the reproductive years against ischemic stroke, but the incidence of stroke increases after menopause, leading to over 50,000 more deaths per year among women compared with men. Significant research shows that the decrease of ovarian hormone levels and estrogen receptor expression correlates with the loss of stroke protection, but much remains unclear. Estrogen is one of the female hormones, affecting vascular function via estrogen receptors (ERs). The chronic effects of estrogen are mediated by estrogen receptors □ and □□(ER□ and ER□), whereas GPR30 is involved in estrogen's acute actions. ER□ and ER□□have been shown to primarily localize in the cell nucleus, while ER□□expression was observed on cerebrovascular mitochondria. It has been shown that mitochondria are not only energy producing organelles, they form an interconnected network within the cells, dynamically change, and are involved in cellular protection, apoptosis, and control of vascular one. We and others have demonstrated that estrogen enhances mitochondrial oxidative phosphorylation and endothelial nitric oxide synthase (eNOS) activity in the rodent vasculature. These important interactions among estrogen, eNOS, and mitochondrial dynamics in large cerebral arteries might explain resistance to ischemic brain injury in female rodents compared with males. Furthermore, we have found a significantly increased mitochondrial DNA and phosphorylated eNOS levels in male middle cerebral arteries 48 h after ischemia compared with the non-ischemic side, indicating that nitric oxide contributes to an enhanced mitochondrial biogenesis. The critical role of mitochondria, in mitigating the effects of experimental stroke has been demonstrated by us and others using rodent models of ischemia reperfusion as well as in *in vitro* oxygen glucose deprivation in cultured brain microvascular endothelial cells and cortical neurons.

Rachel Sabol
Tulane University School of Medicine- LA CaTS, Pre-Doc Trainee
rsabol@tulane.edu



Poster Session B: Friday, April 20, 2:15 pm- 3:15 pm and Friday, April 20, 6 -7:30 pm

High Intensity Focused Ultrasound (HIFU) can be used synergistically with tamoxifen to overcome resistance in preclinical and patient derived xenograft models

Tamoxifen (tam) is the most commonly used anti-cancer therapeutic agent in estrogen receptor positive (ER+) breast cancer (BC) which accounts for ~70% of BC cases. Tam treatment decreases a woman's risk of recurrence by 50%; however, BC that is initially responsive to tam often develops resistance. In this study we evaluate a potential strategy to overcome resistance by using tam in combination with high intensity focused ultrasound (HIFU). HIFU is a clinically used non-invasive tumor ablative therapy that uses acoustic energy deposition. Previous studies have demonstrated that HIFU in combination with cancer therapeutics can have synergistic effects. In this study we found that treatment of MCF7 cells with HIFU and tam has additive anti-proliferative effects and mediates increased cell death. Additionally, we used tam resistant (TR) MCF7 cells that had been exposed to low dose tam over time until they acquired resistance. When MCF7 TR are treated with tam there is no change in viability; however, treatment with HIFU in combination with tam decreased viability of both MCF7 and MCF7 TR to 19% and the viability of the cell lines was indistinguishable. We next evaluated the effect on MCF7 Y537S mutant ESR1, where ER is mutated to be constitutively active. Treatment of MCF7 Y537S had no significant decrease in viability of combination therapy compared to viability after HIFU alone. Analysis of ERalpha gene expression showed that HIFU treatment increased ERalpha expression in MCF7 TR cells, thus resensitizing these cells to tam and allowing these therapies to work synergistically. Our team developed a system to evaluate the potential of this combination of therapies in a patient-derived xenografts (PDX) model. PDX have emerged as a novel translational tool for cancer research with the potential to more accurately recapitulate the molecular and behavioral aspects of cancer. The WHIM20 PDX is a tamoxifen resistant tumor where the patient developed the Y537S mutation in ESR1. *Ex vivo* experiments on PDX tumor pieces demonstrated that combination therapy of HIFU and tam work synergistically to increase cell death of these tumors. Further, cryo SEM demonstrates ablation of cells when these

therapies are used together. These studies present a novel translational strategy to overcome tamoxifen resistance in ER+BC.

Ramya Singireddy
UAB, Pre-Doc Trainee
ramyas@uab.edu

Saturday, April 21, Roosevelt 5

Exploring Müller cell-cone interactions in human fovea using 3-dimensional volume electron microscopy (EM): Müller cells, radial glial cells of the retina, are the principal repository of xanthophyll pigment (lutein, zeaxanthin, meso-zeaxanthin), which are modifiable by diet and visible clinically by autofluorescence imaging. To understand the structural basis of xanthophyll visualization in vivo, we used 3-dimensional electron microscopic (EM) reconstruction of Müller cells surrounding one cone in a healthy human fovea.
From a 21-year-old male organ donor, dissected retinas were rejuvenated by oxygenated Ames medium then fixed in 4% glutaraldehyde. A tissue block 3.5 mm^2 centered on the fovea was prepared for Automated Tape Ultramicrotomy (Kasthuri et al., Cell 162:648-661, 2015). From 1462 serial 65 nm horizontal sections, an area ~250 x 250 µm was imaged at 6 nm xy resolution. Images were stitched and aligned. TrackEM software on a pen display was used to trace, reconstruct, and display cone #5 (of 186) and its contacting Müller cells. Cone 5 is ensheathed by two types of Müller cells, Outer and Inner (Dacey ARVO 2016). The Outer Cell is first seen at the external limiting membrane (ELM) between cones 5 and 17. Moving inward from the ELM, it tightly wraps around cone 5's fiber in a C-shape profile for 78 µm. This Müller cell also intermittently projects to neighboring cones, two of which were close to cone 5 at the ELM. As cone 5's axon approaches the pedicle, it contorts into a corkscrew. The Outer Cell fluidly molds to this changing shape. At this level, this Müller cell doubles in volume to encompass not only cone 5, but also cone 17 and another Müller cell. In the final 17 µm of the block the Müller cell's volume quickly dissipates as it sends a small projection towards the internal limiting membrane, eventually encasing an OFF midget bipolar cell also associated with cone 5. In contrast to this Outer Cell, an Inner Müller Cell adjoining cone 5 spans only 19 µm, interacting directly with cone 5 and the Outer cell for 3.9 µm. Neural-glial relationships in a human fovea are visible through 3-dimensional volume EM. The volume of Müller cells in the fovea was impressive, consistent with a pivotal role in the health of cone photoreceptors and xanthophyll homeostasis. It is possible that individual glia also ensheath the post-receptoral neurons in a cone-driven circuit, supporting the concept that xanthophylls contribute to neural efficiency in vision.

Molly Wasko
UAB, Faculty
mwasko@uab.edu

Friday, April 20; 1:00 PM - 2:00 PM, Roosevelt 4

Enabling entrepreneurship

This session will describe resources available through nine NCATS hubs available for training in entrepreneurship. They will demonstrate the I-Corps methodology developed by the National Science Foundation and engage session participants in real-world entrepreneurial experiences.

Roy Weiner
Tulane University School of Medicine- LA CaTS, Faculty/Scientist
rweiner@tulane.edu

James Willig, MD, MSPH
UAB, Faculty/Scientist
jwillig@uabmc.edu

Karam Zakharia
Tulane University Medical center, Pre-Doc Trainee
kzakharia@hotmail.com

CHOP-R IS AN EFFICIENT TREATMENT FOR PRIMARY DURAL DIFFUSE LARGE B-CELL LYMPHOMA (PD-DLBCL): A SYSTEMATIC REVIEW OF 45 CASES.
Purpose of Study: PD-DLBCL is an aggressive lymphoma that affects the Dura mater, imitating other central nervous system tumors, and remains with unclear optimal management. We conducted a retrospective review of the literature on pathologically confirmed PD-DLBCL and analyzed data on biology, treatment outcomes, and survival. Summary of Results: Out of 245 screened cases, 45 cases of PD-DLBCL were detected. 16 cases were intra-cranial and 29 were intra-spinal. Median age at diagnosis was 59 years. Incidence was nearly equal between women (22/45) and men. When tested, CD20 was positive in each instance (21/21). Using Hans criteria when possible to determine cell of origin, 3 cases were classified as ABC-DLBCL and 5 as GCB-DLBCL, confirming the representation of both subtypes in PD-DLBCL. All cases were stage IE and 6 of the 9 cases which provided Ki-67 data were less than 70%, reflecting an overall less aggressive behavior. Survival data available from 40 cases showed an OS of 4% at 1 year, and 81% at 5 years, which compares favorably to PCNSL and matches early-stage DLBCL. Tumor location (intracranial vs. intra-spinal) did not impact OS (P=0.82). Treatment was reported in 19 cases with available survival data. 11 patients received CHOP, 6 of which additionally received rituximab (CHOP-R). Eight patients received highdose methotrexate (MTX)-based therapy. Interestingly, no difference in OS was observed between CHOP vs. MTXbased therapy (P=0.97), suggesting that PD-DLBCL should be treated as DLBCL rather than PCNSL. Moreover, all patients who received CHOP-R remained disease free and alive. Radiation therapy was given often (25/29) in treatment of spinal disease, but rarely (4/16) when treating cranial disease, but did not impact OS.

Kathrin Zimmerman
UAB, Pre-Doc Trainee
kzimm1@uab.edu

Poster Session B: Friday, April 20, 2:15 - 3:15 pm and Friday, April 20, 6 - 7:30 pm
Post-Traumatic Stress Symptoms n Caregivers of Pediatric Hydrocephalus Population
The goal of this study is to characterize traumatic events and post-traumatic stress symptom severity experienced by caregivers of children with hydrocephalus. Results will eventually e evaluated and compared to demographic and medical characterizes. This study is part of a larger research project that aims to 1. Determine the prevalence and risk factors for post-traumatic stress symptoms in pediatric hydrocephalus patients and their caregivers; 2. Develop a targeted intervention to mitigate its effects and pilot test the intervention.

***Mai Do, MD, MPH, DrPH and Jennifer McCleary, MSW, PhD**
Tulane University School of Medicine
Pilot Award (Poster will be presented by a community member)*
Social, cultural, and cognitive factors that facilitate or impede and individual's use of behavioral health care

Mission of CCTS

The mission of the Center for Clinical and Translational Science is to **serve** our region and a population heavily burdened with cardio-metabolic, vascular and cancer-related diseases in order to **ameliorate** disparities in these and other conditions that disproportionately affect minority and special populations represented within our region. This mission will be accomplished by leveraging the investigative and healthcare **capacity** of our region to continually enhance excellence in clinical and translational research and its delivery for human health.