**11:00-12:30 Cancer Biology**

**(Co-Chairs: Drs. Ma (OUHSC) and Zempleni (UNL))**

**Name:** Sandeep Singhal **Institution:** University of North Dakota **Email:** sandeep.singhal@und.edu **Research area:** Cancer Biology

**Title:** Racial disparity and molecular biology of breast cancer: A multi-omics approach

**Authors:** Sandeep K Singhal1,2, Donald Sens1, Kevin Gardner3
1. Department of Pathology, School of Medicine and Health Sciences, University of North Dakota, ND

2. Department of Biomedical Engineering, College of Eng. & Mines, University of North Dakota, ND

3. Department of Pathology and Cell Biology, Columbia University Medical Centre, NY

**Abstract:** Purpose: The incidence of breast cancer (BC) has risen dramatically during the last four decades. In 2021, an estimated 281,550 women were newly diagnosed with invasive breast cancer and it is expected that, by the year’s end, over 49,290 women, living with breast cancer, may die. In the national effort to reduce the burden of breast cancer, there remains a significant urgent need for the development of predictive and prognostic biomarkers with sufficient precision to empower clinicians with the appropriate treatment. Recent implication of the role of genetic ancestry in patient stratification and prognosis increases the urgency of this need. Meeting this need, we aimed to develop new diagnostic biomarkers and modes of biomarker assessment capable of patient-specific stratification and assignment to the most appropriate risk and treatment groups.  Here we uncover biological factors underlying this disparity by comparing functional expression and prognostic significance of difference biomarkers.

Method: The recent application of artificial intelligence and machine learning to the histomorphologic profiling of pathological specimens is expanding the sensitivity and specificity of quantitative tissue analysis at an unprecedented scale. As a result, this expanded technology has provided new opportunities for the precise characterization of novel and functionally relevant histological features with both predictive and prognostic significance. These advances have provided a template that has enriched the quantitative determination of biomarker abundance to include more precise distinctions based on assessment of subcellular distribution (e.g. membrane versus cytoplasm vs nucleus).

Data and biospecimens from 262 AA and 293 EA patients diagnosed with breast cancer from 2001 to 2010 at a major medical center were analyzed by IHC for functional biomarkers. Integrated comparison of protein levels with network-level gene expression analysis uncovered predictive correlations with race and survival.

Results: Univariate or multivariate HRs for overall survival, estimated from digital IHC scoring of nuclear antigen, show distinct differences in the magnitude and significance of these biomarkers to predict survival based on race: ESR1 [EA HR = 0.47; 95% confidence interval (CI), 0.31–0.72 and AA HR = 0.77; 95% CI, 0.48–1.18]; FOXA1 (EA HR = 0.38; 95% CI, 0.23–0.63 and AA HR = 0.53; 95% CI, 0.31–0.88), and GATA3 (EA HR = 0.36; 95% CI, 0.23–0.56; AA HR = 0.57; CI, 0.56–1.4). In addition, we identify genes in the downstream regulons of these biomarkers highly correlated with race and survival.

Conclusions: Even within clinically homogeneous tumor groups, regulatory networks that drive mammary luminal differentiation reveal race-specific differences in their association with clinical outcome. Understanding these biomarkers and their downstream regulons will elucidate the intrinsic mechanisms that drive racial disparities in breast cancer survival.

**Name:** Joshua Corbin **Institution:** Oklahoma University Health Sciences Center **Email:** joshua-corbin@ouhsc.edu **Research area:** Other **Title:** AN-DISE: A potential RNA interference-based therapy for prostate cancer

**Authors:** Joshua M. Corbin1,2, Constantin Georgescu3, Jonathan D. Wren3, Chao Xu1,4, Adam S. Asch1,5, Maria J. Ruiz-Echevarría1,2,5
1. Stephenson Cancer Center, Oklahoma City, OK.
2. Department of Pathology, Oklahoma University Health Sciences Center, Oklahoma City, OK.
3. Genes and Human Disease Research Program, Division of Genomics and Data Sciences, Oklahoma Medical Research Foundation, Oklahoma City, OK.
4. Department of Biostatistics and Epidemiology, Oklahoma University Health Sciences Center, Oklahoma City, OK.
5. Department of Medicine, Oklahoma University Health Sciences Center, Oklahoma City, OK.

Funding Sources: OCAST HR18-037(M.J.R.E.), INBRE C3145217, Stephenson Cancer Center/NCI/NIH (P20 GM103639, P30 CA225520), NIH 5U54GM104938 (J.D.W.).

**Abstract:** Androgen receptor (AR) signaling is a critical driver of therapeutic response in patients with advanced prostate cancer (PCa). First- and second-generation therapies targeting AR signaling are initially effective, but the benefits are short lived, and most patients relapse with castration resistant prostate cancer (CRPC) which is lethal. Therapeutic resistance and disease progression develop, in most cases, because of molecular adaptation of the AR, AR-coregulators and oncogenic pathways, resulting in persistent AR signaling activation. Therefore, development of effective therapies against advanced PCa remains a critical unmet clinical need.
 We have identified specific small RNAs (sh/si RNAs) that trigger potent androgen signaling inhibition and prostate cancer cell death. Transcriptomic and sh/siRNA seed sequence analyses indicate that expression of these toxic shRNAs lead to downregulation of androgen receptor-coregulatory genes through mRNA 3’-UTR sequence complementarity to the seed sequence of the toxic shRNAs. These findings reveal a specialized form of the “Death Induced by Survival gene Elimination --DISE” mechanism in prostate cancer cells, that we have termed Androgen Network (AN)-DISE. Here we present mechanistic details of AN-DISE and discuss its therapeutic potential for rapid translation into clinical trials.

**Name:** Fangfang Qiao **Institution:** University of Nebraska Medical Center **Email:** fangfang.qiao@unmc.edu **Research area:** Other **Title:** Ctdp1 deficiency results in early embryonic lethality and lactation defects in mice

**Authors:** Fangfang Qiao and Nicholas Woods

**Abstract:** Carboxy-Terminal Domain Phosphatase 1 (CTDP1) is largely known for its defined function in the regulation of transcriptional machinery, but emerging evidence suggests an expanded functional repertoire in the cell cycle and DNA damage response. To explore its physiological function in vivo, we generated the first conditional Ctdp1 knockout mouse model. Deletion of Ctdp1 results in lethality before embryonic day 7.5, with morphological features indicating embryo cell death and resorption. Mechanistically, we found deletion of Ctdp1 in MEFs causes cell death preceded by impaired proliferation associated with cell cycle arrest and aberrant expression of cell cycle regulators, which associates with E2F-mediated transcription. In addition, CTDP1 knockdown inhibits breast cancer cell growth in vitro and in vivo, suggesting it is an essential breast cancer gene. Mammary-specific Ctdp1 knockout in parous female mice results in reduced pup body weight and disruption in the balance and function of mammary epithelial cells. Together, these results reveal that Ctdp1 has a significant role in mouse embryogenesis and mammary gland development.

**Name:** Horrick Sharma **Institution:** Southwestern Oklahoma State University **Email:** horrick.sharma@swosu.edu **Research area:** Other

**Title:** Discovery of a Novel Class of LDH inhibitors against Cancer

**Abstract:** Metabolic reprogramming and metabolic plasticity are emerging as major determinants of pancreatic cancer's growth and metastasis. Recent studies have shown that inhibition of both isoforms of lactate dehydrogenases, LDHA and LDHB, may be needed for effective inhibition of tumorigenesis. So far, there is only one potent and specific dual inhibitor (GNE-140) of LDHA and LDHB known in the literature. We discovered compounds that inhibit both LDHA and LDHB, with the most potent inhibitor showing IC50 in submicromolar concentration. Molecular docking studies revealed the binding mode and key ligand-protein interactions in the LDHA active site. Compounds inhibited lactate production in MiaPaca-2 cells and demonstrated promising anticancer activity in low micromolar levels against human PANC-1, MiaPaca-2 pancreatic cancer cell lines, and against murine PDA FC1199 cells derived from the KPC tumor model. Further, compounds were relatively non-toxic to normal cells. Western blotting analysis of one of the lead compounds revealed activation of intrinsic apoptosis pathway as a regulator of cell death. HPLC was used to determine the chemical stability of lead compounds under acid and basic conditions. We expect to test the most promising lead compound in animal models and develop chemical tools to target metabolic plasticity in pancreatic cancer.

**Name:** Dianna Huisman **Institution:** University of Nebraska Medical Center **Email:** dianna.huisman@unmc.edu **Research area:** Cancer Biology

**Title:** Molecular Characterization of Tumor Initiation in Small-cell Lung Carcinoma

**Authors:** Dianna H. Huisman1, Danielle E. Frodyma1, Kurt W. Fisher1, Robert E. Lewis1
1University of Nebraska Medical Center, Omaha, NE

**Abstract:** Small-cell lung carcinoma (SCLC) is an aggressive, lethal, and highly metastatic disease accounting for 15% of lung cancers. Kinase Suppressor of Ras 2 (KSR2), a molecular scaffold for the MAPK pathway, is expressed in the brain, pituitary gland, and adrenal glands. Pulmonary neuroendocrine cells (PNECs), the cell of origin of most SCLCs, express ASCL1 and undergo self-renewal to repair lung injury. Our analysis reveals KSR2 is highly expressed in PNECs, as well as the ASCL1 subtype of SCLC, which makes up 70% of SCLC tumors. SCLC tumors are comprised of a small stem-like tumor-propagating cell (TPC) population responsible for long term propagation and metastasis, and a proliferative non-tumor propagating cell population. SCLC TPCs are defined by high expression of CD24 and EpCAM, and low expression of CD44. Disruption of KSR2 by inducible RNAi significantly reduces colony forming ability (an index of clonogenicity and self-renewal) of individual SCLC TPCs isolated by fluorescence activated cell sorting (FACS). In vivo extreme limiting dilution analysis (ELDA) of SCLC cells ± KSR2 reduces TPC frequency 10-fold. These data suggest that KSR2 is necessary for the formation and self-renewal of the SCLC tumor-propagating cell population and may serve as a targetable vulnerability in ASCL1 subtype SCLC.

**Name:** Derek Baldwin **Institution:** Wichita State University **Email:** derekb96@hotmail.com **Research area:** Other

**Title:** Observing actin structures and organization to reveal Palladin’s role in metastasis

**Authors:** Derek Baldwin, Sharifah Albraiki, Moriah Beck

**Abstract:** Metastatic cancer cells use invasive structures composed of polymerized actin to migrate throughout the body. An actin-binding protein named palladin is often overexpressed in metastatic cancer cells. Previous research has shown that an actin binding region of palladin (Ig3) causes an increase in actin’s polymerization rate. Now we aim to compare the effects on actin polymerization and organization by the Ig3 domain to that of full-length palladin. We hypothesize that palladin plays a part in promoting the motility of cancer cells throughout the body by increasing polymerization and coordinating the structure of actin filaments. Our focus is to use Total Internal Reflection Fluorescence (TIRF) microscopy to observe actin in the process of polymerization. Our microscopy images capture instances of filament organization and crosslinking, examples of how palladin influences actin filament organization. In comparing the effects of full length palladin to those seen with Ig3, we have found significant changes in the rate of polymerization and filament organization. Future plans include using image quantification programs to measure crosslinking between filaments, in order to better define palladin’s ability to promote branched actin structures. Defining this capability would reveal palladin’s responsibility in constructing the invasive cellular structures that allow cancerous cells to metastasize.

**11:00-12:30 Viruses and Bacteria**

**(Co-Chairs: Drs. Huber (USD) and Liu (OSU))**

 **Name:** Sydney Newsom **Institution:** University of Oklahoma **Email:** sydney.n.newsom-1@ou.edu **Research area:** COVID-19

**Title:** Ranking potential drug targets in coronavirus spike protein by analyzing amino acid functional conservation and evolutionary pressure

**Authors:** Newsom, Sydney N; Van, Richard; Shao, Yihan; Rajan, Rakhi
Department of Chemistry and Biochemistry, Price Family Foundation Structural Biology Center, Stephenson Life Sciences Research Center, University of Oklahoma, Norman, OK

**Abstract:** Initial contact between human cells and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is mediated by the viral Spike (S) protein. The objective of this research is to identify antiviral target sites in S protein and predict which ones will maintain potency against future viral strains as the coronavirus S protein structure continues to evolve. The hypothesis is that based on the level of amino acid conservation in S protein, we can identify regions that are highly evolving and selective against the current SARS-CoV-2 strain or highly conserved in a range of human- and animal-infecting coronaviruses. To test this hypothesis, two complementary in silico methods were used to analyze S protein sequence conservation among 20 (representative of 949) severe strains from humans (including MERS, SARS-CoV, and SARS-CoV-2) and 10 (representative of 88) strains from animals. To identify S protein drug targets, we performed molecular docking of the S protein receptor binding domain with a compound library. Four pockets and six compounds were identified with pocket 4 being the most promising target for antivirals against a broad range of future and present coronaviruses including SARS-CoV-2. These results advance our long-term goal of informing development of antiviral drugs effective against SARS-CoV-2 variants.

**Name:** Miruthula Tamil Selvan **Institution:** Oklahoma State University **Email:** miruthula.tamil\_selvan@okstate.edu **Research area:** COVID-19

**Title:** Establishing a naturally occurring Feline model for SARS CoV-2 infection and disease

**Authors:** Miruthula Tamil Selvan1, Jennifer M. Rudd1, Shannon Cowan1, Yun-Fan Kao1, Cecily C. Midkiff2, Jerry W. Ritchey1, Craig A. Miller1
1Department of Veterinary Pathobiology, College of Veterinary Medicine, Oklahoma State University; Stillwater, OK, USA; 2Division of Comparative Pathology, National Primate Research Center, Tulane University; Covington, LA, USA

**Abstract:** The arrival and persistence of COVID -19 has created an urgent need for an efficient animal model to unravel the pathogenesis of SARS CoV-2 infection. Shortcomings of current animal models for SARS-CoV-2 include limited lower respiratory disease, divergence from clinical COVID-19 disease, and requirements for host genetic modifications to permit infection. The objective of this study was to establish a clinically applicable animal model of SARS-CoV-2 infection that mimics moderate to severe COVID-19 in humans. Specific pathogen free cats were infected with 1.2 x 106 TCID50 SARS-CoV-2 virus via intratracheal inoculation, while a subset of cats remained uninfected as controls. A novel clinical scoring system for feline respiratory disease was developed and utilized, documenting a significant degree of lethargy, fever, dyspnea, and dry cough in SARS-CoV-2 infected cats. Significant histopathologic pulmonary lesions such as diffuse alveolar damage, hyaline membrane formation and fibrin deposition was observed during SARS-CoV-2 infection, replicating lesions identified in COVID-19 patients hospitalized with ARDS. Viral loads and ACE2 expression were quantified in nasal turbinates, distal trachea, lung, and other organs. Natural ACE2 expression, paired with clinicopathologic correlates between this feline model and human COVID-19, encourage use of this model for future translational studies.

**Name:** Phoebe Peña **Institution:** University of Nebraska-Lincoln **Email:** ppena@huskers.unl.edu **Research area:** COVID-19

**Title:** Impact of pre-existing serological cross-reactivity against SARS-CoV-2 on cancer patients in sub-Saharan Africa

**Authors:** Phoebe Peña\* et. al University of Nebraska-Lincoln

**Abstract:** At the time of research, the mortality rates and incidence of COVID-19 in most of sub-Saharan Africa (SSA) were relatively lower than in much of the world. This was unexpected considering the high prevalence of cancers, other diseases, and comparatively limited access to healthcare in many rural areas in SSA. One possible reason is prior exposure to other coronaviruses, eliciting a cross-reactive humoral response against SARS-CoV-2. Cross-reactive antibodies can bind to similarly-shaped epitopes and are important for protection against infections. It is unknown whether these cross-reactive antibodies will prevent the development of COVID-19 and/or reduce its severity. Cancer is a comorbidity for developing severe cases of COVID-19. It is important to examine the effect of pre-existing cross-reactive humoral responses against SARS-CoV-2 on cancer patients. We examined pre-pandemic plasma samples collected from SSA and U.S. adults of both sexes for cross-reactive antibodies against SARS-CoV-2 and six known human coronaviruses using immunofluorescence assays. Preliminary results indicated a higher prevalence of SARS-CoV-2 cross-reactive antibodies in pre-pandemic samples collected from SSA compared to samples from the U.S. We also found exposure to human coronaviruses NL-63 and/or 229E as the likely source of SARS-CoV-2 cross-reactive antibodies. We are currently recruiting cancer and non-cancer study participants in SSA to determine the prevalence of anti-SARS-CoV-2 and cross-reactive antibodies in these individuals during this pandemic compared to those recruited pre-pandemic, and determine the impact of SARS-CoV-2 cross-reactive antibodies on COVID-19 in infected cancer patients.

**Name:** Lauren Zenewicz **Institution:** University of Oklahoma Health Sciences Center **Email:** lauren-zenewicz@ouhsc.edu **Research area:** Other **Title:** A *Clostridioides difficile* toxin induces activation of innate lymphocytes

**Abstract:** Group 3 innate lymphocytes (ILC3s) are rare immune cells often localized in mucosal tissues. Upon activation, ILC3s are a major source of the cytokine interleukin-22 (IL-22). IL-22 modulates tissue responses during inflammation and minimizes dissemination of bacterial pathogens through barrier maintenance, making IL-22 protective in many infections, including Clostridioides difficile. C. difficile is a pathobiont in the GI tract of many healthy individuals, but after certain perturbations causes disease. In this study, we identified a mechanism of how C. difficile modulates host immune responses. A virulence factor, toxin B (TcdB), induced production of IL-22 in ILC3s. This was dependent on the glucosyltransferase activity of TcdB, which inhibits small GTPases. Pharmacological inhibition of Cdc42 phenocopied the TcdB effect and increased IL-22 production by ILC3s, suggesting Cdc42 is a negative regulator of ILC3 activation. C. difficile may perturb the immune system to increase levels of a cytokine that regulates its microenvironment.

**Name:** Austin Nuxoll **Institution:** University of Nebraska Kearney  **Email:** nuxollas@unk.edu **Research area:** Other

**Title:** Decreased Tricarboxylic acid (TCA) cycle in *Staphylococcus* aureus increases survival to innate immunity

**Abstract:** Staphylococcus aureus is responsible for a large array of infections, varying from minor skin and soft tissue infections to more serious infections such as bacteremia or endocarditis. Chronic and relapsing S. aureus bacteremia occurs in 10% of infections and can occur in as high as 15%, even with the use of antibiotics. One potential reason for this is the presence of persister cells - a dormant type of cell that exhibits high tolerance for antibiotics. While major strides have recently been made, persister cells’ role in pathogenesis remains unclear. Initial studies have demonstrated that a fumC knockout (TCA cycle gene) survives challenge from innate immune components - antimicrobial peptides – better than wild type S. aureus. Additionally, the fumC knockout exhibited increased survival within a macrophage. These data led us to hypothesize the fumC knockout is better suited for survival when challenged by innate immune components. Following a biofilm-associated catheter 9-day infection, female mice infected with wild type HG003 were trending towards more frequently clearing the infection compared to female mice infected with the fumC knockout strain. These data suggest that persisters not only present a challenge during antimicrobial therapy but also for the innate immune system.

**Name:** Cheyenne Loo **Institution:** University of Kansas **Email:** cheyenneloo@me.com **Research area:** Other

**Title:** Promiscuity of the *Chromobacterium subtsugae* QS receptor CviR and its role in interspecies competition

**Authors:** Cheyenne Loo, Pratik Koirala, Kara Evans, Saida Benomar, Josephine Chandler

**Abstract:** Quorum sensing (QS) is a type of bacterial communication that coordinates targeted gene transcription among a population in response to population density. QS plays a role in many bacterial functions, such as biofilm formation and the production of virulence factors. Previous experimentation shows that the QS signal receptor of the soil saprophyte Chromobacterium subtsugae (CviR) is able to respond to signals that are structurally distinct from the native C. subtsugae signal. A co-culture competition model between C. subtsugae and fellow QS-abled soil bacterium Burkholderia thailandensis has shown that the promiscuity of CviR allows it to “eavesdrop” on signals produced by B. thailandensis and subsequently activate the secretion of toxins that are important for C. subtsugae to compete with B. thailandensis. Here, we show that the primary QS-controlled toxin involved in eavesdropping is hydrogen cyanide (HCN). We also show that all three of the native B. thailandensis QS signals are able to stimulate production of HCN through CviR to varying degrees. Our results are consistent with the idea that the promiscuity of CviR and subsequent activation of HCN and other toxins might be important for C. subtsugae to compete for space and nutrients in polymicrobial soil communities.

**2:15-3:45 CTR**

**(Co-Chairs: Drs. Basson (UND) and VanWagoner (OUHSC))**

 **Name:** Michael G. Nichols **Institution:** Creighton University **Email:** mnichols@creighton.edu **Research area:** Clinical-translational

**Title:** *In vivo* quantification of metabolic and tissue architectural changes associated with UVA-induced skin cancer in SKH1 Mice

**Authors:** Kristine Au, Carter Cross, Hayden Hubbs, Kelsey A. Jackson, Connor J. Kalhorn, Cecilia Myers, Sam Rogers, Megan Schultz, Thien Q. Tran, George Varghese, Daniel H. Wood, Laura A. Hansen(2), Michael G. Nichols(1), Departments of Physics(1) and Biomedical Sciences(2), Creighton University, NE 68178

**Abstract:** Several of the recognized hallmarks of cancer reflect both the distinct shift in cellular metabolism and remodeling of the extracellular matrix to accommodate increased cellular growth and proliferation. We have developed a non-linear imaging approach that allows simultaneous assessment of cellular NAD(P)H to discern shifts in metabolism, by fluorescence lifetime imaging (FLIM), as well as collagen structure, by Second Harmonic Generation (SHG) of pulsed near-infrared light. While the ratio of forward- to backward-propagating SHG has proven to be diagnostically relevant for biopsy samples, this ratio cannot be obtained directly in vivo. However, confocal detection of multiply scattered and diffusely reflected SHG may provide an approach to measure this ratio in vivo as well. Preliminary results obtained in chronically UV-exposed SKH1 mice reveals a shift in the ratio of free to bound cellular NAD(P)H consistent with increased glycolysis. In addition, the SHG forwards-to-backwards ratio associated with dermal collagen appears to increase in UV-exposed mice. This technique shows promise as a sensitive diagnostic tool for early-stage skin cancer detection.

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**Name:** Kathryn Burge **Institution:** University of Oklahoma Health Sciences Center **Email:** kathryn-burge@ouhsc.edu **Research area:** Clinical-translational **Title:** Hyaluronic acid 35 kDa protects against necrotizing enterocolitis in a hyperosmotic, formula feeding mouse model

**Authors:** Burge, K.Y., Eckert, J.V., Wilson, A.P., Chaaban, H.

**Abstract:** Necrotizing enterocolitis (NEC), an inflammatory disease of the intestine, is the most common gastrointestinal emergency in preterm infants. Dysfunction of the intestinal barrier, premature immune status, dysbiosis, and bacterial translocation of the intestinal epithelium are thought to play major roles in the disease. Animal models for NEC have generally failed translationally due to the incorporation of only a subset of the many risk factors for the condition. Breast milk (BM) is known to be protective against NEC, but the mechanism(s) are unclear. Our group has demonstrated a bioactive component of BM, hyaluronic acid, specifically of 35 kDa molecular weight (HA35), is protective in a mouse model of NEC based on Paneth cell ablation and Gram-negative bacterial translocation. However, therapeutics and preventatives for NEC are rarely validated in a second in vivo model. We tested the efficacy of HA35 in a second mouse model incorporating both Paneth cell ablation and a different NEC risk factor, formula feeding. HA35 significantly reduced mortality and severity of illness in the formula feeding model, potentially implicating broad importance of HA35 across multiple, well-defined risk factors for NEC. Whether these mouse models share similar mechanisms of injury, and whether HA35 is protective through similar pathways, is a pending source of inquiry.

**Name:** James Fletcher **Institution:** Creighton University **Email:** jamesfletcher@creighton.edu **Research area:** Clinical-translational

**Title:** Synthesis and antimicrobial evaluation of 1,2,3-triazole-containing phenanthridines

**Authors:** Lindsey R. Theut and James T. Fletcher\*, Department of Chemistry, Creighton University, NE 68178

**Abstract:** 1,3,4-Trisubstituted-1,2,3-triazolium salts, a newly reported class of quaternary ammonium compounds (QACs), have been shown to possess antimicrobial properties that vary with substituent identity. This project’s aim was to compare the antimicrobial properties of ring-fused 1,2,3-triazolium salt analogs representing the 1,2,3-triazole-containing phenanthridine ring system to their analogous non-fused diaryl triazolium salts. This effectively allows the comparison of rigid, flat arene systems with their flexible structural counterparts. 1,5-Disubstituted-1,2,3-triazoles were prepared from base-catalyzed click reactions between terminal alkyne and aryl azide reactants. Ring-fused 1,2,3-triazole-containing phenanthridine analogs were prepared by intramolecular Pd-catalyzed cross-coupling “fusion” reactions of 2-bromoaryl-substituted triazole precursors. Triazolium salts of fused and non-fused analogs were prepared by N3 benzylation and were screened for antimicrobial properties via microdilution minimum inhibitory concentration assays against Gram-positive bacteria, Gram-negative bacteria and yeast. The majority of fused-ring analogs studied were significantly more potent than their non-fused counterparts. Details regarding the synthesis, characterization, and antimicrobial assays of these compounds will be presented. This publication was made possible by grants from the National Institute for General Medical Science (NIGMS) (5P20GM103427), a component of the National Institutes of Health (NIH), and its contents are the sole responsibility of the authors and do not necessarily represent the official views of NIGMS or NIH.

**Name:** Mark K. Larson **Institution:** Augustana University **Email:** mark.larson@augie.edu **Research area:** Clinical-translational

**Title:** Differential Platelet Responses in Native Americans

**Abstract:** Native Americans disproportionately suffer from thrombotic diseases such as myocardial infarction. Further, existing anti-thrombotic therapies were historically not tested on substantial numbers of Native Americans prior to approval, clouding the breadth of their effectiveness. And, recent findings in other ethnic populations suggest that enriched single nucleotide polymorphisms correlate to both increased platelet reactivity that can contribute to thrombosis and refractory responses to current pharmacologic therapies. Therefore, we hypothesized that similar increases in platelet reactivity could be identified in Native Americans, and that the presence of specific SNPs would in part explain differences in platelet reactivity. Over 50 Native American subjects consented to blood draw, and their platelets were stimulated with a variety of platelet agonists. Platelet reactivity was measured by both GPIIb/IIIa integrin conformational change and platelet alpha granule secretion. Early results suggest that found that Native American platelets are generally more sensitive to ADP and thrombin agonism, responding to lower concentrations than Caucasian platelets. We also identified SNPs present in receptor genes that are enriched in the highest-responding Native American subjects. As such, we provide evidence for the first time that SNP-correlated platelet reactivity may account for some of the increased level of thrombotic disorders in Native Americans.

**Name:** George Varghese **Institution:** Creighton University **Email:** gjv35727@creighton.edu **Research area:** Clinical-translational **Title:** Early detection of Squamous Cell Carcinoma by NADH Phasor FLIM in SKH1 Mice

**Authors:** George Varghese, Kelsey A. Jackson, Connor J. Kalhorn, Cecilia Myers, Thien Q. Tran, Daniel H. Wood, Laura A. Hansen, Michael G. Nichols, Department of Physics, Creighton University, NE 68178

**Abstract:** The hallmarks of cancer include metabolic and structural changes to tissue. These alterations manifest long before gross morphological abnormalities are visible to the human eye. Our research explores the application of Phasor-Fluorescence Lifetime Imaging Microscopy (FLIM) in the early detection of Squamous Cell Carcinoma via non-invasive optical biopsy. Mice are treated with chronic UV-radiation to generate skin cancer while being imaged periodically. We utilize Phasor-FLIM imaging of metabolic co-factors Nicotinamide Adenine Dinucleotide (NADH) and flavoproteins to assess the metabolic state of the imaged tissue. Images from regular microscopy sessions undergo sine-cosine transforms to allow for the generation of phasor-plots. These phasors allow for quantification of the sample’s NADH bound-to-free ratio, revealing metabolic changes before tumors have become visible. Previous trials have indicated a lower bound-to-free index in UV-exposed mice compared to sham irradiated controls, representative of increased glycolytic metabolism associated with cancer. In this study, we utilized a larger sample size while improving our microscope to allow for second harmonic generation imaging (SHG) of collagen. SHG imaging allows us to observe the architectural shifts caused by cancer.

This publication was made possible by grants from the National Institute for General Medical Science (NIGMS) (5P20GM103427), a component of the National Institutes of Health (NIH), and its contents are the sole responsibility of the authors and do not necessarily represent the official views of NIGMS or NIH.

**Name:** Shane Scholten **Institution:** Augustana University **Email:** sscholten@augie.edu **Research area:** Other

**Title:** Ischemic preconditioning effects on physical performance.

 **Abstract:** Initially used for cardioprotective measures, ischemic preconditioning (IPC) has transitioned into the athletic world as a noninvasive technique to improve one’s performance. Anaerobic cycling performance has shown to benefit from this technique; however, IPC’s effects on aerobic cycling performance has been inconclusive.
PURPOSE: To determine the acute effects of IPC on a 3-minute cycling time trial performance in active individuals.
METHODS: In a randomized, single-blind crossover study, 11 physically active individuals, nine men and two women (26.4 ± 10.7 yr), performed a 3 minute maximum effort cycling test preceded by alternating bilateral IPC (3 x 5 minute ischemia, 5 minute reperfusion) or SHAM (3 x 1 minute ischemia, 1 minute reperfusion). Both the IPC and SHAM protocols induced 100% occlusion using a Delfi Personal Tourniquet System (PTS). The PTS was used to individualize proper limb occlusion pressure for complete blood flow occlusion to the leg muscles distal to the blood pressure cuff.
RESULTS: Statistical significance was found between the type of treatment (SHAM vs IPC) and 3-minute time trial performance (p=0.03).
CONCLUSION: IPC was found to increase average power output across 3-minute time trial performance in active individuals.

**2:15-3:45 Neuroscience**

**(Co-Chairs: Drs. Kirkpatrick (KSU) and Dunavesky (UNMC))**

 **Name:** Nishama De Silva Mohotti **Institution:** The University of Kansas **Email:** nishama@ku.edu **Research area:** Neuroscience

**Title:** Defining lipid changes during demyelination & myelin repair using a novel genetic muse model

**Authors:** Nishama D.S Mohotti1, Rashmi B. Binjawadagi1, Meredith Hartley1
1Department of Chemistry, University of Kansas, Lawrence, KS, USA

**Abstract:** Multiple sclerosis is a chronic autoimmune, neurodegenerative central nervous system disease where the axonal myelin sheaths are subjected to repeated inflammatory episodes of demyelination resulting in disability in patients. Knowing that lipids are the main component in myelin membranes, identification of lipids and lipid signaling pathways is very crucial for the development of new therapeutics for multiple sclerosis. Previous lipidomic studies have been limited by the availability of mouse models that feature global demyelination and the ability to correlate myelin damage with disability. This study features the induced conditional knockout- myelin regulatory factor (iCKO- Myrf) mouse model, which has defined stages of myelin damage and repair has a measurable motor disability that correlates with peak demyelination. A full profile lipidomic analysis was performed on brain, spinal cord and serum samples at both demyelination and remyelination stages to map the lipid profile. Lipidomic dynamics will be analyzed to identify lipid signaling pathways that are critical during remyelination. This study will enable us to identify novel therapeutic targets for promoting remyelination, which would have clinical benefits for people living with multiple sclerosis.

**Name:** Jennifer Sexton **Institution:** University of Nebraska Medical Center **Email:** Jennifer.sexton@unmc.edu **Research area:** Neuroscience

**Title:** Investigating the association between Hippocampal volume and neuropsychological abilities vulnerable to Alzheimer's Disease: A developmental approach

 **Authors:** Jennifer N. Sexton, Connor J. Phipps, Lillian Behm, Thomas A. DeCesare, Abi M. Heller, Arthur C. Maerlender, Vaishali S. Phatak, Justin A. Cramer, James Blair, Daniel L. Murman, and David E. Warren

**Abstract:** Significant changes in neuropsychological abilities and brain structure are known to occur during childhood development. Improved memory ability, including memory for arbitrary relations, exemplifies cognitive changes that occur during periadolescence. This pattern suggests that brain regions associated with relational memory may exhibit associated structural changes. Our ongoing NIA-funded research project, the Polygenic Risk of Alzheimer’s Disease in Nebraska Kids (PRANK) study, measures brain structure, brain function, cognitive abilities, and Alzheimer’s polygenic risk score in periadolescent children (age 8-13). Here, we report preliminary data measuring the association between hippocampal volume and relational memory abilities in the study’s periadolescent sample (N = 40). Structural MRI data were collected using protocols adapted from the Human Connectome Project. Neuropsychological abilities included relational memory operationalized as performance on the Picture Sequence Memory Task (PSMT) from the NIH Toolbox. We then calculated the correlation between hippocampal volume and performance on PSMT. Our preliminary observations were consistent with positive correlations between regional hippocampal volume and memory performance on the PSMT. Future work from this study will investigate whether genetic risk for Alzheimer’s Disease is associated with individual differences in brain structure and outcomes on neuropsychological measures in early life.

**Name:** Danielle Germundson **Institution:** University of North Dakota School of Medicine and Health Sciences **Email:** danielle.germundso.1@und.edu **Research area:** Neuroscience **Title:** Repeated allergen exposure triggers neuroinflammation and behavioral changes in a mouse model of asymptomatic cow’s milk allergy

**Authors:** Danielle L. Germundson, Afrina Brishti, Nicholas A. Smith, and Kumi Nagamoto-Combs
Department of Biomedical Sciences and Clinical and Translational Science Graduate Program, University of North Dakota School of Medicine & Health Sciences, Grand Forks, ND

**Abstract:** Neuropsychiatric disorders are often comorbid with food allergies. Despite this association, the effects of allergen exposure on the brain, particularly when prolonged, are not understood. We hypothesized that repeated allergen consumption by mildly allergic individuals could sustain chronic inflammation, promoting behavioral changes via increased neuroinflammation. To test our hypothesis, we sensitized 4-week-old C57BL/6J male mice to a bovine whey allergen, β-lactoglobulin (BLG). Mice were then placed on a whey-containing diet for 2-weeks to simulate repeated allergen exposure, and their behavior was observed. Although BLG-sensitized mice did not exhibit visible allergic reactions, they showed depression-like behavior after allergen consumption. Despite having no anaphylaxis, elevated serum histamine and allergen-specific IgE indicated sensitization was successful. In addition, BLG-sensitized mouse brains had increased IgG extravasation and perivascular astrogliosis, suggestive of ‘leaky’ blood-brain barriers and neuroinflammation. Greater numbers of mast cells and histamine were also found in the brains of BLG-sensitized mice, potentially contributing to the increased vascular permeability. Together, our findings indicate that repeated allergen exposure significantly altered the behavior and brain physiology of BLG-sensitized mice. These results support the notion that mildly symptomatic food allergy can trigger or worsen neuropsychiatric symptoms and highlight the possibility of allergen avoidance to reduce neuroinflammation.

**Name:** Carly Baker **Institution:** Creighton University **Email:** carlybaker@creighton.edu **Research area:** Neuroscience

**Title:** Characterization of CPTII Knockdown on Zebrafish Body and Brain Development and Function

**Authors:** Carly Baker, Aaron Marta, and Annemarie Shibata, Department of Biology, Creighton University, Omaha NE 68178

**Abstract:** Carnitine palmitoyltransferase II (CPTII) facilitates the conversion of palmitoylcarnitine to palmitoyl-CoA. CPTII deficiency is associated with neurodevelopmental and neuropsychological disorders such as epilepsy, schizophrenia, and intellectual disabilities. The specific role of CPTII in the development of functional neural networks is unknown. We hypothesize that CPTII’s role in the carnitine shuttle is essential for proper metabolic intracellular signaling and a loss of function disrupts nervous system development. To investigate our hypothesis, transitional and splice-blocking morpholinos (0.5 µM) are used to knockdown CPTII expression in the zebrafish model system. At 2- and 5-days post CPTII knockdown, viability, morphological analyses, neural network structure, lipid deposition, mitochondrial function, and behavioral assessment will be compared to scrambled morpholino injected and uninjected zebrafish. We confirmed the loss of CPTII pre-mRNA through q-PCR and protein knockdown via LC-MS/MS. LC-MS/MS is also used to confirm specific changes in Palmitoyl-CoA associated with CPTII knockdown. Results show significant disruption of whole larval and central system development. These studies indicate a critical role for metabolic intracellular signaling in brain development and are likely to show significant effects on neurological function in future physiological studies.

**Name:** Anastasia Kerr-German  **Institution:** Boys Town National Research Hospital  **Email:** anastasia.kerr-german@boystown.org **Research area:** Neuroscience

**Title:** Moving Towards a viable characterization of the neurocognitive mechanisms underlying the development of ADHD **Abstract:** ADHD is a disorder impacting 9-11% of children and is defined by difficulties in vigilance, often measured using go/no-go (GNG) tasks. In older youth, ADHD symptoms are associated with dysfunction in dorsolateral prefrontal and parietal cortices during GNG. However, little is known about the early neurodevelopmental risk factors for ADHD due to the difficulty of using fMRI in very young children. The current study employed functional near-infrared spectroscopy (fNIRS) to investigate neural differences associated with ADHD risk (based on parental symptoms) in typically developing (TD) children (2-5-years old, N=40) and with ADHD in children with diagnoses (6-8-years old, N=16) during a GNG task. Controlling for age, increased risk of ADHD within TD youth and ADHD diagnosis was associated with significantly lower accuracy during low, but not high, frequency Go blocks. Neural data showed increased activation of right parietal cortex was associated with risk and diagnosis of ADHD during low frequency blocks. Notably, these data indicate similar pathophysiology between risk for ADHD based on parental ADHD symptoms and diagnosed ADHD. Using fNIRS may facilitate a better understanding of the neurodevelopment of ADHD, potentially leading to earlier diagnosis and intervention, and better outcomes.

**Name:** Lara Bergdolt **Institution:** University of Nebraska Medical Center **Email:** lara.bergdolt@unmc.edu **Research area:** Neuroscience

**Title:** Astrocytic contribution to audiogenic seizure susceptibility in a mouse model of fragile X syndrome

**Abstract:** Fragile X syndrome (FXS) is caused by silencing of the fmr1 gene, which encodes fragile X mental retardation protein (FMRP). Patients with FXS are often also diagnosed with autism spectrum disorder and exhibit additional symptoms which may include intellectual disability, seizures, and sensory hypersensitivity. The effects of FMRP silencing on astrocyte physiology and the contribution of astrocytes to FXS symptoms, particularly sensory hypersensitivity, remain understudied. We have found that astrocyte-specific deletion of FMRP in mice confers susceptibility to audiogenic seizures, an indication of auditory hypersensitivity, while selective restoration of FMRP in astrocytes decreases the propensity for audiogenic seizures. In addition, we have found enhanced spontaneous and ATP-induced somatic calcium signaling in astrocytes in acute brain slices from fmr1 knockout mice. Enhanced calcium signaling is normalized by pretreatment with a P2Y1 antagonist. Fmr1 knockout mice also exhibit enhanced calcium signaling in vivo. We also observed a smaller enhancement of ATP-induced calcium signaling in mice in which FMRP is selectively deleted in astrocytes. This suggests that the mechanisms underlying elevated calcium signaling in the knockout are both intrinsic and extrinsic, and that altered astrocytic function may contribute to sensory hypersensitivity in FXS.

**9:45-11:15 Drug Addiction and Targets**

**(Co-Chairs: Drs. Paulus (UO) and Bevins (UNL))**

 **Name:** Manali Kamath **Institution:** The University of Oklahoma Health Sciences Center **Email:** manali-kamath@ouhsc.edu **Research area:** Other

**Title:** The unfolded protein response is essential for the corneal pathogenesis of *Aspergillus fumigatus*

**Abstract:** Fungal keratitis (FK) is a potentially blinding infection of the cornea for which better treatments are required. The site of fungal growth during FK is the corneal stroma, which is rich in collagen and other proteins, but ostensibly poor in glucose or freely diffusible nutrients. We, therefore, predicted that (1) fungi breakdown these proteins as a primary nutrient source during infection, and (2) fungal pathways that support protein catabolism (e.g. protease secretion) represent important virulence factors and putative drug targets. Using a predominant agent of FK, Aspergillus fumigatus, the work described here supports both parts. First, fungal protease expression was up-regulated in A. fumigatus isolated from infected mouse corneas, suggesting the fungus is indeed catabolizing stromal protein. Second, an A. fumigatus mutant defective in protease secretion, ΔhacA, was unable to establish corneal infection in the murine model of FK. The hacA gene encodes a transcription factor that plays a critical role in the unfolded protein response (UPR), a pathway that detects and resolves the accumulation of misfolded proteins in the endoplasmic reticulum and promotes traffic through the ER-Golgi pathway. Future studies will determine if UPR repression during an active infection leads to reduced disease severity and improved visual outcomes.

**Name:** Nathan Zimmerman **Institution:** Creighton University **Email:** ndz94541@creighton.edu **Research area:** Drug Addition

**Title:** Effects of Psychopharmaceuticals on neuronal sterol synthesis

**Abstract:** Genetic mutations in sterol synthesis enzymes are characterized by elevated 7-DHC, reduced cholesterol and desmosterol, and altered acylcarnitine levels. Recently, our collaborators showed antipsychotics, antidepressants, and anti-arrhythmics alter sterol composition of neurons and astrocytes. These drugs caused an increase in 7-DHC and a reduction in desmosterol levels. Given the prevalence of neurological disorders associated with developmental deficiencies, novel in vivo model systems are needed to improve our understanding of how commonly prescribed drugs influence fetal body and nervous system development. Zebrafish are ideal for screening pharmaceutical effects on vertebrate development. Zebrafish and humans express many of the same genes needed for sterol synthesis. We will utilize zebrafish to test the hypothesis that exposure to pharmaceuticals will alter cholesterol biosynthesis and acylcarnitine levels and disrupt whole body and brain development resulting in abnormal behavior. Zebrafish will be exposed to one of 20 pharmaceuticals that alter sterol synthesis and cross the blood brain barrier. After drug exposure, zebrafish will be assessed for sterol synthesis, morphology, protein and RNA expression, neuronal network activity, and behavior. These tests will determine whether commonly prescribed pharmaceuticals that disrupt cholesterol and acylcarnitine synthesis and alter metabolism result in abnormalities in whole body and brain development and function.

**Name:** Sarah Alsuleiman **Institution:** University of Nebraska at Omaha **Email:** salsuleiman@unomaha.edu **Research area:** Other

**Title:** Bone marrow transcriptomics suggest immunomodulation of promising anti-Schistosoma analog SA01

**Authors:** Sarah Alsuleiman, Thomas Schulze, Andrew Neville, and Paul H. Davis
Department of Biology, University of Nebraska Omaha, 6001 Dodge St, Omaha, NE 68182

**Abstract:** Schistosomiasis, a commonly neglected tropical disease, is a waterborne parasitic worm infection able to infect through direct skin penetration. This disease affects approximately 270 million people worldwide and ranks only second to malaria as a leading infectious disease. Although some possible alternatives are emerging, currently, the most effective drug treatment is praziquantel (PZQ). However, PZQ is only effective against the adult stage of the worm, allowing juvenile worms to progress in the infection. Additionally, Schistosoma worms are developing resistance to this drug as reduced efficacy has been noted. Thus, the need for drug discovery and testing is increased. SA01, a worm clearing derivative of aryl hydantoin Ro 13-3978 is being investigated to treat Schistosomiasis. Previous data points to the compound acting on the host’s immune system as opposed to directly on the worms. Single cell transcriptomics was conducted, and a notable change was significant increase in neutrophil population. Furthermore, there were significant changes in the erythroidal lineage indicative of splenic erythropoiesis, which is consistent with an inflammation type response. To explore these immunological phenotypes, bone marrow transcriptomics is conducted to analyze expression patterns for genes associated with neutrophil granulopoiesis as well as splenic erythropoiesis to elucidate SA01’s mechanism of action.

**Name:** Julie Soukup **Institution:** Creighton University **Email:** jksoukup@creighton.edu **Research area:** Other

**Title:** Evolutionary conservation of ornithine decarboxylase antizyme pseudoknot RNA binding to spermine

**Authors:** Juliane K. Soukup, Samantha Stoupa, Spencer Thompson, Sid Venkatraman, Emma Curran, Diego Gomez, Rhiannon McCracken, and Garrett Soukup
Department of Chemistry & Biochemistry, Creighton University, Omaha, NE, USA

**Abstract:** Nearly all organisms possess the capability to synthesize polyamines, which are essential for cell growth and differentiation. Not surprisingly, the transport and metabolism of polyamines are highly regulated by complex feedback mechanisms. Ornithine decarboxylase (ODC) is the key regulatory enzyme in polyamine biosynthesis. Both ODC and cellular uptake of polyamines are inhibited by Ornithine Decarboxylase Antizyme (OAZ). Mammalian OAZ mRNAs further possess a pseudoknot (PK) structure. Although the role of the OAZ pseudoknot RNA element (further designated OAZ-PK) in polyamine biosynthesis has been investigated, it has not been examined as a distinct polyamine “sensor”.
 Riboswitches are elements within noncoding regions of mRNAs that directly bind to cellular metabolites and modulate gene expression. Many riboswitches provide a mechanism of feedback regulation for gene products within the biosynthetic pathway of the cognate metabolite. Although riboswitches are widespread among bacteria, no riboswitches have been found in animals. We propose that the highly conserved OAZ-PK RNA functions as a riboswitch. Utilizing in-line probing and equilibrium dialysis, apparent binding affinity and specificity for polyamines was determined. The mouse OAZ1-PK RNA binds to spermine with greater affinity than to other polyamines, and spermine binding to OAZ1-PK RNA specifically elicits conformational change, a fundamental property of riboswitches. Closely related spermine analogs (with identical or greater overall positive charge) have lesser affinity and specificity for the OAZ1-PK RNA.
 Our current work is focused on investigating OAZ-PK RNAs from other organisms. Variations in the structures of these RNAs may or may not result in similar functioning to the mouse OAZ1-PK RNA. The function of OAZ-PK RNA as a spermine “sensor” suggests a substantially broader distribution of riboswitches among eukaryotic organisms and represents a potential new drug target in a key metabolic process.

**Name:** Jetty Duffy-Matzner **Institution:** Augustana University **Email:** duffy@augie.edu **Research area:** Other **Title:** Chitosan, hyaluronic acid biopolymer (LbL) assembly on siloxy amino functionalized balafilcon A contact lenses

**Authors:** Ashlee Cain, Ted Van Alstyne, William Raymond, Whitney Twitero, Jetty Duffy-Matzner
Augustana University, Department of Chemistry and Biochemistry
2001 S. Summit Avenue, Sioux Falls, SD 57197

**Abstract:** Contact lenses are generally known for their vision-correcting and cosmetic purposes. This work targets potential remedies for dry eyes and other illnesses that could be more effective and less invasive than traditional treatments. Pure Vision 2 hybrid lenses underwent surface modification utilizing siloxy groups to attach primary amino groups onto the lens’ surface. Chitosan and hyaluronic acid, biopolymers that provide proven health benefits, were then applied to the treated contacts using an electrostatic layer by layer (LbL) technique. Fluorescent-tagged chitosan was synthesized and used to examine the LbL method. Protein deposition, surface charge, water contact angle, and wettability of the layered lenses were compared to untreated lenses. An antibiotic, norfloxacin, was incorporated via a modified LbL technique and tested for resistance to bacterial growth. Timolol, which reduces ocular pressure, was also layered onto lenses using the same method. The elution times of both drugs were measured. The wettability and water contact angle measurements revealed a higher hydrophilicity present in the layered contacts when compared to unlayered. The tagged chitosan data provided considerable proof that the LbL process occurred as theorized. Zeta potential measurements are ongoing to examine the surface charge of the lenses. These results suggest that hybrid lenses can successfully be modified via LbL techniques to increase both water retention and drug elution time.

**Name:** Caleb Sandall **Institution:** University of Nebraska at Omaha **Email:** csandall@unomaha.edu **Research area:** Other **Title:** Changes in Reactive Species Production Caused by the Novel Anti-Schistosomal Compound CS01

**Abstract:** Schistosomiasis is a condition caused by a parasitic worm infection that predominantly affects developing countries. We are investigating a novel drug-like compound, CS01, with demonstrated efficacy against worm infection, but which exhibits no observable effects on the worm itself. Preliminary data from our lab suggests that granulocyte surface markers are upregulated alongside these cells’ ability to produce reactive species in murine splenocytes post treatment. We examined the effects of this novel drug-like compound on granulocytes’ ability to produce reactive oxygen species using ATP and NADH with the goal to understand more about its possible function in vivo.

**9:45-11:15 Molecular Target Discovery and Development/Nanomedicine**

**(Co-Chairs: Drs. West (OU) and Guzman (KU)**

 **Name:** Suman Maharjan **Institution:** Oklahoma State University **Email:** suman.maharjan@okstate.edu **Research area:** Other

 **Title:** Cell shape variation in *Escherichia coli* with point mutations in *mreB*

**Authors:** Suman Maharjan, Jada Lusk, Ryan Sloan, Rose Bevienguevarr, and Randy Morgenstein

**Abstract:** The actin-homolog mreB is a crucial component of the rod-machinery that adds new peptidoglycan material for lateral elongation during growth. It is necessary for maintaining the rod shape of Escherichia coli and many other rod-shaped bacteria. MreB is functionally active as polymeric nanofilaments localized beneath the inner membrane along the long axis of the cell while avoiding the poles. As expected, cells lacking MreB or in the presence of depolymerizing agent A22 suffer loss of rod shape that ultimately leads to cell death. Previous studies looking at random mutations in MreB observed varying degrees of alteration in cell shape and size implying the effect of each amino acid residue for rod-shape dynamics is independent. Here, we have taken a systematic approach by creating an alanine-scanning library to better understand the role of each residue in MreB. We have analyzed over 250-point mutants and observed a varying degree of cell shape modulation. While most mutants-maintained rod-shape morphology with distortions in length and width, fourteen mutants are round-shaped. At this point, it appears certain residues and their positions are critical to retain wild-type rod shape. In addition, the ability to generate stable round shape cells suggests that the lethality of mreB deletion is not due to defects in cell wall synthesis, but another role for MreB in the cell.

**Name:** Isioma Akwanamnye  **Institution:** Chadron State College **Email:** isioma.akwanamnye@eagles.csc.edu **Research area:** Molecular Target Discovery and Development-Nanomedicine **Title:** The title of my presentation is the Effect of Curcumin on gene expression induced by the NF-KB pathway in Triple-Negative breast cancer

**Authors:** Isioma Akwanamnye\*, Lelisse Umeta, and Ann Marie Buchmann, Department of Physical and Life Sciences, Chadron State College, Chadron, Nebraska 69337

**Abstract:** Triple-negative breast cancer (TNBC) accounts for approximately 13 percent of all breast cancer cases. TNBC is characterized by a lack of expression of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptors (HER2) making conventional hormonal therapies less effective in treating this aggressive form of breast cancer. Therefore, de novo treatment models are necessary to targeting different pathway involved in triple-negative breast cancer. Curcumin, a major component of the spice turmeric extracted from the plant Curcuma longa, has long been recognized for its medicinal properties including the inhibition of cancer cell proliferation. The objective of this study was to investigate the effects of curcumin in inhibiting NF-kB pathway in triple-negative breast cancer cells focusing on the expression of NF-kB responsive genes. MDA-MB 231 TNBC cells were treated with different concentrations of curcumin (4M, 8M, 12M & 16M dissolved in DMSO) at 24 & 48-hours intervals and compared to a DMSO-treated control group. RNA was extracted from cells and converted to cDNA using reverse transcriptase protocols. Real-time quantitative PCR (RT-qPCR) was used to quantify expression of different genes using GAPDH as a housekeeping gene control for each treatment concentration. The 2-CT method was used to analyze the relative changes in gene expression from RT-qPCR. After treatment with curcumin for 24 -48 hours, the expression levels of cyclin D1 and c-myc at different concentrations (4M, 8M, 12M & 16M) were decreased compared with those of the control group. These results indicate that curcumin is able to decrease the expression of genes induced by the NF-kB pathway in TNBC.

**Name:** Sadegh Nikfarjam **Institution:** University of Central Oklahoma **Email:** snikfarjam@uco.edu **Research area:** Other

**Title:** Laser microgrooving and nanofiber membrane application for total knee replacement implants using a Caprine model

**Authors:** Morshed Khandaker, Sadegh Nikfarjam, Karim Kari, Helga Progri, Erik Clary, Amgad Haleem

**Abstract:** Aseptic loosening is a well-recognized phenomenon in cementless total knee replacement (TKR) and often carries severe consequences for the patient. Recently, we developed and tested in vitro a novel strategy for enhancing osseointegration and acute mechanical stability of orthopedic implants that employ laser micro grooving and nanofiber membrane application at the bone- implant interface. We report here the results from a pilot study employing three skeletally mature goats. For one goat, the arthroplasty implant surfaces were unaltered from the manufacturer’s mirror-polished (MP) condition. For the other two goats, the TT bone-contact surface was laser-micro grooved (150 μm depth, 200 μm width, 200 μm spacing) and coated with polycaprolactone (PCL) nanofibers. Following surgery, animals received appropriate analgesic therapy and rehabilitative care. Post- operative monitoring included assessment of mentation, vital signs, pain level, digestive function and limb status. By the study’s end all animals had recovered a pre-surgery range of motion in the operated knee and exhibited typical bony changes on radiographic follow-up. Histomorphometric analysis of explanted bone-TT constructs showed the increased new bone surface area in the Lasered - NFM sample compared with the MP sample, suggesting that microgrooves and/or PCL nanofiber coating may improve clinical performance of the implant.

**Name:** Evelyn Carreto **Institution:** University of Nebraska Medical Center **Email:** ecarretoguevara@unmc.edu **Research area:** Molecular Target Discovery and Development-Nanomedicine
**Title:** Investigation of Molecular Adducts Formed with a Novel NTSR1-targetted Radiotherapeutic in the Pancreatic Cancer Cell Line

**Authors:** Evelyn Carreto Guevara, Sue Brusnahan, Katherine Brake, Sadie Allen, and Jered Garrison

**Abstract:** Neurotensin receptor 1 (NTSR1) is upregulated in multiple types of cancer such as colorectal, prostate, and pancreatic. NTSR1 is negligibly expressed in most normal tissues. The Garrison lab at UNMC focuses on the development of radiotherapeutic drugs that target and destroy cancer cells. Their laboratory has synthesized Compound 7 a novel NTSR1-radiotherapeutic with a cysteine cathepsin (CC) trapping agent that increases the retention time in tumors leading to greater radiation dose delivery and cancer cell death. The CC trapping agent forms macromolecular adducts within the endolysosomal compartments of cancer cells. To better elucidate the mechanism and cellular trafficking of this drug and its adducts, we will perform internalization and efflux studies as well as centrifugal filtration techniques to isolate and quantitate formed macromolecular adducts. The control for these experiments will be 177Lu-3BP-227, an NTSR1-targeted agent currently in clinical trials. Both the experimental and control agents will be applied to wells containing cultured HT-29. PC-3, and AsPC-1 cells (NTSR1-positive). Afterwards, we will take the extracellular medium and perform spin filter analysis to separate the radiolabeled components by molecular weight. We expect to find a higher radioactive macromolecule percentage in the extracellular media of the experimental compound compared to the control.

**Name:** Vivek Swami **Institution:** University of Central Oklahoma **Email:** vswami1@uco.edu **Research area:** Other

**Title:** The title of my project is Effect of PCL nanofiber support of an in vitro skin equivalent

 **Authors:** Vivek Swami, Melville Vaughan, PhD, & Morshed Khandaker, PhD

**Abstract:** The goal of this project was to determine the effects of Polycaprolactone (PCL) electrospun nanofibers (ENF) on the generation of skin equivalents composed of collagen, fibroblasts, and keratinocytes. Skin equivalents require mechanical tension to study myofibroblast phenotype induction; thus we used a plastic ring suspended within the collagen to allow tension generation. We prepared skin equivalents with or without tension rings, in the presence or absence of PCL-ENF sheets. Fibroblasts, collagen, +/- tension ring, +/- PCL-ENF were mixed together and allowed to polymerize into a dermal equivalent; culture continued to allow contraction or tension generation. Then, keratinocytes were plated atop the tissues to form a skin equivalent. Subsequent culture at the air/liquid interface (ALI) was conducted to fully mature the tissues; optical coherence tomography was used to monitor culture. 3-week ALI cultures were processed for histological staining. We observed PCL-ENF dermal equivalents were able to generate tension similar to tissues with a plastic ring. The epidermis of skin equivalents appeared similar under the four tested conditions. In some cases, spaces developed between PCL-ENF and collagen; however, this did not affect establishment of dermal or skin equivalents. These models will be useful to study myofibroblasts in fibrotic or wound healing studies.

**Name:** Emily Gilbert **Institution:** College of Saint Mary **Email:** egilbert0586@csm.edu **Research area:** Molecular Target Discovery and Development-Nanomedicine
**Title:** The formulation, development, and analytical characterization of polyphenolic combination

**Authors:** Emily Gilbert, Stacy Thornton, and Dr. Dunesh Kumari\*
\* College of Saint Mary

**Abstract:** Curcumin and quercetin are two naturally occurring antioxidants that inhibit free radicals, reduce superoxide anions and peroxides, and inhibit low-density lipoprotein oxidation and lipid peroxidation. Preliminary studies have shown that these antioxidants can be used to treat and prevent chronic conditions such as cancer and diabetes, but both are very limited in their therapeutic usage due to their low oral bioavailability, gastric permeability, and solubility. This makes it difficult for either drug to reach active sites outside of the gastrointestinal tract. Novel formulations of curcumin-quercetin and their combinations using various excipients; UV-spectroscopic method will be developed in the future for the simultaneous detection of curcumin and quercetin in the developed formulations. Further, drug release studies from the formulation will be carried out using Slide-A-Lyzer Dialysis Cassette.

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**12:30-1:45 INBRE Undergraduate Rising Stars**

**(Julie Soukup, CU)**

 **Name:** Johnny Dinh Phan **Institution:** K-INBRE: University of Kansas Medical Center  **Email:** jdinhphan@ku.edu **Research area:** Other

**Title: TBA**

**Abstract:** Polycystic kidney disease (PKD) is a genetic disease characterized by multiple cysts in the kidneys which enlarge overtime and lead to end-stage renal disease. The incidence of autosomal dominant polycystic kidney disease (ADPKD) is 1/1000 births. About 85% of ADPKD cases have mutations in polycystin 1 (PC1) and the remaining 15% in polycystin 2 (PC2) (proteins encoded by PKD1 and PKD2 respectively). Disruption of multiple signaling and metabolic pathways has been reported in PKD. Previously, we used an iron-chelating drug called ciclopirox olamine (CPX-O) and found that CPX-O ameliorated disease progression in a PKD mouse model. Additionally, CPX-O decreased ferritin levels of the cells and tissues. This led us to identify that iron/ferritin axis is affected in PKD. We found that ferritin levels are elevated in renal epithelial cells from ADPKD patients as well as in a PKD mouse model. Messenger RNA levels of iron-transport protein ferroportin (FPN1) increased and heme oxygenase 1 (HMOX) decreased in ADPKD samples. To determine whether iron and ferritin are important in cyst growth, we grew mini-cysts from ADPKD cells in culture and treated with ferritin or apoferritin (ferritin with no iron), with or without CPX-O. Both ferritin and apoferritin induced cyst enlargement while presence of CPX-O reduced ferritin and apoferritin induced cyst enlargement, suggesting that CPX-O works in an iron-independent manner via ferritin to reduce cyst formation. Taken together, our studies identify ferritin/iron dysregulation as another pathway implicated in PKD and show that CPX-O may qualify as an alternate drug in PKD treatment.

**Name:** Elizabeth Holmes\* & Jason Becker\*

**\***Both authors contributed equally; both will be presenting

**Institution:** Augustana University **Email:** eholmes18@ole.augie.edu **Research area:** Other **Title:** Antimicrobial effects of placenta on*Staphylococcus aureus* biofilms

**Authors:** Ellie Holmes & Jason Becker

**Abstract:** Previous work in our lab has shown that placenta extract has antimicrobial activity on suspensions of bacterial cells. Here, we test the ability of placenta extracts to inhibit biofilm formation. Placentas from four different species were separated into maternal and fetal portions. S. aureus cells were grown in the presence of either maternal or fetal extracts and biofilm and planktonic growth were measured. Several of the placenta samples inhibited biofilm growth, with the fetal portion of cow placenta being the most effective. Consistent with previous results, this activity was enhanced in boiled extracts. Exposure of mature biofilms to placenta extracts did not disrupt the biofilm; however, it did result in damage to cells in the biofilm. The results of this research suggest a promising avenue for the use of placenta tissue in wound treatment and could lead to a greater understanding of role of placenta in innate immunity.

**Name:** LeeAnna Lui **Institution:** University of Nebraska at Omaha **Email:** llui@unomaha.edu **Research area:** Other

**Title:** Developing a combinational drug therapy against the chronic stage of *Toxoplasma gondii*

**Authors:** LeeAnna M. Lui1, Austin G. Sanford1, Alex Wallick1, Braydon Dreher1, and Paul H. Davis1
1Department of Biology, University of Nebraska at Omaha, 6001 Dodge Street, Omaha, NE 68182

**Abstract:** Toxoplasma gondii is an intracellular parasite that infects 30% of the world’s population. Toxoplasmosis, the disease caused by T. gondii infection, causes mild cold symptoms in its host initially. Existing in its acute stage, T. gondii replicates and infects quickly. However, weeks after infection, the parasite transforms into a slow replicating, bradyzoite stage that forms within cells as cysts. As bradyzoites, T. gondii forms in the host’s brain, eyes, and muscle tissue. Currently, there is no treatment for this cyst stage, which can reemerge and cause lethal toxoplasmic encephalitis. Our work suggests that a novel combination of already approved drugs significantly reduces and potentially eradicates cyst burden. Through in vitro tissue culture and in vivo murine drug studies, we examine the efficacy of this cocktail and its ability to clear cyst burden in chronic infection models. If successful, we will be closer to creating a combinational approach with FDA approved drugs that eradicate the chronic infection of T. gondii.

**Name:** Nicholas Bergum **Institution:** University of North Dakota **Email:** nicholas.bergum@und.edu **Research area:** Other

**Title:** Chronic Exposure to Arsenic Increases the Invasiveness of the Luminal Bladder Cancer Cell Line, RT4

**Abstract:** The bladder is a target organ for inorganic arsenic, a carcinogen and common environmental contaminant found in soil and water. Urothelial carcinoma (UC) is the most common type of bladder cancer (BC). Urothelial carcinoma can be molecularly sub-typed as luminal or basal. We hypothesized that chronic arsenic exposure to a luminal bladder cancer would lead to development of basal characteristics and become more aggressive. We treated the human bladder cancer RT4 cell line (luminal sub-type) with 1 µM arsenite (As3+) for twenty passages. Throughout the study, we evaluated key luminal and basal gene/protein markers in vitro and at passage twenty, injected the cells into athymic mice to evaluate tumor histology and measure protein markers using immunohistochemistry in vivo. Our data indicates that chronic As3+ treatment altered cellular morphology and decreased several luminal markers in cell culture. The tumors generated from the As3+-exposed cells histologically looked similar to the parents (non-treated) cells, however, they appeared to be more invasive to the liver and displayed elevated levels of some basal markers. In conclusion, our study demonstrates that chronic As3+ exposure is able to convert a non-invasive luminal sub-type of bladder cancer to an invasive form that has acquired some basal characteristics.

**Name:** Emily Bedea **Institution:** Southwestern Oklahoma State University **Email:** bedeae@student.swosu.edu **Research area:** Other

**Title:** Identification and Characterization of an Important Metabolic Enzyme from Streptococcus Sanguinis

**Abstract:** Streptococcus sanguinis is a pathobiont associated with healthy oral biofilms in humans. S. sanguinis is one of the leading causes of infective endocarditis (IE) and its pathogenesis is linked to its ability to survive in blood. Survival in blood requires nutrients which are scarce in vivo. Pathogens overcome this scarcity by upregulating metabolic pathways required for the biosynthesis of nutrients. Several enzymes involved in biosynthesis of these nutrients utilize bicarbonate. Carbonic anhydrase (CA) catalyzes the hydration of CO2 to bicarbonate. Several studies have shown that inactivating CA’s negatively impacts virulence in pathogens. The goal of this study is to purify CA from S. sanguinis for biochemical and structural studies. We identified an 18.2 kDa protein in S. sanguinis using BLAST analysis with homology to well-studied β-CA’s, and SsaCanB has a α/β fold typical of β-CA’s. In order to over-express SsaCanB, the gene coding for SsaCanB was cloned into the pET28a using traditional cloning strategies. The construct was then transformed into E. coli BL21(DE3) and SsaCanB was over-expressed. SDS-PAGE analysis revealed 19.8 kDa band indicating successful over-expression of SsaCanB. Overexpressed SsaCanB was purified using immobilized metal affinity chromatography. Purified SsaCanB was found to have CA activity using an in-gel protonography assay.