Research Core Fair 2024- Submitted abstracts

Earth, Ocean and Environment

Poster #1
First Author: Allison Brown
PI: Besim Dragovic
Title: Unraveling the Molybdenum (Mo) Cycle at the Subduction Interface: A case study from the Ligurian Alps
Abstract:
Heavy Mo isotope compositions in arc lavas have been interpreted to have resulted from the reactive flow of serpentinite-derived fluids through subducted crustal rocks under oxidizing conditions, while light Mo is retained in the residual subducted oceanic rocks1 (in phases like rutile, ilmenite). However, the effect of high-pressure (HP) metamorphism and metasomatism on Mo systematics remains enigmatic. This study attempts to a) distinguish Mo systematics among exhumed Fe-Ti metagabbros and serpentinites from the Voltri Massif of the Ligurian Alps and b) evaluate the (re)distribution of Mo and its isotopes formed by HP fluid-mediated mass transfer by analyzing a metasomatic reaction zone between juxtaposed serpentinite and metagabbro, wherein serpentinite-derived fluids have been suggested to have infiltrated a large hm-scale metagabbroic body.2 We present both the variability within and correlations between Mo isotopes, [Mo], [fluid-mobile elements; FMEs], and Fe3+/ΣFetotal. Overall, metagabbros (n = 36) across the Voltri Massif exhibit a range of [Mo] (0.07 to 4.4 µg/g; avg. = 1.0 µg/g) and δ98/95Mo (-0.36‰ to 0.93‰; avg. = -0.08‰), comparable to MORB1 (6.1 µg/g and -0.16‰, respectively). Serpentinites (n = 12) exhibit a range of [Mo] (0.01 to 1.9 µg/g; avg. = 0.45 µg/g) and δ98/95Mo (-0.39‰ to 0.49‰; avg. = 0.05‰), displaying overall higher [Mo] and lower δ98/95Mo, compared to oceanic serpentinized peridotite3 (0.11 µg/g and 1.1‰).
For the aforementioned reaction zone, systematic trends in [Mo], [FMEs], Fe3+/ΣFetotal, and δ98/95Mo exist. Metagabbros at the core of the gabbro body maintain MORB-like [Mo] and δ98/95Mo values and low [FMEs], remaining largely unaltered by metasomatism. Metagabbros proximal to the contact with the serpentinite display lower [Mo], Fe3+/ΣFetotal, and δ98/95Mo. Notably, samples at an intermediate distance from the contact (~0.5 m) display elevated δ98/95Mo, [FMEs] and Fe3+/ΣFetotal.
We suggest fluid-mediated mass transfer between serpentinite and crustal rocks as a possible mechanism for generating isotopically heavy Mo that can be delivered to the source of arc magmas. This study helps bridge the gap in understanding the fate of Mo in subduction zones.
1Chen, et al. 2019, Nat. Comm.
2Codillo et al., 2022, G3
3Rojas-Kolomiets et al., 2023, EPSL

Poster # 2
First Author: Gabriel de Souza Franco
PI: Michael Bizimis
Title: Evidence for the opening of Drake Passage before 41Myr using fossil shark teeth from La Meseta Formation, Seymour Island, Antarctica
Abstract:
The opening of Drake Passage allowed the initiation of the Circumpolar Antarctic Current, thus shielding Antarctica from warmer equatorial waters. While the timing of this event has been traced back to 41Myr ago, it is poorly constrained.

Here we test the timing of Drake Passage opening through the use of rare earth element (REE) concentrations, strontium, and neodymium isotope analyses on fossil shark teeth and neodymium isotopes on sediments from the Eocene La Meseta Formation units. Still, this Formation has no age consensus in the literature.
The shark teeth εNd vary from -7 to -4, between present day εNd Pacific and Atlantic seawater values, and typically higher than associated sediments (εNd = -9 to -6) while 87Sr/86Sr show a narrow range 0.707722 to 0.707775. The PAAS-normalized REE patterns show enrichment in the middle ones with respect to both light and heavy ones and no cerium anomalies.
The REE results indicate that the shark teeth underwent some diagenetic alteration. Nevertheless, the Nd isotopic composition of the sediments is similar to the least radiogenic shark teeth, thus implying that there must be at least one end-member whose composition is at least as radiogenic as the most radiogenic teeth. Consequently, the range of εNd in shark still records some of their seawater equivalent signal. Considering the shark teeth were deposited in the Atlantic sector of the Southern Ocean, an Atlantic seawater end-member is a requirement, whose composition is also similar to the sediments in question. The most radiogenic composition, nonetheless, is ascribed to Pacific seawater, hence suggesting Pacific water influx and that Drake Passage was open when La Meseta was deposited.
The Sr isotopic results are consistent with the majority of the current age models for La Meseta deposition. Regardless of which age model is used, however, our data suggests the Drake Passage opened earlier than 41Myr, as all models allocate the two basal La Meseta units as older than this age.

Poster # 3
First Author: Reece Hammond
PI: Michael Bizimis
Title: Hf-Nd-Sr isotope systematics of Alaskan ophiolite complexes: Implications for the origin of marginal ocean basins in East Central Alaska.
Abstract:
Alaska reflects a complex history of accretion of disparate allochthonous terranes. Maficultramafic complexes thought to represent variably complete sections of oceanic lithosphere are presumed to define the paleo boundaries and/or demarcate margins of the accreted allochthonous assemblages in Alaska. We present major, trace-element and Sr-Nd-Hf radiogenic isotopic data of gabbro, diabase and pyroxenite samples from four Paleozoic to Jurassic mafic-ultramafic complexes in interior Alaska: Livengood (ca. 550 Ma), Seventymile (ca. 240 Ma), Kanuti (≤ 180 Ma) and Rampart (ca. 250 Ma). The purpose is to provide insights into their magmatic origin and implications for the tectonic evolution of east-central Alaska.
The Livengood and Seventymile samples have εNd(i) and εHf(i) values that generally overlap Pacific MORB (εNd(i)~ 9-11; εHf(i) ~11-15) . Samples from both assemblages show smooth, LREE depleted patterns and lack HFSE depletions, similar to N-MORBs. The Kanuti complex samples have more variable εNd(i) and εHf(i) that extend to values lower than Pacific MORB. The
LREE/HREE ratios correlate with εNd(i) and εHf(i), indicative of a mixed magma source. They also lack the distinct Nb-Ta depletions, or Pb enrichments, characteristic of arc magmas. The Rampart complex has εNd(i) and εHf(i) values of ~4-5, and 9-11 respectively, with E-MORB-like LREE enrichments and slight Nb-Ta depletions. The pyroxenites are isotopically more depleted than the diabases, suggesting different magma sources.
We interpret the data to suggest that the Seventymile samples represent a marginal basin between ancestral North America and the Yukon-Tanana allochthon with minimal subduction influence. The older Livengood, with a similar mantle source as the Seventymile, may represent earlier obducted oceanic lithosphere now found within the allochthonous assemblage. Assuming Kanuti is part of the Angayucham Terrane of Arctic Alaska, its MORB-EMORB composition suggests an origin as a marginal basin that formed as a consequence of southward subduction at the Koyukuk terrane margin. Rampart still has an ambiguous origin, but provisional data are generally more elementally and isotopically enriched than for the other three mafic complexes, with more of an arc signature.

Poster # 4
First Author: Owen Jensen
PI: Gene Yogodzinski
Title: Boron isotope evidence for deep-slab fluids in Aleutian magmas
Abstract:
Boron (B) abundance and isotope systematics in lavas from the Aleutian volcanic arc point to three sources. Lavas from the eastern Aleutian Islands appear to point to B-rich sources dominated by subducted sediment and altered oceanic crust (AOC). A subset of Aleutian island lavas with relatively low, isotopically light B contents may point to a source in AOC that has lost 11B in prior episodes of dehydration, but more work is needed to better define this source. Compared to arc lavas globally, western Aleutian seafloor lavas have unusually heavy B that is negatively correlated with B concentrations. The heaviest B occurs in samples that have trace element and radiogenic isotope characteristics interpreted to result from partial melting of metamorphosed subducted crust. These lavas point to a B source that contains a small but isotopically heavy B reservoir that is only revealed in the western Aleutians, where the effect of B-rich sediment is removed. This source may be serpentinite in the mantle section of the subducting plate. Dewatering of such "deep-slab serpentinite" into overlying crust that is 200-300° hotter is likely to drive flux melting within the crust. Our dataset provides the most direct geochemical evidence to date for this deep-slab fluid source, the existence of which has so far been indirectly inferred from geophysical and geochemical evidence.

Poster # 5
First Author: Ekaterina Rojas Kolomiets
PI: Michael Bizimis
Title: Light Mo isotopes in sediment cores outboard the Aleutian arc: implications for the Mo cycle in subduction zones
Abstract:
Marine sediments contribute importantly to the chemical composition of magmas produced in subduction zones. Subducting sediments are thought to carry heavy Mo isotopes to depths where subduction magmas are produced. Therefore, heavy Mo isotopes observed in the associated erupted volcanic rocks are often attributed to sediment sources. However, available marine sediment data show high variability in Mo isotopes suggesting that the role of subducted sediments in the arc magmatism is more complex than previously thought. Here, we explore the influence of subducted sediments on the Mo budget of the Aleutian arc by analyzing Mo isotope compositions (δ98/95Mo, relative to NIST 3134) and Mo concentrations (in µg/g) in sediments from ODP 886C (n= 22, 72 m thick), DSDP 183 (n=12, 500 m thick), DSDP 178 (n =10, 777 m thick) and IODP 1417 (n = 9, 708 m thick) cores outboard the Aleutian arc. ODP 886C sediments show a wide range of δ98/95Mo (–2.0 to +1‰) and highly variable Mo concentrations (0.19-1121 µg/g). DSDP 183 sediments have less variable Mo concentrations (0.40-33 µg/g) but also show a wide range of δ98/95Mo (–1.2 to +0.26‰). Sediments from DSDP 178 have a significant range of Mo concentrations (0.45-9.08 µg/g) and the heaviest δ98/95Mo (–0.97 to +1.23) of all cores analyzed in this study. Samples from IODP 1417 display less variable δ98/95Mo (–0.24 to +0.32‰) and Mo concentrations (0.36-4.12 µg/g). The extreme variability of the Mo isotope systematics of these sediments creates large uncertainty in bulk core δ98/95Mo and Mo concentrations estimates. Nonetheless, current estimates for the mean-weighted (weighted by density and thickness) Mo isotope compositions of all sediment cores are light and overlap the MORB (Mid Ocean Ridge Basalt)/mantle range, suggesting that the sediment source for Mo in Aleutian arc magmas may be indistinguishable from mantle contributions. Moreover, the high Mo concentrations (up to 1000 times higher than subducting oceanic crust and mantle) suggest that subducted sediments with predominantly light Mo isotopes should dominate the Mo budget of the Aleutian arc. An important implication from these data is that the sediments outboard the Aleutian arc do not carry the high δ98/95Mo needed to explain the heaviest Mo isotopes

(+0.30%) of Korovin, Seguam and Yunaska lavas. Instead, a serpentinite source with high δ98/95Mo (Rojas-Kolomiets et al., 2023 – EPSL) introduced by the subduction of the Amlia Fracture Zone is likely the dominant source of isotopically heavy Mo in that region of the arc.

Poster # 6 and "Lightning Talk"
First Author: Lance Tully
PI: David L. Barbeau
Title: From the mountains to the sea: Advancing our knowledge of source-to-sink sediment dynamics through detrital zircon geochronology in the Santee River watershed, South Carolina
Abstract:

With implications to sediment budgets, nutrient and contaminant transport, and climate change, a vitally important problem in the Earth sciences is understanding how materials transfer from geologic 'sources' to 'sinks'. Advances in technology (e.g., laser-ablation plasma mass spectrometry) provide powerful sediment provenance tools for understanding source-to-sink sediment dynamics through detrital-zircon geochronology. Despite the tremendous insight into geological problems such advances have enabled, assumptions commonly made during sediment provenance studies could lead to misinterpretations of data. For example, these studies generally assume that sediments are transported geologically instantaneously with little to no fractionation, and therefore, that sedimentary deposits (i.e., sinks) are representative of the source geology from which they were derived. Relatively few studies have sought to challenge and better understand the mechanisms behind these assumptions.

Preliminary results presented herein reveal discrepancies in the observed detrital-zircon age populations in continental shelf samples off-shore of the Santee River delta in South Carolina from what would be expected based on bedrock age characterizations of their up-dip source geologic units. In specific, we have observed a deficiency (approximately 5x less than anticipated) of Neoproterozoic 'Pan-African' zircons in the Santee shelf deposits. This is surprising given that much of the Santee River watershed consists of the 'Pan-African' Carolina Zone, the geologic units of which contain zircons of predominately Neoproterozoic ages. Leading potential hypotheses to explain this discrepancy include: (1) the recycling of 'Pan-African' poor sediments from pre-existing coastal plain deposits; (2) variability related to source rock zircon fertility; and/or (3) "missing" zircons due to sediment fractionation along the transport pathway.

This project sets the stage to test these hypotheses in the next phases of my research. Future work includes detrital-zircon analysis of sediment samples of Cretaceous and younger-aged coastal plain sediments and modern fluvial samples collected from strategic locations from a variety of geological terranes within the Santee River Watershed. Results from this work should yield greater insight into the source-to-sink mechanisms at play within the watershed, broadly applicable to numerous fluvial/coastal systems, and improve the growing detrital-zircon research community's ability to address important geological questions with greater certainty.

Life Sciences/ Cancer

Poster # 32 and "Lightning Talk"
First Author: Niti Jani
PI: Marj Pena
Title: Multiple exposures to antibiotics and increased risk of colorectal cancer
Abstract:
Colorectal cancer (CRC) is the second leading cause of cancer related deaths in the United States and worldwide. When CRC is diagnosed in younger patients (less than 55 years) it is known as early onset colorectal cancer (EOCRC). EOCRC is a global phenomenon whose incidence and mortality has been constantly increasing. EOCRC

incidences increased from 11% to 20% between 1995 to 2019 and is expected to increase by 140% by 2030. The cause and mechanism of EOCRC are unknown. Based on our current knowledge of the disease we believe that exposure to certain exposomes during childhood and young adult years can increase the risk of EOCRC development. In our study, we hypothesized that early life exposure to antibiotic causes dysbiosis and inflammation in the colon which leads to mutation and epigenetic alterations that promotes EOCRC. We treated A/J mice multiple times with commonly prescribed pediatric antibiotics and then exposed them to azoxymethane carcinogen to develop tumors. Our results showed higher tumor burden, systemic inflammation and increased immune cell infiltration in the colon of antibiotic treated mice compared to control mice. Moreover, antibiotic treatment caused dysbiosis in the gut and increased abundance of certain bacterial families in antibiotic treated mice. One of these bacterial species is suspected to be carcinogenic by other studies. Thus, our results suggest possible involvement of antibiotics on increased risk of EOCRC.

Poster # 34
First Author: Zach Mack
PI: Eugenia Broude
Title: Adaptation of breast cancer cells to a CDK4/6 inhibitor
Abstract:
Inhibitors of CDK4/6 have become a major addition to the clinical arsenal against estrogen receptor (ER)-positive breast cancers. In particular, CDK4/6 inhibitor palbociclib (IBRANCETM) has been approved for the treatment of ER-positive breast cancers (in combination with hormone therapy). However, palbociclib treatment eventually fails due to the development of resistance. Laboratory studies based on long-term drug selection revealed several mechanisms of palbociclib resistance. However, it is now understood that drug resistance may first emerge as massive non-genetic adaptation of tumor cells to an anticancer drug, before stable resistant mutants can be selected. The goals of our study were to determine how breast cancer cells adapt to palbociclib, and whether inhibition of CDK8/19 Mediator kinase, a broad-spectrum regulator of transcriptional reprogramming, could affect the process of adaptation to palbociclib.
We have characterized the dynamics of cell growth of MCF7 ER+ breast cancer cells in the presence of different concentrations of palbociclib and found that the cells undergo rapid adaptation to the drug and resume cell growth within 2-3 weeks. Similar results were obtained with other cell lines, including ZR75-1 ER+ breast cancer and SW-620 colon cancer cells, where adaptation took longer (3-4 weeks). Although the adapted cells proliferated in the presence of palbociclib, their resistance was unstable, indicating its non-genetic nature. Remarkably, palbociclib adaptation in all the cell lines was prevented by the addition of CDK8/19 inhibitors (which by themselves had only a moderate antiproliferative effect). To investigate whether palbociclib adaptation is a variable stochastic process, we set up 10 concurrent adaptation studies of MCF-7 cells exposed to 500 nM palbociclib. Adaptation was observed at approximately the same time (28 days) in all 10 replicates, suggesting a similar non-stochastic process.
To delineate transcriptional features of CDK8/19-dependent adaptation to palbociclib, we carried out RNA-Seq analysis of MCF-7 cells after 28-day adaptation and after short-term (3 days) exposure to palbociclib, with or without CDK8/19 inhibitor SNX631. Remarkably, all 10 palbociclib-adapted cell populations showed very similar changes in gene expression, including striking upregulation of interferon-γ and interferon-α pathways. The biggest effects of CDK8/19 inhibition on genes affected by 3-day treatment with palbociclib were downregulation of palbociclib-inducible genes and upregulation of palbociclib-inhibited genes. Our analysis identified a number of changes in gene expression that were associated with both 3-day and 28-day palbociclib treatment and counteracted by CDK8/19 inhibition, as potential mediators of CDK8/19-dependent transcriptional adaptation. One of these changes is upregulation of CDK6, which has been previously linked to palbociclib resistance.
We have also characterized the heterogeneity of MCF-7 cells in regard to their inherent sensitivity to palbociclib, SNX631, and their combination. 44 single-cell clones were isolated and characterized by 7-day growth inhibition

assays. This set of clones showed a wide range of palbociclib resistance but a narrower range of SNX631 sensitivity. All the clones were strongly inhibited when palbociclib was combined with SNX631. These results suggest that palbociclib adaptation is a robust and rapid process driven by phenotypic heterogeneity and by transcriptional reprogramming mediated by CDK8/19.

Poster # 35
First Author: Alissa Marchione
PI: Katie Kathrein
Title: TARGETED SMALL MOLECULE INHIBITORS REMEDIATE THE LOSS OF ING4 EXPRESSION IN SEVERAL CANCERS
Abstract:
Inhibitor of growth 4 (ING4) has been identified as a tumor suppressor protein, yet the exact mechanism of action has not been fully characterized. Previously, ING4 has been shown to promote stem cell-like characteristics in malignant cells through direct interactions with the p53, Hif-1a, c-Myc, and NF-kB pathways. To regulate NF-kB, ING4 binds to the p65 component of NF-kB, a transcription factor complex that promotes cytokine expression. Our laboratory has shown that knockdown of Ing4 expression in zebrafish results in loss of hematopoietic stem and progenitor cell (HSPC) specification and a significant increase in NF-kB target gene expression. Knockdown of NF-kB expression in Ing4 deficient zebrafish recovered HSPC marker expression in the aorta suggesting that NF-kB inhibition could remediate the loss of Ing4 expression. Similarly, several small molecule inhibitors of the NF-kB pathway with varying mechanisms rescue of HSPC marker staining in the zebrafish aorta. Using the NIH DCTD mechanistic drug set VI, we further investigated small molecules that abet the loss of HSPC in our zebrafish Ing4 knockdown model and rescued ING4 deficient phenotypes. Utilizing the targeted small molecules to treat ING4-deficient cancer cell lines T47D and HCT116, we saw significantly reduced colony formation and cell proliferation upon treatment, and a decrease in tumor burden in zebrafish xenograft assays. Our findings provide key tools for further identification and characterization of ING4 pathways that impact both hematopoietic and cancer cell function.

Poster # 36
First Author: Karthik Rangavajhula
PI: Eugenia Broude
Title: Assessing effects of CDK8/19 Inhibition on Metastasis of Triple Negative Breast Cancer
Abstract:
Effective Triple Negative Breast Cancer (TNBC) treatment has been largely hindered by its lack of common physiological targets and limited understanding of the factors that govern metastatic changes. Twin kinases CDK8 and CDK19, in conjunction with the Mediator complex, function as a key transcriptional regulator that modulates enhancer-promoter communication during gene expression reprogramming characteristic to tumor transformation and progression. Analysis of clinical samples revealed that CDK8 gene expression levels correlated to significantly worse outcomes in more aggressive subtypes of prostate, breast, bladder, and GI tract cancer.
Our preliminary data suggests that selective CDK8/19 inhibition lowers TNBC cells viability in vitro and to some extent in vivo. Based on these observations, our project assesses the hypothesis that metastatic potential in TNBC is promoted by transcriptomic changes, the development of which can be therapeutically prevented using Mediator kinase inhibitors (CDK8/19i). Supporting our hypothesis, in vitro experiments demonstrate a decrease in proliferative capability and invasive behavior following treatment with a selective CDK8 inhibitor. Ongoing experiments are exploring the effect of CDK8/19 inhibition on the greater tumor microenvironment in PDX tissue samples. We are also developing human and murine TNBC cells lines with CDK8 and CDK19 with inactivated kinases moieties to further test our hypothesis in assessing the role of the mediator kinase proteins in development of metastatic phenotype. In elucidating this relationship between CDK8/19 expression levels and the

aggressive nature of Triple Negative Breast Cancer, we may warrant further investigation of this previously under-explored “Achilles Heel” in TNBC, by which these stubborn tumor subtypes can be driven and in turn targeted for treatment.

Poster # 37
First Author: Shanshan Shi
PI: Peisheng Xu
Title: EGFR-targeted nanogels for enhanced cancer photodynamic therapy
Abstract:
Photodynamic therapy (PDT) is a non-invasive form of therapy. The combination of near-infrared (NIR) light and photosensitizer offers a potential solution to treat deep tumor tissue. However, most photosensitizers suffer from poor water solubility and rapid clearance in blood circulation, which ultimately lead to low drug bioavailability. In this research, erlotinib (ELT), an epidermal growth factor receptor targeting ligand, and chlorin e6 (Ce6) were conjugated onto poly[(2-(pyridin-2-yldisulfanyl)ethylacrylate)-co-[poly(ethylene glycol)]] (PDA-PEG) to yield ELT Ce6 NGs for enhanced photodynamic therapy. The resulting ELT-Ce6 NGs exhibited excellent biocompatibility, physiological stability, and tumor-targeting properties. In addition, ELT-Ce6 NGs could efficiently generate reactive oxygen species and kill cancer cells upon NIR irradiation because of the release of Ce6 photosensitizer in a microenvironment of elevated GSH levels. The ELT-Ce6 NGs afford enhanced targetability for orthotopic 4T1 breast cancer. Both in vitro and in vivo studies suggest that ELT Ce6 NGs can be promising nanotheranostic agents for cancer photodynamic therapy.

Poster # 38 and “Lightning Talk”
First Author: Mingming Wang
PI: Peisheng Xu
Title: Nano-ERASER based intracellular degradation of PD-L1 and regulate DNA damage response in triple-negative breast cancer through Trim-Away strategy
Abstract:
Programmed cell death ligand 1 (PD-L1) is an immune checkpoint protein, which is a potential target for cancer immunotherapy. Several anti-PD-L1 antibody (Abs) have been approved by the FDA for the treatment of a various cancers. However, for patients with solid tumors, only about 20% respond to anti-PD-L1 Abs. Herein, we utilized a polymeric nanogel based-Trim-Away system, named Nano-ERASER, to reduce the expression of PD-L1 in cancer cells. The anti-PD-L1 Abs loaded-Nano-ERASER can intracellularly deliver and release the Abs and subsequently degrade endogenous PD-L1 protein. The efficacy of Nano-ERASER in depleting PDL1 protein has been validated in 4T1 cells. Due to the efficient degradation of PD-L1, in vitro study found that Nano-ERASER can effectively prevent the proliferation, migration, and invasion of 4T1 cells. Further investigation via immunofluorescence staining and immunoblotting revealed that Nano-ERASER kills 4T1 cells through preventing the repair of DNA damage. Furthermore, Nano-ERASER effectively inhibited the growth of triple negative breast cancer in an orthotopic mouse model and attenuated its metastasis to the liver and lungs. Our study validated that Nano-ERASER technique can serve as a novel antibody-based Trim-Away therapeutic modality for the treatment of cancer and other diseases.

Poster # 31
First Author: Gourab Gupta
PI: Hexin Chen
Title: miR-489 targets FoxM1 to induce cell cycle arrest and apoptosis in triple negative breast cancer cells leading to ICD
Abstract:

It has been well established that microRNAs (miRNAs) have an important role in cancer sustenance and progression. Our previous studies have established the role of miR-489 as a tumor suppressor miRNA in breast cancer. However, the multiple targets of this miRNA have diversified its mechanism from preventing tumor cell proliferation to promoting cell death pathways. In this study we have aimed to establish the role of miR-489 in cell cycle inhibition, leading to Endoplasmic Reticulum stress (ER stress) and ultimately immunogenic cell death (ICD). Firstly, we found that overexpression of miR-489 in triple negative breast cancer (TNBC) cell lines including MDA-MB-231, BT 549, drastically reduced cell proliferation using colony formation assay and real-time cell analysis. Furthermore, studies like GO analysis, sequence analysis and cell cycle analysis demonstrated that miR-489 induces cell cycle arrest and apoptosis in TNBC by directly targeting FOXM1 and regulating other kinases like CDK1. It was also shown for the first time that miR-489 overexpression induces ER stress and the release of damage associated molecular patterns (DAMPs), consistent with hallmarks of ICD like Calreticulin exposure on cellular surface and ATP release, triggering phagocytosis. It was also established that miR-489-induced apoptosis lead to the elevation of cleaved caspase 3, which was responsible for the activation of PANX1 and the consequent release of ATP. In conclusion, we tried to mechanistically understand the role of miR-489 in cell cycle arrest leading to cellular stress. Stress induced apoptosis and consequent ICD was also a possible outcome and it turned out miR-489 overexpression without any other ICD inducer was good enough to trigger the release of DAMPs and elucidate an immunogenic response.

Poster # 33
First Author: Manikanda Raja Keerthi Raja
PI: Hexin Chen
Title: Understanding IL1alpha Mediated Immune Suppression in HER2+ Breast Cancer
Abstract:
The role of the cytokine- Interleukin 1alpha (IL1α) produced by the tumor and the host in during tumor progression is poorly understood. In the present study, we report that IL1a-/- mice regresses HER2 positive breast cancer starting at 2-week time point, while the Wildtype (WT) tumor grows exponential with time. At the 2- week time point, the immune profile showed more tumor infiltrated immune cells of which most immune cells were myeloid cells. Of those myeloid cells, we identified that monocytes failed to differentiate into Tumor Associated Macrophages (TAMs) and transitioned into inflammatory monocytes in IL1a-/- tumor, while in WT the differentiation was successful into TAMs. Of the remaining lymphoid cells (CD4 or CD8) in the tumor, we observed CD8 cells expressing a more proliferative marker (Ki67), memory T cell markers (CD44+Ly6C+) and a significantly less immune inhibitory marker (PD1) was observed. To study if CD4 or CD8 cells played an important role in IL1a-/- tumor regression, we depleted those cells and observed significant tumor growth in IL1a-/-. After depleting CD4 or CD8 cells in IL1a-/- mice, we were able to see tumor successfully established and also monocytes were able to convert into TAMs. Our findings have shed light on how IL1α produced by the host is important for tumor progression in HER2 positive breast cancer by facilitating TAM formation and affecting T cell activity.

Life Sciences/ Cell Biology

Poster # 11
First Author: Elizaveta Korunova
PI: Michael Shtutman
Title: The influence of stress granules on viscoelastic properties of cytoplasm during senescence
Abstract:
The rheological properties of cytoplasm, such as elasticity, diffusion, and viscosity, play a crucial role in regulating cellular processes. However, our understanding of how cells regulate and utilize these properties remains limited. This study presents a model that elucidates the regulation of rheological properties via the formation of stress granules, a type of liquid-liquid phase separation. Stress granules assemble from RNA and proteins in response to various types of stress, including osmotic stress, temperature shock, oxidative stress, and ER stress. While stress granules are typically described in the context of translation arrest, evidence of their involvement in other processes, such as transport and metabolism, has started to emerge. However, there is surprisingly still very limited data regarding the connection between stress granules and the viscoelastic properties of the cytoplasm. The importance of understanding this link is heightened in the context of senescence. Evidence suggests that cell senescence leads to a drastic enlargement of cell volume, resulting in an abnormal decrease in cytoplasm density and an increase in diffusion of macromolecules. However, under stress conditions, senescent cells exhibit increased formation of stress granules, which disassemble at a slower rate and tend to form persistent stress granules. This contradicts the research that showed the positive correlation between the decrease in cytoplasm density and stress granule disassembly under hypoosmotic conditions. We hypothesize that the formation of stress granules in senescent cells compensates for changes in viscoelastic properties during senescence, potentially supporting the functioning of senescence-associated secretory cell phenotypes that contribute to neurodegenerative and age-associated disorders. To test the hypothesis, we measured the viscoelastic properties through particle tracking of 40 nm genetically encoded nanoparticles (GEM) and Fluorescence Recovery After Photobleaching (FRAP) of tdTomato in U2OS cells before and after the induction of oxidative stress-associated stress granules during induced senescence. FRAP of tdTomato is used to elucidate changes in viscoelastic properties of the cytoplasm at the level of cytoplasmic proteins. Tracking of 40 nm nanoparticles shows changes in the level of ribosomes. As a result, we show an increase in diffusion at the level of ribosomes after the formation of stress granules. The changes in viscoelastic properties in normal and senescent conditions will be compared.

Life Sciences/ Metabolism

Poster # 28
First Author: Brooke Bullard
PI: E. Angela Murphy
Title: Panaxynol improves crypt and mucosal architecture, suppresses colitis-enriched microbes, and alters the immune response to mitigate colitis.
Abstract:
Ulcerative colitis (UC) is an idiopathic inflammatory disease of the large intestine, which impacts millions worldwide. Current interventions aimed at treating UC symptoms can have off-target effects, invoking the need for alternatives that may provide similar benefits with less unintended consequences. This study builds on our initial data, which showed that panaxynol can suppress disease severity in murine colitis. Here we explore the underlying mechanisms by which panaxynol improves both chronic and acute murine colitis. 14-week-old C57BL/6 female mice were either given 3 rounds of dextran sulfate sodium (DSS) in drinking water to induce chronic colitis or 1

round to induce acute colitis. Vehicle or panaxynol (2.5 mg/kg) was administered via oral gavage 3x/week for the study duration. Consistent with our previous findings, panaxynol significantly ($p<0.05$) improved the disease activity index and endoscopic scores in both models. Using the acute model to examine potential mechanisms, we show that panaxynol significantly ($p<0.05$) reduced DSS-induced crypt distortion, goblet cell loss, and mucus loss in the colon. 16s sequencing revealed panaxynol altered microbial composition to suppress colitis-enriched genera (i.e., Enterococcus, Eubacterium, and Ruminococcus). Additionally, panaxynol significantly ($p<0.05$) suppressed macrophage polarization and induced regulatory T-cells in the colonic lamina propria. The beneficial effects of panaxynol on mucosal and crypt architecture, combined with its microbial and immune-mediated effects, provide insight into mechanisms by which panaxynol suppresses murine colitis. Overall, this data is promising for the use of panaxynol to improve colitis in the clinic.

Poster # 29 and "Lightning Talk"
First Author: Thomas Cardaci
PI: E. Angela Murphy
Title: Cancer cachexia increases skeletal muscle lipid deposition and decreases lipid droplet-mitochondrial contact.
Abstract:
Cancer cachexia is the unintentional loss of lean mass and directly contributes to functional dependency, poor treatment outcomes, and decreased survival in cancer patients. While the pathogenicity of cachexia is multifactorial, metabolic dysfunction remains a key contributor to its progression. Despite this, there is a lack of evidence investigating the role of altered muscle lipid homeostasis, lipid droplet dynamics, and lipid droplet-mitochondrial interactions in contributing to this wasting syndrome. Therefore, the purpose of this study was to investigate the impact of cancer cachexia on skeletal muscle dysfunction and mass loss, intramyocellular lipid droplet content and morphology, and lipid droplet-mitochondrial contact using the Lewis Lung Carcinoma (LLC) murine model. C57/BL6 male mice (n=20) were implanted with LLC cells in the right flank or underwent sham surgery. Skeletal muscle was excised for transmission electron microscopy (TEM; soleus), oil red o/lipid staining (tibialis anterior), and protein (gastrocnemius) 25 days following implantation. One-way ANOVAs were used to assess statistical differences ($p<.05$). TEM analysis unveiled LLC mice had greater number (232%; $p=0.0055$) and size (130%; $p=0.0226$) of intramyocellular lipid droplets further supported by increased oil-red o positive fibers (87%; $p=0.0109$) compared to controls. Additionally, morphological analyses of lipid droplets show altered morphometrics (i.e. roundness, circularity, aspect ratio, etc.) as well as decreased lipid droplet-mitochondria contact (86%; $p=0.0042$) and dysregulation in lipid droplet regulatory proteins in cachectic muscle ($p<0.05$). Collectively, these data demonstrate that cancer cachexia induces myosteatosis, alters lipid droplet morphology, and decreases mitochondrial interactions likely contributing to the decrements in skeletal muscle mass and function experienced by cancer patients.

Poster Number: 12
First Author: Hunter Cox
PI: Norma Frizzell
Title: Detection of Immunometabolite Derived Cysteine Modifications
Abstract:
The immunometabolite itaconate accumulates during lipopolysaccharide (LPS) stimulation of macrophages and microglia. Itaconate non-enzymatically reacts with cysteine residues to generate 2,3-dicarboxypropylcysteine (2,3-DCP), referred to as protein dicarboxypropylation. The tricarboxylic acid (TCA) cycle metabolite fumarate non-enzymatically reacts with the amino acid cysteine to form S-(2-succino)-cysteine (2SC), resulting in irreversible protein succination. Since fumarate and itaconate levels dynamically change in activated immune cells, the levels of both 2SC and 2,3-DCP reflect the abundance of these metabolites and their capacity to modify protein structure

and function. We generated esters of 2SC and 2,3-DCP from protein hydrolysates and used stable isotope dilution liquid chromatography-tandem mass spectrometry (LC-MS/MS) to determine the abundance of these in LPS-stimulated Highly Aggressively Proliferating Immortalized (HAPI) microglia. Itaconate derived 2,3-DCP, but not fumarate derived 2SC, increased in LPS-treated HAPI microglia. Stoichiometric measurements demonstrated that 2,3-DCP increased from 1.57 to 9.07% of total cysteines upon LPS stimulation. This methodology was extended to the quantification of 2SC in serum from experimental autoimmune encephalitis (EAE) mice treated with the fumarate ester, dimethyl fumarate (DMF), an immunosuppressive compound. As expected, DMF resulted in pronounced succination resulting in elevated 2SC levels. The quantification of 2SC in serum samples may have utility for monitoring DMF exposure in patients treated with DMF for multiple sclerosis (marketed as Tecfidera®). Lymphocyte counts are routinely measured in patients treated with DMF to prevent severe lymphopenia, while also suppressing disease relapses. Monitoring 2SC levels may provide a direct measurement of the effect of fumarate esters on irreversible cysteine modification in at-risk patients.

Poster Number: 13
First Author: Alexander Huss
PI: E. Angela Murphy
Title: Impact of Obesity Induced by High Fat Diet on Lipid Accumulation in Skeletal Muscle
Abstract:
By the year 2030, almost 50% of adults in the United States are expected to be obese. Obesity has been shown to increase the risk of several chronic metabolic diseases, several cancers, and is associated with impaired skeletal muscle function and metabolism. Despite this, little it is known about the role of altered muscle lipid homeostasis, lipid droplet dynamics, and lipid droplet-mitochondrial interactions in contributing to muscle dysfunction in obesity. Therefore, we sought to investigate the impact of high-fat diet induced obesity on overall skeletal muscle lipid deposition, intramyocellular lipid droplet content and morphology, and lipid droplet-mitochondrial contact. Male C57/BL6 mice (n=20) were divided into two groups: one group received LLC cell implants (106 cells) in the right flank, while the other group underwent sham surgery. After 25 days, skeletal muscle samples were collected transmission electron microscopy (TEM; soleus), oil red o/lipid staining (tibialis anterior), and protein analysis (gastrocnemius). Statistical analysis was performed using a Student's T-test with an alpha level of 0.05. Protein analyses revealed dysregulation in key metabolic regulatory proteins (Atrogin-1, Adiponectin, PLIN-2, p:t AKT (S473 & T308), MURF1) accompanied by increases in oil red o staining in obese compared to lean mice. This was further supported by obese mice exhibiting a greater number of intramyocellular lipid droplets. Furthermore, morphological examination of lipid droplets showed alterations in shape parameters (e.g., roundness, circularity, aspect ratio), along with reduced contact between lipid droplets and mitochondria. Collectively, these findings suggest that obesity-induced skeletal muscle dysfunction may be driven, at least in part, due to changes in lipid droplet-mitochondria interactions resulting in excess accumulation of lipids and altered lipid droplet morphology.

Poster # 30
First Author: Mary Mitchell
PI: Melissa Ellermann
Title: Increased endocannabinoid signaling releases host-derived nutrients to stimulate Escherichia coli growth in the gut
Abstract:
Crohn's disease (CD) is a chronic gastrointestinal disease that is characterized by prolonged inflammation mediated by an overactive immune response to the gut microbiota. Linked to CD pathogenesis is the expansion of Escherichia coli, a common signature of gut microbiome dysfunction. Current treatments for CD patients can have adverse side effects and increase long-term risks for co-morbidities, highlighting the importance for ongoing

development of alternative treatment options. The endocannabinoid system has been recognized as a potential therapeutic target due to its anti-inflammatory properties and successful application in other diseases. Endocannabinoids are lipid hormones that signal via the CB1 and CB2 receptors. While CB2 activation is generally anti-inflammatory in models of CD, the effects of CB1 activation on inflammation and microbiome dysfunction are not well described. Therefore, we compared the effects of increased endocannabinoid signaling via the CB1 and CB2 receptors in a murine model of CD. Our results demonstrate that stimulation of endocannabinoid signaling significantly worsened inflammation and increased intestinal E. coli growth. Administration of a CB1 antagonist attenuated inflammation and prevented E. coli proliferation. In contrast, when a CB2 antagonist was administered, E. coli growth remained elevated. These results led us to hypothesize that CB1 activation increases the availability of nutrients that stimulate E. coli growth by allowing an advantageous switch from fermentation to respiration. To test our hypothesis, we repeated our treatments in mice colonized with an E. coli mutant unable to perform anaerobic respiration (moaA). In comparison to the parental E. coli strain, CB1 activation did not stimulate proliferation of the moaA-deficient mutant in the ileum or colon. In contrast, increased growth of moaA-deficient E. coli was still observed in the cecum following CB1 stimulation. Our results suggest that E. coli proliferation in response to CB1 activation varies depending on gut region. Overall, these results suggest that endocannabinoid signaling at the CB1 receptor exacerbates colonic inflammation and stimulates E. coli outgrowth by altering nutrient availability in our CD model. Future studies aim to determine the impacts of CB1 signaling and increased E. coli growth on CD pathogenesis.

Poster # 14
First Author: Christian Unger
PIs: Angela Murphy and Reilly Enos
Title: "Estrogen and its Receptor in Male Liver Glucose Metabolism: A Balancing Act in Diet-Induced Obesity"
Abstract:
BACKGROUND: Obesity is associated with impaired glucose metabolism which is thought to play a role in a variety of obesity-linked comorbidities. These metabolic impairments are evident in the liver as it plays a pivotal role in glucose metabolism. Thus, developing liver-centric therapies is a viable option to remedy the metabolic perturbations seen in obesity. Administration of systemic exogenous sex steroids has previously been shown to beneficially impact metabolic processes, however, the off-target effects and potential negative health risks associated with global steroid therapies hinder their use clinically. Therefore, there is a critical need to understand the tissue-specific effects of steroid action to develop targeted therapeutics which bypass any potential unwanted side effects.
PURPOSE: The purpose of these experiments was to interrogate the role of liver estrogen receptor alpha (ERα) as well as aromatase expression in regulating metabolic outcomes as well as the potential therapeutic applications.
METHODS: We developed three novel mouse models that allow for inducible deletion of liver estrogen receptor alpha (Liver- ERα ID), inducible overexpression of liver ERα (Liver-ERα↑), as well as inducible aromatase overexpression in the liver (Liver-Arom↑). Male mice were fed either a purified LFD or HFD for 13 weeks Liver-Arom↑ and Liver-ERα↑ study, and only HFD was given to the Liver- ERα ID study for 13 weeks. Body weight was assessed throughout the course of the experiment, while body composition (DEXA), glucose tolerance tests, and insulin tolerance tests were performed near the termination of dietary treatment.
RESULTS: Each genetic manipulation had little to no effect on bodyweight, however, glucose tolerance and insulin tolerance test results were impaired with aromatase overexpression and estrogen receptor alpha deletion in the liver, however, estrogen receptor alpha overexpression lead to an improved glucose tolerance test with significantly lowered insulin levels independent of changes to liver weight or adiposity metrics.
CONCLUSION: There appears to be a Goldilocks principle in estrogen receptor signaling within the liver, where an excess of ligand-receptor interaction is undesirable, complete deletion is harmful, and elevated expression of

estrogen receptor alpha could achieve the optimal level. Liver-specific agonists might have potential therapeutic benefits.

Life Sciences/ Neuroscience

Poster # 15
First Author: Courtney Buchanan
PI: Jeffrey Twiss
Title: Testing an autocrine loop that slows axon regeneration using localized protein synthesis
Abstract:
Axons play a crucial role in establishing the long-range connections needed for nervous system function. The considerable length of axons that underlie their functions make the system vulnerable to disruption by injury and disease. Despite the ability of the PNS to spontaneously regenerate, axon regeneration is extremely slow (1-2 mm per day). Therefore, there is a critical need to develop strategies to accelerate axon regeneration. We recently showed that KHSRP slows PNS regeneration, with regeneration accelerated in mice lacking neuronal KHSRP. KHSRP is an RNA splicing factor that also promotes RNA decay and our data indicate that deletion of KHSRP stabilizes its target mRNAs in axons. KHSRP levels increase rapidly in axons after nerve injury through increased axoplasmic Ca2+, remaining elevated for up to 28 days after axotomy (Patel et al., 2022). Our data suggest that it is the accumulation of axonal KHSRP that slows axon growth. Here we sought to determine the mechanism underlying the sustained elevation of KHSRP after injury. We had previously shown that Reg3a mRNA, which encodes a secreted lectin-like protein, is transcriptionally upregulated in L4/5 DRGs following axotomy and localizes to axons including regenerating spinal cord axons (Kalinski et al., 2015). Exogenous REG3A protein increases axonal Ca2+, activates PERK-->eIF2aPS51 pathway, and increases translation of axonal Khsrp mRNA. Depletion of Reg3a mRNA using shRNA increases axon regeneration and decreases axonal KHSRP protein in regenerating axons. These initial observations suggest that axonal translation of Reg3a mRNA provides an autocrine loop to sustain translation of Khsrp mRNA in regenerating axons and slow axon regeneration.

Poster # 16
First Author: Irene Dalla Costa
PI: Jeffrey Twiss
Title: Acetylation of axonal G3BP1 increases overall protein synthesis and promotes axonal growth and regeneration
Abstract:
Peripheral Nervous System (PNS) injury activates local translation of specific mRNAs in axons. We previously showed that the stress granule (SG) protein G3BP1 stores axonal mRNAs, which slows axon growth but also provides a level of protein synthesis regulation that is essential for injury responses and regeneration (Sahoo et al., 2018, Nat Comm). G3BP1 forms SGs through liquid-liquid phase separation (LLPS), and its threshold for LLPS is modulated by post-translational modifications. Phosphorylation of G3BP1 on Ser 149 (G3BP1PS149) leads to SG disassembly in axons, and releases G3BP1-associated mRNAs to promote axon regeneration (Sahoo et al., 2020, Curr Biol). Lys 376 acetylation of G3BP1 (G3BP1AcK376) also triggers SG disassembly (Gal et al., 2019, MCB), raising the possibility that G3BP1 acetylation could also modulate axon growth. We find that G3BP1AcK376 rapidly increases after PNS axon injury with subsequent accumulation at a proximally placed nerve ligation consistent with retrograde movement of G3BP1AcK376. By live imaging, G3BP1 acetylmimetic (G3BP1K376Q) vs. non-acetylatable (G3BP1K376R) mutants show distinct motilities in axons compared to wild type (WT) G3BP1. Expression of G3BP1K376Q in cultured dorsal root ganglion neurons significantly increases axon growth compared to WT, G3BP1K376R, and phosphomimetic G3BP1S149E. Expression of G3BP1K376Q increases axonal protein synthesis, likely due to the release of regeneration-associated mRNAs. Consistent with this, in vivo expression of

G3BP1K376Q significantly increases PNS nerve regeneration compared to WT and G3BP1K376R. Taken together, these data indicate that axonal G3BP1 undergoes both acetylation and phosphorylation following nerve injury, resulting in the disassembly of SGs and enhanced axon regeneration. Future studies will be needed to resolve the distinct roles of G3BP1 acetylation and phosphorylation. Nevertheless, it is appealing to speculate that different G3BP1 post-translational modifications may regulate different pools of mRNAs involved in axonal injury response and subsequent regeneration.

Poster # 17
First Author: Marla Frick
PI: Jim R. Fadel
Title: Orexin/hypocretin modulation of neuroinflammation in a rodent model: implications for age-related cognitive decline
Abstract:
The orexin/hypocretin neuropeptide system, primarily found in the lateral hypothalamus and perifornical region, modulates sleep, wakefulness, appetite, and cognitive function. One region with dense orexinergic projections is the basal forebrain (BF), which is the major source of acetylcholine in the neocortex and limbic structures such as the hippocampus. The basal forebrain cholinergic system mediates cognition and dysfunction is one of the key hallmarks of Alzheimer's disease. We have previously shown significant reductions in orexin signaling and orexinergic innervation of cholinergic cells within the BF of aged rodents. Loss of orexin impairs cholinergic neurotransmission and cognition, but the mechanisms responsible remain poorly understood. Recent evidence suggests neuroinflammation as a contributing factor to the pathogenesis of Alzheimer's disease. It has been suggested that orexin may be neuroprotective, and we hypothesize that the age-related loss of orexin neurons diminishes the brain's anti-inflammatory response, leading to basal forebrain cholinergic dysfunction.
Here, we administered lentivirus mediated expression of Preproorexin antisense or sense into the lateral hypothalamus of young adult (3 months; antisense) and aged (22-26 months; sense), male and female Fisher 344/Brown Norway F1 hybrid rats. Three weeks later, a neuroinflammatory response was induced with an acute lipopolysaccharide (1 mg/kg, intraperitoneal) challenge. 6 hours later, brains were removed and bilaterally dissected with one hemisphere post-fixed for immunohistochemical analysis and one hemisphere frozen for cytokine analysis.
Lentivirus efficacy was verified using immunohistochemistry for green fluorescent protein expression and changes in orexin expression within the lateral hypothalamus and terminal regions. There was no significant difference in total Iba-1 (a marker of microglia—the brain's resident immune cells) in the basal forebrain, but there was a shift in activation state towards a pro- inflammatory, "M1" phenotype in the orexin antisense-treated rats. In addition, there was an increase in the inflammatory cytokines, IL-6 and TNF-alpha in the prefrontal cortex of orexin antisense treated male rats.
Loss of orexin expression in aging may facilitate neuroinflammatory processes in key regions, such as the BF and prefrontal cortex, and thereby contribute to neurodegeneration and cognitive decline.
Supported by NIH R01 AG050518 and 2RF1 AG050518.

Life Sciences/ Stem Cells

Poster # 18
First Author: Carlos Alfaro Quinde
PI: Katie Kathrein
Title: Characterizing the role of Ing4 in hematopoietic stem cells: an experimental and computational approach.
Abstract:
Hematopoiesis is a finely regulated process that fluctuates to meet demand, generating fully matured cells from hematopoietic stem cells (HSCs) through controlled self-renewal and differentiation. The inhibitor of growth 4 (Ing4) is a tumor suppressor that has been well-characterized in several cancers, but its role in hematopoiesis remains unclear. Our research has shown a pivotal role of Ing4 in HSC regulation. Using an Ing4 knockdown mouse model (Ing4 -/-), we observed that HSCs exhibit increased quiescence compared to wild-type HSCs, yet surprisingly display a transcriptome profile similar to proliferating cells. Additionally, Ing4 loss enhances the regenerative capacity of HSCs, providing stress resistance against chronic inflammation. These findings suggest Ing4 as a potential candidate for improving hematopoiesis due to robust HSC function, therefore, further investigation into the biological pathways modulating HSC proliferation and differentiation must be performed. To elucidate these pathways, HSCs are extracted from both Ing4 -/- and WT bone marrows and cultured in vitro for seven days to assess how inhibitors targeting different pathways modify HSC proliferation capacity. On the other hand, a profound understanding of complex systems like hematopoiesis can be challenging, often limited by experimental constraints. To overcome this, we developed an agent-based stochastic computational model to elucidate HSC dynamics in both WT and Ing4 -/- systems. The model integrates experimental data and theoretical work, taking into consideration quiescence, self-renewal, differentiation, and apoptosis. This model will be tested and calibrated until matching the experimental data. After that, it will enable the exploration of scenarios that cannot be observed experimentally. Both complementary approaches will aim to enhance our understanding of stem cell biology and contribute to elucidating the characteristics of Ing4-modulated HSCs during bone marrow transplantations.

Poster # 19
First Author: Marco Hernandez
PI: Katie Kathrein
Title: Exploring Metabolic Responses in Hematopoietic Stem Cells in Absence of protein Inhibitor of Growth-4 (Ing4)
Abstract:
Hematopoiesis, the differentiation process of stem and progenitor cells within the bone marrow (BM), is vital for maintaining the circulatory system's homeostatic fitness and immunological defense. Hematopoietic stem cells (HSCs) play a crucial role in replenishing the stem cell compartment, preventing hematopoietic depletion. However, chronic infection, inflammation, and cellular stress can lead to BM failure (BMF), requiring hematopoietic stem cell transplantation (HSCT). Despite advances, post-transplantation challenges contribute to 42.9% of fatal relapses in BMF patients.
Recent research identified the inhibitor of growth 4 (Ing4) as a key epigenetic regulator of hematopoiesis. Ing4 is a regulatory protein whose function is dysregulated in numerous types of cancers and other hematopoietic malignancies. Unexpectedly, our preliminary studies showed that Ing4-deficient HSCs, usually in a quiescent state, exhibit increased gene expression of metabolic markers associated with oxidative phosphorylation (OxPhos) and ribosomal biogenesis (RiBi), which is typically linked to activated HSCs. This paradoxical observation raises intriguing questions about how cellular metabolic pathways including translation and mitochondrial respiration contribute to maintaining HSC quiescence while promoting BM repopulation. Here,

we hypothesize that Ing4 deficiency leads to the upregulation of both Ribi and OxPhos, with minimal impact on downstream metabolic pathways such as translation and OxPhos.
Contrary to conventional notions associating quiescence with low mitochondrial activity, our preliminary data suggests an increased mitochondrial activity in Ing4-deficient HSCs. We explored the effect of Ing4 deficiency on OxPhos in quiescent HSCs by employing tetramethylrhodamine methyl ester (TMRM) to analyze active mitochondria undergoing OxPhos. We found no difference in the membrane potential activity between Ing4-deficient and wildtype HSCs, indicating that high expression of genes involved in OxPhos does not necessarily correspond with increased cellular respiration, preventing overwork of the mitochondrial machinery.
Additionally, we examined the impacts of increased Ribi-associated gene expression on translational rates in Ing4-deficient HSCs by utilizing the RiboPuromycylation Method ex vivo and evaluated ribosomal translation rates in Ing4-deficient HSCs. We are currently in the process of analyzing additional data that will be incorporated into the final poster presentation.
Together, these results contribute to our understanding of HSC behavior in BM environments, presenting Ing4 deficiency as a model for abnormal hematopoiesis function. The outcomes promise not only a mechanistic understanding of HSC function but also open avenues for targeted therapeutic interventions, addressing challenges in BM transplantation and related disorders.

Poster # 20
First Author: Vi Nguyen
PI: Wenbin Tan
Title: Generation and Characterization of Clinically Relevant Disease Models for Port Wine Birthmark using iPSCs
Abstract:
Background/Introduction: Port Wine Birthmark (PWB) is a congenital vascular malformation with a progressive development to be darkened and raised as a result of nodules. The current
treatments for PWB are Pulse Dye Laser (PDL) and Photodynamic Laser Treatment (PDT).
However, the efficacy of blanching the birthmark is inadequate, and the reoccurrence after
treatment is a significant clinical barrier. Developing clinically relevant disease models that can be used for mechanistic and therapeutic development studies is a critical unmet need. Induced
pluripotent stem cell (iPSC) is a powerful tool in different disease models and drug discovery because of its pluripotency characteristics. In addition, iPSC-derived cells can retain and exhibit the disease phenotypes from the original donors. Therefore, iPSC and their derived vascular cells could be potential cell models for the study of PWB.
Research Questions/ Hypothesis: It was hypothesized that PWB iPSC-derived endothelial cells (ECs) could preserve the disease phenotypes, thus serving as clinically relevant disease models.
Goal/ Aim: To generate iPSC lines from PWB skin lesions and characterize the molecular and functional phenotypes of those iPSC-derived ECs.
Method/ Approach: PWB lesional and normal skin biopsies were cultured for outgrowths of human dermal fibroblasts (hDFs), followed by reprogramming using a CytoTune-iPS Kit (ThermoFisher). IPSC colonies were formed, picked, and expanded. The induction of iPSC into ECs was performed using reported protocols with tailored modifications. Bulk RNA-seq and ATAC-seq were performed on both iPSC and iPSC-derived ECs. The functional phenotypes of iPSC-derived ECs were characterized using in vitro capillary formation and in vivo Matrigel plug-in assays.
Result/ Data: We successfully generated and maintained human PWB (#3921) and normal (#52521) iPSCs. IPSC generated from normal and PWS lesional hDFs expressed stem cell biomarkers such as Oct4, Nanog, Tra1-60, and SOX2. The differentiation of iPSC into ECs allowed the production an EC population of approximately 95% purity based on CD31+ cell profile in flow cytometry. Expressions of EC biomarkers, including CD31, CD144, VEGFR2, and eNOS further confirmed in iPSC-derived ECs. PWB EC_3921 showed impaired capillary-tube formation in vitro

with larger perimeters (p=6.22x10-24) and thicker branches (p=1.07x10-77) comparing with normal EC_52521. In the plug-in assay, the formation of perfused human vasculature was evident 10 days after intradermal xenograft of normal and PWB ECs with the corresponding MSCs into SCID mice, which were characterized by using anti-human UEA1 and anti-human CD31 antibodies. Perfused vasculature formed by PWB iPSC-derived ECs showed bigger perimeters (p=8.45x10-6) and greater densities (p=7.34x10-8) than those formed by normal ECs. 16.6% of perfused vessels formed by PWB iPSC-derived ECs showed perimeters over 300 μm. KEGG analysis of RNA-seq differentially expressed genes (DEGs) showed significantly dysregulated pathways related to cell differentiation, organ development, and cell lipid metabolism in PWB iPSCs and ECs compared to normal ones.
Conclusion: PWB-derived ECs retained critical disease-related phenotypes, including forming vessels with enlarged perimeters and thick branches in vitro and in vivo. These cells are valuable and unique cell models that can be used for PWB studies.

Life Sciences/ Vascular

Poster # 21
First Author: Mrinmay Chakrabarti
PI: Mohamad Azhar
Title: The role of sex hormones in Calcific Aortic Valve Diseases
Abstract:
Calcific Aortic Valve Disease (CAVD) is the third most common cardiovascular disease and the leading cause of valve disease in the developed world. It affects 25% of people older than 65 years and 50% of people older than 85 years of age. Tissue samples collected from patients suffering from CAVD have shown elevated levels of the TGFβ1 in heart valves. We also observed upregulation of TGFβ1 in the valve interstitial cells (VIC) of Tgfb1TG/PostnCre mice. Our earlier studies clearly showed induction of CAVD in both male and female mice at 1-3 months of age. However, males advanced to calcific AS at a higher rate by 1-2 years of age than female mice. Thus, we aim to understand the role of female hormones that protects females from developing advanced CAVD. We have isolated valve interstitial cells (VICs) from 4-6-weeks old Ts(H2-K1-tsA58) (i.e., immortomouse) male or female mice aortic valves and culture them in osteogenic media in presence or absence of estradiol (10-100 nM) or di-hydro-testosterone (10 nM). Ovariectomy (OVX)/sham OVX female and castration (CAST)/sham CAST male Tgfb1TG/PostnCre mice of 3-7 months of age were used for our in vivo study. Our alizarin red staining confirmed the calcification of VICs in osteogenic media. Our cell culture studies also indicated that estradiol plays a protective role in preventing the VICs of females, whereas testosterone promotes calcification of female VICs. For male VICs, estrogen has no protective role against calcification and leads to the same amount of calcification as testosterone. Our animal studies suggest the protective role of estrogen in female mice is outweighed by the pro-osteogenic effects of increased levels of TGFβ1 in the VICs of the AV.

Poster # 22
First Author: Ridha Fatima
PI: Holly LaVoie
Title: Pregnancy affects left ventricle collagen and MMP2 in wildtype and Matrix Metalloproteinase 14 overexpressing mice
Abstract:
During pregnancy, the heart enlarges to accommodate increased blood volume. Peri- or post-partum cardiomyopathy occurs when the heart fails to return to its original size following delivery. Matrix-metalloproteinase 14 (MMP14) helps remodel the heart by cleaving extracellular matrix proteins surrounding blood vessels and cardiomyocytes. Our goal was to compare mice expressing a human MMP14 transgene (hMMP14) in fibroblasts with wildtypes before, during, and after pregnancy for left ventricle (LV) collagen types I and III and

MMP2 mRNAs and proteins. Mouse LV tissue was isolated at pregnancy day 17 (ed17) and postpartum day 49 (ppd49); age-matched virgin LVs were also isolated. Real-time PCR (n=5-8/group) was performed with cDNA and mouse Mmp2, Col1a1, Col1a2, and Col3a1 primers, and Rplp0 for normalization. Western Blots (n=3/group) evaluated isoforms of Collagens I and III between 100 and 200 kDa using non-reducing gels and COL1A1 and COL3A1 antibodies with tubulin for normalization. Zymography assessed MMP2 activity. Data were analyzed by Two-way ANOVA and Sidak's (genotype) or Tukey's (reproductive status within genotype) post-hoc test; $P<0.05$ was significant. Two-way ANOVA revealed a significant interaction of reproductive status and genotype for Col1a1 mRNA and a main effect of reproductive status on several COL1A1 isoforms. Col1a1 mRNA showed lower levels in hMMP14 ppd49 mice compared to wildtypes. In ed17 wildtype mice, COL1A1 isoforms (120-160 kDa) were lower than wildtype ppd49 mice and age-matched virgin groups. There was a non-significant trend for these COL1A1 isoforms to be lower in hMMP14 ed17 than ppd49 mice ($P = 0.058$). There was a significant main effect of reproductive status on MMP2 activity but no post-hoc test difference. No significant differences were found for Mmp2, Col1a2, and Col3a1 mRNA or COL3A1 protein. Col1a1 mRNA level differences between genotypes were not reflected in COL1A1 isoform abundance. In conclusion, late pregnancy tended to have lower levels of specific COL1A1 isoforms suggesting lower new collagen I synthesis. Although a genotype related difference in collagen or MMP2 proteins was not observed, lower new collagen synthesis suggested controlled remodeling during late pregnancy in both genotypes. Supported by Magellan & SCHC Research awards, SC INBRE P20GM103499, USC ASPIRE I.

Poster # 23
First Author: Thanh Le
PI: Mohamad Azhar
Title: Micro-Computed Tomography Imaging Reveals Ethylenediaminetetraacetic Acid Nanoparticles Reverses Medial Arterial Calcification in Mouse Model Of Adenine Diet Induced Chronic Kidney Disease
Abstract:
Medial arterial calcification (MAC) is a form of vascular calcification in the medial layer of arteries, often linked with aging, diabetes, and chronic kidney disease. To induce MAC in mice, we used a twelve-week adenine diet (uremic) in C57BL/6 mice. Experimental mice were fed a normal (0.9%) and a high (1.8%) phosphate adenine diet (AD). Control mice were given a standard chow diet (CD). Following the AD diet, experimental mice were switched to CD diet and received injections of Ethylenediaminetetraacetic Acid Nanoparticles (EDTA-NPs) twice a week for eight weeks. We monitored the progression of calcification 'before' treatment and changes in calcium deposits during treatment using live micro-computed tomography (micro-CT) imaging. Calcification in the aorta and soft tissues was annotated using ITK-Snap and an AI model developed by our team. Then, we quantified calcification using ImageJ to compare 'before' and 'after' treatment results. Analysis indicated that aortic calcification began after eight weeks of adenine diet and continued to increase throughout the experimental period. Mice treated with EDTA-NPs had a gradual reduction in calcium deposits within the aorta and other soft tissues of the medial wall. The untreated group showed an overall increase in aortic calcification, while the treated group showed a decrease, with a significant difference indicated by an independent t-test ($p=0.0116$). Our results suggest the potential efficacy of EDTA-NPs as a non-surgical approach to reverse MAC.

Poster # 24
First Author: Laena Pernomian
PI: Camilla Ferreira Wenceslau
Title: A Single-Short Partial Reprogramming of the Endothelial Cells In Vivo decreases Blood Pressure and Vascular Contractility Through the Attenuation of Endothelial-to-Mesenchymal Transition in Male Hypertensive Mice

Abstract:
The Schlager hypertensive (BPH/2J) mouse strain is a genetic model of spontaneous hypertension. Endothelial dysfunction is a hallmark characteristic of hypertension, including the phenotypic transitioning of endothelial cells to adopt mesenchymal features (EndMT). We hypothesized that treating endothelial cells with Oct4, Sox2, and Klf4 transcription factors will lead to partial reprogramming, reduce EndMT, and prevent vascular dysfunction. Mouse endothelial cells were transduced with a lentiviral vector containing Cadherin5-Oct4-Sox2-Klf4-EGFP (LV-OSK), control lentivirus (LVCO), or phosphate-buffered saline (PBS). Cell migration, proliferation, and endothelial progenitor cell (EPC) markers were evaluated. Male or female BPH/2J mice (~44-week-old) and their age-matched controls BPN/3J (normotensive) received a single injection of LVCO or LV-OSK (100µL) via the tail vein and were evaluated after ten days. Systolic blood pressure (SBP) was measured directly by catheterizing the left carotid artery. Mesenteric resistance arteries were isolated and mounted on wire myographs to evaluate phenylephrine-induced contraction, and the EndMT was investigated in aortas by confocal microscopy. Data were analyzed using One-way or Two-way ANOVA, with Tukey post-hoc ($p<0.05$). LV-OSK treatment increased the mouse transcription factors Oct4, Sox2 and Klf4 (Oct4: 5.6±0.7%; Sox2: 0.6±0.1A.U.; Klf4: 0.35±0.05U) compared to LVCO (Oct4: 1.8±0.2%; Sox2: 0.2±0.1A.U.; Klf4: 0.04±0.02U) or PBS (Oct4: 1.5±0.4%; Sox2: 0.2±0.1A.U.; Klf4: 0.02±0.01U, n=3-6), and it increased the EPC marker CD133 (11.7±0.8%) vs. LVCO (7.6±0.3%) or PBS (6.5±0.6%, n=3), but not CD34 or cell proliferation. Cell migration was lower in LV-OSK (68±4%) than in LVCO cells (89±2%, n=5). Male and female BPH/2J treated with LVCO had higher SBP (male: 105±2mmHg, female: 97±2mmHg, n=6) compared to BPN/3J mice (male: 80±2mmHg, female: 77±5mmHg, n=3-4), and LV-OSK treatment decreased SBP in male BPH/2J (90±2mmHg, n=5) but not in female mice (98±5mmHg, n=5). The phenylephrine-induced contraction was reduced in arteries from male BPH/2J treated with LV-OSK (7.12±0.6mN, n=5) but not in female mice (10.01±1.06mN, n=5) compared to LVCO (male: 10.50±0.82mN; female: 8.84±1.36mN; n=5). EndMT was detected in male hypertensive mice treated with LVCO (0.041±0.01A.U.), and LV-OSK prevented it (0.007±0.004, n=3). These data reveal that partial endothelial cell reprogramming in vivo is a new strategy to prevent endothelial dysfunction in male hypertensive mice.

Poster # 25
First Author: Yana Udani
PI: Mohamad Azhar
Title: Effect of alcohol on aortic valve calcification
Abstract:
Aortic valve calcification is a calcium mineral deposition in the heart's aortic valves, leading to narrow valve opening, and in severe cases aortic valve stenosis. It is a marker of early-stage heart disease and often common in older age. Ethanol, when ingested, has been known to decrease vitamin D activity and induce phosphate-mediated mineralization leading to an increase in calcium absorption and mineralization. An increase in blood fat levels and fast heartbeat are common consequences, creating additional plaque deposition and higher risk of calcific aortic valve disease (CAVD). The objective of this research has been to replicate common concentrations of ethanol found in light to heavy drinkers and grow valvular interstitial cells (VICs) in these conditions plus osteogenic media to determine whether higher concentration of ethanol induces calcification. The mouse VICs grown in osteogenic media without ethanol were compared to cells treated with ethanol in osteogenic media for analysis a month after starting ethanol treatment. Cells were stained with Alizarin red dye and quantified through microscopic image analysis. We used ethanol concentrations of 0 mM (no alcohol), 10 mM, 25 mM, 50 mM, and 100 mM in our experimental protocol. A p-value of 0.005 was quantified using a t-test of VICs in untreated control plus osteogenic media and 10 mM ethanol plus osteogenic media, indicating an increase in calcification but when compared to the 25 mM, 50 mM, and 100 mM ethanol plus osteogenic media a decrease was observed in the percent of calcified area. Due to high variation in the data of each group of cells, we plan to find another method for quantifying calcium mineral deposits and/or data analysis procedure to reduce variation and to provide more reliable results.

Poster # 26
First Author: Shalin Vasi
PI: Mohamad Azhar
Title: Identification of Differentially Expressed Genes Involved in Thoracic Aortopathy
Abstract:
Introduction: Transforming growth factor beta (TGFβ) is a member of evolutionarily conserved family of cytokines which involve in different biological processes such as cell proliferation, differentiation, migration, adhesion, apoptosis, and extracellular matrix synthesis. The loss of function mutation in TGFB2 results in thoracic aortic aneurysm (TAA) seen in LDS type 4 patients.
Goal of Study: The objective of this research was to evaluate the change in gene expression during development of aneurysm and its reversal by pentagalloyl glucose (PGG) nanoparticle (NP) therapy.
Methods: We generated tamoxifen-inducible smooth muscle-specific Tgfb2 conditional knockout (i.e., Tgfb2 iCKO) mice. Tamoxifen (5 daily i.p. injections) was injected at 4wk of age. We compared performed bulk RNA sequencing (USC Genomics Core Facility) and compared gene expression in thoracic aorta from 17 weeks old wildtype, Tgfb2 iCKO (with established aneurysm), and Tgfb2 iCKO (in which aneurysm was reversed/treated by PGG-NP therapy).
Results: Venn diagram and heatmap data showed that 95 genes that were upregulated in the Tgfb2 iCKO with an established TAA and downregulated following PGG NP treatment. On the other hand, 49 genes that were downregulated in the Tgfb2 iCKO mice with TAA upregulated following the treatment with PGG NP. There were no genes that upregulated or downregulated in the same direction (i.e., upregulated in both Tgfb2 iCKO and Tgfb2 iCKO/PGG NP treatment or downregulated in both groups). This suggests that PGG NP therapy could be very beneficial and specific to the TAA reversal phenotype with minimal side-effects (or off-target effects). We found that genes that were upregulated in TAA and reversed or downregulated by PGG NP are known aortic aneurysm related genes (e.g., ANGPTL8, APLN, C3, CYSLTR1, KIT, PLA2G7, S1PR3, VDR). Furthermore, we found genes such as NR4A, ADAMTS1, and SEMA3A which were downregulated in TAA but were upregulated by PGG NP are also associated with aortic aneurysm.
Conclusions: Disruption of Tgfb2 in vascular smooth muscle cells in young mice alters the expression of genes involved in SMC phenotype, ECM composition, and cell-ECM binding and communication and inflammation, which in turn lead to aortic aneurysm and dissection. Furthermore, altered genes associated with the established TAA are reversed following PGG NP treatment. Our data suggest that PGG NP treatment has minimal side-effects and strong therapeutic potential to non-surgically reverse or treat thoracic aortic aneurysm.

Poster # 27
First Author: Emily Waigi
PI: Camilla F. Wenceslau
Title: Vascular Dysfunction in the Mesenteric Resistance Arteries Occurs Prior to the occurrence of Early-Onset Alzheimer's Disease.
Abstract:
Alzheimer's Disease (AD) and cardiovascular diseases (CVDs) are a major cause of disability and death among the older population. Familial Alzheimer's Disease (FAD) is linked with an early onset AD (EOAD) pathology (<65years) that manifests through pathogenic mutations in the presenilin (PSEN)1 and PSEN2 genes, leading to the increased production of central amyloid β (Aβ) peptides. We hypothesized that peripheral vascular remodeling and vascular dysfunction in the aorta and mesenteric resistance arteries (MRA) would be observed prior to the development of EOAD. The MRA of male and female C57Bl/6J (control) and AD mice (B6.
CApptm1DboTg(APPswe,PSEN1dE9)85Dbo) at 9-weeks-old were isolated prior to the onset of AD. Acetylcholine-induced relaxation (1pM-30μM) and phenylephrine-induced contraction (0.1nM-30μM) were evaluated using wire myography. H&E staining was used to evaluate aorta morphology. Data were analyzed as non-linear curve

regression and maximum response (Rmax) using the Student t test ($p<0.05^*$). MRA from AD mice showed impaired relaxation in both males and females. Interestingly, phenylephrine-induced contraction was reduced in arteries from males but not in arteries from female mice. However, no differences were observed in the aorta wall thickness in the male or female AD mice. These data suggest that the changes observed in the peripheral microvasculature prior to the onset of AD could later have direct effects on cerebral blood flow leading to areas of altered blood perfusion and microvascular damage, thus contributing to the genesis and maintenance of AD.

Public Health

Poster # 7
First Author: Sabrina Carrel
PI: Anna Blenda
Title: The Creation and Implementation of a Novel Database for Medical School Research Tracking and Student Research Opportunities
Abstract:
For medical students, conducting research improves critical thinking skills, introduces students to mentors, and provides the groundwork for future physicians to both interpret and contribute to future evidence-based medicine. Despite these benefits, medical schools lack a centralized infrastructure to track career outcomes and promote the availability of research opportunities to students. The utilization of a singular database for these purposes could increase student satisfaction and productivity, improve communication between research mentors and students, and increase future funding to institutions based on measurable results of research productivity. Our novel creation of the Database of Projects and Experiences was constructed to centralize student and researcher information, increase student autonomy, and track research productivity at the University of South Carolina School of Medicine Greenville (USCSOMG). Our first step in creating a database was to identify the needs of students and faculty. The results from a survey of the M1 class in 2023 combined with the needs as described by our clinical and faculty collaborators were used to build the foundation of the database. Our working team consisted of computer scientists, research faculty and medical students. The database is divided into two parts: A Faculty portal and a Student portal. From this division, each portal has a unique set of fields that were created to address medical school research needs. Fields for data collection were vetted by USCSOMG clinical collaborators and approved by school leadership before its' release to students. The Database of Projects and Experiences is currently being piloted by a sample at the USCSOMG. The M1 class can create an account allowing them access to the internal summer research application and project reporting services. Current utilization of the database is focused on matching students with research mentors and reporting research outcomes over the M1/M2 summer. The focus is limited to the M1 class as the system is being deployed incrementally so that improvements can be made as needed. The team plans to onboard all current USCSOMG students and each future class as they begin their medical school experience for the most accurate longitudinal data tracking. There is a clear need for a centralized database for students, faculty, and administrative personnel within and across medical schools to track and provide research activity. USCSOMG is continuing to work with collaborators to develop this system, and early feedback from stakeholders has been promising. Future directions for the Database of Projects and Experiences are to implement the program for all students and begin data analysis on student productivity to improve longitudinal research experiences and overall student and university satisfaction.

Poster # 8 and "Lightning Talk"
First Author: Denise Davis
PI: Elizabeth Regan
Title: Secondary Use Of Real-World Data For Patient Selection and Analysis In End-Of-Life Care Study.

Abstract:
This project focused on an end-of-life (EOL) Care study that could address the disparities in EOL care, including sociodemographic, physical health, and clinical aspects. Another focus was the impact of 2016 Medicare policies on advanced care delivery. Secondary analysis was based on several clinical outcomes and EOL Care services over a lifetime. The added goal was to simplify access to data for use in probabilistic learning algorithms.
The multidisciplinary research team consisted of a medical oncologist, a palliative care physician, a statistician, a health informatician, and a doctoral student(data engineer). An Extract-Transform-Load data pipeline was built to harmonize the data, and the characteristics and usability of data elements were assessed.
Data collection and analysis presented for this study was comprehensive across 20 hospitals and 600 provider services over the lifetime of 15306 cancer decedents. A significant increase in palliative care consults was observed for two three-year windows: 29.5% to 36.8% (p=0.0000). This increase was supported by the 2016 Medicare changes.
Several challenges were addressed, including mapping clinical requirements to EPIC Cogito data elements, transforming cancer registry data into an analytical schema, determining EOL Care indicators in the presence of missing data and anomalies, and simplifying access to data for analysis with probabilistic and statistical AI learning algorithms. Capturing timed events over the deceased's lifetime was also a crucial component of our analytical model.
Many of the required variables for the study did not exist in native form within the EHR. As a result, the measures of EOL Care were engineered from timed events over the lifetime of patients. Such events include the diagnosis of cancer and services leading up to the death of individual patients. It was impossible to model and relate all life-prolonging and life-sustaining treatments for each patient due to the limitations of structured data in the EHR. Evaluating EOL Care is complex ongoing clinical research. Research that could improve EOL care and decrease the likelihood of burdensome, low-value, and perhaps unwanted care.
This work was supported by the BDHSC grant and received approval from institutional IRB to use decedent data as the source for EOL care research.

Poster # 9
First Author: Shrikant Pawar, Assistant Professor
PI: Shrikant Pawar
Title: Cyclical Learning Rates (CLR'S) for Improving Training Accuracies and Lowering Computational Cost
Abstract:
Prediction of different lung pathologies using chest X-ray images is a challenging task requiring robust training and testing accuracies. In this article, one-class classifier (OCC) and binary classification algorithms have been tested to classify 14 different diseases (atelectasis, cardiomegaly, consolidation, effusion, edema, emphysema, fibrosis, hernia, infiltration, mass, nodule, pneumonia, pneumothorax and pleural-thickening). We have utilized 3 different neural network architectures (MobileNetV1, Alexnet, and DenseNet-121) with four different optimizers (SGD, Adam, and RMSProp) for comparing best possible accuracies. Cyclical learning rate (CLR), a tuning hyperparameters technique was found to have a faster convergence of the cost towards the minima of cost function. Here, we present a unique approach of utilizing previously trained binary classification models with a learning rate decay technique for re-training models using CLR's. Doing so, we found significant improvement in training accuracies for each of the selected conditions. Thus, utilizing CLR's in callback functions seems a promising strategy for image classification problems.

Poster # 10

First Author: ZIFEI ZHONG

PI: Srihari Nelakuditi

Title: WATCHER: Wearables and Apps for Tracking Core for Healthcare Research

Abstract:

Many healthcare research studies require monitoring the activity, sleep, gait, etc., of human participants, which in turn requires the continuous tracking of their motion and vitals. Despite the wide availability of wearables and apps designed for this purpose, they often fail to meet the precision, efficiency, flexibility, and battery life demands of public health researchers. To bridge this gap, we have been developing the Wearables and Apps for Tracking Core for Healthcare Research (WATCHER), which offers a versatile infrastructure for the collection and analysis of wearable sensor data. It can provide an end-to-end pipeline that includes gathering raw sensor data from wearable devices, uploading it to a central server, extracting aggregated statistics and features, and applying machine learning models to these features to derive insights pertinent to each healthcare study. At the Research Core Fair, we plan to showcase some of the capabilities of WATCHER using devices such as Fitbit, Google Pixel, and Samsung Galaxy watches and invite feedback on how it can be further refined to advance healthcare research at USC.