2026 Great Plains Rare Disease Summit

Poster Presenter Guide

(Highlighted names represent Data Blitz Presenters)

Position: 1
Name: Sofia Hollmann
Organization: Sanford Research
Title: Characterization of the function of E3 ubiquitin ligase RNF12 in muscle stem cells
Authors: Hollmann Sofia*; Olguin, Hugo; Bustos, Francisco
Affiliations: Pediatrics and Rare Diseases Group, Sanford Research
Pontifical Catholic University of Chile, Laboratory of tissue regeneration and adult stem cells, Santiago, Chile.
Abstract: The maintenance and regenerative capacity of the skeletal muscle depends on tissue-specific stem cells known as satellite cells (SCs). Under basal conditions, satellite cells (SCs) remain in a quiescent state; however, when faced with certain stimuli, they regain the ability to re-enter the cell cycle, proliferate, and differentiate. One of the systems that regulates this process is the ubiquitin–proteasome system (UPS), which consists of an enzymatic cascade in which E3 ligase specifically recognizes its substrate, conferring specificity to the process. It has recently been observed that levels of the E3 ligase RNF12 fluctuate during the differentiation process. Therefore, our objective in this study is to obtain more information about this variation and gain insight of a possible role of this protein during the differentiation process. In order to address this objective, a differentiation assay was performed in C2C12 cells and primary cultures, collecting samples at different time points. These analyses revealed a decrease in RNF12 levels as the cells transitioned from a proliferative state to a differentiated state. Subsequently, RNF12 gain-of-function and loss-of-function assays were performed to further investigate its role during the differentiation process. To this end, C2C12 cells and primary cultures were transfected with siRNA targeting RNF12 (loss of function) or with the pCAGGS-RNF12-HA plasmid (gain of function). In this context, although it was not possible to establish a conclusive relationship, the results suggest that an increase in RNF12 expression is associated with a reduced capacity for cell differentiation. Together, these findings indicate that RNF12 levels decrease during myogenic differentiation and suggest that RNF12 may be playing a role during this process.

Position 2
Name: Sneha Acharya
Organization: Sanford Research
Title: Adenine Base Editors as a Novel Gene Therapy for CLN2 Disease
Authors: Acharya, Sneha.*; Rechtzigel, Mitchell J.; Pratt, Melissa A.; Randolph, Peyton E.; Newby, Greg.; Leppert, Hannah G.; Booth, Clarissa D.; Anderson, Joelle;= T.; Timm, Kaylie J.; Liu, David R.; Weimer, Jill M.
Affiliations: Center for Genetics and Rare Diseases at Sanford Research Institute
Institute of MIT and Harvard, Cambridge
Sanford School of Medicine at the University of South Dakota, Vermillion, SD, USA
Abstract: Neuronal ceroid lipofuscinoses (NCLs), collectively known as Batten disease, comprise a group of fatal lysosomal storage disorders. CLN2 Batten disease results from loss or dysfunction of the soluble lysosomal enzyme tripeptidyl peptidase 1 (TPP1), most commonly due to the nonsense mutation p.R208X. Using a CLN2R207X mouse model that closely mirrors the p.R208X patient mutation, we evaluated the therapeutic potential of an AAV9-delivered adenine base editor (ABE7.10), administered via intracerebroventricular injection at postnatal day 1. Gene editing led to increased TPP1 enzymatic activity and mitigated disease-associated pathology across multiple brain regions by 11 weeks of age. Despite the promising CNS-specific outcomes, treated animals did not exhibit extended survival. Given the emergent evidence indicating peripheral involvement in CLN2 Batten disease, these findings suggest that pathology outside the CNS remains unaddressed by CNS-restricted delivery. To address this limitation, we implemented a dual-administration strategy, delivering ABE7.10 through both intracerebroventricular and intravenous routes at postnatal day 1, and assessed the resulting effects on survival and disease pathology. This work supports the continued advancement of adenine base editing as a promising therapeutic strategy for CLN2 Batten disease.

Position 3
Name: Jared Wollman
Organization: Sanford Research
Title: Flow Cytometry Core Facility
Authors: Wollman, Jared*; de la Puente, Pilar
Affiliations: Sanford Research Institute
Abstract: The Flow Cytometry Core was established in 2011 through funding provided by the NIH CoBRE Grant – Cancer Biology Research Center. The Core is housed within the Sanford Research Center; employing experienced, technically proficient staff; and maintains, operates, and supports multiple research instruments for flow cytometry, flow sorting, and sample preparation. The Core's primary mission is to fulfill the flow cytometry-based needs of Sanford Research's principal investigators and neighboring institutions.

Position 4
Name: Venkateshwarlu Bandi
Organization: Sanford Research
Title: The XLID105-associated USP27X variant K509E disrupts deubiquitylation activity and protein localization.
Authors: Bandi, Venkateshwarlu*; Schmelyun, Dhane; Harel, Tamar; Wolberger, Cynthia; Bustos, Francisco
Affiliations: Pediatrics and Rare Diseases Group, Sanford Research
Department of Biophysics and Biophysical Chemistry, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.
Department of Genetics, Hadassah Medical Center, Jerusalem, Israel.
Abstract: X-linked intellectual disability 105 (XLID105) is a neurodevelopmental genetic disorder associated with variants in the USP27X gene, located on the X chromosome. XLID105 majorly affects males as compared with females, with intellectual disabilities, relative macrocephaly, motor delay, speech delay, autism, epilepsy, dysmorphic features, anxiety, and psychosis, other neurodevelopmental symptoms. Most XLID105 variants cause USP27X protein functional disturbance, which impacts its functions, such as deubiquitylation. We identified and functionally assessed the USP27X variants H346R, W349C, R466W, K509E, T580I, S609R, and H623P with an assay based on their activity towards ubiquitylated histone H2B (H2B-Ub) in HEK293T-17 cells. We found that the variant K509E showed disturbed USP27X-deubiquitinase activity. We also investigated the localization effects of these mutations, and we found that while wild type USP27X is localized in the nucleus, K509E and S609R variants are localized to cytoplasmic aggregates. Protein stability analysis with flow cytometry reporters showed that K509E and S609R are less stable than WT and other variants. Our studies indicate that the neurodevelopmental disorder-associated variant USP27X-K509E disrupts deubiquitylation activity. Further studies will aim at understanding the role of USP27X variant effects in human neurodevelopment and use this information in the development of targeted therapies for these patients.

Position 5
Name: Ashley VanCleave
Organization: Sanford Research
Title: Mesenchyme-specific inactivation of Sav1 impairs skeletal development in mice
Authors: VanCleave, Ashley*; Torres, Haydee M.; Kim, Jihyun; Tecleab, Yohannes; Zeng, Erliang; Tao, Jianning
Affiliations: Sanford Research Institute
Abstract: The Flow Cytometry Core was established in 2011 through funding provided by the NIH CoBRE Grant – Cancer Biology Research Center. The Core is housed within the Sanford Research Center; employing experienced, technically proficient staff; and maintains, operates, and supports multiple research instruments for flow cytometry, flow sorting, and sample preparation. The Core's primary mission is to fulfill the flow cytometry-based needs of Sanford Research's principal investigators and neighboring institutions.

Position 6
Name: Soe Maung Maung Phone Myint
Organization: Sanford Research
Title: Mutation in Wdr45 leads to early motor dysfunction and widespread aberrant axon terminals in a beta-propeller protein associated neurodegeneration (BPAN) patient-inspired mouse model
Authors: Phone Myint, Soe Maung Maung,* Krishna Karia, Tetiana Kovalenko, Mitchell Rechtzigel, Prithvi Patthi, Ariana Edwards, Jessica Howard, Elizabeth Aaseng, Shamiq Aftab, Eugenia Trushina, Jill Weimer, Louis-Jan Pilaz, Brandon Meyerink
Affiliations: Pediatrics and Rare Diseases Group, Sanford Research Mayo Clinic, Department of Molecular Pharmacology and Experimental Therapeutics
Abstract: Neurons are highly compartmentalized, specialized cells that are foundational to brain function. Moreover, the neurons we have early in life are the same cells that we carry through our entire life. For these cells to stay healthy and functional over this long period, a process called autophagy is used to clear unwanted, toxic, or unneeded materials from the cell. Alterations in autophagy caused by genetic mutations can lead to the death of neurons and neurodegenerative disease. Here, we used CRISPR editing to modify the autophagy gene WDR45 in mice to generate a model of Beta-propeller Protein Associated Neurodegeneration (BPAN). We show these mice have robust behavior phenotypes consistent with BPAN. We further found that this mutation leads to profound effects on neurons as they develop large, dysmorphic compartments, referred to as spheroids, in the distal portions of their axons. Spheroids form early in the development of the animals and affect numerous types of neurons throughout the brain. These phenotypes are accompanied by changes in expression of several genes involved in synaptic maintenance, vesicular function, ER-associated calcium maintenance, and iron regulation including ferroptosis. We found WDR45 mutant neurons have fewer autophagosomes and an accumulation of mitochondria in their projections as well as significant changes in the proteins residing in their synapses. Finally, we discovered WDR45 associated spheroids contain large accumulations of endoplasmic reticulum and structures for synaptic function. Together, this work establishes WDR45 as a critical regulator of axon homeostasis.

Position 7
Name: Moin Talukder
Organization: Sanford Research
Title: Metabolic Starvation Activates YAP1 to Drive Cellular Reprogramming in Hepatoblastoma
Authors: Talukder, Md Moin Uddin*; Rashid, Naira, Petrik, Olivia, Khurshid, Safiya
Affiliations: Sanford Research
Abstract: Hepatoblastoma (HB), the most common pediatric liver cancer, develops within a metabolically constrained tumor microenvironment characterized by limited nutrient availability. While cancer cells adapt to such stress through metabolic rewiring, the impact of nutrient deprivation on key oncogenic signaling pathways in HB remains unclear. In this study, we investigated how combined glucose and glutamine deprivation (GQ starvation) affects Yes-associated protein 1 (YAP1), a central effector of the Hippo pathway implicated in hepatoblastoma biology. Using HepG2 cells, we assessed YAP1 activity, downstream targets, and cellular phenotypes under metabolic stress conditions. We found that metabolic starvation increases nuclear YAP1 levels, indicating enhanced YAP1 activity. This was accompanied by a significant reduction in CCN2 protein expression, suggesting regulation at the post-transcriptional level. Loss of CCN2 correlated with decreased expression of the hepatocyte differentiation marker HNF4α and increased cell aggregation behavior. Functional assays further showed that CCN2 knockdown alters proliferative dynamics, supporting its role in maintaining cellular homeostasis. Together, these findings suggest that metabolic stress induces YAP1 activation and promotes cellular reprogramming in hepatoblastoma cells, characterized by altered differentiation state and cell-cell interaction behavior. This study highlights a potential adaptive mechanism by which hepatoblastoma cells respond to nutrient deprivation and identifies the YAP1-CCN2 axis as a key regulator of cell state under metabolic stress.

Position 8
Name: Michael Kareta
Organization: Sanford Research
Title: Page & Gage Family Cancer Testis Antigens Promote Small Cell Lung Cancer Chemoresistance by the Regulation of Cell Cycle Pathways
Authors: Jillian Stamp, Malini Mukherjee, Ashley Van Asma, Ella Bakken, Danielle May, Rachel Chrisopulos, Kyle Roux, Michael S. Kareta*
Affiliations: University of South Dakota, Sanford School of MedicinBiomedical Research Division, Sanford Research Institute Functional Genomics & Bioinformatics Core, Sanford Research Institute, Augustana University, Sioux Falls, SD, Protein Biochemistry Core, Sanford Research Institute Department of Chemistry & Biochemistry, South Dakota State University
Abstract: Small cell lung cancer (SCLC) is a devastating disease, constituting 15% of all lung cancer diagnoses. Molecularly, the hallmarks of SCLC include universal loss of Rb and TP53 tumor suppressor genes, tremendous mutational burden, and marked heterogeneity resulting in the rapid acquisition of chemoresistance. Despite an impressive initial response to the standard of care combination cisplatin and etoposide, the near-universal acquisition of chemoresistance presents a decades-long challenge in achieving positive patient outcomes. We have previously shown that two specific Cancer Testis Antigen (CTA) gene families, the GAGEs and PAGEs, are significantly overexpressed in chemotherapy-relapsed human CDX models by scRNA-seq. Importantly, we uncovered that representative members of these families, GAGE2A and PAGE5, functionally contribute to SCLC chemoresistance. Given the existence of over 200 CTA genes, selective upregulation of individual gene families in different cancers reflects a multifaceted mechanism of regulation. This present study aims to understand the mechanism of upregulation of specific CTA families in SCLC, and their role in mediated chemoresistance. We describe epigenetic mechanisms behind CTA upregulation using DNMT inhibitors and whole-genome methyl- and hydroxymethyl-sequencing were used to further validate differences in DNA methylation upon chemotherapy treatment. Our data indicate that DNA demethylation plays a role in CTA expression, while also uncovering a shared putative enhancer for the GAGE and PAGE families. Furthermore, we have found that both PAGE5 and GAGE2A bind to and regulate key members of the cell cycle machinery. This regulation of the cell cycle is not limited to transcriptional means only, but also at the direct protein::protein levels as discovered using BioID. In addition, the localization of GAGE2A was extensively characterized and found to also be on the cell surface reflecting novel roles amongst the CTAs. Together, these observations provide mechanistic evidence for how SCLC chemoresistance is mediated by the PAGE and GAGE families and provide novel pathways and targets for investigation with the goal of clinical intervention in resistant disease.

Position 9
Name: Mangalam Bajpai
Organization: Sanford Research / University of South Dakota
Title: Characterization of Novel Murine Rhabdomyosarcoma Cell Lines Driven by Muscle Cell-specific Notch1 Gain-of-function
Authors: Bajpai, Mangalam*; Hinojosa, Leetoria; Huang, Zhangzan; Smithback, Austyn; Czarnecki, Rebecca; Kim, Jihyun; Fang, Fang; Cao, Yuxia1; Stromberg, Gage1; Aftab, Shamiq; May, Danielle; Pilaz, L.J.; Muirhead, DesiRae; Roux, Kyle; Zeng, Erliang; Torres, Haydee; Tao, Jianning.
Affiliations: Cancer Biology & Immunotherapies Group, Sanford Research, Division of Biomedical and Translational Sciences, University of South Dakota, Department of Chemistry and Biochemistry, South Dakota State University, Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN, USA4, Division of Biostatistics and Computational Biology, University of Iowa, Pediatrics and Rare Diseases Group, Sanford Research, Enabling Technologies Group, Sanford Research, Sioux Falls. Department of Pathology & Department of Pediatrics at Sanford School of Medicine, University of South Dakota
Abstract: Rhabdomyosarcoma (RMS) is an aggressive soft-tissue cancer caused by impaired myogenic differentiation. The Notch signaling pathway plays a key role in cell self-renewal and differentiation. Dysregulated Notch1 signaling in RMS contributes to maintaining cancer stemness. However, current models do not fully capture the impaired Notch1 function that drives RMS progression. To address this issue, we have created two new mouse cell lines: RMS1 and RMS2. These were derived from tumors that occurred spontaneously in a transgenic mouse model expressing the NOTCH1 intracellular domain (NICD) in MLC-Cre positive cells. In this study, we characterized these two cell lines in vitro using genotyping, Western blot analysis and colony formation and proliferation assays. We characterized the cell lines by assessing their ability to undergo cellular differentiation and RNA-sequencing. PCR analysis of genomic DNA confirmed the MLC-Cre; NICD genotype, and immunoblot analysis confirmed the presence of NICD. RMS1 and RMS2 exhibited robust proliferative capacity but limited ability to differentiate into myocytes, adipocytes or osteoblasts under differentiation conditions. Further, we performed transcriptional profiling on both cell lines using RNA-seq. The data revealed higher expression of HES1 and histone deacetylase (HDAC) genes than in the mouse myoblast cell line C2C12. Given the role of HDACs in epigenetic regulation and cancer progression, we evaluated the FDA-approved HDAC inhibitor Romidepsin at low doses. Romidepsin and PAK4 inhibitors significantly reduced cell proliferation and colony formation, thus supporting a functional role for HDAC and PAK4 activity in maintaining RMS cell stemness. The newly developed RMS1 and RMS2 cell lines are therefore valuable preclinical models for studying impaired Notch1 function and evaluating targeted therapies for RMS.

Position 10
Name: Allison Hoefakker
Organization: Sanford Research
Title: Exploring the mechanisms of Marbach-Rustad Progeroid Syndrome
Authors: Hoefakker, Allison* Sears, Rhiannon Roux, Kyle
Affiliations: Center for Genetics and Rare Diseases Research, Sanford Research Institute, Division of Biomedical and Translational Sciences, Sanford School of Medicine, University of South Dakota. Department of Pediatrics, Sanford School of Medicine, University of South Dakota.
Abstract: The nuclear envelope (NE) is an organelle critical to numerous eukaryotic cellular processes. Unsurprisingly, mutations in many of the protein constituents of the NE lead to a variety of diseases. One of these NE-associated diseases is Marbach-Rustad Progeroid Syndrome (MARUPS), a rare form of progeria that was recently identified. MARUPS is caused by an autosomal dominant mutation in LEMD2 that leads to p.Ser479Phe missense mutation in the encoded LEMD2 protein. LEMD2 is a multi-pass transmembrane protein that resides in the inner nuclear membrane and binds to BAF and A-type lamins, mutations in which are associated with other forms of progeria. This project aims to examine the cellular mechanisms underlying MARUPS by employing multiple methods, including fixed and live-cell imaging and BioID to compare the behavior of wild-type (wt) and mutant (m)LEMD2 as well as consequences of its expression. Our initial results identified a reduced mobility of mLEMD2 within the NE as well as altered interactions with protein binding partners. We hypothesize that these altered interactions caused by the p.Ser479Phe mutation within LEMD2 are perturbing the process of nuclear envelope resealing during envelope rupture repair and postmitotic envelope reformation and suggest a shared mechanism with other forms of NE-associated progerias.

Position 11
Name: Casey McKenzie
Organization: Sanford Research
Title: Identifying the Response of Mouse Testis Cells to Flagellar Dysfunction in Primary Ciliary Dyskinesia
Authors: McKenzie, Casey* Isaiah, Oduduabasi Kareta, Michael Lee, Lance
Affiliations: Pediatrics and Rare Diseases Group, Sanford Research. Functional Genomics & Bioinformatics Core, Sanford Research. Genetics and Genomics Group, Sanford Research. Department of Pediatrics, Sanford School of Medicine of the University of South Dakota.
Abstract: Purpose/Background: Dysfunction of motile cilia and flagella cause the pediatric syndrome primary ciliary dyskinesia (PCD), which affects approximately 1 in 7,500 live births and is characterized by chronic respiratory infection, bronchiectasis, and infertility, as well as occasional laterality defects and hydrocephalus. We have previously shown that mice lacking the ciliary central pair proteins Cfap221, Spef2, and Cfap54 develop a PCD phenotype that includes respiratory abnormalities and male infertility. Transcriptomic studies identified multiple pathways altered in respiratory epithelial cells in response to cilia dysfunction, but little is known about testis responses to flagellar dysfunction despite a severe histopathological phenotype of aborted spermatogenesis. In this study, we use these mouse models to elucidate the response of testis cells to flagellar defects resulting from loss of these proteins. The use of single cell RNA sequencing (scRNAseq) and analysis of differentially expressed genes enables exploration of cellular functions that may play a role in disease pathogenesis. Design/Methods: We used the 10x Genomics chromium single cell sorter to perform scRNAseq on samples of cells isolated and purified from the testis of wild type and PCD mutant mice. Differential gene expression was investigated via bioinformatics analysis to identify changes within the mutant testis cell types. Findings/Results: To determine high-priority differentially expressed genes, we identified cell clusters associated with each step of the developing germ cells and the trajectory of their differentiation. Analysis of differentially expressed genes in the germ cell types from each PCD mutant mouse uncovers changes in the PCD mutants during disease pathogenesis. Conclusion/Discussion: Identifying how the testis cell types respond to flagellar defects improves our understanding of PCD pathogenesis, reveals tissue-specific differences in response to ciliary and flagellar dysfunction, and has the potential to lead to new therapies for PCD-associated phenotypes.

Position 12
Name: Naira Rashid
Organization: Sanford Research
Title: Metabolic Stress Driven Alternative Splicing Programs Promote EMT and Invasion in Hepatoblastoma
Authors: Rashid, Naira*
Affiliations: Sanford Research
Abstract: Metastatic hepatoblastoma has a very poor prognosis, with 5-year survival rates of only 20–50%. Tumor cells are known to survive within a hostile, nutrient-deprived microenvironment and adapt to survive and disseminate; however, the molecular mechanisms underlying this adaptation remain poorly defined. To address this gap, we modelled metabolic stress by culturing hepatoblastoma cells under combined glucose and glutamine deprivation and perform integrated RNA sequencing to define stress-induced changes in gene expression and alternative splicing. We systematically compared these profiles with transcriptomic data from hepatoblastoma patient tumors to identify clinically conserved stress-responsive programs. Our analyses reveal robust, conserved alternative splicing events such as those in FLNB, NUMB and ITGA6 and RNA-binding protein networks including RBPs such as MBNL1, 2 and IGF2BP2 that regulate epithelial–mesenchymal transition and promote invasive phenotypes under metabolic stress. These programs are shared between starved hepatoblastoma cells and metastatic patient samples, highlighting their clinical relevance.Collectively, our findings demonstrate that metabolic stress reshapes the alternative splicing landscape, revealing an additional layer of gene regulation that enables hepatoblastoma cells to adapt to nutrient-deprived conditions. Given that hepatoblastomas are inherently nutrient-starved, these results provide a framework for targeting stress-adaptive pathways and developing improved therapeutic strategies for children with advanced disease.

Position 13
Name: Attila Kovacs
Organization: Sanford Research
Title: Assessing cancer-related pain by behavioral tests in mice with oral tumors
Authors: Kovács, Attila* Vermeer, Paola
Affiliations: Cancer Biology and Immunotherapies Group, Sanford Research. Sanford School of Medicine, University of South Dakota.
Abstract: Introduction: Quantifying oro-facial pain is complicated as this richly innervated area contains multiple overlapping fields associated with different sensory modalities. Here, we tested the utility of marble bury, burrowing, and our newly developed facial von Frey test to assess oral cancer-related pain. Methods: C57BL/6J mice were separated into four experimental groups (10 mice/group) as follows: 1) oral MOC2-7 tumor implantation; 2) oral tumor implantation + carprofen (non-steroidal anti-inflammatory drug commonly used for pain); 3) No tumor; 4) No tumor + carprofen. All groups underwent behavioral testing twice a week before and after tumor implantation. While the marble bury test classically assesses obsessive/compulsive and anxiety-like behaviors, it can also serve as a measure of pain. The burrowing test measures a mouse's innate behavior to remove food from a tube. While it is a test of general well-being, it also serves as a measure of pain. Facial von Frey tests the mechanical sensitivity of the right (tumor-bearing) and left (no tumor) cheeks. For this, the mouse’s movements are gently restricted by holding its tail while von Frey filaments are used to touch each cheek using the simplified up-down method. Results: On days 28 and 30 post-tumor implantation, male mice buried significantly less marbles than no tumor control animals; treatment with carprofen prevented this decline. On day 30 post-tumor implantation, tumor-bearing mice showed a significant decrease in the amount of food pellets removed from the tube; carprofen had no effect on this behavior. Starting on day 10 post-tumor implantation, the mechanical sensitivity of the tumor-bearing right cheek markedly increased as compared to no tumor control animals. Carprofen treatment prevented this increased sensitivity. Surprisingly, carprofen treatment caused a pronounced reduction in tumor growth in female but not male mice. Conclusion: Our newly developed facial von Frey test does not require repeated conditioning or training and can detect increased mechanical sensitivity at the tumor site as early as 10 days after tumor implantation.

Position 14

Name: Karama Hamdi
Organization: Sanford Research

Title: Identifying the Cliliary Perturbations in OKUR-CHUNG Neurodevelopmental Syndrome

Authors: Hamdi, Karama* Menzel, Elizabeth Loukil, Abdelhalim
Affiliations: Sanford Research Institute

Abstract: The primary cilium is a sensory, microtubule-based organelle that mediates extracellular signals from the neighboring environment into the cell. It mediates key developmental signaling pathways, including the Sonic Hedgehog pathway (SHH). Primary cilia are therefore essential for embryonic development and the homeostasis of multiple organs and tissues. Mutations in ciliary genes cause a variety of rare disorders, commonly termed ciliopathies, with a wide range of developmental deficits. We previously identified the casein kinase II alpha I, CSNK2A1, as being enriched at the basal body and mediating cilia trafficking, signaling, and stability. CSNK2A1 mutations cause Okur-Chung neurodevelopmental syndrome (OCNDS), an autosomal dominant condition with neurological abnormalities comparable to those of cilia-related disorders. The molecular and cellular mechanisms underlying the pathogenesis of OCNDS remain unknown. Since CSNK2A1 modulates ciliary processes, we wondered whether OCNDS mutations might affect primary cilia regulation and function. Hence, we assessed cilia in OCNDS patients' cells, which are skin fibroblasts heterozygous for CSNK2A1 missense mutations (p.R47G, p.D156E, and p.K198R; two control cell lines). Our findings showed that all OCNDS cell lines displayed shorter cilia and abnormal signaling, with no change in ciliogenesis. We also found that SHH proteins exhibit abnormal levels in OCNDS cilia. While SMO ciliary levels were reduced, GLI2 and KIF7 were increased at the ciliary tip in the presence of SMO agonist (SAG). These findings were consistent with our quantitative PCR results. Both SHH target genes, Gli1 and Patched, exhibited abnormal expressions in all OCNDS cell lines compared to controls. These findings indicate that OCNDS variants disrupt primary cilia trafficking and signaling, similarly across OCNDS lines. This suggests a unifying ciliary mechanism(s) likely driven by the CSNK2A1 mutated version. Csnk2a1 genomic changes in OCNDS are missense point mutations affecting one of the two gene alleles. It is plausible that these mutations might cause changes in the CSNK2A1 kinase activity and its substrate signature. We therefore performed quantitative phosphoproteomics analysis to define phosphorylation shifts in OCNDS compared to control cells. Multiple comparisons were performed between each OCNDS cell line and a control cell line. To identify unifying hits, we overlapped either enriched or depleted phosphoproteins from all or most comparisons. Our stringent strategy allowed us to identify only two consistently enriched hits, KRI1 (Cysteine endopeptidase) and TRAPPC10 (Trafficking Protein Particle Complex Subunit 10). We deployed super-resolution microscopy (Nikon, SORA) and showed that both hits localized to the centrosome. KRI1 and TRAPPC10 exhibited ring-like structures at the basal body in control cells. Interestingly, this subcellular organization was disrupted in all OCNDS cell lines. In addition, their centrosomal levels were significantly reduced in all patients' cells. This centrosomal reduction is likely to be a protein mislocalization and/or a failure in its recruitment. This is because the total protein levels of TRAPPC10 and KRI1 appeared unchanged in the presence or absence of cycloheximide. Even though OCNDS cells are from different individuals with different mutations, their ciliary phenotypes appear similar. Consistent with this, our phosphoproteomics results unbiasedly identified two centrosomal hits that are potentially hyperphosphorylated by OCNDS variants. Further work is needed to investigate the ciliary roles of KRI1 and TRAPPC10, with the latter already shown to be required for cilia assembly. Our future work will build on our findings to holistically identify the underlying molecular mechanisms of OCNDS. This is expected to provide novel insights into the potential disease causality between primary cilia dysregulation and OCNDS. In the long term, we hope our work will help enhance the discovery of new therapeutics that can target cilia recovery and, in turn, relieve some of the neurological deficits.

Position 15
Name: Dane Rasmussen
Organization: Sanford Research
Title: CAR-Tregs: A Drive Towards a Type I Diabetes Treatment
Authors: Rasmussen, Dane* Bhattarai, Ram* Savinov, Alexei
Affiliations: Diabetes Research Group, Sanford Research
Abstract: Type 1 diabetes (T1D) is an autoimmune disease in which autoreactive effector T cells destroy pancreatic β cells, abolishing insulin production and resulting in chronic hyperglycemia and associated metabolic complications. Although exogenous insulin administration is lifesaving, it does not address the underlying autoimmune pathology. One promising immunomodulatory approach is the engineering of regulatory T cells (Tregs) expressing a β cell–specific chimeric antigen receptor (CAR-Tregs). These CAR-Tregs could localize to the pancreas and provide immune protection to β cells, thereby preserving endogenous insulin production. A major obstacle to CAR-Treg therapy is the relative rarity of natural Tregs (nTregs) in peripheral blood, making it difficult to obtain sufficient cells for therapeutic dosing. Induction of naïve $CD4^+$ T cells into induced Tregs (iTregs) offers a potential solution; however, iTregs often exhibit reduced immunosuppressive function and declining Treg identity after extended culture, as indicated by loss of FOXP3 expression. Notably, Sakaguchi et al. demonstrated that deletion of the transcriptional regulator RBPJ can stabilize FOXP3 expression and maintain Treg identity in iTregs. Here, we generated both CAR-nTregs and CAR-iTregs targeting the β cell–specific marker NTPDase3 using a retroviral system. Following sorting and expansion of CAR-positive cells, both populations maintained Treg identity, as assessed by FOXP3 expression via flow cytometry. Additionally, we produced CRISPR-induced RBPJ knockout iTregs. These cells retained stable FOXP3 expression and Treg-like identity over multiple weeks in culture. Together, these findings support the feasibility of generating stable CAR-Treg populations and highlight new avenues for developing durable, antigen-specific immunotherapies for T1D.

Position 16
Name: Derick Peters
Organization: Sanford Research
Title: Leveraging Blood-Based Multi-Omic Analyses for Diagnostic Classification of Batten Disease Subtypes
Authors: Peters, Derick* Rechtzigel, Mitchelle Leppert, Hannah Anderson, Joelle Michelle, K Ortmeier, Steve Pratt, Melissa Booth, Clarissa Posern, C Schulz, April Brudvig, Jonathan Weimer, Jill
Affiliations: Pediatrics and Rare Diseases Group, Sanford Research, Department of Pediatrics, Sanford School of Medicine.
Abstract: Batten disease is a rare neurodegenerative disorder caused by mutations in one of several genes, including TPP1 (CLN2) and CLN3 — both heavily implicated in lysosomal homeostasis. Current biomarkers, such as neurofilament light (NfL), lack specificity and may not capture non-neuronal aspects of disease pathology. A deeper understanding of blood biomolecule changes in affected individuals would clarify core disease mechanisms and enable more targeted biomarkers for refined clinical assessment and early detection. To this end, we used blood drawn from wild-type, CLN2R208X and CLN3Δex7/8 Yucatan miniature pigs for novel disease biomarker discovery and validation. Metabolomic, lipidomic, and proteomic analyses were performed across all three genotypes at multiple timepoints, yielding over 500 altered metabolites and over 800 altered proteins in late-stage disease. From these data, we identified the most dysregulated analytes in the CLN3Δex7/8 model and developed a classification system capable of identifying CLN3-specific disease subtype from blood samples and assessing disease severity at the time of sample collection. Our next step is to extend the CLN3-specific framework to the CLN2R208X model with the goal of developing a diagnostic tool capable of distinguishing different disease subtypes and their respective phenotypes, including heterozygous carriers, in humans carrying analogous mutations. Beyond diagnosis, this tool would offer clinicians and researchers a much-needed means to monitor disease progression and evaluate efficacy of emerging therapeutics — a critical gap in the Batten disease community.

Position 17
Name: Clarissa Booth
Organization: Sanford Research
Title: Designing and Executing In Vivo Studies: An Integrated Research Platform Provided by the Animal Hub at Sanford Research Institute
Authors: Booth, Clarissa* Pilaz, LJ Michelle, Kaitlyn Bastain, Abby Karia, Krishna members of the Animal Hub team
Affiliations: Sanford Research, Animal Hub
Abstract: Progress in rare disease research is often driven by innovative animal models and robust in vivo experimentation, yet these studies can be technically complex and resource-intensive. The Animal Hub at Sanford Research Institute was established to provide a centralized, integrated platform to support animal-based research, bringing together expertise in model generation, behavioral and phenotypic assessment, and preclinical therapeutic evaluation. By combining multidisciplinary expertise, the Hub connects investigators with shared infrastructure, technical training, and experimental design guidance to support reproducible and efficient experiments and studies. Through the Experimental Therapeutics Screening Facility (ETSF), the Hub can also partner directly with investigators to design and execute collaborative in vivo experiments, including preclinical efficacy, pharmacokinetic, and safety studies, as well as basic science applications. This poster provides an overview of the Animal Hub's structure and services and illustrates how coordinated animal research support can facilitate discovery, improve study quality, and accelerate translational efforts in rare disease research.

Position 18
Name: Elizabeth Menzel
Organization: Sanford Research
Title: Cilia SubQ suite: modular pipelines for analysis of primary cilia subcompartments and trafficking
Authors: Menzel, Elizabeth* Hamdi, Karama Hoffman, Gracie Loukil, Abdelhalim
Affiliations: Pediatrics and Rare Diseases Group, Sanford Research. Department of Pediatrics, Sanford School of Medicine, University of South Dakota. Biomedical and Translational Sciences Program, University of South Dakota.
Abstract:
Primary cilia are microtubule-based, antenna-like organelles that protrude from the surface of most vertebrate cells and play critical roles in sensing extracellular signals, regulating developmental pathways, and maintaining cellular homeostasis. To form and function properly, these organelles rely on precise spatial and temporal coordination of protein composition in their distinct structural subdomains, including the basal body, transition zone, ciliary shaft, and ciliary tip. Disruptions in ciliary subdomain organization can lead to a range of human disorders known as ciliopathies. However, to capture subtle phenotypic changes in both healthy and disease states, accurate, high-resolution quantification of each subdomain is essential.
Therefore, we have developed Cilia-SubQ, a versatile collection of flexible pipelines for the arivis Pro software designed to detect the primary cilium, pericentriolar material, basal body, transition zone compartment, and ciliary tip, enabling rapid and reproducible quantification of immunofluorescent signals from ciliary-centrosomal proteins. Through the Arivis Cloud-learning toolkit, we trained an AI model to robustly detect primary cilia, which could then be imported and expanded upon with additional commands to isolate each subdomain for quantification. The suite also includes a readily deployable script for generating kymographs of IFT trafficking in mammalian primary cilia, as well as a script for FIJI to be used in conjunction with the arivis Pro to quantify cilia length. Altogether, Cilia-SubQ is a toolkit that has the potential to expedite immunofluorescence quantification in an unbiased, reliable manner.

Position 19
Name: Jeffrey Barr
Organization: Sanford Research
Title: Microglia and Astroglial activation in a mouse orofacial cancer model and the impact of various treatments
Authors: Barr, Jeffrey* Walz, Austin Vermeer, Paola
Affiliations: Sanford Research
Abstract: Sensory information from oral and facial regions is initially processed in the spinal trigeminal nucleus, specifically in the caudalis (Vc) subregion. Using a mouse model of head and neck cancer, we've previously demonstrated that tumor-infiltrating nerves connect to distinct brain areas via the ipsilateral trigeminal ganglion, and that this neuronal circuit is activated in the presence of cancer. The aim of this study was to investigate whether astroglia and microglia in the Vc and associated brain regions may be involved in the alterations observed in the presence of orofacial cancer. The effects were tested on Vc astroglia hyperactivity, as revealed by glial fibrillary acid protein (GFAP) labeling or microglial hyperactivity, as revealed by Ionized calcium binding adaptor molecule 1 (Iba1) labeling. Compared with contralateral regions and tumor-naïve mice, a significant increase of Iba1-positive cells was found in ipsilateral Vc, principal sensory nucleus of trigeminal nerve (PrV), Facial motor nucleus (VII), and a significant increase of GFAP-positive cells in the facial motor nucleus of male and female mice. These increases in both Iba1 and GFAP were significantly inhibited by administration of carprofen, by selective ablation of TRPV1-expressing sensory neurons by Resiniferatoxin (RTX), or by treatment of the cancer with cisplatin-based chemoradiation. The increases in glia activity did not correspond completely with previous measures of neuronal activity via fos labeling. These various findings suggest that glial hyperactivity may not be involved in the enhanced responses of cancer-associated neurons, but may play a role in hyperalgesia associated with orofacial cancer.

Position 20
Name: Rachel Chrisopulos
Organization: Sanford Research
Title: Biochemistry Core: Exploring Protein Networks with Cutting Edge Techniques
Authors: Chrisopulos, Rachel J.* May, Danielle G. Roux, Kyle J.
Affiliations: Enabling Technologies Group, Sanford Research. Department of Pediatrics, Sanford School of Medicine, University of South Dakota.
Abstract: In the post-genome era there is increased emphasis on understanding protein function. A powerful approach to study protein function is to monitor protein-protein interactions (PPIs). Traditional methods to screen for PPIs, including yeast two-hybrid and affinity-protein complex purification, have been successful but have substantial limitations. To overcome some of these limitations and provide a complementary approach, the Biochemistry Core (BC) at Sanford Research primarily functions to provide BioID services. BioID (for proximity-dependent biotin identification) is a fundamentally unique method to generate a history of PPIs over time by using a promiscuous biotin ligase fused to a bait protein or targeting motif. When expressed in cells the BioID fusion protein biotinylates proximate proteins enabling their capture and identification by mass-spectrometry analysis. Unlike other approaches, BioID is applicable to insoluble proteins and enables detection of weak and transient PPIs. Since we developed the method in 2012, BioID has become an established method with over 300+ publications citing or using BioID to monitor PPIs in a wide variety of cellular and animal models. The BC also works to improve the BioID method by advancing the “BioID-Toolbox” by creating BioID2 biotin ligase, expanding zipcode BioID, and testing a recently engineered, faster version of BioID termed TurboID. In addition to BioID services, the BC assists researchers investigate PPIs by providing training, and performing conventional co-immunoprecipitation and gel/membrane imaging.

Position 21
Name: Destiny Brockhaus
Organization: University of South Dakota / Sanford Research
Title: Early brain responses to peripheral melanoma and the role of TRPV1⁺ sensory neurons
Authors: Brockhaus, Destiny S.* Kovács, Attila D. Welbon, Craig Barr, Jeffrey Vermeer, Paola D.
Affiliations: University of South Dakota. Sanford Research.
Abstract: Brain metastasis remains a leading cause of mortality in melanoma, yet how the brain responds to peripheral tumors prior to CNS colonization is poorly understood. TRPV1-expressing sensory nerves infiltrate primary melanomas, but their role in tumor–brain communication and metastasis is unknown. In other cancers, tumors engage TRPV1⁺ neurons to form circuits projecting to the brain, suggesting that primary tumor–neuron interactions may influence central responses and metastatic spread.
Here, we investigate the establishment of tumor–brain circuitry in melanoma, assess central neuronal and glial activation, and evaluate the contribution of TRPV1⁺ tumor-infiltrating neurons (TINs). Juvenile C57BL/6 mice underwent chemical ablation of TRPV1⁺ neurons using resiniferatoxin (RTX) prior to intradermal injection of YUMMER1.7 melanoma cells. Six days prior to euthanasia, tumors were injected with Wheat Germ Agglutinin (WGA) for neural tracing, and tumors and brains were collected for analysis. Confocal microscopy assessed WGA-labeled circuitry, while immunofluorescence for neuronal (ΔFos) and glial (CD68, GFAP) markers indicated altered activation.
Early tracing data suggest that TRPV1⁺ TINs establish functional connections with central circuits, potentially enabling tumor-to-brain communication. Notably, female mice exhibit reduced tumor growth relative to males, with a trend toward increased TRPV1⁺ tumor innervation in primary melanomas. Together, these findings suggest that the brain may respond to peripheral melanoma at early stages and highlight tumor–brain communication pathways as potential therapeutic targets.

Position 22
Name: Destiny Brockhaus
Organization: University of South Dakota / Sanford Research
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Affiliations: University of South Dakota. Sanford Research.
Abstract: Brain metastasis remains a leading cause of mortality in melanoma, yet how the brain responds to peripheral tumors prior to CNS colonization is poorly understood. TRPV1-expressing sensory nerves infiltrate primary melanomas, but their role in tumor–brain communication and metastasis is unknown. In other cancers, tumors engage TRPV1⁺ neurons to form circuits projecting to the brain, suggesting that primary tumor–neuron interactions may influence central responses and metastatic spread.
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Position 23
Name: Leetoria Hinojosa
Organization: Sanford Research / Mayo Clinic
Title: Investigating the Molecular Mechanisms of Lateral Meningocele Syndrome (LMS) and Potential Therapeutic Targets in Notch-Related Skeletal Disorders
Authors: Torres, H Hinojosa, L VanCleave, A Rodezno, T May, D Mukherjee, M Tecleab, Y Kim, J Pilaz, L Weimer, J Zeng, E Roux, K Westendorf, J Tao, J
Affiliations: Sanford Research. Mayo Clinic.
Abstract: Lateral Meningocele Syndrome (LMS) is a rare congenital disorder marked by musculoskeletal anomalies and neurological impairments due to NOTCH3 mutations. This study explores the underlying disease mechanisms and assesses potential therapeutic interventions using the Humpback (hpbk) mouse model. We employed the hpbk model, carrying a Notch3 gain-of-function mutation, to evaluate phenotypic manifestations and therapeutic responses. Methods included skeletal staining, micro-CT, single-nucleus RNA-seq, bulk RNA-seq analyses, histological examinations, functional assessments like the Rotarod test, in vitro luciferase reporter assays, and proximity-dependent biotin identification (BioID) screening assays. Two-month-old hpbk/hpbk mice exhibited reduced body weight, skeletal muscle size, and grip strength, along with kyphosis, unlike their heterozygous counterparts. Transcriptomic analyses highlighted dysregulated pathways, notably involving the Farnesoid X receptor (FXR)/Retinoid X receptor (RXR) and interactions with histone deacetylases (HDACs). The HPBK Notch3 protein demonstrated reduced transactivation activities, and BioID screening identified unique interactors, retaining approximately 40% of known and unknown interactors with the WT Notch3 protein, including RBPJ, HDAC1, and TCF20. Early intervention with an HDAC inhibitor prevented kyphosis and restored skeletal muscle weight in mutant mice. Our findings suggest that NOTCH3 mutations in LMS disrupt multiple metabolic and developmental pathways, underscore the potential of targeted HDAC inhibition as a therapeutic avenue, and reveal complex protein interactions that may inform future treatment strategies. Ongoing studies aim to further delineate functional discrepancies between mutant and wild-type NOTCH3 proteins.

Position 24

Name: Christina Jackson
Organization: University of Minnesota

Title: Gene Therapy for Cockayne Syndrome B (CSB) and Establishing a Stress-Induced Mouse Model

Authors: Jackson, Christina G.* Luo, Hanyang Venigalla, Sree Aslanidi, George Kang, Peter Pacak, Christina A**.**
Affiliations: Department of Neurology, University of Minnesota Medical School. The Hormel Institute, University of Minnesota.

Abstract: Cockayne syndrome (CS) is a rare autosomal recessive disorder caused by pathogenic variants in the ERCC8 or ERCC6 genes encoding for the proteins CSA and CSB, respectively. These genes are essential for repairing damage to DNA and are involved in the transcription-coupled repair sub pathway of nucleotide excision repair. Clinically, CS presents a variety of symptoms including features of premature aging, growth failure, microcephaly, photosensitivity, neurological/neurodevelopmental abnormalities, liver and digestive problems, and damaged kidneys. Because there are currently no disease-altering therapies available for CS, this project seeks to develop a gene therapy for CSB. We are evaluating the potential to restore CSB function by delivering an adeno-associated virus (AAV)-based gene therapy to alleviate disease features.The specific capsid serotype being used is AAVDJ, which has been proven superior to other serotypes for targeting the brain and spinal cord while de-targeting the liver across multiple delivery routes in mice. The vector contains codon optimized ERCC6 (CSB) under the control of a specialized mini-promoter (CP040) designed to specifically accommodate the large size of the gene being delivered. The project tests how the route of administration of the virus influences behavior, phenotype, biodistribution and safety by comparing intravenous (IV), intrathecal (IT), and combined IV and IT injections of the vector in age and sex matched wild-type (WT) and CSB ($Csb^{-/-}$) mice with the aim of understanding how efficiently the therapy reaches target tissues in the CNS and periphery. Mice in one of three experimental groups (WT, $Csb^{-/-}$, and $Csb^{-/-}$ + AAVDJ), will be treated at 12 weeks of age, followed by behavioral assays including ActiTrack, and Elevated Plus Maze. The mice will be sacrificed at 25 weeks of age for tissue analysis, quantification of AAV vector genomes, ERCC6 transgene expression levels, CSB protein expression, and markers of oxidative stress using 8 OH-DG. This is an ongoing study in which the aforementioned cohorts are being established, with some mice in the IT $Csb^{-/-}$ + AAVDJ group having been treated and are undergoing further evaluation. In addition, the particularly mild nature of our $Csb^{-/-}$ mouse model has prompted us to explore methods that may induce chronic oxidative stress. We are performing a pilot study in which WT and $Csb^{-/-}$ mice are subject to drinking ad libitum .03% H_2O_2 in their regular water and compared to control drinking normal water. Given the DNA damage–sensitive nature of CSB, the goals of this study are to evaluate how chronic low-level hydrogen peroxide exposure affects disease-relevant pathways and to establish a more robust model for testing therapeutic interventions. Future findings from this project will inform optimal treatment strategies and therapeutic feasibility of our gene delivery for future clinical translation as it relates to pathogenic variants associated with CSB and Cockayne syndrome

Position 25
Name: Sree Venigalla
Organization: University of Minnesota
Title: Human 3D Engineered tissue models for studying rare cardiac and skeletal muscle disorders
Authors: Venigalla, Sree* Tinklenberg, Jennifer Pakkiriswami, Shanmugasundaram Liu, Julia Kang, Peter Cade, Todd Pacak, Christina
Affiliations: Greg Marzolf Jr. Muscular Dystrophy Center and Department of Neurology, University of Minnesota Medical School. Department of Integrative Biology and Physiology, University of Minnesota Medical School. University School of Medicine, Doctor of Physical Therapy Division, Duke University School of Medicine.
Abstract: Background: Rare disorders affect ~300 million people worldwide, with 80% having genetic origins but only 5% having approved treatments. While mouse models are vital for therapeutic development, they often fail to replicate human phenotypes or account for diverse genetic backgrounds. 3D engineered tissue models using patient-derived induced pluripotent stem cells (iPSCs) offer a complementary platform, retaining the genetic drivers of disease while enabling tissue-level functional analysis. Methods: This study utilizes Curi Bio's Magnetometric Analyzer for eNgineered Tissue ARRAY (Mantarray) to develop 3D Engineered Muscle Tissues (EMTs) for Duchenne muscular dystrophy (DMD) and Engineered Heart Tissues (EHTs) for Barth syndrome (BTHS). Constructs were generated by combining iPSC-derived skeletal myoblasts or cardiomyocytes with fibroblasts in a fibrin-based hydrogel. Using a 24-well plate format with integrated graphite electrodes, tissues undergo simultaneous electrical stimulation to assess contractile properties between days 5 and 14. Results: We demonstrate that both DMD and BTHS constructs exhibited distinct, impaired contractile phenotypes compared to healthy controls. In addition, we demonstrate the ability to measure oxygen consumption and reactive oxygen species (ROS) measurements using a next generation O2K-Fluo-respirometry (Oroboros) with healthy and BTHS 3D EHTs. ROS measurements were significantly elevated in BTHS 3D EHTs compared to healthy EHTs. Ongoing work includes immunofluorescence, western blotting, RT-PCR, and mitochondrial activity measurements to further characterize these models. Conclusion: Overall, the Mantarray platform provides a high-throughput, physiologically relevant environment for studying disorders that impair muscle contraction. These results demonstrate the platform's utility for investigating disease mechanisms and performing human-centric drug screening for rare genetic disorders.

Position 26
Name: Venessa Agyapong
Organization: University of Minnesota
Title: The Senolytics Dasatinib and Quercetin (D+Q) and 3TC Modulate Inflammation and Senescence-Associated Features in DMD Muscle
Authors: Agyapong, Venessa* Venigalla, Sree Tinklenberg, Jennifer Sedivy, John Robbins, Paul Kang, Peter B. Pacak, Christina A.
Affiliations: Department of Neurology and Greg Marzolf Jr. Muscular Dystrophy Center, University of Minnesota. Department of Molecular Biology, Cell Biology, and Biochemistry, Brown University. Institute of the Biology of Aging and Metabolism, University of Minnesota.
Abstract: Ineffective myofiber repair mechanisms in Duchenne Muscular Dystrophy (DMD) result in progressive muscle tissue degeneration. We and others have found that DMD aligns with 8 of the 12 hallmarks of aging, with the presence of senescent cells and stem cell exhaustion heavily impairing the regenerative capacity of muscle. As muscle cells are progressively lost and replaced with fat deposits and fibrosis, secondary disease mechanisms give rise to phenotypes associated with premature aging that worsen over time. The aim of this study is to evaluate the effectiveness of the senolytics Dasatinib and Quercetin (D+Q), as well as lamivudine (3TC), in reducing accelerated aging phenotypes and improving regenerative capacity in DMD (D2-mdx) mouse myofibers. 3TC, an antiviral agent, has been shown to reduce senescence, potentially through anti-inflammatory mechanisms. D+Q has been used synergistically in cancer therapy to reduce senescence and inflammation by inducing apoptosis in senescent cells. We hypothesized that both treatments would reduce chronic senescent cell accumulation, decrease inflammation, and promote more effective muscle regeneration. 3TC was administered to D2-WT and D2-mdx mice starting at 6 weeks of age for 4 weeks via drinking water, with untreated controls receiving water alone. D+Q was administered starting at 3 weeks of age for 22 weeks via oral gavage twice weekly. Behavioral assessments were conducted at early, middle, and late stages of treatment using Actitrack, inverted wire, rotarod, and grip strength tests, and muscle mass was collected at necropsy. Neither treatment improved muscle function or mass. However, fluorescence-activated cell sorting (FACS) of tibialis anterior muscle revealed reduced resident macrophages, increased endothelial cell populations, and decreased inflammatory markers. Ongoing analyses of tissue structure, gene expression, and protein expression will further clarify treatment effects and guide future therapeutic strategies targeting senescence in DMD.

Position 27

Name: Usman Zeb
Organization: Institute of Biotechnology and Genetic Engineering, University of Agriculture Peshawar / The University of Chicago

Title: PADI4 gene mutation impact on Synovial lining in Rheumatoid arthritis disease using whole exome sequencing

Authors: Zeb, Usman Dawood, Ahmad He, Tong Chuan
Affiliations: Institute of Biotechnology and Genetic Engineering, University of Agriculture Peshawar. The University of Chicago.

Abstract: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent inflammation and joint damage, with a strong genetic component. The PADI4 gene encodes peptidyl arginine deiminase 4, an enzyme involved in citrullination, which converts arginine residues into citrulline, leading to the formation of anti-citrullinated protein antibodies (ACPAs), a hallmark of RA.

In this study, we investigated the segregation and variant spectrum of the PADI4 gene in RA-affected families using whole exome sequencing followed by Sanger sequencing validation. The gene showed strong segregation among affected individuals. Three key variants were identified: rs11203366 (c.163G>A; p.Arg55His), rs11203367 (c.281C>T; p.Pro94Leu), and rs874881 (c.245T>C; p.Leu82Pro). These missense changes are predicted to alter protein structure and enzymatic activity, potentially enhancing aberrant citrullination and promoting autoimmune responses.

Statistical analysis demonstrated a significant association between PADI4 variants and RA susceptibility ($P < 0.05$), with increased odds ratios indicating elevated genetic risk. In conclusion, these findings highlight the critical role of PADI4 variants in RA pathogenesis and support their potential as genetic biomarkers for disease susceptibility and targeted therapeutic strategies.

Position 28

Name: Grace Hoffman

Organization: Sanford Research / University of South Dakota

Title: Investigating the Roles of the ciliary kinase CSNK2A1 in mediating Neural Tube Patterning During Neurogenesis

Authors: Hoffman, Grace* Hamdi, Karama Loukil, Abdelhalim

Affiliations: Sanford Research. Biomedical and Translational Sciences Program, University of South Dakota. Department of Pediatrics, Sanford School of Medicine, University of South Dakota.

Abstract: Primary cilia act as the antennae of the cell that detect extracellular signals to transduce the proper cellular response. Ciliary signaling regulates major developmental signaling pathways such as the Sonic Hedgehog (SHH) and WNT signaling. Therefore, this signaling hub is vital for embryonic development and the homeostasis of several organs and tissues. Mutations in ciliary genes lead to a broad spectrum of rare human diseases, often affecting several organs including the central nervous system. We previously identified Casein kinase 2 alpha 1 (CSNK2A1) as a modulator of ciliary trafficking and stability, acting as a negative regulator of SHH signaling. Mutations in Csnk2a1 gene cause Okur Chung Neurodevelopmental Syndrome (OCNDS), a neurodevelopmental disorder. Individuals with OCNDS exhibit a range of neurological deficits and clinical features that broadly overlap with those seen in cilia-related disorders. We evaluated the effect of Csnk2a1 disease-associated variants on primary cilia and found cells from OCNDS patients exhibit shorter cilia with impaired SHH activation. This led us to investigate the in vivo role of CSNK2A1 in SHH-mediated neural development. To this end, we utilized the patterning of the neural tube, mediated by primary cilia at midgestation, as a readout of SHH pathway activity during neurogenesis. In addition, we sought to compare the effect of the OCNDS variant with that of the Csnk2a1 null allele on neurogenesis and embryogenesis. To test this, we assembled an allelic series that combines the Csnk2a1 null and the OCNDS (K198T or mu) alleles [Csnk2a1 +/+, +/-, -/-, +/198mu, -/198mu, and 198mu/198mu]. The K198T point mutation located in the CSNK2A1 kinase domain is a confirmed pathogenic mutation in multiple OCNDS patients. Embryos exhibited various developmental abnormalities, including brain malformations, partially open neural tubes, and cardiac fluid accumulation. Embryos with Csnk2a1 -/- mutations were non-viable by embryonic day (E)11.5, Csnk2a1 -/198mu mutants by E11, and Csnk2a1 K198T/K198T mutants by E9.5. The earlier lethality of embryos possessing Csnk2a1 K198T suggests that this mutation is more disruptive than the null allele, suggesting a gain-of-function effect. Embryos were collected at multiple developmental stages, sectioned, and stained with markers for dorsal and ventral progenitors OLIG2, PAX6, FOXA2, Islet 1/2, NKX2.2, PAX7, and OLIG3. The lengths of each progenitor domain were normalized to total neural tube length and statistically compared between mutant and control embryos. We observed significant disruptions across multiple neural tube domains in all disease variant Csnk2a1 embryos. Analysis of this allelic series suggests that SHH signaling pathway is preferentially disrupted in the OCNDS variant, while WNT signaling levels appear at canonical levels. In the future, we aim to investigate the specific neural progenitor populations that are disrupted in OCNDS and explore their potential downstream effects on brain development, as well as the molecular abnormalities within these populations. Our data suggests that primary cilia signaling may be impaired early during neurogenesis in OCNDS, potentially contributing to the neurodevelopmental defects observed in affected individuals.

Position 29
Name: Kimberly Turner
Organization: Sanford Research Institute
Title: Characterizing a Multinational Rare Disease Registry: Demographics, Diagnoses, and Age at Presentation
Authors: Turner, Kimberly R. Scott, Rebecca Mendel, Alyssa Free, Colette Chan, Chun Hung
Affiliations: Sanford Research Institute
Abstract: Rare and undiagnosed diseases affect millions of individuals worldwide, yet many conditions remain poorly characterized due to limited cohort sizes and fragmented data collection. Patient registries offer an important mechanism for aggregating patient-reported data across diverse diagnoses and geographic regions. Here, we present a descriptive overview of a multinational rare disease registry, focusing on participant demographics, primary diagnoses, age at diagnosis, geographic distribution, and reported modes of diagnosis. By summarizing normalized participant-level data, this work highlights the diversity of rare disease populations and diagnostic pathways represented within the registry.

Position 30
NName
Organization: Sanford Research
Title: Adenine Base Editors as a Novel Gene Therapy for CLN2 Disease
Authors: Acharya, Sneha* Rechtzigel, Mitchell J. Pratt, Melissa A. Randolph, Peyton E. Newby, Greg Leppert, Hannah G. Booth, Clarissa D. Anderson, Joelle T. Timm, Kaylie J. Liu, David R. Weimer, Jill M.
Affiliations: Center for Genetics and Rare Diseases at Sanford Research Institute. Broad Institute of MIT and Harvard. Harvard Medical School. Sanford School of Medicine, University of South Dakota.
Abstract: Neuronal ceroid lipofuscinoses (NCLs), collectively known as Batten disease, comprise a group of fatal lysosomal storage disorders. CLN2 Batten disease results from loss or dysfunction of the soluble lysosomal enzyme tripeptidyl peptidase 1 (TPP1), most commonly due to the nonsense mutation p.R208X. Using a CLN2R207X mouse model that closely mirrors the p.R208X patient mutation, we evaluated the therapeutic potential of an AAV9-delivered adenine base editor (ABE7.10), administered via intracerebroventricular injection at postnatal day 1. Gene editing led to increased TPP1 enzymatic activity and mitigated disease-associated pathology across multiple brain regions by 11 weeks of age. Despite the promising CNS-specific outcomes, treated animals did not exhibit extended survival. Given the emergent evidence indicating peripheral involvement in CLN2 Batten disease, these findings suggest that pathology outside the CNS remains unaddressed by CNS-restricted delivery. To address this limitation, we implemented a dual-administration strategy, delivering ABE7.10 through both intracerebroventricular and intravenous routes at postnatal day 1, and assessed the resulting effects on survival and disease pathology. This work supports the continued advancement of adenine base editing as a promising therapeutic strategy for CLN2 Batten disease.

Position 31
Name: Megan Manotti, BSN, RN OCN
Organization: Beyond Primrose ZBTB20 Foundation
Authors: Manotti, Megan
Affiliations: Beyond Primrose ZBTB20 Foundation