



UNIVERSITY OF
SOUTH DAKOTA
SANFORD SCHOOL OF MEDICINE

Annual Medical Student Research Forum 2019

Friday, July 19th
9:00 AM to 12:00 PM

Room 111
Lee Medical Building

Sanford School of Medicine
The University of South Dakota
414 East Clark Street
Vermillion, SD

Program and Abstracts

Program Schedule

- 9:00-9:15 Opening Remarks by Dr. Manzerra on the Summer Research Program, T-35 CHIRP Program, Scholarship Pathways, and Independent Research opportunities.
- 9:15-9:30 Alexander Clem-Evolution of Professionalism in Medicine.
(Henry Travers)
- 9:30-09:45 Stephanie Jahnz-Detection of virus in vaccinated pregnant sows infected with Influenza A.
(Victor Huber, PhD)
- 9:45-10:00 Claire Kittock-Using human umbilical mesenchymal stem cells to understand the influence of prenatal diabetes exposure on early human development. (Michelle Baack, MD)
- 10:00-10:15 Mykayla Palmer- Dual targeting Notch-regulated histone deacetylase and demethylase in a Cellular model of human osteosarcoma. (Jianning Tao, PhD)
- 10:15-10:30 Luke Smith-Gene networks driving muscle performance in *Anolis* lizards.
(Andrea Liebl, PhD)
- 10:30-10:45 Break
- 10:45-11:00 Patrick Wilson-Characterizing the type I interferon response against influenza D viruses in human cells (Victor Huber, PhD)
- 11:00-11:15 Nicholas Wixon-M2e as a potential universal vaccine target through antibody-dependent Cellular cytotoxicity.
(Victor Huber, PhD)
- 11:15-11:30 Sarah Scott, Scholarship Pathways- A self-directed video-based course to improve medical students' note writing. (Val Kozmenko, MD & Valerie Hearn, MD)
- 11:30-11:45 Michael Blankespoor, Scholarship Pathways- The Suture Suspension Technique as a Surgical Treatment for Carpometacarpal (CMC) Joint Arthritis. (Robert VanDemark, MD)
- 11:45-12:00 Kayla Knutson-CHIRP-Conditional deletion of CLN3 using cell type specific Cre recombinase drivers. (Jill Weimer, PhD)
- 12:00-1:00 Lunch with Advisors.

Abstracts

Evolution of Professionalism in Medicine

Alexander Clem, Henry Travers

Introduction: The art of healing, from its origin 3500 years ago, has evolved with other elements of human society. Transformations in basic societal structure, changing religious influences, and accumulating secular resources led in stages to its relatively recent emergence as a profession in the late 18th and 19th centuries. Analogous influences in the 20th and early 21st centuries challenged the very definition of medicine as a profession, affecting modern-day health care's education, practice, influence on peoples' health and preservation of its work force. It was the general aim of the investigation to uncover how medicine became established as a profession, to define its founding characteristics and to determine the influences on the profession that have or could potentially have modified those characteristics. We focused our research on medicine in the United States in the 20th and 21st centuries. Our initial hypotheses were:

- Medicine's evolution into a profession is a relatively recent phenomenon
- Social, religious, economic and scientific influences on medical professionalism have not changed in millennia and continue to transform health care
- Medicine has become a service industry rather than a profession

Methods: Books and articles about the history of medicine as a profession were located through systematic searches of library catalogues both through computer-based databases and through references cited by other works. These were systematically catalogued to develop predominantly sociological evaluations of information to address our primary hypotheses.

Results: Ancient medicine was an art of healing, a common trade with no regulatory body or standard of education. It evolved in stages to a profession in the 19th century. Medical education became standardized in the United States following the Flexner Report in 1910. From this developmental pinnacle, the profession has slowly been losing autonomy through legislation, medical enterprises and insurance companies. Modern-day medicine has become an industry service.

Conclusions: The field of medicine has transformed into a service industry rather than an art. The practice of medicine has rapidly expanded to meet the needs of society at the cost of the autonomy of the profession. What will be the next evolution of medicine?

Starr, P. (1982). *The social transformation of American medicine*. New York: Basic Books.

Flexner, A., Updike, D. B. (1910). *Medical education in the United States and Canada: A report to the Carnegie foundation for the advancement of teaching*. 576 Fifth Avenue, New York City.

Inui, T (2003). *A Flag in the Wind: Educating for Professionalism in Medicine*. *Association of American Medical Colleges*.

Professionalism; medical history; medical practice

Detection of virus in vaccinated pregnant sows infected with Influenza A

Stephanie Jahnz Victor Huber, Ph.D.

Introduction: The Influenza A (IAV) virus is a respiratory pathogen that is easily transmitted from infected patients to other vulnerable hosts via contact with and uptake of respiratory droplets (Deng, et al. 2015). Women in the second and third trimesters of pregnancy have increased hospitalization rates compared to non-pregnant women. The Huber lab has developed a vaccine with broad immunity to IAV. To study the vaccine's effects on pregnant women and their fetuses, a pregnant sow model has been developed by the Huber lab and collaborators.

Methods: Groups of vaccinated and unvaccinated pigs were challenged with IAV, and lung homogenates, bronchoalveolar lavage (BAL) fluid, and nasal swabs were collected. Using traditional cell infection assays, samples were analyzed for presence of virus. Results were obtained by incubating monolayers of influenza-permissive cells with dilutions of individual tissue samples, and presence of virus was confirmed using red blood cells. Results are reported as 50% tissue culture infectious doses (TCID₅₀).

Results: Virus was not detected in lung homogenates, BAL fluid, or nasal swabs collected from sows that were vaccinated with vehicle only or vaccine but not challenged with IAV. Similarly, virus was not detected in sows that were vaccinated with vaccine but not challenged with IAV. Alternatively, sows that were vaccinated with PBS only and challenged with IAV were positive for virus in lung homogenate, bronchoalveolar lavage fluid, and nasal swabs

Conclusions: Sows that received vaccine and were challenged with IAV were negative for the presence of virus, indicating that the vaccine prevented the development of the viral infection. Future research will test samples collected from the fetal samples, as well as samples collected from newborns that are challenged with multiple IAVs within the H1N1 subtype. Furthermore, the efficacy of the vaccine in pregnant sows against different strains of IAV will be tested using in another pregnant sow study.

Neuzil, K. M.; Reed, G. W.; Mitchel, E. F.; Simonsen, L.; Griffin, M. R. (1998). Impact of Influenza on Acute Cardiopulmonary Hospitalizations in Pregnant Women. *Am. J. Epidemiology*, 148, 1094-1102.

Wang, J.; Xu, H.; Mu, C.; Chen, C.; Guo, L.; Chen, L.; Huang, J.; Guo, Q. (2018). A Study on Mother-to-Fetus/Infant Transmission of Influenza A(H7N9) Virus: Two Case Reports and a Review of Literature. *Clin. Respir. J.* 19, 2539-2545.

McMillan, M.; Porritt, K.; Kralik, D.; Costi, L.; Marshall, H. (2015). Influenza Vaccination During Pregnancy: A Systematic Review of Fetal Death, Spontaneous Abortion, and Congenital Malformation Safety Outcomes. *Vaccine*, 33, 2108-2117.

Influenza A; vaccine; sow model

Using human umbilical mesenchymal stem cells to understand the influence of prenatal diabetes exposure on early human development

Claire Kittock Michelle Baack, MD

Introduction: Infants born to diabetic mothers (IDM) have a higher incidence of birth defects. The mechanism for this is unknown, but is likely due to developmental aberrations from exposure to a diabetic milieu during organogenesis. Diabetic pregnancy can lead to intrinsic cell differences or altered cell signaling from an abnormal developmental microenvironment (DME). Mesenchymal stem cells derived from human umbilical cords (hu-MSCs) are genetically similar to the developing fetus and exposed to the same in utero conditions. Cord blood contains personalized nutrients, cytokines and growth factors that influence development. We created a novel, precision-based model called InVitroWOMB that uses hu-MSC and a cord blood-derived scaffold replicating the DME to help uncover mechanisms of embryopathy in diabetic pregnancy.

Methods: Following consent, hu-MSCs were extracted from umbilical cords collected after diabetic and non-diabetic pregnancies. To determine intrinsic cellular differences, hu-MSCs were plated in 2D culture for proliferation and viability analysis. Cell counts were assessed at 24, 48, 72, and 96 hours. Viability was assessed at 96 hours using Invitrogen's LIVE/DEAD kit. A cross-over study was used to analyze the differential impact of cell-intrinsic factors and signaling from the DME on adipogenic and osteogenic differentiation. Acellular InVitroWOMBs were analyzed for differences in DME. InVitroWOMBs were either fixed for imaging or frozen for analysis of protein and RNA. Protein extracted from InVitroWOMBs were also analyzed via Western Blot with antibodies against markers for MSCs (THY1) and adipocytes (PLIN1).

Results: Preliminary data indicate that diabetic exposed hu-MSCs have impaired proliferative capacity (n=2) and higher rate of cell death compared to non-diabetic exposed hu-MSCs (n=2). Preliminary InVitroWOMB analysis included Oil Red O staining of adipocytes as a measure of lipid droplets and Western Blotting for protein expression.

Conclusions: Preliminary results indicate that diabetic exposed hu-MSCs had intrinsic cell abnormalities that could contribute to embryopathy. Completing each arm of the cross-over study will provide insight into the role of diabetic DME on hu-MSCs and give insight about interventions that can be implemented to prevent birth defects in IDM.

References:

- Beccera, JE et al (1990). Diabetes mellitus during pregnancy and the risks for specific birth defects: a population-based case-control study. *Pediatrics*. 85; 1-9.
- Correa, A et al (2007). Diabetes mellitus and birth defects. *Am J Obstet Gynecol*. 199;e1-9.
- Mushahary, D et al (2017). Isolation, cultivation, and characterization of human mesenchymal stem cells. *Cytometry*. 93:19-31.

Keywords: mesenchymal stem cells; diabetes; development

Dual targeting Notch-regulated histone deacetylase and demethylase in a cellular model of human osteosarcoma

Mykayla L. Palmer Dr. Jianning Tao

Introduction: The aim of this study was to test the drug Domatinostat, also known as 4SC-202, which is currently used in clinical trials for varying cancer treatments. 4SC-202 is suggested to target the class 1 histone deacetylase inhibitor (HDAC1) and the lysine-specific histone demethylase (LSD1), which both form a complex with Notch1 NICD.^{1,2} Most recently, somatic mutations resulting in gain of function of Notch signaling pathway have been found in more than 11% of human osteosarcoma.³ However, 4SC-202 has not been studied in osteosarcoma. For this study, SJSA1, a human osteosarcoma cell line, was used to test the effects of 4SC-202 *in vitro*. Preliminary data from the Tao lab shows that SJSA1 presents high levels of Notch activity. The hypothesis of this study is that 4SC-202 will inhibit SJSA1 cell growth through inhibiting HDAC1 and LSD1 and, therefore, suppressing Notch function.

Methods: The effects of 4SC-202 were examined on the SJSA1 cell line *in vitro* through proliferation, invasion, colony formation, adipocyte differentiation, osteoblast differentiation, and wound-healing assays. In addition, the ability for 4SC-202 to inhibit Notch function was examined molecularly using Western blot and qRT-PCR.

Results: It was discovered that as little as 1 μ M of 4SC-202 inhibits cell proliferation, invasion, colony formation, differentiation, and wound-healing *in vitro*. While further studies must be done to confirm results, it is suggested that in the SJSA1 cell line 4SC-202 directly inhibits the Notch pathway. This is shown through inhibited cell growth and a decrease in Notch3, HDAC1, and LSD1, as well as a change in deacetylation and demethylation, seen through H3k9Ac and H4k4Me2, respectively. These results give us insight to the mechanisms of both the 4SC-202 and the Notch pathway.

Conclusion: By studying the use of 4SC-202 on the SJSA1 cell line, we may better understand the Notch pathway and effects of inhibition by therapeutic drugs. The significance of the research on 4SC-202 and the SJSA1 cell line is important for the future of cancer patients and could lead to genome-informed targeted therapy. In the future, this drug will be tested *in vivo* on mouse models to further study 4SC-202.

1. Tresckow, B. et al. "Phase I study of domatinostat (4SC-202), a class I histone deacetylase inhibitor in patients with advanced hematological malignancies." *European Journal of Hematology* (2018): 163-173.
2. Wobser, M. et al. "Elucidating the mechanism of action of domatinostat (4SC-202) in cutaneous T cell lymphoma cells." *Journal of Hematology & Oncology* (2019).
3. Sayles, L. et al. "Genome-Informed Targeted Therapy for Osteosarcoma." *American Association for Cancer Research Journal* (2019): 46-63.

Osteosarcoma; Notch pathway; 4SC-202

Gene networks driving muscle performance in *Anolis* lizards

Luke Smith Andrea Liebl, PhD

Animal muscles are exceptionally diverse in structure and function as they meet a variety of demands for an individual to survive. Muscles coordinate with each other so that individuals can survive in their environments. However, muscles vary in performance to best suit their role in promoting organism survival, and differences in gene expression among muscles likely accounts for much of this variation. *Anolis* lizards, a genus that has undergone considerable adaptive radiation, live in a wide range of habitats and ecotypes to which each species has had to evolve appropriately to survive. These habitats require different muscles of the anole to perform extremely variable tasks. Unsurprisingly, muscle performance of these lizards (e.g. twitch time and peak contractile velocity) varies among muscle types. Specifically, the performance of jaw and leg muscles, diverges strongly because their importance for survival (e.g., to escape predation and to bite prey) differs both across and within individuals. Here, I use RNA-seq to measure the differential gene expression generating differences in muscle performance between the jaw and leg muscles. The observed discrepancy in gene expression may explain the divergence in performance observed between the muscles. A weighted gene co-expression network was created to identify modules of genes with expression that correlates significantly to muscle performance metrics. Analysis of these particular genes using DAVID and the String database reveals the key functions of these groups of genes in creating the muscle performance differences observed between the jaw and leg muscle. Determining these underlying differences in gene expression between muscles and individuals helps explain how performance metrics (e.g., twitch time and peak contractile velocity) change over time. Additionally, differential gene expression could show how the ecology and evolution of an individual influences its muscle performance.

Langfelder, P., & Horvath, S. (2008). WGCNA: an R package for weighted correlation network analysis. *BMC Bioinformatics*, 9(1), 559. doi:10.1186/1471-2105-9-559

Leng, N., Dawson, J. A., Thomson, J. A., Ruotti, V., Rissman, A. I., Smits, B. M., . . . Kendziorski, C. (2013). EBSeq: an empirical Bayes hierarchical model for inference in RNA-seq experiments. *Bioinformatics*, 29(8), 1035-1043.

Rome, L. C., & Klimov, A. A. (2000). Superfast contractions without superfast energetics: ATP usage by SR-Ca²⁺ pumps and crossbridges in toadfish swimbladder muscle. *The Journal of Physiology*, 526(2), 279-286. doi:10.1111/j.1469-7793.2000.t01-1-00279.x

Keywords: *Anolis* lizards; RNA-seq; muscle performance

M2e as a potential universal vaccine target through antibody-dependent cellular cytotoxicity

Nicholas Wixon Victor Huber PhD

With the constant threat of an influenza pandemic, it becomes necessary to look at options that could protect against all strains. Influenza A viruses, regardless of the subtype or isolate, possess M2e, a protein derived from the matrix gene that expresses 23 amino acids externally. While not universally conserved, there are only a handful of variants of M2e that have been identified to-date.

Introduction: In theory, if effective vaccines could be generated that induce antibodies against all immunologic variants of this protein, vaccinated individuals could have broad immunity across all influenza strains. Within the normal virus infection cycle, the expressed M2e surface protein is at very low levels in comparison to hemagglutinin and neuraminidase. This makes M2e a poor target for neutralizing antibodies, however, the M2e produced during infection does get expressed at the surface of infected cells. Which makes it a target for antibodies that can cause the death of infected cells through a process known as antibody-dependent cellular cytotoxicity, or ADCC. We hypothesized that M2e antibodies produced in response to vaccination will recognize M2e expressed on the surface of host cells and induce ADCC.

Methods: We are currently infecting A549 cells with whole virus to determine if our ferret M2e antibodies bind to the protein when expressed on the cell surface. We are also attempting to establish an A549 cell line that stably expresses M2e through transfection. If this is successful, we will be able to test our antibody's ADCC conduction without having to infect them with influenza beforehand.

Results: are currently unavailable because data collection is still underway.

Conclusions: If our ferret antibodies successfully bind to M2e expressed on the infected cells, we will test if these antibodies can induce ADCC through the respective assay. Once we establish an A549 cell line that can stably express M2e it will streamline our experiments by eliminating the infection step.

Guo, Y., He, L., Song, N., Li, P., Sun, S., Zhao, G., . . . Zhou, Y. (2017). Highly conserved M2e and hemagglutinin epitope-based recombinant proteins induce protection against influenza virus infection. *Microbes and Infection*, 19(12), 641-647. doi:10.1016/j.micinf.2017.08.010

Zaman, M., Good, M. F., & Toth, I. (2013). Nanovaccines and their mode of action. *Methods*, 60(3), 226-231. doi:10.1016/j.ymeth.2013.04.014

Zhong, W., He, J., Tang, X., Liu, F., Lu, X., Zeng, H., . . . Hancock, K. (2011). Development and evaluation of an M2-293FT cell-based flow cytometric assay for quantification of antibody response to native form of matrix protein 2 of influenza A viruses. *Journal of Immunological Methods*, 369(1-2), 115-124. doi:10.1016/j.jim.2011.04.010

M2e, Influenza, Nanovaccine

Characterizing the type I interferon response against influenza D viruses in human cells

Patrick Wilson Victor Huber

Introduction: Accepted as the newest type of influenza virus in the Orthomyxoviridae family is the influenza D virus (IDV). This virus resides in bovine, but it is known to infect swine and other small ruminants. Although present in these animals, it has not yet been associated with illness in humans. Previous studies suggest that influenza A viruses regulate type I interferon (IFN) expression during primary viral infection and can affect the susceptibility of the host towards a secondary bacterial infection. It was hypothesized that epithelial cells infected with IDV would produce type I IFNs at levels that are similar to those seen with influenza A viruses (IAV) that are not associated with secondary bacterial infections.

Methods: Whole IDV virus (D/swine/Oklahoma/1334/2011) supplied from SDSU was grown in Madin-Darby Canine Kidney (MDCK) cells to generate a stock of virus that was utilized for infection. Adenocarcinomic human alveolar basal epithelial cells (A549) were infected with the stock of IDV and RNA was collected at 5-time points (6 hours post-infection (HPI), 12 HPI, 24 HPI, 48 HPI, and 72 HPI). RT-PCR was performed on the RNA samples and analyzed.

Results: RT-PCR data revealed low levels of IFN expression in A549 cells infected with D/OK at all timepoints for all interferons tested. The most notable increase in IFNs produced a 4-fold to 9-fold increase in expression versus the negative controls. Increased IFN expression was not reserved for a specific interferon subtype and was observed in type I, II, and III interferon responses.

Conclusions: The data shows that this specific cell line (A549) infected with a low multiplicity of infection (MOI = 0.001) of IDV does not become infected to a high degree nor does it produce a robust innate immune response. Low infectivity, along with low IFN levels, suggest that D/OK cannot infect A549 cells at a low viral dose—which could be due to low viral concentrations or possibly due to virus:cell incompatibility. A future experiment infecting A549 cells with a higher MOI should be conducted and compared to current data to assess the cause of the low IFN response more completely.

Collin, E. A., Sheng, Z., Lang, Y., Ma, W., Hause, B. M., & Li, F. (2015). Cocirculation of two distinct genetic and antigenic lineages of proposed influenza D virus in cattle. *Journal of virology*, 89(2), 1036-1042.

Hause, B. M., Ducatez, M., Collin, E. A., Ran, Z., Liu, R., Sheng, Z., ... & Webby, R. J. (2013). Isolation of a novel swine influenza virus from Oklahoma in 2011 which is distantly related to human influenza C viruses. *PLoS pathogens*, 9(2), e1003176.

Su, S., Fu, X., Li, G., Kerlin, F., & Veit, M. (2017). Novel Influenza D virus: epidemiology, pathology, evolution, and biological characteristics. *Virulence* 8: 1580–1591.

Influenza D; interferon; A549

A self-directed video-based course to improve medical students' note writing

Sarah Scott, Valeriy Kozmenko & Valerie Hearn

Scholarship Pathways, Sanford School of Medical, USD

Introduction: The high stakes Objective Structured Clinical Examination (HS-OSCE) is a required University of South Dakota Sanford School of Medicine (USD SSOM) test that medical students need to pass at the end of Pillar 2. It closely represents the United States Medical License Examination Step 2 Clinical Skills national board exam. Previously, around 42% of students needed to remediate the note-writing component. The USD SSOM developed an Enhanced Patient Note Writer (EPNW) program for students to practice writing notes, but it failed to improve students' note writing skills tested at the HS-OSCE. We hypothesized that supplementing the EPNW with video content and individual feedback to the students regarding their note writing skills would improve their note-writing performance during the HS-OSCE.

Methods: Eight cases were created, along with encounter checklists, patient scripts, and note-grading rubrics. Each case was portrayed by a standardized patient and a student doctor and filmed in an exam room. The videos were then used in conjunction with the EPNW software. Using the video-enhanced patient note writer (VEPNW), students watched a video and wrote a patient note within 10 minutes. After completing notes, case-specific note-grading checklists became available for students. Students self-graded their notes, and the scores were saved on the server. Students' progress with note writing was monitored during four weeks of preparation for the HS-OSCE.

Results: A total of 68 students had access to the VEPNW program in preparation for the HS-OSCE. Of those, 35 were considered participants by the criteria that they each used the VEPNW program greater than four times. In comparing participants (>4x) to non-participants (<4x), participants were found to have higher mean scores for the HS-OSCE note score (77.54% vs. 74.33%) and for the HS-OSCE overall score (83.2% vs. 81.53%). Of those that needed to remediate notes, 22.2% were participants and 77.8% were non-participants.

Conclusions: Creation of an automated system that provided individualized feedback to students regarding their note writing skills improved their performance in handling patient documentation. The participant group performed better on the HS-OSCE note writing and overall scores. The participant group also had less students require note writing remediation.

Ecker, D.J., Milan, F.B., Cassese, T., Farnan, J.M., Madigosky, W.S., Massie, F.S.,... Ovitsh, R.K.. (2018). Step up -not on- the Step 2 Clinical Skills exam: Directors of Clinical Skills Courses (DOCS) oppose ending Step 2 CS. *Academic Medicine*, 93(5), 693-698.

Harden, R.M., Stevenson, M., Downie, W.W., & Wilson, G.M. (1975). Assessment of clinical competence using objective structured examination. *British Medical Journal*, 1(5955), 447-451.

Tervo, R.C., Dimitrievich, E., Trujillo, A.L., Whittle, K., Redinius, P., & Wellman, L. (1997). The Objective Structured Clinical Examination (OSCE) in the clinical clerkship: an overview. *South Dakota Journal of Medicine*, 50(5), 153-156.

Clinical skills, education, note-writing

The Suture Suspension Technique as a Surgical Treatment for Carpometacarpal (CMC) Joint Arthritis

Michael Blankespoor Robert VanDermark, MD

Scholarship Pathways, Sanford School of Medicine, USD

Carpometacarpal (CMC) joint arthritis is a common, disabling form of osteoarthritis affecting the hand that causes swelling, stiffness, and discomfort at the base of the thumb. There are various techniques for the treatment of CMC joint arthritis including surgical options of arthrodesis (fusion) of the CMC joint, various forms of arthroplasty which include partial or complete trapezial excision with or without ligament reconstruction, and prosthetic replacement of the CMC joint. These surgical techniques have similar outcomes; however, some of the methods do involve more surgical work and may incur greater risk and cost for the patient. In this study, we prospectively analyze patient satisfaction, patient rated outcome scores, the postoperative clinical course, and cost for the CMC suture suspension technique, a treatment of CMC joint arthritis that involves trapezial excision and suspension with suture to stabilize the joint postoperatively.

Conditional deletion of CLN3 using cell type specific Cre recombinase drivers

Kayla Knutson Jill Weimer, PhD

CLN3-Batten disease is an autosomal recessive disorder that is caused by mutations in *CLN3*, the most common mutation being a 1.02 kb deletion of exons 7-8. CLN3-Batten disease is characterized by the accumulation of autofluorescent storage material along with neurodegeneration and glial activation, suggesting the involvement of multiple different cell types in the disease progression. The *Cln3^{Δex7/8}* mouse model recapitulates the common mutation, and currently represents the best available tool to investigate disease mechanisms. However, it does not allow us to study the contribution of each cell type to disease processes. Thus, to understand cell-type specific functions of CLN3, we developed a novel mouse line that allows for selective deletion of exons 7-8 in CLN3 by flanking these exons with loxP sites. In this study, we used this novel *Cln3^{loxΔ7/8}* mouse to specifically focus on the role of CLN3 pathogenesis in multiple cell types: in excitatory projection neurons by crossing these mice with a NEX-cre recombinase driven line, in interneurons using an NKX2.1-cre recombinase driven line, and in microglia using a CX3CR1-cre line. Histopathological analysis at 9 or 10 months of age was performed to assess glial and neuronal pathologies. Selective loss of CLN3 in excitatory projection neurons led to increased gliosis and accumulation of autofluorescent storage material, recapitulating pathology seen in the *Cln3^{loxΔ7/8}* mouse. This suggests CLN3 specifically plays a vital role in the health of excitatory projection neurons within the brain, leading to the pathology and neurodegeneration indicative of disease. Understanding the mechanisms of how CLN3 contributes to essential transport in neuronal processes and how these processes are perturbed in CLN3-Batten disease will aid in our critical need to find a successful treatment for this disease that rescues neurodegeneration.

Cotman, SL, and Staropoli, JF (2012). The juvenile Batten disease protein, CLN3, and its role in regulating anterograde and retrograde post-Golgi trafficking. *Clinical Lipidology*, 7:(1), 79-91.

Phillips, SN, Benedict, JW, Weimer, JM, and Pearce, DA (2005). CLN3, the protein associated with batten disease: structure, function and localization. *J Neurosci Res*, 79(5):573-83.

Carcel-Trullols, J, Kovacs, AD, and Pearce, DA (2015). Cell biology of the NCL proteins: What they do and don't do. *Biochim Biophys Acta*, 1852(10 Pt B):2242-55.

CLN3; Batten disease; neuronal trafficking

Posters

Daniel Pfeifle, M4; Benson Hsu, MD, MBA, FAAP:

Healthcare costs and resource utilization in pediatric patients with bronchiolitis: A comparison of rural and urban Emergency Department patients.

Sarah Scott MS4, Valeriy Kozmenko MD Valerie Hearn MD, Shane Schellpfeffer EdD

An innovative self-directed video-based course to improve medical students' note writing skills.

Luke Fuhrman MSIV, Thayne Munce, PhD:

A prospective study of heat intolerance and recent concussion among athletes.

Jake N. Johnson, MSIII, Jennifer L. Dalland, MA ATC, Lisa N. MacFadden, PhD:

Assessing the effectiveness of RTS testing in identifying patients at risk for anterior cruciate ligament graft failure.

Nick Goodhope, PharmD MS4, Laura Rasmussen, MD, Jennifer Giroux, MD MPH:

Hepatitis C Registry for Great Plains Tribes.

Brisk B, MSIV; Jordre B, PT, DPT, GCS, CEEAA, Cert MDT; Schweinle W, PhD:

Cardiovascular disease, diabetes and anthropometric measures in competitive aging athletes.

Anthony Restaino, Jianning Tao, PhD

Production of NOTCH1 and NOTCH3 Knockdown SJSA-1 Osteosarcoma Cell Lines

Research Programs and Opportunities for SSOM Students

The USD-SSOM Medical Student Research Program (MSRP) strives to create and support opportunities for medical students in the areas of research, service, and education. Three of our programs are described below. In addition, we can assist medical students who are not enrolled in these programs by helping find mentors and funding small projects and travel to conferences.

Contact Laura Rumohr, Program Assistant, Medical Student Research Committee (msrp@usd.edu).

The Medical Student Summer Research Program is an 8 week research experience for students newly accepted to the medical school. Students receive a \$5,000 stipend and the hosting lab receives up to \$2,000 for supplies. To apply, students choose a faculty member as a research mentor and submit an application to the Medical Student Research Committee.

For more information, please contact Laura Rumohr, Program Assistant, Medical Student Research Committee (msrp@usd.edu).

The Scholarship Pathways Program is an elective opportunity developed to enrich the medical school experience by promoting rigorous independent scholarship and scholarly excellence as well as produce leaders in medical education, research and service. The program spans all four years and develops critical thinking and independent learning skills.

For more information, please contact Candace N. Zeigler, M.D., FACP (Candace.Zeigler@usd.edu), 605-357-1572, 1400 W. 22nd Street, Sioux Falls, SD 57105.

NIH T-35 Children's Health Innovative Research Program (CHIRP) at the Sanford School of Medicine and Sanford Research is focused on providing research training in clinical biomedical sciences to medical students. The ultimate goal of the CHIRP is to help meet the future needs of health-related research by contributing to the development of physicians who will be well-prepared to use evidence-based medicine in practice and contribute to translational research. This research program is self-paced, allowing participants to work closely with their mentors to complete 320 hours of research time during pillars 1 & 2 of their medical school curriculum. All participants receive a generous stipend. Additionally, participants are required to participate in a responsible conduct in research training program, meet routinely with their mentoring team and are encouraged to present their research at regional/national research conferences. Applications are now open for Year 2 of this competitive program. For more information and to apply, visit the Medical Student Research webpage.

All of these programs can be found at the Medical Student Research Website:

www.usd.edu/medicine/basic-biomedical-sciences/research/medical-student-research-program