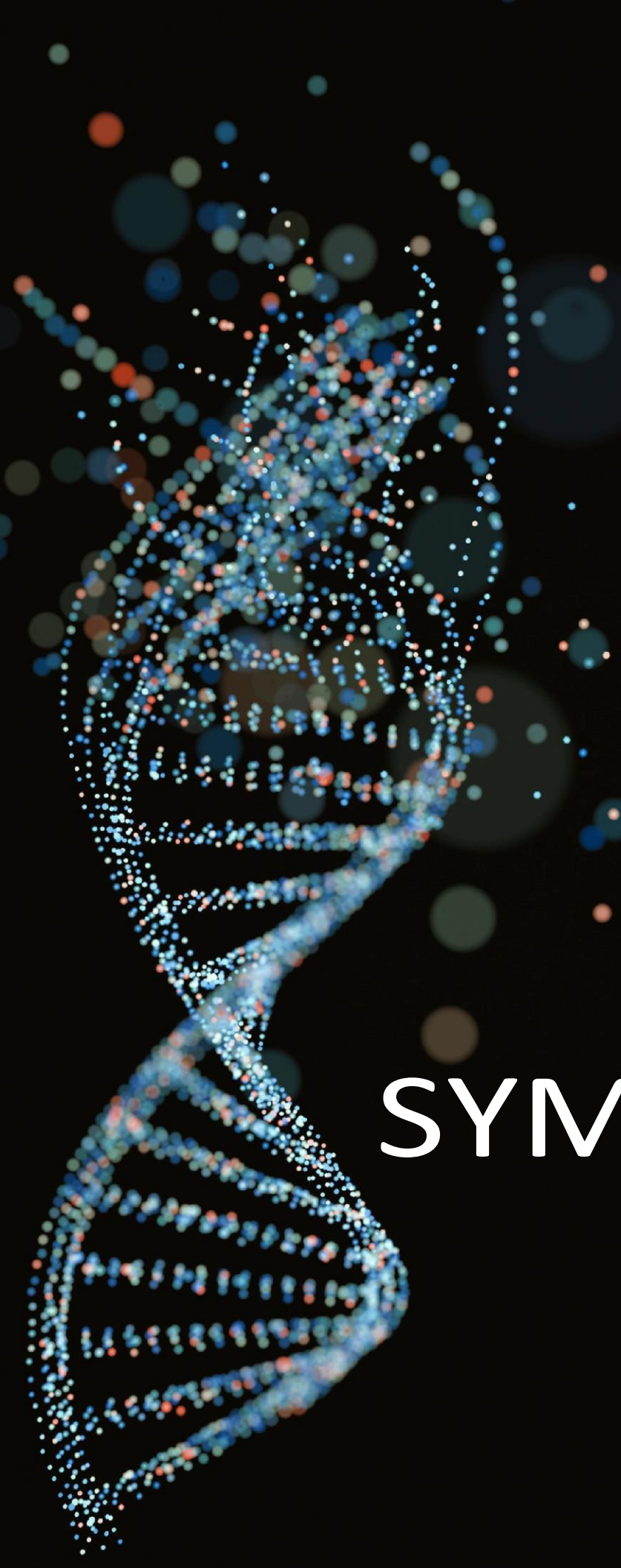

PROGRAM

DaCCoTA

DAKOTA COMMUNITY COLLABORATIVE ON TRANSLATIONAL ACTIVITY

ANNUAL SYMPOSIUM

July 27, 2023

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DaCCoTA ANNUAL SYMPOSIUM | July 27, 2023

DaCCoTA Website: https://med.und.edu/daccota/

Pathfinder Web Portal: https://pathfinder.med.und.edu/

The DaCCoTA is supported by the National Institute of General Medical Sciences of the National Institute of Health under Award Number U54GM128729.

STATEMENT OF EDUCATIONAL OBJECTIVES

1. Increase familiarity with principles of clinical and translational research study design.
2. Demonstrate an understanding of the data archiving requirements from federal agencies.
3. Recognize the tools necessary to establish and maintain successful community and academic partnerships.
4. Establish solutions to overcome research resource limitations.
5. Obtain a better understanding of data sovereignty when working with Tribal Nations.
6. Identify characteristics of private research grants.
7. Obtain tools for navigating collaborations with industry partners.

CONTINUING MEDICAL EDUCATION CREDIT INFORMATION

CME: This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Sanford Health, the University of South Dakota, University of North Dakota, and North Dakota State University. Sanford Health is accredited by the ACCME to provide continuing medical education for physicians.

Sanford Health designates this live activity for a maximum of 2.0 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Requirements for Successful Completion of this Activity

- Report attendance as requested by event planners.
- Attendance at one or more sessions.
- Be present no later than 10 minutes after starting time of the session.

DISCLOSURE INFORMATION

Presence or Absence of Relevant Financial Relationship(s) for Planners & Faculty/Content Specialist(s)

a. None of the planners for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

b. The following Faculty/Presenters disclosed the following relevant financial relationship(s) with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:
    - Jill Weimer, PhD, Chief Science Officer for Amicus Therapeutics
        - All relevant financial relationships listed for these individual have been mitigated.

c. All remaining Faculty/Presenters have returned disclosure forms indicating that they have no affiliation or financial interest in any organization(s) that may have a direct interest in the subject matter of their presentation(s).

d. Educational content integrity is maintained, and bias prevented through adherence to the Standards for Integrity and Independence in Accredited Continuing Education as outlined by ACCME and ANCC.

Post-Symposium Survey

Evaluation: We invite your feedback via an electronic evaluation. ***A post-activity evaluation will be sent to you via the email you used when registering for the symposium. There is a QR code and link listed below that will also take you to the post-symposium survey to complete.***

Link: ***https://app.smartsheet.com/b/form/e1f2f9901e4649a4996d8287a9b7a1e3***

CME Certificate of Verification Survey

A CME Verification of Completion Survey will be sent to you via the email you used when registering for the symposium to complete the Survey. There is also a QR code and link listed below that will take you to the CME Verification of Completion Survey to complete. This survey will generate an email to be sent to you for your records. This survey and email confirmation will serve as your certificate for this conference. Be sure to track the session(s) you participated in and keep a copy for your records.

Link: **https://app.smartsheet.com/b/form/6e8dd8d10e7e4bdab93fee23d0cc1644**

SCHEDULE

7:30 – 8:00	**Registration**
8:00 – 8:10	**Welcome** Gary Schwartz, PhD
8:15 – 9:15	**Concurrent Sessions** **Session 1 – Federal Data Archiving Requirements: Considerations when Working with Sovereign Nation Partners** Bridget Diamond-Welch, PhD; Anna Kosloski, PhD; Katie Edwards, PhD **Session 2 – Handy Research Tools for Immediate Use** Mark Williamson, PhD; Kent Ripplinger, MS; Nick Bittner **Session 3 – How to Develop a Research Project with Limited Resources** Soojung Kim, PhD, MPH; Lyle Best, MD; Brent Voels, PhD
9:15 – 9:45	**Poster Session – Group A**
9:45 – 10:00	**Break**
10:00 – 12:00	**Awardee Updates** Jonathan Bleeker, MD Kevin Francis, PhD Soojung Kim, PhD Motoki Takaku, PhD Victor Huber, PhD & Khosrow Rezvani, PhD, MD
12:00 – 1:00	**Lunch & Discussion Groups** **Real World Biometrics for Tracking Health** Matthew Rizzo, MD **A Circle of Trust: Opportunities to Engage Indigenous Populations in Clinical Trials** Allison Kelliher, MD **Unlocking the Potential of the National COVID Cohort Collaborative (N3C)** Kent Ripplinger, MS
1:00 – 2:00	**Concurrent Sessions** **Session 1 – Until Health Equity Do Us Part: Ways to Initiate & Sustain Partnerships** Keyonna King, DrPH, MA; Emily Frankel, MPH **Session 2 – Exploring Private Research Grants** Khosrow Rezvani, PhD, MD; Jill Weimer, PhD; Michelle Baack, MD **Session 3 – Sanford PLEDGE: Integrating Screening for Type 1 Diabetes Risk into Routine Pediatric Cares** Kurt Griffin, MD, PhD
2:00 – 2:30	**Poster Session – Group B**
2:30 – 2:45	**Break**
2:45 – 4:45	**Awardee Updates** Cheryl Hysjulien, RN, PsyD Dinesh Katti, PhD Marijo Roiko, PhD Melanie Nadeau, PhD, MPH Dali Sun, PhD
4:45	**Closing/Wrap Up/Awards**

SPEAKERS

Concurrent Sessions – 8:15 – 9:15

Session 1 – Federal Data Archiving Requirements: Considerations when Working with Sovereign Nation Partners

Bridget Diamond-Welch, PhD
Anna Kosloski, PhD
Katie Edwards, PhD

In 2022, the co-authors returned over 1.5 million in federal dollars to the National Institute of Justice because of federal data archiving requirements conflict with tribal sovereignty including tribe's data sovereignty. This presentation will review data archiving requirements including the reasons for archiving, different types and forms of archiving, and different agency requirements. We will then discuss what data sovereignty means and how different tribes assert their sovereignty. We will discuss how researchers can work with tribes to understand each tribe's view on data archiving and why/when archiving may not be possible.

Dr. Bridget Diamond-Welch, Ph.D., is the Director of Research & Innovation in the School of Health Sciences at the University of South Dakota. Her research expertise is in sexualized violence, specifically with vulnerable populations. She takes part in several Indigenous-led community-based participatory projects. She is currently PI on three such federally funded grants, is co-I on several related projects, and has several grants and projects to improve sexual assault systems response across South Dakota and the region. She has also been instrumental in procuring several million dollars of grant funding to support programs and efforts to improve services for victims of interpersonal violence across South Dakota.

Anna Kosloski is an Associate Professor in the School of Public Affairs at the University of Colorado at Colorado Springs. She received her Ph.D. from Iowa State University in 2012. Dr. Kosloski's research is focused on the intersection of gender and crime. She explores this intersect by focusing on the needs and behavioral risks of women in correctional institutions and human trafficking crimes. Her current research examines females as both victim and offenders of crime. She believes that only in understanding the pathways to criminality, can we develop policy and programs that foster intervention and prevention measures. Dr. Kosloski is also interested in the intersections of race, class, gender and crime. Dr. Kosloski believes research can be an impetus for action. Therefore she has made great efforts to partner with community organizations on research initiatives. Finally, Dr. Kosloski is committed to teaching and tries to incorporate research centered on student learning and pedagogy to her scholarly initiatives.

Dr. Katie Edwards, Ph.D., is an Associate Professor at the University of Nebraska—Lincoln where she directs the Interpersonal Violence Research Laboratory. Using community-based participatory action research, Dr. Edwards seeks to answer two questions in her work: (1) *How do we prevent sexual and related forms of violence?* and (2) *How do we most effectively support survivors in the aftermath of violent victimization?* Much of Dr. Edwards work focuses on minoritized populations, specifically Native American/Indigenous youth and families as well as LGBTQ2S+ youth and emerging adults. Dr. Edwards highly values community leadership in

developing and evaluating strengths-focused, affirming, culturally grounded initiatives to prevent and respond to sexual and related forms of violence. To date, she has published more than 200 peer reviewed journal articles, and over the past 10 years has accrued over 22 million dollars in funding for her research, predominately from federal (U.S.) agencies.

Learning Objectives

1. Discuss data archiving requirements from federal agencies.
2. Explore issues around data sovereignty when working with Tribal Nations.

Session 2 – Handy Research Tools for Immediate Use

Mark Williamson, PhD
Kent Ripplinger, MS
Nick Bittner

Researchers are often dedicated specialists with great expertise in their given discipline, be it xenograft mouse models for pancreatic cancer or clinical trials testing the effect of maternal nutrition on infant gut microbiomes. In other topics across the full gambit of research—from inception to publication—they may be less experienced. There lies the tension; the research topics need to be dealt with, taking time and energy away from the expertise where the researcher really shines. This talk's goal is to address that tension, providing handy tools that can be immediately implemented. So researchers can get back to the science they love.

Dr. Mark Williamson is a research professor for the Department of Population Health at UND. He is also the Statistician for the DaCCoTA Biostatistics Core and Director of the upcoming ROAR Radon Test Chamber. His research interests include radon, statistical methods, bioinformatics, and epidemiology.

Kent Ripplinger is the Database Investigator Navigator for the DaCCoTA. He assists clinical researchers in using large administrative databases to help answer research questions. One of his primary areas of support is with the National COVID Cohort Collaborative (N3C) Data Enclave where he assists with onboarding requirements, creating project proposals, submitting Data Use Requests, and acting as a liaison between N3C resources and investigators. He also provides training on a variety of databases to promote potential opportunities for using datasets in research.

Nicholas Bittner is currently pursuing a biomedical engineering degree at the University of North Dakota. He is an ASME certified manufacturer associate along with being the advanced manufacturing instructor for Cankdeska Cikana Community College. He also works as a digital engineering technician for the computational research center found at UND where he assists the Epscor Program in developing innovative ways to pursue advanced manufacturing techniques for culturing applications.

Learning Objectives

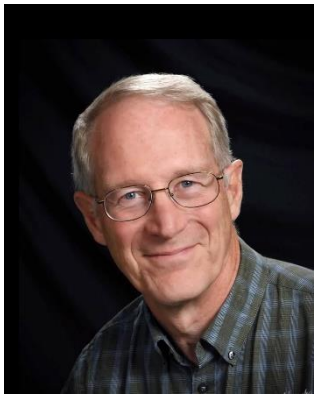
1. Examine DaCCoTA resources/collaborations that can immediately impact their research.

Session 3 – How to Develop a Research Project with Limited Resources

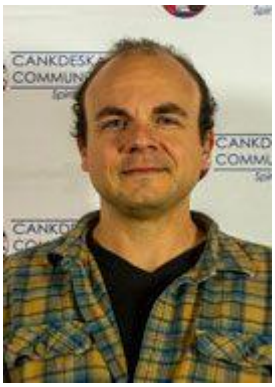
Soojung Kim, PhD, MPH
Lyle Best, MD
Brent Voels, PhD

In ideal circumstances, scientists and clinicians would have no resource limitations in their research. In practice, limitations are inevitable. Limitations may include lack of funding, equipment, personnel, infrastructure, or expertise. Therefore, it is instructive to examine potential limitations as well as examples of how to overcome such limitations. Research is done in the real world, so projects must be designed to overcome real-world obstacles like resource limitations.

Soojung Kim is an Associate Professor and Chair in the Department of Communication at the University of North Dakota. She received both M.A. and Ph.D. in Mass Communication from the University of Minnesota, an M.P.H. from the University of North Dakota, and a B.A. in Mass Communication and Psychology from Korea University. Her research focuses on increasing the awareness of public health issues and changing health behaviors by using effective social and mobile media strategies. Her research has been supported by the National Institute of General Medical Sciences of the National Institutes Health, North Dakota Department of Health and Human Services, Prevent Cancer Foundation, National Center for Healthy Housing, and Grand Forks Public Health.



Dr. Lyle Best is a North Dakota researcher. He began his professional career with the Indian Health Service (ISS) and served as a clinical director and Maternal Child Health consultant. He later worked at the DNA Diagnostic Laboratory in Canada, taught "Introduction to Human Genetics" at Turtle Mountain Community College (TMCC), conducted genetic and other research in American Indian (AI) communities, and served as principal investigator for the Strong Heart Study (SHS), Dakota Center, continuing as a co-investigator through the present. Dr. Best has supervised the Genetics and Pre-eclampsia Study (GPS) at TMCC since 2004, which has resulted in the training and engagement of tribal college students into biomedical research and was the first study to report genetic variants in the C-reactive protein (CRP) gene increasing risk of pre-eclampsia. He also supervised a case/control and randomized-controlled trial of an educational intervention to improve control of asthma in the Cheyenne River Sioux community.



Brent Voels has held his position at Cankdeska Cikana Community College since 2014, completed his graduate work at the University of North Dakota in 2015 where his research focused on gene expression in breast cancer cell lines. He has continued to collaborate in research efforts with his mentors from UND, and focuses on providing Tribal College students research opportunities in the place they call home.

Learning Objectives

1. Describe sources of resource limitation in their research and understand potential solutions.

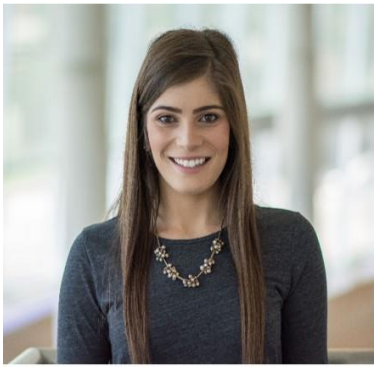
Concurrent Sessions – 1:00 – 2:00

Session 1 – Until Health Equity Do Us Part: Ways to Initiate & Sustain Partnerships

Keyonna King, DrPH, MA
Emily Frankel, MPH

"Until Health Equity Do Us Part, Ways to Initiate and Sustain Partnerships" will describe the three dimensions of partnership sustainability and highlight best-practices for sustaining partnerships. By the conclusion of the talk, audience members will understand how to build community-academic partnerships and sustain the relationship in a healthy manner.

Dr. King is an Assistant Professor at University of Nebraska Medical Center in the College of Public Health, Department of Health Promotion. She teaches the Applications of CBPR to graduate students and practices the CBPR approach to engage community in projects to address health disparities through UNMC's Center for Reducing Health Disparities. Specifically, she partners with the North Omaha community to address priority health needs identified by the community. Some of her past and current projects focus on addressing mental health, chronic disease intervention and prevention, violence, and improving the diversity of the healthcare workforce. Dr. King is the Director of the Community Engagement & Outreach core of the Great Plains IDeA Clinical Translational Research Network at UNMC. She leads the core in developing and implementing community engagement and outreach trainings and dissemination of resources to ensure the research/work is relevant and meeting the needs of underserved people and areas of Nebraska. Dr. King focuses her independent research efforts on using CBPR to understand and address depression in Black men; and improving mental and physical health outcomes for systematically marginalized and excluded populations such as Black Americans and American Indians.



Emily currently serves as the Practice-Based Research Network (PBRN) Community Program Manager for the Great Plains IDeA-CTR, headquartered at the University of Nebraska Medical Center. She serves as the central coordinator for the development, planning, implementation, and assessment of community-engaged clinical and translational health initiatives. Emily also coordinates the Community Engagement and Outreach Core for the Great Plains IDeA-CTR, ensuring adequate training and resources are available for community partners and researchers conducting Community-Engaged Research. Emily is passionate about supporting older adult's quality of life through nutrition, especially those residing in rural communities.

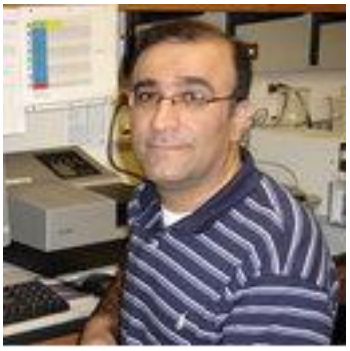
Learning Objectives

1. Establish ways to build community-academic partnerships.
2. Describe the dimensions of partnership sustainability.
3. Recognize best practices for partnership sustainability.

Session 2 – Exploring Private Research Grants

Khosrow Rezvani, PhD, MD
Jill Weimer, PhD
Michelle Baack, MD

Researchers need to consider all possibilities for receiving research funding. We often think of public sources such as state and federal agencies. In this session, we'll consider private research grants, how they differ from public research grants, and how you can set yourself up for success. The primary goal of this session is to highlight the potential of private research grants and opportunities for funding.



Primarily, Dr. Rezvani trained as a medical doctor, followed by an internship and four years' clinical practice in private offices and hospitals. His experiences with patients as a clinician and his interest in basic sciences inspired him to apply for a PhD program. He completed his PhD in molecular and cell biology as part of Professor John R. Mayer's group at the University of Nottingham in the United Kingdom. Dr. Mayer is one of the pioneers in the field of ubiquitin research, with more than 150 peer-reviewed articles. Dr. Rezvani's training in ubiquitin-proteasome research continued under the guidance of Professor Mariella De Biasi at Baylor College of Medicine in Houston, TX. While there, he was able to show for the first time that the nicotine molecule inhibits proteasomal catalytic activities (Rezvani, 2007 and 2010). He discovered a novel function for a ubiquitin-like (UBX)-domain-containing protein, UBXN2A, in 2009 (Rezvani et al., 2009) before joining the University of South Dakota as an independent researcher in the Division of Basic Biomedical Sciences in 2010. Convincing evidence regarding the potential function of UBXN2A in solid tumors led Dr. Rezvani to make a major transition to the cancer biology field. His group focused on the anti-cancer function of UBXN2A in colon cancer, the third most common cancer in both men and women in the United States. His projects have led to several major publications in the journals *Cell Death & Disease* (2014), *Cell Death and Discovery* (2021), and the *Journal of Oncogene* (2023). His current project focuses on Veratridine, a natural plant molecule capable of enhancing the expression of UBXN2A *in vivo*. His ultimate plan is to move Veratridine forward in pre-clinical development using a unique UBXN2A mouse model. Ultimately, his drug development project could improve existing chemotherapy regimens for colon cancer patients, providing a better survival rate with a lower incidence of side effects.

Dr. Jill Weimer is a developmental neuroscientist and oversees the management and continued development of the translational arm of Sanford Research in Sioux Falls, South Dakota. She started at Sanford Research in 2009, and her research program focuses on the molecular mechanisms mediating development of the cerebral cortex and how disruption in these processes can lead to a whole host of neural pediatric disorders, including Batten's disease and Neurofibromatosis Type 1. Work in Dr. Weimer's lab helped lead to the first ever gene therapy trial programs for CLN3 and CLN6 – Batten disease. In June 2019, Dr. Weimer joined the Amicus Therapeutics team as the Senior Vice President of Discovery Research and Gene Therapy Science and now serves as the Chief Science Officer. She plays a unique dual role holding leadership positions with both Sanford Research and Amicus, in addition to leading her research lab. Dr. Weimer grew up in north central Missouri and moved to upstate New York where she received her bachelor's degree and Ph.D. in neuroscience from the University of Rochester. She completed her postdoctoral training in the

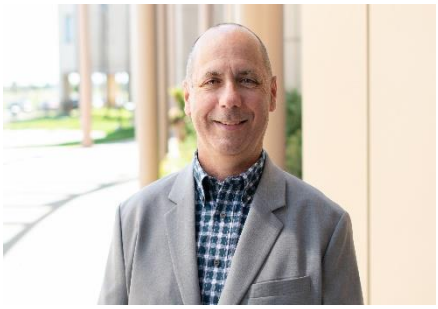
Neuroscience Research Center at the University of North Carolina in Chapel Hill with a focus on developmental neuroscience. Dr. Weimer also serves as a scientific advisor to a number of rare disease foundation as well as serving as the President of the Alumni Council for her alma mater, the University of Rochester School of Medicine and Dentistry.

Dr. Baack completed her undergraduate training at South Dakota State University (SDSU) College of Pharmacy, Medical School at the University of South Dakota Sanford School of Medicine and a Pediatric Residency at Creighton - University of Nebraska Medical Center Joint Pediatric Residency Program in Omaha. She practiced as a general pediatrician for 10 years in Pierre, SD before returning to a fellowship in Neonatal and Perinatal Medicine at the University of Iowa. There she developed a passion for perinatal and neonatal research. She is currently a neonatologist in the Boekelheide Neonatal Intensive Care Unit at Sanford Children's Hospital, Professor and the Chair of Pediatrics at the University of South Dakota – Sanford School of Medicine and an Associate Scientist in the Environmental Influences on Health and Disease Group at Sanford Research. Her primary research objective is to understand the role of maternal and neonatal lipid abnormalities in the developmental origin of health and disease (DOHaD) and to develop preventative strategies to decrease the risk of both short and long-term disease in high-risk populations including infants born to obese or diabetic mothers. To meet this objective, she has both clinical and basic science research projects. As the Sanford – site principal investigator for NICHD Neonatal Research Networks (NRN), her clinical research in the NICU strives to improve the outcomes of high-risk babies Her clinical and translational work focus primarily on discovering dietary interventions during pregnancy, lactation or the neonatal period that improve outcomes of premature infants and infants born to diabetic or obese mothers. Basic and translational research in the Baack lab focuses on understanding the molecular and metabolic mechanisms of developmental programming in offspring exposed to maternal dyslipidemia or diabetic pregnancy. The lab's overarching goal is to find translational interventions that improve mitochondrial function, cardiometabolic health and prevent heart disease in not only one, but subsequent generations.

Learning Objectives

1. Identify important characteristics of private research grants.

Session 3 – Sanford PLEDGE: Integrating Screening for Type 1 Diabetes Risk into Routine Pediatric Cares



Kurt J. Griffin, MD, PhD
Todd and Linda Broin Chair for Diabetes Research and
Director of Clinical Trials, The Sanford Project, Sanford Research
Associate Professor, Pediatric Endocrinology, Sanford School of Medicine,
University of South Dakota

Kurt Griffin is the director of clinical trials for the Sanford Project and associate professor of pediatric endocrinology at the University of South Dakota. Dr. Griffin earned his Ph.D. in cell and developmental biology and his M.D. at the University of Colorado. He completed his pediatric residency at Rainbow Babies and Children's Hospital in Cleveland and then a fellowship in pediatric endocrinology at NIH. As faculty at the University of Arizona, he built a portfolio of basic and clinical research in type 1 diabetes (T1D). Dr. Griffin was recruited to Sanford in 2013 to accelerate clinical trials in T1D.

Dr. Griffin's research efforts span the natural history of T1D, with emphases on 1) multicenter clinical trials to rebalance the underlying autoimmunity that causes this disease, and 2) general population screening to identify which children might benefit from an earlier intervention.

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Learning Objectives

1. Describe assessments of genetic risk for Type 1 Diabetes.
2. Describe available assessments of immunologic progression of Type 1 DiabetesT1D.
3. Describe the risk of progression to clinical (Stage 3) type 1 diabetes based on antibody measurements.
4. Describe how the PLEDGE Screening program is automated and integrated into routine pediatric care.

AWARDEES

AWARDEE **Jonathan Bleeker, MD** **FEASIBILITY PILOT GRANT AWARDEE**

Title: **Investigating the utility of circulating tumor DNA in predicting outcomes following definitive multimodality therapy for locally advanced esophageal/gastroesophageal junction cancer**

Team: **Jonathan S. Bleeker MD**, Michael Kareta PhD, Mark Williamson, PhD

Abstract: **INTRODUCTION:** Locally advanced esophageal and GE junction cancer is typically treated with concurrent chemoradiation (CRT) followed by surgical resection, with 5 year overall survival rates ranging from 39-47% utilizing a number of concurrent chemotherapy regimens. The benefit of surgery following CRT in patients with locally advanced esophageal and GEJ cancers is controversial with some retrospective series and database data supporting a survival benefit from surgery, while other series and randomized trials call this benefit into question. Biomarkers to guide the intensity of therapy and inform the need for trimodality treatment are lacking. This protocol aims to identify the potential role of ctDNA evaluation in predicting efficacy of therapy and outcomes in patients with locally advanced esophageal and GE junction malignancies. **METHODS:** Between November 2020 and November 2022, 12 patients with locally advanced esophageal/GE junction carcinoma were enrolled and underwent genomic testing on a biopsy from their primary tumor at diagnosis and serial ctDNA testing at diagnosis, after chemoradiation but before surgery and after surgery. These results were analyzed to assess correlation between solid tumor and ctDNA testing, whether pre-treatment ctDNA results correlate with outcomes and if clearance of ctDNA during treatment may predict positive outcomes. **RESULTS:** All 12 patients underwent tissue and ctDNA genomic testing; in 5/12 patients (42%), ctDNA correlating with tissue genomic results was detected. At the time of last reporting, 8/12 patients remained alive; 2/5 patients with ctDNA positivity at diagnosis remain alive as opposed to 6/7 of those without detectable ctDNA at diagnosis. The median overall survival of the ctDNA positive group was 225 days vs. 493 days in the ctDNA negative group. This difference was not statistically significant and clearance of ctDNA during therapy was not correlated with better outcomes. **CONCLUSION:** This trial demonstrates both the feasibility as well as the difficulties in developing ctDNA as a predictive biomarkers in patients undergoing cancer therapies given imperfect correlation between ctDNA and tissue based therapy even prior to treatment. The data presented here would suggest that presence of ctDNA detectable prior to surgery may be correlated with poorer outcomes; further data from this trial and other similar studies will be needed to confirm this trend.

AWARDEE **Kevin Francis, PhD** **FEASIBILITY PILOT GRANT AWARDEE**

Title: **Interplay between cholesterol metabolism and extracellular vesicles in head and neck cancer**

Team: Jazmine D. W. Yaeger, Austin L. Walz, Caitlin S. Williamson, W. Chad Spanos, Paola D. Vermeer, **Kevin R. Francis**

Abstract: Head and neck squamous cell carcinoma (HNSCC) is the 6th most common type of cancer, presents formidable treatment challenges, and exhibits a propensity for metastatic outgrowth. Patient survival rates correlate to the classification of HNSCC as human papilloma virus positive (HPV+) or negative (HPV-) with the former having a more favorable prognosis. Defining the mechanisms underlying HNSCC pathogenicity are needed. Our previous published work demonstrated that small extracellular vesicles (EVs) termed exosomes promote tumorigenicity. We hypothesized that based upon the critical role lipid content plays in EV formation and function, targeting cholesterol metabolism within EV producing cells may represent a novel mechanism to impact HNSCC. Through a robust comparison of the impact of pharmacological inhibitors of cholesterol synthesis, we demonstrate that EV production and release is unexpectedly increased upon cholesterol inhibition in multiple cell types, including HNSCC-derived cell models. We also demonstrate that EVs produced from cholesterol-inhibited cell types exhibit altered molecular profiles and surface markers which may impact EV function. Within HNSCC models, HPV- cell lines are more sensitive to cholesterol inhibition compared to HPV+ HNSCC models. Our ongoing work is detailing the lipids present within normal and HNSCC-derived EVs, quantifying cholesterol impacts on EV cargo, and examining cholesterol impacts on EVs in other model systems. These studies have implications to HNSCC pathogenesis and suggest lipid-impacted EVs may also play a role in other diseases as well.

AWARDEE **Soojung Kim, PhD, MPH** **FEASIBILITY PILOT GRANT AWARDEE**

Title: **Interventions to Promote Home Radon Testing: A Randomized Clinical Trial of a Smartphone App vs. Printed Brochures**

Team: **Soojung Kim, PhD, MPH**, Tiffany Chiu, MA, Marilyn G. Klug, PhD, David Schmitz, MD, & Gary G. Schwartz, PhD, MPH, PhD

Abstract: Purpose: Radon is a preventable cause of lung cancer, but the percentage of homes tested for radon is low. We previously developed a smartphone app that informs users about radon and allows them to request a free radon test.

Method: We conducted a randomized, controlled trial comparing the radon app versus printed brochures on radon knowledge, attitudes, and behaviors, including the proportion of participants requesting radon tests. Participants (N = 138) were undergraduates at a midwestern university. Data were analyzed by t-tests, general linear models, and logistic regression.

Results: App users showed significantly greater increases in radon knowledge ($p = 0.010$) and self-efficacy ($p < 0.001$) and requested tests three times more often than brochure recipients (41.4% vs. 13.2%, $p < 0.001$). However, the rate of test usage in each condition was low, ~3%.

Conclusion: The radon app markedly outperformed brochures in increasing knowledge and requests for radon tests. Future work should focus on methods to increase test usage.

AWARDEE **Motoki Takaku, PhD** **FEASIBILITY PILOT GRANT AWARDEE**

Title: **Deep learning based development of early cancer detection by chromatin architecture in cell-free DNA**

Team: **Motoki Takaku,** Nazim Belabbaci, Aerica Nagornyuk, Sakuntha Gunarathna, Kincaid Rowbotham, and Xusheng Wang

Abstract: Cell-free DNA (cfDNA) is a promising biomarker for cancer detection, with oncogenic mutations identifiable through cfDNA sequencing analysis. Importantly, cfDNAs partially retain epigenetic information such as DNA methylation and chromatin structure, including nucleosome positioning. This information can be used to predict the cell-of-origin and the presence of cancerous tissues. Several studies have demonstrated the potential of cfDNA profiling, alongside systemic analyses, to detect cancer at early stages and predict both the type and stage of the disease. Despite this potential, most existing studies have focused on genetic information (DNA mutations) and cfDNA concentration in plasma, with limited attention paid to chromatin studies.

In this project, we aimed to establish a computational pipeline that distinguishes between cancer patients and healthy donors using only cell-free nucleosome data. The nucleosome, as the fundamental unit of chromatin, possesses unique positioning in each cell type, thus providing a means to detect cancer cell-derived nucleosomes. In collaboration with Sanford Health, we developed a purification method to obtain sufficient cell-free nucleosomes for next-generation sequencing from less than 500 µl of plasma sample. We acquired about 40 sets of next-generation sequencing data from individuals with breast cancer, pancreatic cancer, and from healthy donors. Our data show enrichment of cancer-derived cell-free nucleosomes at tissue-specific active chromatin regions. Furthermore, we found that cell-free nucleosome signals at these regulatory regions can be employed for machine learning prediction. The model we established achieved high prediction accuracy, underscoring the potential of this approach for early cancer detection.

AWARDEE **Victor Huber, PhD & Khosrow Rezvani, PhD, MD** **COVID-19 PILOT GRANT AWARDEE**

Title: **Comparison of antibodies against SARS-CoV-2 in cancer and non-cancer pediatric patients in South Dakota**

Team: Santiago Lopez, Khaled Ismail, Fernando Bula-Rudas, Maria D Paez, Eduardo Callegari, PhD, Sanam Sane, PhD, **Khosrow Rezvani, PhD, MD, Victor Huber, PhD**

Abstract:

In late 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), began circulating in humans. This virus causes coronavirus disease of 2019 (COVID-19), and a COVID-19 pandemic was declared on March 11, 2020. Our research focuses on understanding the impact of SARS-CoV-2 infection on antibody-mediated immunity and biomarkers in pediatric cancer patients. Similar to the work of others, our data show that antibody levels are generally low after natural SARS-CoV-2 infection, and this was seen in all patient populations. Our most recent work has evaluated antibody levels in vaccinated individuals to determine how host immune responses differ after vaccination. Work toward defining the biomarkers associated with SARS-CoV-2 infection is currently underway, with a direct focus on patient populations with specific cancer diagnoses.

AWARDEE **Cheryl Hysjulien, RN, PsyD** **READY-TO-GO PILOT GRANT AWARDEE**

Title: **A Comprehensive Approach to Head and Neck Cancer Prehabilitation**

Team: **Cheryl A Hysjulien RN, PsyD,** Amy Schmidt CNP, Klaus Cavalheri, PhD

Abstract:

Purpose: The diagnosis and treatment for head and neck cancer is considered one of “the most devastating and debilitating of all cancers” (Clarke & Dropkin, 2006, p. 1). Patients have preexisting psychosocial barriers that impact their treatment and outcomes. Patients are twice as likely to die from suicide than other cancer patients. In addition, the treatment course has significant physical impacts on quality of life. This study sought to improve head and neck cancer patient outcomes and quality of life through an innovative prehabilitation program.

Method: Study group patients participated in a four-hour multidisciplinary Prehabilitation Clinic. The clinic included: Integrative Essentials Pre-treatment group, consultation with a physical therapist, speech therapist, registered dietician, and social worker. Assessments and interventions were individualized. Assessment measures were repeated at 6-8 weeks and 5-6 months post treatment. A prospective control group in another region of Sanford Health was used for comparison. Retrospective data was collected from Fargo patients prior to initiation of the study. A repeated measures design was utilized to monitor and assess success of the program.

Results: Prehabilitation clinics improve head and neck cancer patient outcomes and quality of life.

Conclusions: This multidisciplinary prehabilitation clinic for head and neck cancer patients improved patient functionality, quality of life and emotional well-being. It is now the standard of care at Sanford Health Fargo, ND.

AWARDEE **Dinesh Katti, PhD** **READY-TO-GO PILOT GRANT AWARDEE**

Title: **Prostate Cancer Bone Metastasis Testbed for Regenerative Bone Therapies for Bone Metastasis**

Team: Quyen Hoang, Preetham Ravi, Sharad Jaswandkar, Hanmant Gaikwad, Shrinwanti Ghosh, Jiha Kim, Parth Vyas, Samy Heshmat, **Dinesh R Katti**, Kalpana Katti

Abstract: Prostate cancer metastasizing to the bones poses substantial challenges, causing profound pain and escalating mortality rates in affected patients. Consequently, there is a need to develop innovative treatment approaches. This research introduces a unique test platform for studying bone metastasis in prostate cancer, which is specifically designed to integrate tumor therapy and bone regeneration. The testbed consists of 3D nanoclay bone-mimetic scaffolds, human mesenchymal stem cells (hMSCs), and patient-derived prostate cancer cell lines (CTR_PCA 3001-3006). By accurately replicating the bone microenvironment affected by metastasis, this testbed allows comprehensive investigations into the molecular characteristics and behavior of patient-derived cancer cells within the bone niche. Building on previous achievements, this study focuses on evaluating the effectiveness of targeted drug treatments using the sandwich model for local drug delivery. By tailoring drug regimens to individual patients, the aim is to develop personalized treatment strategies that effectively target prostate cancer cells while promoting bone regeneration. The insights gained from this study have the potential to advance the fields of integrative tumor therapy and bone regeneration in prostate cancer. In conclusion, the establishment of a patient-derived experimental platform for bone metastasis, which incorporates the sandwich model for drug delivery, presents a valuable tool for investigating the biology of prostate cancer, refining targeted therapies, and fostering bone regeneration. The integrative nature of this testbed opens new possibilities for advancing personalized medicine in the treatment of prostate cancer.

AWARDEE **Marijo Roiko, PhD** **CLINICAL RESEARCH OPPORTUNITY PROGRAM GRANT AWARDEE**

Title: **SARS-CoV-2 Whole Genome Sequencing and Metagenomic Analysis**

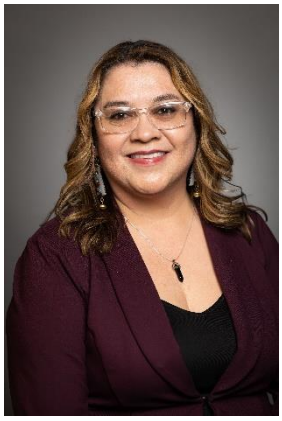
Team: Brett McGregor[1], Antariksh Tyagi[1], Sergei Nechaev[1], Bony DeKumar[1], Sara Nausheen[2], Junguk Hur[1], **Marijo Roiko[2]**

Abstract: SARS-CoV-2 infection causes a wide variety of symptoms from asymptomatic infections to acute respiratory failure and death. Multiple factors have been associated with severity of infection including age and comorbid conditions. One such factor that requires further investigation is microbiome dysbiosis which has previously been associated with other disease conditions. To further examine the impact of SARS-CoV-2 infection on the nasopharyngeal microbiome, we performed microbiome sequencing on a large cohort of samples submitted for SARS-CoV-2 diagnostic testing. Study samples were randomly selected from nasopharyngeal swabs collected in 3 mL of viral or universal transport medium tested by an FDA EUA NAAT

(Cepheid, Roche, BioFire, Diasorin, Hologic) for SARS-CoV-2 at Altru Pathology and Laboratory Services. Total nucleic acid was isolated and whole-genome sequencing, following the Artic protocol, and 16S metagenomic sequencing, using Nanopore, were performed. Sample metadata and clinical variables were recovered from the electronic medical record (Epic) for each sample submitted for sequencing.

From 1,058 samples submitted to UND, 975 passed QC and 923 had metadata available for analysis. SARS-CoV-2 whole genome sequences were obtained from 550 samples, of which 495 had metadata. WGS identified 29 viral variants, including 5 variants of interest, currently classified as variants being monitored which accounted for ~14% of samples sequenced. Microbiome analyses identified a potential shift in the microbiome between SARS-CoV-2 positive and negative samples. Differences were also observed across viral variants present in significant quantities in the study cohort. No significant differences were observed by gender or hospitalization status. In conclusion, SARS-CoV-2 infection is associated with changes in the nasopharyngeal microbiome. These shifts may be impacted by viral variants but are independent of gender and hospitalization status. Further work is required to identify the impact of COVID-19 severity and viral genome on microbiome composition.

AWARDEE **Melanie Nadeau, PhD, MPH** **COMMUNITY ENGAGEMENT SCHOLARS GRANT AWARDEE**



Title: **Creating a Tribally Informed Risk and Protective Factor Survey utilizing an Indigenous Mixed Study Approach**

Team: **Melanie Nadeau, PhD, MPH**; Tyler Parisien, Ed.D.

Abstract: Traditionally American Indians have not informed the tool development for surveys used to collect data in their communities. Currently the Youth Risk Behavior Surveillance System (YRBSS) monitors health-related behaviors among youth. The behaviors are categorized into six themes, three of which are cancer related, including sexual health, substance use, and dietary/physical activity. The YRBSS is designed to determine the prevalence of health behaviors and assess changes over time. Although the YRBSS disseminates useful results for youth across the nation, it is not representative for Tribal nations. As a result, a multitude of issues exist with data collection efforts in American Indian communities. Of particular concern, indicators are not community informed. As a result, the cancer related risk and protective factor profile for American Indian youth is unknown. The significant gaps in current data efforts call for more culturally informed community driven approaches. The overarching study goal is to determine the prevalence of community level protective and cancer related risk factors among tribal youth by creating and administering a community informed data collection tool. This presentation will provide an overview of current data collection efforts, the mixed studies process, key findings and future directions.

AWARDEE **Dali Sun, PhD** **BASIC SCHOLARS PROGRAM GRANT AWARDEE**

Title: **Exosomal collective attributes for PDAC screening**

Team: **Sun, Dali**

Abstract:

Purpose: Exosomes are of great interest as biomarkers of cancer. Most exosome-based cancer diagnostic studies have focused on establishing exosome assays that detect increased expression of a single cancer-associated marker or marker signatures based on multiplex detection of these biomarkers. However, these biomarkers can be obscured by high background signal from exosomes of nonmalignant cells. The lack of exosome quality assessment methods is also a barrier to applying results from these studies since differences in exosome collection and isolation protocols among different studies can produce significant variations in exosome sample composition.

Methods: We introduced multiple approaches to utilize exosomes for clinical cancer diagnosis. In these methods, exosome collective attribute components, rather than specific exosome factors, are used to distinguish exosomes derived from malignant and non-malignant cells.

Results: Our data indicate these collective attributes are cell-specific, and thus represent a practical use of exosome. These exosome collective markers can also be employed to distinguish serum exosomes from patients with and without malignant disease, in conjunction with other biomarkers.

Conclusion: We investigated the multiple collective attributes of exosomes as cell-specific characteristics. These collective attributes can discriminate tumor-derived exosomes at low-cost, and can be employed to screen cancer patients from serum samples.

POSTER PRESENTATIONS

Poster Session – Group A

Pilar de la Puente, PhD

Title: **Engineering a physiologically relevant *ex vivo* 3D ovarian cancer culture model for precision-based drug screening**

Team: Kristin Calar, Simona Plesselova, Megan Jorgense, Hailey Axemaker, Maria Bell, **Pilar de la Puente**

Abstract: Purpose: Ovarian cancer (OC) is one of the deadliest forms of cancer in women where 80% of patients develop resistance within 5 years. The overall objective of this investigation is to provide a translationally relevant 100% patient-derived *ex vivo* 3D culture platform with controlled physiologically relevant physical properties to perform clinically relevant analysis of OC treatment responses. Method: Our model contains patient-derived tumoroids grown within a 100% human patient-derived plasma 3D matrix. The model was fully characterized and compared to matched parental tumors. Primary biospecimens were categorized as sensitive and resistant by Response Evaluation Criteria in Solid Tumors (RECIST) score, and precision-based high-throughput drug screens were performed to establish a predictive score that would be able to distinguish sensitive from resistant patients using several read-outs such as proliferation, apoptosis, and viability. Results: The model was shown to recapitulate structural complexity, biochemical composition, and morphological features of OC tumors. The model supported growth better than other traditional culture assays. Our model was able to retrospectively predict patient treatment response *ex vivo* in only 7 days. Conclusion: Our results present a reproducible and clinically translatable preclinical model assessing effective treatment options by predicting therapeutic efficacy and avoiding treatment with drugs that the tumor will be resistant to. Moreover, our results are expected to have an important positive impact because they will provide a valuable tool in predicting each individual patients' response to therapy and permit a much more in-depth and clinically relevant analysis of OC treatment responses than is currently possible.

Ramkumar Mathur, PhD

Title: **Regulation of mTOR signaling in colon cancer pathology**

Team: Abby Lund, Mansib Rehman, Robert Sticca, Donald A Jurivich, **Ramkumar Mathur**

Abstract: Colorectal cancer (CRC) is the third leading cause of cancer deaths globally. More than two-thirds of CRC patients are over the age of 70, with over 43% of those patients being over 75. Given the higher mortality rate of elderly cancer patients, it is vital to understand the underlying causes to design a personalized CRC therapeutic regimen. Our understanding has been focused on young animal models, and age-related transcriptome and cellular alterations that raise cancer risk are poorly understood. The risk of tumor recurrence through metastasis remains a substantial challenge, regardless of early identification. Cellular or molecular mechanisms that affect gene regulation and cancer emergence are still unknown. The long-term goal of our research is to determine how aging-induced immune dysregulation affects the tumor microenvironment (TME) and contributes to metastases. Age-related alterations in epithelial and immune cell diversity make it challenging to examine tumor microenvironment transcriptomic and molecular features in the older adult. In our study, we found that aging immune cells had an effect on tumorigenic pathways. Our published and preliminary research demonstrates that IL22 cytokines have a significant role in oncogenesis in aging. We identify that IL22/mTOR signaling controls aging CRC development and that understanding the tumor immune milieu may improve colorectal cancer treatment (CRC). Based on we hypothesized that IL22/mTOR signaling promotes the growth of age-related colon cancer and that knowing the transcriptome and molecular components of the tumor immune microenvironment might improve the therapy of CRC in the elderly. We investigate this hypothesis using two distinct objectives. Aim 1. The role of mTOR function in tumor permissive environment. Aim 2. determine if blocking of mTOR to alleviate colon cancer in older adults. IMPACT. The planned research will assist in the development of innovative translational and therapeutic strategies for the treatment of aging and colorectal cancer. Based on the planned study, we will be able to design personalized therapy for advanced CRC patients.

James Foster, PhD

Title: **Environmental Lead Exposure and Dopaminergic Dysfunction**

Team: **James D. Foster**, Marilyn G. Klug, Gary G. Schwartz

Abstract: Parkinson Disease (PD) is a chronic and progressive neurodegenerative disorder that affects millions of Americans. Although several genes have been identified in the pathology of PD, approximately 90% of PD cases are of unknown origin. Epidemiological studies have recently shown the prevalence of PD in US states is positively associated with the quantity of acid rain where it is hypothesized that acid rain could mobilize metals, such as lead (Pb^{2+}), from the soil increasing their levels in drinking water. In addition, there is a significant positive correlation between lead municipal drinking water service lines still utilized in the US with the prevalence of PD. Exposure to Pb^{2+} has been implicated in neurotoxicity especially with regard to dopamine (DA) producing neurons. Dopaminergic (DAergic) neurons release DA which controls motor function, mood, reward and cognition. Extraneuronal DA levels are controlled spatially and temporally by DA transporter (DAT)-mediated uptake of released transmitter back into presynaptic neurons. The experiments proposed in this study are consistent with the priorities and goals of the DaCCoTA Translating Epidemiology to Experiments (TREE) pilot grant mechanism where we translate the epidemiologic findings implicating Pb^{2+} in drinking water with the risk of PD to potential altered DAT function and extraneuronal DA clearance in cellular and animal model systems. Preliminary results suggest that DA uptake in kidney epithelial cells expressing the DAT are not affected by acute exposure to Pb^{2+} (0-500 µM), however, ongoing studies in neuronal and animal models system may reveal effects of chronic exposure.

Sijo Mathew, PhD

Title: **Talin-1 promotes Fibrosis in Clear Cell Renal Cell Carcinoma (ccRCC) through Renin-Angiotensin Signaling**

Team: Md Saimon Mia, Preston Steen, **Sijo Mathew**

Abstract: Background: Fibrosis in ccRCC activates various pro-proliferative cell signaling pathways and promotes tumor growth. Since the integrin-talin complex is a primary mediator of reciprocal signal transduction from fibrotic stroma, the major molecular pathways through which talin-1 promotes fibrosis in ccRCC were investigated. Method: Genetic downregulation of talin-1 in the renal cancer cell (Caki-1) was achieved with talin-1 shRNA; clones with lower talin-1 expression (talin-1 KD) were isolated. Cell functional assays, migration, proliferation, and pro-tumorogenic signaling were identified using talin-1 KD cells and control shRNA-treated (talin-1 WT) cells. In addition, using immunoblotting and qRT-PCR, the major profibrotic molecular pathway was determined. Results: Downregulation of talin-1 in Caki-1 cells led to a significant decrease in cell adhesion and spreading on collagen-1 or vitronectin-coated plates. In addition, a significant decrease in focal adhesion, cell proliferation, and migration was also observed with the knockdown of talin-1. Furthermore, the profibrotic signaling pathways AKT and ERK 1/2 were significantly decreased in talin-1KD cells compared to talin-1 WT cells. In contrast, a significant increase in the phosphorylation of p38 was observed in talin-1KD cells than in control shRNA treated (talin-1 WT) cells. Furthermore, angiotensin-converting enzyme (ACE) and angiotensin II (ANGII) receptor 1 (AGT1R) showed a significant decrease in talin-1 KD cells. Moreover, an increase in ANG II receptor 2 (AGT2R) was observed in talin-1KD cells. Conclusion: This study illustrates the significance of talin-1 in ANG-II-mediated profibrotic signaling in renal cell carcinoma.

Soonhee Roh, PhD

Title: **Cognitive Impairment and Social Determinants of Health among Indigenous Women**

Team: **Soonhee Roh**, Yeon-Shim Lee

Abstract: Purpose: This study aimed to assess the levels of cognitive impairment and Alzheimer's disease knowledge among 123 Indigenous women aged 40 to 70 years in partnership with a tribe in the Northern Plains. The study utilized the social determinants of health (SDOH) framework to examine the associations between selected SDOH factors and cognitive impairment status. Method: The data for this study were extracted from the 2021 Intervention to Promote Breast Cancer Screening Among Indigenous Women, which aimed to improve breast cancer screening and overall health among Indigenous women. Cognitive impairment was measured using the Alzheimer's Disease 8 instrument. The SDOH variables considered in the analysis included education, health literacy, social engagement, religious activity and participation, depression, chronic conditions, and demographic information. Results: The results of the study indicated that more than half of the respondents were likely to have cognitive impairment, and they exhibited lower income and education levels compared to the group with normal cognition. Higher levels of Alzheimer's disease knowledge in treatment and management and life impact were associated with lower odds of cognitive impairment. Conversely, higher levels of depression and participation in religious activities were associated with higher odds of cognitive impairment. Conclusion: Future research should use culturally grounded tools or wellness instruments that are validated and appropriate for use with Indigenous populations. Historical and cultural factors should be incorporated into social determinants of health frameworks tailored for Indigenous populations, leading to better health outcomes and ultimately enhancing leading to better health outcomes and ultimately enhancing Alzheimer's Disease-Related Dementia health equality.

Paola Vermeer, PhD

Title: **Tumor innervation in high-grade serous ovarian carcinoma**

Team: Anthony C. Restaino, Austin Walz, Samuel J. Vermeer, Jeffrey Barr, Attila Kovács, Robin R. Fettig, Daniel W. Vermeer, Hunter Reavis, Caitlin S. Williamson, Christopher T. Lucido, Tuany Eichwald, Dalia K. Omran, Euihye Jung, Lauren E. Schwartz, Maria Bell, DesiRae M. Muirhead, Jody E. Hooper, William C. Spanos, Ronny Drapkin, Sebastien Talbot, **Paola D. Vermeer**

Abstract: Purpose: Patients with densely innervated tumors suffer a worse prognosis than those with sparsely innervated disease. Given the poor survival of ovarian cancer patients, we wondered if intra-tumoral neurons remain functional at the tumor bed and functionally contribute to disease progression. Method: We analyzed ovarian cancers in The Cancer Genome Atlas (TCGA) for expression of neuronal genes. We used Proximity Ligation Assay (PLA) with pre-and post-synaptic markers to determine if synapse-like structures form at the tumor bed. We electrophysiologically analyzed HGSOC patient samples using Microelectrode Arrays (MEA) to determine if measurable activity is present in these malignancies. We also orthotopically implanted syngeneic HGSOC tumors into control and transgenic mice lacking tumor-infiltrating neurons and analyzed the electrophysiologic impact on tumors. Since we had previously defined tumor-infiltrating nerves as sensory, we tested the impact of Substance P on tumor cell proliferation and migration. Results: Analysis of TCGA for neuronal genes shows that high neuronal gene expression correlated with low survival in high-grade serous ovarian carcinosm (HGSOC). PLA shows that cases of HGSOC harbor significantly higher PLA signal as compared to benign or normal ovary suggesting that intra-tumoral nerves form synapse-like structures in the malignancies. Consistent with this, MEA analysis shows significantly increased electrical activity in cases of HGSOC as compared to benign or normal tissues. Importantly, tumors grown in transgenic animals lacking tumor-infiltrating neurons harbor significantly decreased intra-tumoral electrical activity suggesting that at least some of this activity comes from intra-tumoral neurons. In vitro assays demonstrate that HGSOC cells respond to Substance P with increased proliferation and migration. These effects are blocked by inclusion of an NK1R antagonist. NK1R is the receptor for Subtance P and these studies indicate that the proliferative and migration impact of Substance P on HGSOC cells is mediated directly by binding of this neuropeptide to its receptor. Conclusions: HGSOCs are densely innervated by sensory nerves that remain functional at the tumor bed. Release of Substance P by these tumor-infiltrating nerves contributes to tumor cell proliferation and migration.

Bailey Pickering

Title: **Childbearing Education Classes in South Dakota**

Team: Kaihlen Smith, **Bailey Pickering**, Tayler Modlin

Abstract: In 1960, childbearing education classes (CEC) were created to educate women about the labor and delivery process. Women who attend CEC have higher rates of vaginal deliveries versus cesarean deliveries. Other benefits of CEC are increased confidence, increased likelihood of breastfeeding, better communication between the patient and their care team, a decrease in analgesic use, and increased labor and delivery satisfaction. Knowledge is powerful in situations of the unknown. Demographics of women who attend CEC are most commonly white, have a college degree, and are considered above the poverty line. One theory behind these findings is a lack of availability of CEC to women of lower education and lower socioeconomic status. We created a list of counties in South Dakota and their respective clinics and contacted each clinic to see if they offer CEC. If they did not, we asked for a referral location. There are only 17 CECs held in the state of South Dakota. 13 of which are offered full-time and 4 are offered on a periodic or individual basis. We found the average distance between each CEC to be 50.49 miles. CEC are lacking in the state of South Dakota, especially in rural areas. South Dakota has the highest birth rate per 1,000 people in the nation, creating a need for CEC and education before delivery. This information shows the disparity in South Dakota and can serve as a reference point for other rural areas to bring attention to the importance of CEC and geographic obstacles.

Madison Kovar

Title: **AK072019: A Molecular Inhibitor of MRSA Acetate Kinase Exhibiting Cellular-Level Efficacy against *Staphylococcus aureus***

Team: **Madison Kovar**, Mitchell Lonnem, Chun Wu

Abstract: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections pose a significant therapeutic challenge, driving the need for novel antibiotics. Our lab targeted the bacterial central metabolism, specifically MRSA acetate kinase (ACK), as a potential drug target for MRSA infection due to its in silico essentiality to MRSA and absence in humans. MRSA ACK was successfully cloned, expressed, purified, and characterized. High-throughput inhibitor screening identified 38 potential hits, with compound AK072019 ranking high in our priority list. This poster displayed the inhibition kinetics, antibacterial activity, and selectivity of AK072019 at the molecular and cellular levels. Kinetic assays revealed AK072019 to be a competitive inhibitor of MRSA ACK, exhibiting a Ki value of 448.0 μM. Comparative analysis of antibacterial activity of inhibitor AK072019 against 17 species of representative Gram positive and Gram-negative bacteria was conducted by Kirby-Bauer disk diffusion method. The results demonstrated that AK072019 selectively inhibit the growth of Gram-positive bacteria Staphylococcus aureus, Staphylococcus epidermidis and Bacillus cereus without inhibiting the rest of Gram-positive and Gram-negative bacteria tested. The observed efficacy and selectivity of AK072019 underscore its potential as a candidate of narrow-spectrum antibiotic. Despite AK072019 displaying micromolar-level inhibition, it is remarkable that this molecular inhibitor of a newly identified drug target exhibits selective efficacy at the cellular level. These findings provide the foundation for further investigations aiming to develop secondary inhibitors of MRSA ACK with improved inhibitory activity and cellular efficacy, that holds significant promise for combating MRSA infections effectively.

Komila Rasuleva

Title: **EvIPqPCR, A Noninvasive Detection of Circulating Tumorous Extracellular Vesicles for Pancreatic Cancer Screening**

Team: **Komila Rasuleva**, Dali Sun

Abstract: Pancreatic cancer is often diagnosed at advanced stages, resulting in high mortality rates. Noninvasive and efficient screening techniques are urgently needed for detection. Tumor-derived extracellular vesicles (tdEVs) have emerged as potential diagnostic biomarkers for cancer. However, current tdEV-based assays have limitations, including high sample volumes, complexity, and cost. To address these challenges, we developed a novel diagnostic method called EvIPqPCR for pancreatic cancer screening. EvIPqPCR utilizes the ratio of mitochondrial DNA to nuclear DNA (mtDNA/nDNA) in tdEVs as a cell-specific characteristic to target both malignant and nonmalignant EVs. We observed that tumorous EVs exhibited higher mtDNA content compared to healthy EVs. EvIPqPCR method combines immunoprecipitation (IP) and qPCR to directly detect tdEVs in patient serum. Notably, this technique eliminates the need for DNA isolation and employs duplexing probes for qPCR, reducing the assay time by at least 3 hours. Our study demonstrates that EvIPqPCR is a fast and specific method for detecting pancreatic cancer. The assay shows a weak correlation with prognosis biomarkers and exhibits sufficient discriminatory power between healthy individuals, pancreatitis patients, and pancreatic cancer cases. It requires a small sample volume (200 µL), less time-consuming (<1.5 hr.), is cost-effective (<$10/sample), and easily scaled for high-throughput analysis. These features make it an attractive option for cancer screening. In summary, our study represents a significant advancement in noninvasive diagnostic approaches for pancreatic cancer. The utilization of the EV mtDNA/nDNA ratio as a tumor marker, along with the isolation-free approach and duplexing qPCR probes, enhances the accuracy and efficiency of cancer diagnosis.

Alyssa Schumacher

Title: **Midwest Health Disparities in Pregnancy Outcomes before, during, and after Covid-19**

Team: **Alyssa N. Schumacher**, Hilla I. Sang PhD, Anna M. Strahm

Abstract: Purpose: To describe birthweight and preterm birth outcomes before, during, and after the psychosocial stressor impact of COVID-19 among pregnant women including Indigenous American, Black and White individuals. Methods: We reviewed a large retrospective data set spanning April 2011-September 2022, that included 9,541 de-identified primigravida pregnancies between the ages of 18-45 who gave birth in the Midwest at a gestational length of <43 weeks. COVID-19 epochs were delineated into pregnancies occurring in periods "Before," "Transitional," and "After" February 25th 2020 (CDC, 2023). From this data set we categorized race from the participant's medical charts limiting to three categories including Black (N=262), Indigenous American (IA; N=294), and White (N=8,985). Results: While there was not an overall discernable trend of lower birthweight or gestational length across COVID-19 epochs, the gestational length of Black and IA individuals tended to be shorter than their White counterparts. Additionally, we observed an increase among Black individuals, and decrease among IA individuals, in preterm births during the After COVID-19 epoch. Further analyses are necessary to determine whether COVID-19 stress, racial discrimination, or other relevant factors predict these changes. Conclusion: Our results describing trends across COVID-19 epochs in both Black and IA pregnancies suggest an unequal impact of the pandemic for these communities. Further analyses are planned using propensity matching, to reduce between group variance, and determine if models including race and COVID-19 epochs predict birthweight and gestational length. Additionally, future research might consider the role of racially mediated stress differences during analyses of these or similar epochs.

Jadyn Gasper

Title: **Racial Disparities in Glucose Tolerance and Delivery Intervention**

Team: **Jadyn Gasper**, Hilla I. Sang PhD, Anna M. Strahm

Abstract: Purpose: The COVID-19 pandemic created new stressors influencing psychosomatic symptoms during pregnancy. Historically devalued racial groups were theorized to be disproportionately affected. This may have implications for pregnancy health and outcomes as stress can affect glucose tolerance and delivery interventions. In this report we describe how combinations of racial identity and COVID-19 timing during pregnancy impacted Oral Glucose Challenge Test (OGCT) values, and delivery interventions. Method: We reviewed 44,891 de-identified medical records from a large Midwestern healthcare system from 2011-2021. Records included pregnant women aged 18-45 with a gestational length of <43 weeks, had information on OGCT and delivery intervention use, and were identified as either Indigenous American (IA; N=3494), Black (N=2231), or White (N=39166). Results: Across predetermined COVID-19 epochs, there appears to be an increase in OGCT scores among IA and Black women peaking before the vaccine was available, followed by a decrease with vaccine availability. Among IA women the percentage of cesarean deliveries appears to increase until right before the vaccine is available and then decrease. Conversely, cesarean deliveries for Black women decrease until right before the vaccine is available and then increases. The OGCT scores and cesarean deliveries for White women appear relatively unchanged across COVID-19 epochs. Conclusion: Health disparities relevant to COVID-19 may be present among IA and Black women due to the appearance of a fluctuation of OGCT values and delivery interventions while White women were seemingly unaffected. Further analysis will be done to discern if the differences are statistically significant using a predictive model.

Poster Session – Group B

Elisabetta Liverani, PhD

Title: **Investigating the role of platelets in cancer patients undergoing treatment with PD-1/PD-L1 inhibitors**

Team: Ying Kang, Philomena Entsie, Emmanuel Boadi Amoafo, Steven F. Powell, MD, **Elisabetta Liverani**

Abstract: Purpose: we aimed to investigate whether targeting the PD-1/PD-L1 pathway alters platelet functions and interaction with the T cells. Programmed cell death protein 1 ((PD-1) is a cell surface receptor on T lymphocytes that once bound to its ligand, (PD-L1), negatively regulates immune cell functions. Platelets contribute to cancer growth and inactivate the immune system favoring cancer growth. Platelets are a significant source of PD-L1. Our hypothesis is that upon PD-1/PD-L1 inhibitor treatment, the platelet activation and platelet-T cell interaction will be diminished. Methods: we collected blood samples from cancer patients before and 3 weeks after PD-1/PD-L1 immunotherapy. We analyzed platelet activation by measuring surface p-selectin and collagen and ADP-induced aggregation and secretion. We measured platelet and CD4+ or CD8+ T cell aggregate formation in vivo and in vitro. Results: platelets from cancer patients had an increased p-selectin surface expression which is not observed in healthy control. In cancer patient blood samples, we observed a significant percentage of platelet-CD4+ and platelet-CD8+ aggregate formation, while they are not observed in healthy individuals. Three weeks after immunotherapy, it showed a trend toward a decrease in p-selectin surface expression on platelets and a trend toward a decrease in platelets-CD8+ T cell aggregates. Conclusion: platelets from cancer patients were activated. Immunotherapy has shown the potential to restore healthy platelet functions and diminished their interaction with CD8+ T lymphocytes.

Steven Wu, PhD

Title: **All-in-One nanoparticle for breast cancer treatment based on phototherapy and chemodynamic therapy**

Team: Mingjian Chen, Shuyi He**, Steven Xu Wu**

Abstract: Chemodynamic therapy (CDT) has emerged as an outstanding antitumor therapeutic method due to its selectivity and utilization of tumor microenvironment. However, there are still unmet requirements to achieve high antitumor efficiency. Here, an iron-loaded semiconducting polymer dot modified with glucose oxidase (Pdots@Fe@GOx) is reported to deliver iron ions into tumor tissues and in situ generation of hydrogen peroxide in tumors. On one hand, Pdots@Fe@GOx converts glucose to gluconic acid and hydrogen peroxide (H2O2) in tumor, which not only consumes glucose of tumor cells, but also provides the H2O2 for the following Fenton reaction. On the other hand, the Pdots@Fe@GOx delivers active iron ions in tumor to perform CDT with the combination of the generated H2O2. In addition, the Pdots@Fe@GOx has both photothermal and photodynamic effects under the irradiation of near-infrared laser, which can improve and compensate the CDT effect to kill cancer cells. This Pdots@Fe@GOx-based multiple-mode therapeutic strategy has successfully achieved a synergistic anticancer effect with minimal side effects.

Sabha Ganai, MD, PhD

Title: **An Explanatory Sequential Mixed-Methods Investigation of Colorectal Cancer Care Disparities in North Dakota**

Team: **Sabha Ganai, MD, PhD, MPH,** Joel T. Zimmerman, Hilla I. Sang, PhD, Cameryn Ryan, Shawnda Schroeder, PhD

Abstract: Rural populations experience disparities in access to care which can lead to inferior cancer outcomes. Colorectal cancer (CRC) is the second-leading cause of cancer mortality in the United States, despite being highly preventable, detectable, and treatable. Over the last decade, CRC incidence rates have decreased by 30% in the US, presumably secondary to screening as a public health measure. However, the pace of improvements from screening has not been equal within the United States, with North Dakota lower that the median of states for colorectal screening rates, while having a higher than average cancer incidence. We present the hypothesis that spatial and aspatial barriers exist that influence CRC outcomes in North Dakota. We present the first phase of an explanatory sequential mixed-methods study focusing on CRC mortality-incidence ratio hot-spot and low-spot counties in North Dakota that will elucidate attitudes, behaviors, beliefs, and barriers that may influence CRC incidence, screening rates, stage of presentation, and mortality. This study will specifically explore quantitative data analyzed using spatial techniques and use this data to inform qualitative analyses in a population-centered fashion. We present the quantitative phase of the study, including data from spatial analysis of ND cancer registry data (n=6368; 2002-2018) and compared rural (RUCA 4-10) and urban patients. We used ArcGIS to calculate rural driving distance to various specialists and noted significant differences in travel distance for access to endoscopists, colorectal surgeons, and hepatobiliary surgeons. Increasing travel distance to HPB surgical care was associated with worse survival. We then examined age adjusted mortality to incidence ratio and subdivided counties by quintile, with the highest MIR quintile designated as “hot spots” and lowest MIR quintile as “low spots”. We noted a significant difference in survival between cohorts, with medial survival of 3.9y in hot spot counties and 6.7 years in low spot counties. Next, we created an ecologic cohort study and submitted surveys by random purposeful sampling to ND residents in specific counties by MIR quintile and received responses from residents of low-spot counties (n=44), middle quintile counties (n=42), and hot-spot counties (n=35). We examined demographics, EUROQOL 5L-5D perceptions of current health state, and validated questions examining mistrust in health care, and questions relevant to cost of travel and health expenditures. In addition, we examined travel time to various services ranging from food, dental care, regular health care visits, colonoscopy, minor/major surgery, and cancer care, with additional comparisons between travel during winter months and summer months. We are currently structuring focus groups in hot-spot and low-spot counties. These will be conducted in gender-specific community member cohorts to explain data and explore community attitudes, behaviors, values, and beliefs. We will later conduct provider interviews, comparing/contrasting provider attitudes, behaviors, values, and beliefs in hot-spot and low-spot counties. Following Kilbourne’s conceptual framework for disparities research, we will work towards defining and developing an intervention to improve outcomes in North Dakota.

Buddhadev Layek, PhD

Title: **Mesenchymal Stem Cell-Based Targeted Combined Therapy for Lung Cancer Management**

Team: Paras Mani Giri, Cornelius McKown Dyke, **Buddhadev Layek**

Abstract: Purpose. Lung cancer is the leading cancer killer in both men and women, accounting for ~25% of all cancer deaths. The ineffective delivery of conventional chemotherapeutics to tumor tissue and the tumor's innate resistance to chemotherapy are the main causes of the dismal treatment results. The proposed research aims to evaluate tumor-targeted delivery of nano-encapsulated entinostat and paclitaxel combination using engineered mesenchymal stem cells (MSCs). Methods. A549 cells were treated with paclitaxel, entinostat, or their combination, and cell viability was determined via MTT assay. The combination interactions between free oxaliplatin and entinostat were evaluated using Combenefit® software. Western blotting techniques were performed to determine acetylated histone H3 and H4 and cleave caspase expression. Both drugs were individually encapsulated into poly(lactic-co-glycolic) acid nanoparticles using the emulsion solvent evaporation technique and characterized for their physicochemical properties. In vitro cytotoxicity of drug-loaded nanoparticles was performed using A549 cells. Currently, we are performing in vivo efficacy of the combination therapy using a patient-derived xenograft (PDX) model of lung cancer. Results. Drug combinations showed synergistic potential at various combination ranges. Western blot analysis revealed higher expression of acetylated H3, H4, and cleaved caspase 3 in combination treatment compared to individual treatment. Both paclitaxel and entinostat nanoparticles were spherical with a size of ~280 nm and showed sustained in vitro drug release profiles. Our preliminary in vivo data exhibited promising anticancer effects of combination treatment against the PDX tumor model. Conclusion. Our results demonstrate that nano-MSCs-mediated combination therapy can be a potential alternative strategy for lung cancer management.

Khosrow Rezvani, PhD, MD

Title: **Mechanistic studies of UBXN2A-RICTOR-mTORC2 axis in human colorectal cancer**

Team: Sanam Sane, Rekha Srinivasan, Rashaun A. Potts, Morgan Eikanger, Jessica Freeling, Ryan M. Antony, Douglas Lynch, Jonathan Bleeker, Hassan Turaihi, Angela Pillatzki, **Khosrow Rezvani**

Abstract: There is a clear need to develop more effective targeted therapies to decrease the high mortality associated with metastatic colorectal cancer (CRC). Recent evidence points to inhibiting a signaling pathway regulated by the mTORC2 complex as a promising approach for effective targeted therapy in CRC. Suppression of mTORC2 signaling inhibits CRC cell proliferation and sensitizes CRC cells to standard-of-care therapies. The Rictor protein is a critical component of the mTORC2 complex that increases CRC and drives aberrant mTORC2 and AKT signaling in CRC cells. The current study leverages evidence that the downregulation of Rictor may be a promising approach for targeting mTORC2 signaling for therapeutic benefit in CRC patients. We found a tumor-suppressive ubiquitin-like protein, UBXN2A, induces degradation of Rictor in CRC cells, inhibiting downstream Rictor-mTORC2-regulated cancer-associated processes such as cell growth, survival, and migration. UBXN2A induction in patient tumor-derived organoids suppresses the mTORC2 pathway. These findings provide new insights into the potent anti-cancer function of a Ubiquitin-like protein in patients with CRC.

Estelle Leclerc, PhD

Title: **Effects of RAGE inhibition during melanoma chemotherapy in PDX mouse models of melanoma**

Team: Md. Zahidul Hasan, Yousuf Alam, Daniel Tuvin, David Bradley, **Estelle Leclerc**

Abstract: We previously showed that the Receptor for Advanced Glycation End products (RAGE) enhances resistance towards the cytotoxic DNA alkylating agent dacarbazine in a xenograft mouse model of melanoma tumors. The purpose of the present study was to investigate if RAGE also enhances resistance towards the current standard of care vemurafenib and trametinib. These two drugs inhibit key molecules of the BRAF/MEK signaling pathway, a pathway that is responsible for melanoma tumor growth. We chose to test the effect of these drugs using a patient-derived xenograft (PDX) mouse model, a method of choice, because PDX models closely recapitulate the pathophysiological conditions of patients' tumors. The first objective of our study was to generate PDX mouse models of melanoma. Through our collaboration with Dr. Tuvin, we successfully expanded the tumors from 3 distinct patients in mice, out of the 5 patients' tumors that we received from Sanford. We also generated cell-lines from 2 distinct tumors. We tested the sensitivity of one cell-line against the DNA alkylating agent temozolomide and the BRAF mutant inhibitor vemurafenib. We observed that the PDX derived cell-line was resistant to temozolomide but was sensitive to vemurafenib. Our next objective will be to determine if i) the treatment of the PDX carrying mice with vemurafenib and trametinib is more effecting in reducing cell proliferation and/or tumor growth than vemurafenib alone, and ii) RAGE inhibition combined with vemurafenib and trametinib is more effective in reducing or tumor growth than vemurafenib and trametinib combined.

Jiha Kim, PhD

Title: **Pathological perivascular phenotype contributes to hypoxia, impaired immune response, and reduced therapeutic efficacy**

Team: Vikneshwari Natarajan., Isabel Kallmeyer, Sangdeuk Ha, **Jiha Kim**

Abstract: Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer death in men and women in the U.S., with a 5-year survival rate of 12%. One of the reasons for such a poor prognosis is its complex and dense tumor microenvironment (TME) and lack of effective treatment options. Within the PDAC TME, morphologically aberrant leaky vessels are responsible for hypoxia and impaired immune response, which likely reduces the efficacy of cancer therapies. Therefore, we hypothesize that correcting such undesirable phenotype via vascular normalization will alleviate the harsh TME and enhance the treatment efficacy. Our study revealed that tumor-associated pericytes across all PDAC tumor tissues exhibited ectopic αSMA expression, which was correlated with vascular leakiness and hypoxia. We also showed that such aberrant pericyte phenotype was due to pancreatic cancer cell-derived extracellular vesicles (PC-Exo). In addition, PC-Exo stimulated, tumor-conditioned αSMA+ pericytes present mechanical abnormalities and immune-suppressive features. We performed single-cell RNA sequencing to further determine the pathological signature of tumor pericytes and identify potential target molecules toward vascular normalization. Pericytes were isolated from WT pancreas and KPC tumors at 15-20 weeks to obtain a viable single-cell population for scRNA seq. In addition, to define the influence of pericyte phenotypes on PDAC TME evolution, multispectral imaging was utilized. Various combinations of pericytes and immune markers are examined to study the relationship between pericyte phenotype and immune composition in TME.

Kennedy Forest

Title: **Alcohol use as a risk factor for drug-induced liver injury with amoxicillin-clavulanate in the All of Us Research Program**

Team: **Kennedy Forest**, Tiffany Knecht, Shaopeng Gu, Eric A. Larson, Russell A. Wilke

Abstract: Purpose: Idiosyncratic drug-induced liver injury (DILI) is an extremely rare adverse drug reaction (occurring in less than 1 in 10,000 patients exposed), but it has the potential to be lethal. Antibiotics, such as amoxicillin-clavulanate, are a known cause of idiosyncratic DILI. Demographic factors and relevant clinical covariates may help clinicians risk stratify patients for DILI with antibiotic use. There is great interest in identifying genetic and environmental risk determinants that could be used to avoid DILI specifically with amoxicillin-clavulanate. Methods: Retrospective analyses were conducted applying a standardized phenotyping algorithm to de-identified electronic health record (EHR)-linked clinical data available for 318,598 study participants in the All of Us database. Phenome scanning and exclusion criteria were applied to identify DILI cases from among the 36,794 patients exposed to amoxicillin-clavulanate. Results: Thirty cases of acute DILI were identified with amoxicillin-clavulanate. Assessment of clinical covariates revealed a trend toward higher mean alcohol intake in case patients, when compared to non-DILI controls. Nether BMI nor age were associated with case status. Conclusion: Data from the EHR-linked research cohorts can be efficiently mined to identify DILI cases related to antibiotic use. In All of Us, analysis of clinical covariates revealed a higher mean alcohol intake in acute DILI cases compared to controls. This suggests that reducing alcohol use may favorably modify the risk for DILI with amoxicillin-clavulanate.

Andrew Guymon

Title: **Do We Need a Saline Bolus? – The Necessary Refinement of Pediatric Propofol Sedation**

Team: **Andrew Guymon**, Madigan Moore, Laura Nelson, Mir Ali

Abstract: Purpose: US healthcare costs have risen dramatically encompassing 20% of the nation's GDP. Propofol sedation is used ubiquitously for pediatric MRIs to ensure minimal patient movement. Normally, patients receive a 20 ml/kg saline bolus in hopes of maintaining blood pressure throughout sedation. The goal of this study was to determine if a 10 ml/kg saline bolus was as equally efficacious as a 20 ml/kg saline bolus at completing pediatric propofol sedations and maintaining MAP in aims of reducing healthcare costs. Method: The study had two phases. The first phase was a six-month review of saline bolus dosing using the standard 20 ml/kg bolus. The second phase introduced a goal saline bolus of 10 ml/kg. A successful sedation was determined by completing the MRI without any complications or signs of cardiovascular distress. Results: A total of 114 pediatric patients were recruited. The percentage of successful sedations with a 20 ml/kg bolus and 10 ml/kg bolus was 94% and 100%, respectively. The average total saline bolus was reduced by 49% from phase 1 to phase 2. Importantly, the average MAP throughout sedation (20 ml/kg: 57±2 mmHg, 10 ml/kg: 58±2 mmHg, p = 0.425), minimal MAP (20 ml/kg: 50±2 mmHg, 10 ml/kg: 52±1 mmHg, p = 0.125) and end-sedation MAP (20 ml/kg: 58±1 mmHg, 10 ml/kg: 57±1 mmHg, p = 0.610) were equivocal between the two groups. Conclusion: We conclude that a saline bolus dose of 10 ml/kg would preserve blood pressure, and allow for successful sedation, but prevent excess dosing.

Morgan Eikanger

Title: **Veratridine functions as a potential anti-mTORC2-Rictor tumorigenic pathway inhibitor in human colorectal cancer**

Team: **Morgan Eikanger**, Khosrow Rezvani

Abstract: Despite advances in treatment regimens, the high mortality rates due to colorectal cancer (CRC) have remained unchanged. Understanding the mechanisms underlying the multistep metastatic programs activated in CRC tumors is critical for developing novel therapies to improve the management of this advanced disease. We have previously shown that veratridine (VTD), a lipid-soluble alkaloid extracted from Liliaceae plants, can transcriptionally increase UBXN2A, a known tumor suppressor protein in CRC. UBXN2A induces 26S proteasomal degradation of the Rictor protein, a key member in the mTORC2 tumorigenic signaling pathway. The VTD-UBXN2A axis inhibits the overactive Rictor-mTORC2 pathway in CRC, resulting in the suppression of mTORC2's downstream pathways, including the angiogenesis pathway. VTD induces apoptosis in CRC-originated primary, metastatic, and cancer stem cells. VTD-dependent induction of UBXN2A suppresses epithelial-mesenchymal transition (EMT) and interferes with cancer cell migration and invasion. To examine the anti-tumor growth potential of VTD in animal models, we used a mouse model of CRC with progressing tumor masses in the colon and rectum. Vehicle and VTD-treated mice revealed that intraperitoneal injection of VTD (0.1 mg/kg, q.o.d for 30 days) significantly decreases tumor growth. These findings provide an attractive and promising target for the next generation of drugs capable of targeting metastatic CRC.

Valentina Catalan

Title: **Factors impacting gestational diabetes mellitus health disparities in the Midwestern U.S**

Team: **Valentina Ayala Catalan**, Hilla I. Sang, Anna M. Strahm

Abstract: Purpose: In the USA, gestational diabetes mellitus (GDM) impacts up to 10% of pregnancies, and is reported to have greater prevalence and impact on women of historically marginalized racial/ethnic identity. Recent findings suggest underlying factors including maternal age, BMI, and healthcare contributes to these health disparities. We examined the influence of racial/ethnic identity, maternal age, and BMI on rates of GDM diagnosis, as well as fetal growth. Methods: We examined 9,720 de-identified medical records between 2011-2021, from a large Midwestern healthcare system. These records were limited to primipara pregnancies, with a maternal age between 18-45, and gestational length <43 weeks, with BMI information, and analyzable race categories including Indigenous American (IA; N=294), Asian (N=162) Black (N=262), Native Hawaiian/Pacific Islanders (NH; N=17), and White (N=8985) women. Results: After entering covariates of maternal age, BMI, and fetal sex, Black women were less likely ($p<.01$), while Asian ($p<.001$) and NH women ($p<.05$) were more likely to be diagnosed with GDM than White women. Furthermore, after entering covariates for maternal age, BMI, fetal sex, GDM diagnosis, and gestational length neonates of IA women ($p<.001$) were heavier, while Black women ($p<.001$) had babies that weighed less than White women. Conclusion: While the maternal age and BMI significantly contribute to GDM risk and fetal growth models, related health disparities persist, even when limited to women with access to the same health system for their prenatal care. Prenatal care that addresses culturally specific risks for groups experiencing health disparities continues to be important in reproductive health care.

Shanta Messerli

Title: **Neuroprotection and cognitive improvement using VACNO and SanFlow in the scopolamine model for Alzheimer's Disease**

Team: **Shanta M. Messerli**, Roland Rabl, Manuela Prokesch, Bohdan Soltys, Jan Simoni, Carleton Hsia, Keith Miskimins

Abstract: We investigated the efficacy of two novel drugs, VACNO and Sanflow, in preventing memory loss in an animal model of Alzheimer's Disease (AD). These drugs function as extracellular superoxide dismutase (SOD) mimetics, reducing oxidative stress, and have previously demonstrated neuroprotective effects in stroke and traumatic brain injury models. In our study, we compared the effects of VACNO and Sanflow in a scopolamine induced rat model of AD. Rats were injected with scopolamine, and we evaluated the therapeutic potential of VACNO and Sanflow in preventing or reversing learning and memory impairments. We assessed amygdala and hippocampal-dependent memory using a step-through passive avoidance test, where increased latency time to enter the dark compartment indicates improved memory retention. Long-term memory retention was evaluated 24 hours after the training phase. No statistically significant differences between treatment groups were observed during the training phase. However, during the testing phase, animals treated with Scopolamine + Sanflow exhibited a statistically significant increase in latency to enter the dark compartment compared to those treated with Scopolamine alone, suggesting enhanced memory retention. Additionally, reduced immunoreactivity of Glial fibrillary acidic protein (GFAP) in rats treated with scopolamine + VACNO and scopolamine + Sanflow, compared to those treated with scopolamine alone, suggests that both VACNO and Sanflow reduce scopolamine-induced astrocyte infiltration, potentially indicating a protective effect on neurons and a decrease in astrogliosis. Considering the potential benefits of Sanflow in memory improvement, further exploration of the effects of these SOD mimetics on cognitive impairment and neuronal changes in AD is warranted.

LUNCH DISCUSSION GROUPS

Group 1 – Unlocking the Potential of the National COVID Cohort (N3C)

Kent Ripplinger, MS

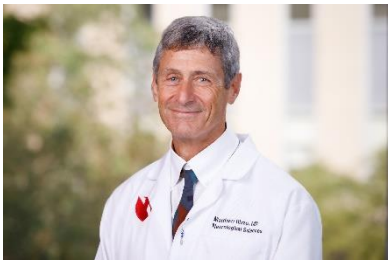
Are you passionate about harnessing the power of data to advance healthcare research and improve patient outcomes? Join us for an engaging lunchtime discussion group focused on “Unlocking the Potential of the N3C”! The National COVID Cohort Collaborative (N3C) is an ambitious initiative established in response to the COVID-19 pandemic. It is a groundbreaking effort that brings together a vast repository of clinical, laboratory, and demographic data from millions of COVID-19 patients across the United States. This unique resource is free to use, housed in a secure and centralized platform, and designed to facilitate research and collaboration among scientists, clinicians, and data experts. Don’t miss out on this fantastic opportunity to be part of the discussion surrounding the N3C and its potential to transform healthcare research. Please join us as we work together to Unlock the Potential of the N3C!

Kent Ripplinger is the Database Investigator Navigator for the DaCCoTA. He assists clinical researchers in using large administrative databases to help answer research questions. One of his primary areas of support is with the National COVID Cohort Collaborative (N3C) Data Enclave where he assists with onboarding requirements, creating project proposals, submitting Data Use Requests, and acting as a liaison between N3C resources and investigators. He also provides training on a variety of databases to promote potential opportunities for using datasets in research.

Group 2 – Real World Biometrics for Tracking Health

Matthew Rizzo, MD

Relevant service spans the US National Academy of Sciences Board on Human-Systems Integration, US FDA Panel for PNS and CNS Drugs, and FMCSA Medical Advisory Committee (appointed by US Secretary of Transportation), and extensive science and policy service and leadership with the American Academy of Neurology, the American Neurological Association, and multiple universities. He also serves on the Association for Clinical and Translation Science (ACTS) Executive Committee to empower members to develop, implement, and evaluate the impact of research and education programs. He has extensive experience working with other leaders, investigators, and trainees from academic medical centers, government, industry, and philanthropy. As a cellist, he founded the Nebraska Medical Orchestra. He is a clinician scientist who believes strongly in silo-spanning work, as promoted by CP Snow and EO Wilson.



Dr. Rizzo is 1) Reynolds Professor and Chair, Department of Neurological Sciences, 2) Chief Physician for Neurological Services (Neurology, Neurosurgery, Pain, PM&R, Psychiatry) at the University of Nebraska Medical Center (UNMC), 3) Founding Director NIH NIGMS Great Plains IDeA-CTR network spanning all NE University Institutions, Creighton, Omaha VA, Children's Hospital, Children's Health Research Initiative, Boys Town, and the Dakotas; and 4) Director, NE Practice Based Research Network spanning 70 sites. His principal previous employment (until 2014) was at the University of Iowa as 1) Professor of Neurology, Engineering, and Public Policy; 2) Vice Chair of Translational and Clinical Research; 3) Director, Division of Neuroergonomics; and 4) Founding Director, Aging Brain and Mind Initiative, spanning Colleges of Medicine, Nursing, Engineering, Public Health, and Liberal Arts and Sciences.

Dr. Rizzo proudly serves the Chair for the Executive Committee of the American Brain Coalition (ABC), a 501(c)3 organization comprising nearly 150 partner organizations (patient advocacy, industry, medical professional, and government groups), advocating to advance research for neurological cures. He has made distinct, sustained, original contributions to US biomedical science and education. His work on cerebral substrates of human vision creatively combined the human lesion method with visual psychophysics and cognitive science. Building on ethological principles pioneered by Lorenz, he helped forge Neuroergonomics, a new field bridging medicine, neuroscience, and engineering. He pioneered simulation and "brain-in the wild" work using sensors in a person's own vehicle and devices as egalitarian, passive-detection systems for flagging age- and disease-related aberrant behavior and physiology ("digital biomarkers") that may signal early signs of functional decline or incipient disease (e.g., degenerative).

DaCCoTA Resource Cores

Biostatistics, Epidemiology, and Research Design Core

Director – Gary Schwartz, PhD, gary.schwartz@und.edu
Co-Director – Ross D. Crosby, PhD, Ross.Crosby@SanfordHealth.org
Statistician – Mark Williamson, PhD, mark.williamson.2@und.edu
Database Navigator – Kent Ripplinger, MS kent.p.ripplinger@und.edu
Website: https://med.und.edu/daccota/biostatistics-epidemiology-research-design-core.html

The Biostatistics, Epidemiology, and Research Design Core (BERDC) offers both pre-award and post-award grant support services including assistance with research design, statistical analysis, data collection and management, regulatory services, and data access.
The BERDC also provides consulting services to address a wide range of biostatistical approaches relevant to cancer research as well as opportunities to mentor DaCCoTA investigators, junior faculty, and graduate students.
Additionally, the BERDC provides a variety of data informatics services including a secure web application designed to support data capture for research studies, extensive computational infrastructure, and data storage.

Community Engagement and Outreach Core

Director – Julie Smith-Yliniemi, PhD, LPCC, MPH, Julie.smithyliniemi@und.edu
Co-Director – Shannon Bacon, MSW, LSW, shannon@communityhealthcare.net
Coordinator – Susan Thompson, MA, susan.thompson2@und.edu
Website: https://med.und.edu/daccota/community-engagement-outreach-core.html

The Community Engagement and Outreach Core (CEOC) focuses on engaging communities and groups that are disproportionately affected by cancer with the long-term goal of developing community-based research priorities that can be translated into improved health outcomes. The CEOC has the following key objectives:

- Engage communities to assist in a research agenda-setting process that is based on population health needs and community priorities
- Expand research that is culturally appropriate for rural and American Indian communities through training and research
- Promote dialogue and collaborate with communities and other stakeholders to assess findings from completed research projects

In order to meet these objectives, the CEOC will conduct interviews and focus groups with key informants and stakeholders, establish accessible training modules and materials on culturally appropriate research strategies for working with rural and American Indian communities, and organize a communication plan that promotes inclusion and dialogue regarding the results of research projects.

Clinical Research Resources and Facilities Core

Director – Lora Black, RN, MPH, Lora.Black@SanfordHealth.org
Co-Director – Kimberly Hammer, PhD, Kimberly.Hammer@va.gov
Project Manager – Miranda Leitheiser, ACRP-CP, MPH, Miranda.Ruiter@SanfordHealth.org
Project Manager – Cassy Garry, ACRP-CP Cassy.Garry@SanfordHealth.org

Website: https://med.und.edu/daccota/clinical-research-resources-facilities-core.html

The overall goal of the Clinical Research Resources and Facilities Core (CRRFC) is to provide synergy and expansion opportunities to the existing clinical services and technology cores available through the partnering institutes, thereby fostering an ideal environment for the competitive execution of clinical and translational cancer research. Below is a summary of the services provided by the CRRFC:

- Facilitate access to patient samples
- Facilitate access to patient data sets
- Assist with identification of collaborators or clinician/non-clinician teams
- Increase operational support for clinical research and provide oversight for research involving human subjects
- Assist with study design, human subjects sections, form creation, patient recruitment, sample and data collection
- Assist PIs in navigation of workflows and resources across the DaCCoTA footprint
- Assist PIs with study closeout

Professional Development Core

Director – Lee Baugh, PhD, Lee.Baugh@usd.edu
Co-Director – Donald Sens, PhD, donald.sens@und.edu
Coordinator –
Website: https://med.und.edu/daccota/professional-development-core.html

The primary goal of the Professional Development Core (PDC) is to build an integrated program of education and career development. The PDC offers the following training opportunities to support clinical and translational cancer research:

- DaCCoTA Scholars Program - The purpose of this award is to stimulate the development of new Clinical and Translational Research (CTR) investigators. Applications are expected to address health-related translational research of importance to North and South Dakota. Each awardee will receive salary support (50% FTE plus fringe) that guarantees a minimum of 50% protected research time for the project. The DaCCoTA will provide the first three years of funding, and the final two years will be funded by the applicant's home institution (contingent on adequate progress). The awardee will also receive up to $160,000 in annual research support for up to 5 years. The DaCCoTA Scholars Program offers both a basic and community engagement track, and early career faculty are encouraged to apply.
- Clinical Research Opportunities Program - The Clinical Research Opportunities Program provides salary support (up to 20% of the NIH salary cap) for community-practicing hospital-based clinicians to allow them to participate in training activities and collaborate with basic science investigators to conduct translational research.

Pilot Projects Program

Director – Holly Brown-Borg, PhD, holly.brown.borg@und.edu
Co-Director – Sathish Venkatachalem, PhD, s.venkatachalem@ndsu.edu
Coordinator – Savannah Macias-Daugherty, savannah.m.daugherty@und.edu
Website: https://med.und.edu/daccota/pilot-projects-program.html

The goal of the Pilot Projects Program is to stimulate growth of expertise and engagement in clinical and translational research. This program funds a variety of awards and provides a

mechanism for clinician/non-clinician teams to develop promising new translational research projects focused on cancer. The Pilot Projects Program offers the following pilot grants:

- Introduction to Research Pilot Award - The Introduction to Research Award offers up to $15K and is intended to allow non-faculty clinicians or early-stage investigators (ESIs; residents/postdoctoral scholars) to engage in research. This award aims to recruit a: 1) clinician from the American Indian Collaborative Rural Research Network (AICoRN) or rural and tribal communities; or 2) ESIs who have interest but no experience managing a research project or preparing a grant. Clinician applicants will be recruited as adjunct faculty into one of the partner institutions and partnered with the Cores to assist with delivering the intended outcomes of refining a hypothesis, designing a CTR study, and step-by-step introduction to grant components that would be required for a subsequent Feasibility application. Similarly, ESIs awardees will be assigned a mentor to assist in developing an individualized training plan (ITP). Successful completion of these proposals should result in a more research savvy clinician and a submitted Feasibility proposal or ESIs that are more interested and prepared to engage in translational research.
- Feasibility - The feasibility pilot awards provide up to $40K to allow a clinician/non-clinician team to form around a novel cancer-related hypothesis. Awardees will receive assistance with research design, determination of data required, and the final preparation of a competitive “ready-to-go” or community engagement award application. The primary goal of this award is to allow a team to form and connect with the Biostatistics, Epidemiology, and Research Design Core, Clinical Research Resources and Facilities Core, and the Pilot Projects Program to generate competitive proposals for the CTR Ready-to-Go Pilot Award mechanism.
- Ready-to-Go - The ready-to-go pilot awards represent a larger investment of up to $75K for 1 year and are intended for those projects with existing significant preliminary data in support of a novel clinical/translational hypothesis. These proposals should result in sufficient findings to support a collaborative extramural grant application (involving a clinician and non-clinician team) and a peer-reviewed publication.
- TREE - The Translating Epidemiology to Experiments (TREE) Pilot Grant Award offers up to $50K and is intended to provide seed funding for a public health/laboratory scientist team towards highly innovative projects that seek to translate promising epidemiological findings at the population level to relevant in vitro and/or in vivo experiments and/or the reverse, from in vitro and in vivo observations to a population setting. Proposals are envisioned to focus on T0-T1 translational research, whereas T2-T4 studies are a better fit for other Pilot Project funding mechanisms.