

Sanford researcher explores American Indian breast cancer management and prognosis



Dr. Anu Gaba, a specialist in oncology and hematology at Sanford Health, worked with a team of researchers on breast cancer through her DaCCoTA Clinical Research Opportunities Grant. The team's goal was to assess the impact of Medicaid expansion under the Affordable Care Act on the gap between American Indians and Whites in breast cancer management and prognosis.

Prior studies have shown that over a 20-year span (1990-2009), breast cancer death rates in the U.S. have not significantly declined for American Indians (AIs) in comparison to the White population. Dr. Gaba's team examined whether the 2010 Medicaid expansion as part of the Affordable Care Act (ACA) resulted in the improvement of breast cancer management and prognosis for American Indians relative to the White population.

They abstracted information from the National Cancer Data Base for AIs and White breast cancer patients diagnosed between the years 2004-2016 who lived in states that expanded Medicaid in January 2014, and those that did not expand Medicaid. Breast cancer outcomes—stage at diagnosis, insurance status, definitive treatment initiation within 30 days of diagnosis, and 3-year mortality—were analyzed.

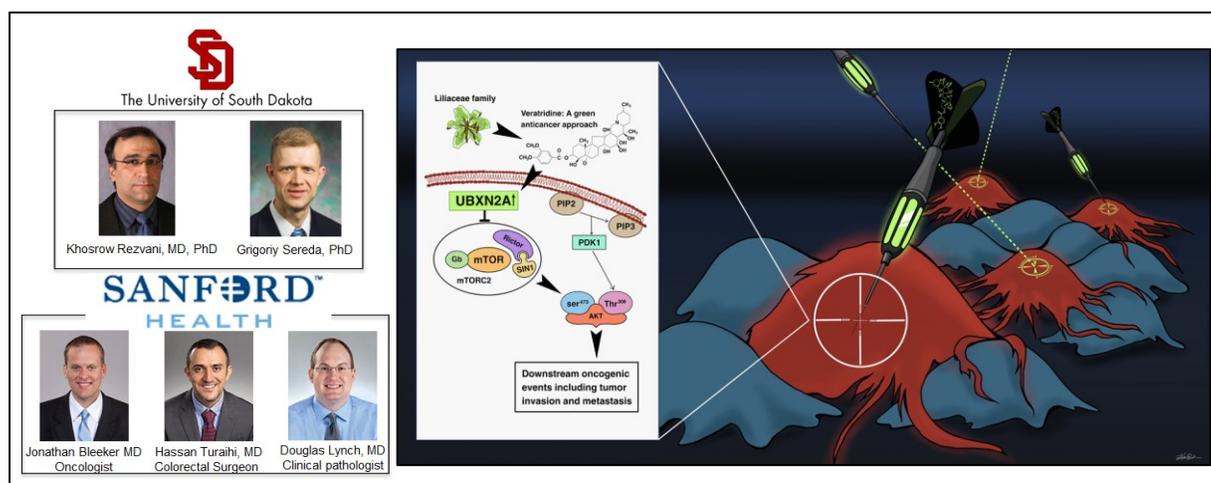
There were over a million newly diagnosed White and AI breast cancers between the years 2004-2016. More than 99% were Whites and 0.3% were AIs. Of these, 46.9% resided in states that expanded Medicaid in January 2014 and 53.1% in states that did not expand Medicaid.

Their analysis showed that in patients newly diagnosed with breast cancer, the proportion of uninsured declined significantly with Medicaid expansion (OR=0.53, 95% CI: 0.52-0.54; $p < 0.001$) in Whites and AIs, and the proportion of patients who received first definitive treatment within 30 days of diagnosis decreased significantly less in states that expanded Medicaid (decrease from 51% to 42%) than in non-expansion states (decrease from 55% to 44%) ($p = 0.041$) under the ACA. Most notably, Medicaid expansion increased early breast cancer diagnosis in AIs; this effect was not seen in non-expansion states ($p = 0.001$). Medicaid expansion could not be associated with changes in the three-year mortality rate.

In conclusion, Dr. Gaba and her team found that Medicaid expansion has improved breast health for both Whites and AIs in the United States. The team is currently in the process of publishing this research. Dr. Gaba would like to acknowledge the other team members who worked hard on this project – Li Cao from the Sanford Biostatistics Core and Rebecca Renfrew from the Sanford Cancer Registry, as well as Dr. Ross Crosby (Sanford Research) and Dr. Kristi Eglund (SAB Biotherapeutics) who served as mentors for this project.

Smart nanocarrier-based drug delivery of an anti-cancer plant alkaloid targets colorectal tumors

A collaborative translational research project between the University of South Dakota and Sanford Health in Sioux Falls has led to an advanced drug discovery and a new delivery method.



USD and Sanford Health have developed a novel drug that suppresses colon cancer cells through a new method of targeted delivery.

Despite advanced treatment regimens, one third of patients with colorectal cancer (CRC) ultimately die from metastatic (disseminated) disease. The prognosis for patients with metastatic CRC is an abysmal $\leq 12\%$, and there have been no significant treatment innovations in the past ten years. In addition to 50,000 deaths due to CRC in the United States annually, the incidence of CRC is rising rapidly among young adults. According to the American Cancer Society, 18,000 people under the age of 50 were diagnosed with CRC in the United States in 2020. Thus, there is an urgent need to develop safer and more effective targeted therapies that can significantly decrease the mortality rates among patients with CRC.

Small molecules extracted from plants have made significant contributions to anticancer drug development in the past 50 years. Two examples are taxol and camptothecin, alkaloids isolated from plants that are currently used in clinic as FDA-approved anti-cancer drugs with annual sales in the billion-dollar range.

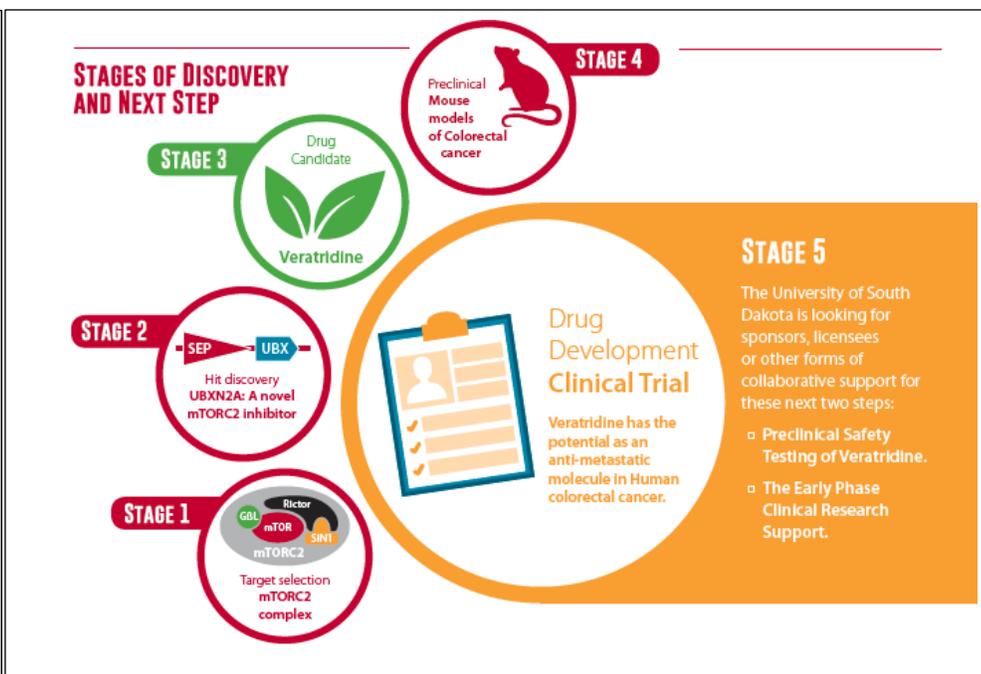
Dr. Khosrow Rezvani, an associate professor in the University of South Dakota's Division of Basic Biomedical Sciences, and a team of researchers have discovered that a known plant-derived anti-hypertensive supplement named veratridine can target and induce death in human colon cancer cells. The team found that veratridine mechanistically interferes with the mTORC2 signaling pathway involved in tumor formation, progression, and metastasis. Dr. Rezvani and his team have shown that veratridine acts as an anti-growth and anti-metastatic cancer therapeutic in colon cancer cells and in animal models of CRC. The discovery of new agents that interfere with specific molecular pathways involved in cancer metastasis can significantly change the course of treatment for patients with advanced CRC, thereby improving patients' quality of life.

The involvement of Sanford Health clinicians (Dr. Bleeker, Dr. Turaihi, and Dr. Lynch) and the Sanford Health clinical coordinator team (Janet Wernisch, Tabatha Lemke, Ryan Sprecher, and Miranda Ruitter) have turned this project into successful translational research supported by the DaCCoTA Cancer Collaborative Program.

During the execution of the above study, Dr. Grigoriy Sereda from the USD Department of Chemistry began a collaborative project with Dr. Rezvani's group to optimize the delivery of veratridine to cancer cells while leaving normal cells intact. Dr. Sereda and his team were able to seal veratridine inside of nanoparticles by using large molecules of metalloproteins to block the pore exits, keeping the drug inside. When the nanoparticles encounter cancer cells, the cancer cells produce an enzyme that splits the blocking proteins, opens the pores, and releases the anticancer drug precisely at the locations of the cancer cells. The precisely tuned surface charge of the nanoparticles enables them to selectively adhere to cancerous cells, leaving normal fibroblasts intact. The selective drug delivery and release will drastically reduce the dosage required for treatment and the exposure of non-cancerous tissues and neurons to the drug. The first set of results was published in the journal *Bioconjugate Chemistry* in 2021 with the title "Targeting Colon Cancer Cells with Enzyme-Triggered Casein-Gated Release of Cargo from Mesoporous Silica-Based Nanoparticles" (*Bioconjugate Chemistry*, **2021**, 32(11), 2353-2365).

USD and Sanford Health are the first to create this tumor suppressing drug, which has been examined in a preclinical model and is ready to move to the next step and undergo human clinical trial. This team is also the first to be able to deliver the drug to the tumor site only through a new method of highly targeted nanoparticle delivery.

Rezvani started drug screening in 2014; currently, Rezvani's and Sereda's teams are conducting further tests to prove their drug delivery technology. Their goal is to test the effectiveness of veratridine in a human clinical trial in the near future.



Core Component Highlight: Introducing AICoRN



The American Indian Collaborative Research Network (AICoRN) is the new practice-based research network (PBRN) for the DaCCoTA Project. AICoRN operates as a network of health providers in the Dakota region who want to do clinical research in a focused way. Additionally, AICoRN includes practitioners, clinics and tribal organizations in Wyoming and Montana. These partners provide the “laboratory” – the clinics – for studying broad populations of patients in community-based settings. The project’s goal is to address the health needs of American Indian populations, as well as other underserved populations, such as rural Dakotans.

Current Network Members:

CHAD: Community Healthcare Association of the Dakotas

- Network of Federally Qualified Health Centers
- 65 sites, 53 communities

Monument Health: Based in Rapid City

- 31 specialties, 12 communities across western SD
- 5,000 physicians and caregivers, 5 hospitals, 38 clinics and centers

Oyate Health: Tribally owned community driven health care system

- Black Hills and Badlands region of western SD
- Primary Care, Urgent Care, specialty clinics

Family Medicine Centers UND Family Medicine Residencies

- Bismarck & Minot Family Medicine Residencies
- Trains Family Physicians, and partners with over 100 specialists

Current Projects:

- Clinical Trials Network – Ohio Valley Node partnership with Great Plains Behavioral Health Directors. Define tribal research agenda and explore telemedicine-based medication assisted treatment for opiate use disorder.
- American Heart Association – partnership to define gaps in research for American Indian and Alaska Native cardiovascular and cerebrovascular health.
- PASC (Post-Acute Sequelae of Covid) Community Advisory Board – national study to explore treatment for long-haul COVID-19.
- Collaboration with CTR and COBRE studies – Dr. Nicole Redvers clinical trial with traditional American Indian medicine chokeberry.

“All Dakotans deserve access to meaningful healthcare that is provided in a relevant way. AICoRN continues to partner with providers and communities to define meaningful projects that translate the existing body of knowledge into practice to improve our overall health.”

-Dr. Allison Kelliher, Director of AICoRN

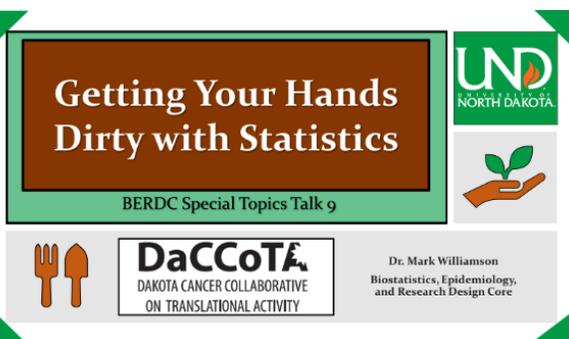
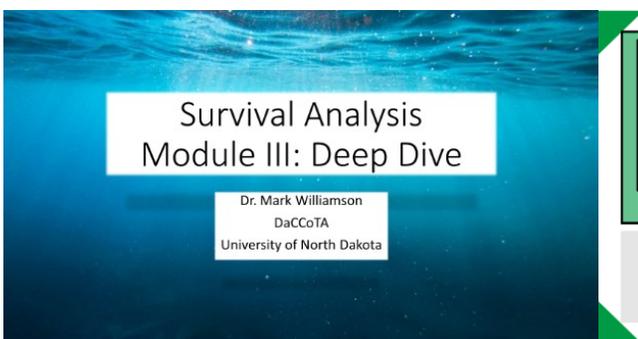
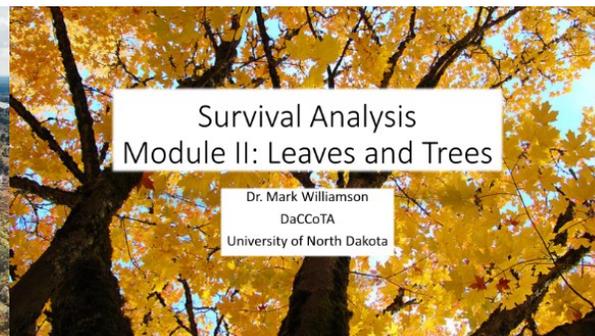
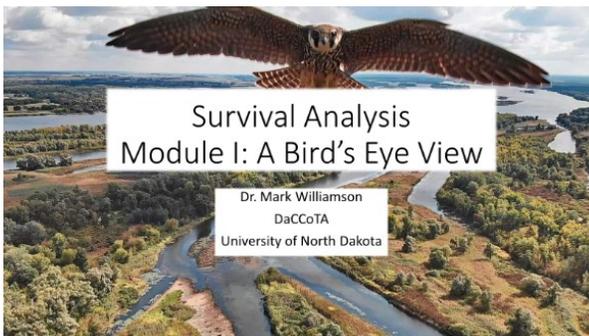
Upcoming Calls for Applications

The goal of the Dakota Cancer Collaborative on Translational Activity (DaCCoTA) is to stimulate growth of expertise and engagement in disease-related clinical and translational research (CTR) in the Dakota region. Several calls for applications from different funding mechanisms will be launching soon. Translating Epidemiology to Experiments (TREE) Pilot Grants will open in January 2022. Professional Development Awards will open in March 2022.

Recent Training Resources

Statistical Training Resources (<https://med.und.edu/daccota/berdc-resources.html>)

- Survival Analysis Module 1: A Bird's Eye View
- Survival Analysis Module 2: Leaves and Trees
- Survival Analysis Module 3: Deep Dive
- Getting Your Hands Dirty with Statistics (Special Topics Talk #9)



Recent Events

- Professional Development Core Virtual Info Session (Sept 15)
 - Tribal IRB Workshop (Oct 6)
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Upcoming Events

- February 2022
 - Virtual Informational Session, co-hosted by AICoRN and the Professional Development Core (PDC) focused on Clinical Research Opportunities Program (CROP) Applicants
 - March 2022
 - Virtual Informational Session, hosted by the PDC
 - Mock Peer Review, hosted by the PDC
 - Intellectual Property Session for DaCCoTA awardees, hosted by the PDC
 - April 2022
 - Core Training Event: Biostatistics Resource Overview
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Annual Symposium: Save the Date

2022 DaCCoTA Annual Symposium & AICoRN Summit

August 4-5, 2022

Sanford Center, Sioux Falls, SD

(Virtual Option Available)

- Educational Opportunities
- Poster Session
- DaCCoTA Awardee Presentations
- Networking Opportunities
- Additional information coming soon
- Please check the DaCCoTA Symposium Website for updates as additional information becomes available:
<https://med.und.edu/daccota/symposium.html>