

Facilities and Other Resources-University of North Dakota School of Medicine and Health Sciences

The **UND School of Medicine and Health Sciences** completed construction of a 325,000-square-foot, four-story, state-of-the-art building in August 2016. It is the only medical school in North Dakota and houses eight degree programs, including Athletic Training, Biomedical Sciences, Medicine, Medical Laboratory Sciences, Occupational Therapy, Physical Therapy, Physician Assistants and Public Health. Its entire west wing is devoted to biomedical research and includes open labs with office suites for researchers and students nearby.

The **Biomedical Sciences Department** was formed by combining the Departments of Pharmacology/Physiology/Therapeutics, Microbiology & Immunology, Anatomy & Cell Biology, and Biochemistry & Molecular Biology in 2013. This created a multi-discipline research environment and graduate/fellow training program, beneficial to all involved. The merging created an abundance of shared equipment resources available to faculty, students, fellows, and staff. Combined seminars, journal clubs, laboratory meetings, yearly retreats, and coursework produce an integrated research environment with a collective expertise far beyond what was present in any single department. This vibrant atmosphere stimulates an ongoing variety of collaborative, cross-discipline projects.

The Biomedical Sciences Department occupies four floors of the research wing of the new **UND School of Medicine & Health Sciences** as well as the Neuroscience Research Facility and the first floor of the Edwin James Research Facility in Columbia Hall. The Department's space in the newly completed School of Medicine houses open design, state-of-the-art laboratories, and offices spanning all 4 floors, occupying approximately 42,000 sq. ft., as well as 5,500 sq. ft. in the Edwin C. James Research Facility, and 14,000 sq. ft. in the adjacent Neuroscience Research Facility. The Biomedical Sciences Department also maintains or has access to the Flow Cytometry Core (see below), the Imaging Core (see below), Mass Spectrometry Core (see below), Histology Core (see below), Genomics Core (see below), and Behavioral Core (see below).

The **Edwin C. James Research Facility**, located in Columbia Hall, houses a portion of the Biomedical Sciences Department and is adjacent to the Center for Biomedical Research animal facility as well as the Neuroscience Research Facility. It provides all weather connections to the Center for Biomedical Research Facility and spacious, state-of-the-art laboratories and offices. The Facility contains 5 floors of research and office space occupying over 45,000 sq. ft. The building provides recently renovated space for those Departmental faculty whose interests include epigenetics. Its open lab design is conducive to increased collegial interaction.

The **Neuroscience Research Facility** was established at UND in 2004. The goal of the Facility is to help investigators develop expertise in multidisciplinary approaches toward the understanding of brain function. The Facility is research-oriented involving faculty from the Biomedical Sciences Department. The Facility building is located on the UND campus adjacent to the School of Medicine. This single story building is approximately 14,000 sq. ft. and provides ten laboratories and office space as well as a conference/seminar room, atrium, and dining area for UND researchers engaged in the study of neurological disease and treatment. It is a highly interactive environment with shared space, equipment, combined lab meetings/seminars and very collegial with abundant opportunities for collaborative projects.

Overall Research Environment

The research environment within the UNDSMHS is multi-discipline and vibrant due to targeted recruitment, integration of all basic science departments into Biomedical Sciences, and specific development of research foci described below.

The **Center for Neurodegenerative Disorder Research** was established at UND in 2002 through the NIH COBRE, an acronym for Centers of Biomedical Research Excellence, program to cultivate research expertise among junior faculty and strengthen the research infrastructure of states that do not receive as much NIH funding as some large states. Since its inception, the program has grown to become one of the defining research strengths of UND and includes a large cohort of multi-discipline faculty spanning the School of Medicine, the College of Arts and Sciences, and the College of Engineering and Mines. Although the original scope of the Center focused on pathophysiology and neurodegenerative disease, recruitment and targeted initiatives have expanded current interests to include numerous areas such as aging, development, neurogenesis, addiction, and

psychiatric disease.

The **Center of Biomedical Research Excellence (COBRE) in the Epigenomics of Development and Disease** was established at UND in 2013. The Epigenetics Working Group at UND unites multiple research teams across disciplines and departments using different conceptual frameworks and experimental approaches to study epigenetic mechanisms regulating development and aging. Using a wide range of experimental systems, research teams are aiming to uncover how exposure to developmental and environmental stress leads to the accumulation of genome-wide epigenetic changes and whether these changes can eventually cause or exacerbate development of aging-associated diseases such as cancer, neurodegenerative disorders, and cardiovascular diseases. As a group, these faculty are targeting molecular mechanisms of local and reversible genome-wide reprogramming, cellular heritability of epigenetic changes, fine-tuning of local gene activity that can be recruited for clinical applications.

The **Center of Biomedical Research Excellence (COBRE) in Host-Pathogen Interaction** was initiated at UND in 2016. The objective of the COBRE in Host-Pathogen interaction is to establish a highly interactive and dynamic group of junior investigators whose research focuses on the intersection between the host and microbial agents. These investigators with expertise in viral, bacterial and parasitic infections are working in a cohesive and collaborative manner to uncover immune mechanisms regulating the pathogenesis of these diverse infectious diseases, likely identifying novel treatment targets, and to identify microbial influences altering susceptibility and onset of disease. The cutting edge, critical research proposed in this grant will be accomplished by utilizing state-of-the-art infrastructure supported by core facilities equipped with modern instrumentation and technology (Flow Cytometry, Imaging, Histology). To enhance the program further, we have included a translational component as a key facet of this COBRE (Bioinformatics Core), which is consistent with our global, strategic mission to address the needs of North Dakota's aging, largely rural population that are prone to infectious diseases such as pulmonary infections, sepsis, neuroinflammation and vector-borne disease. This center nurtures a focused group of investigators working to establish a collaborative and sustainable Center of Excellence in Host-Pathogen Interactions capable of attracting the brightest and most talented faculty, students and fellows to conduct world-class research in the burgeoning field of infectious disease. UND is fully committed to ensuring the growth and sustainability of this group even after the COBRE grant ends, which will establish and maintain UND as an emerging infectious disease center in the US.

The goal of the **North Dakota IDEa Network of Biomedical Research Excellence (INBRE)** is to build biomedical research capacity by serving research universities, baccalaureate institutions, and tribal colleges within the state. Specifically, it aims to initiate competitive, sustainable research programs at four predominantly undergraduate institutions (PUIs), increase the number of students from PUIs who choose to pursue advanced training in the biomedical sciences, increase the number of students from tribal colleges who matriculate into baccalaureate degree programs in the sciences, enhance the state's access to computational and electronic resources supporting biomedical research, and enhance existing core facilities. The INBRE supports a statewide network of faculty, staff, and all levels of students working to understand the environmental impact of ND in the broader setting of environmental science.

The NIH CTR program funded, **Dakota Cancer Collaborative on Translational Activity (DaCCoTA)**, is designed to bring together researchers and clinicians with diverse experience from across the region to develop unique and innovative means of combating cancer in North and South Dakota. This consortium arrangement is between UND, NDSU and the University of South Dakota (USD) as academic partners. Clinical partners include Fargo VA Health Care System, Sioux Falls VA Health Care System, Altru Health System, Essentia Health, Trinity Health, Regional Health, and Catholic Health Initiative. The DaCCoTA program works to advance cancer treatment through broad approaches mounted by collective groups of clinical and basic researchers who are focused on conducting clinical/translational research.

Laboratory/Office:

The investigator has a dedicated laboratory with approximately 1000 sq feet of bench space along with a dedicated room for cell culture and a separate dedicated room for histology. The laboratory is located in the Biomedical Science Research West Wing of the School of Medicine. The laboratory is modern and well equipped with benches, sinks, cabinets, air and natural gas. The lighting and ventilation are excellent. The laboratory and office spaces are equipped with multiple internet connections and telephones as well as wireless service

throughout the building. The P.I. has a private 100 sq. ft. office located separate from the laboratory space with two networked Dell computers. Offices of PIs, fellows, and students are contained within an office suite adjacent to the laboratory space. Department shared photocopier/printers, administrative staff, office supplies/resources are all located within the office suite and available to all. SMHS IT and library support are located on the 2nd floor of the SMHS. Students, fellows, and staff also have individual desk spaces and computer/internet access within the office suite.

Animal:

The **Center for Biomedical Research** Facility at UND is a state-of-the-art research AALAC approved animal facility. This 20,000 sq. ft. facility is equipped with a quarantine room, surgical suite (with separate prep, scrub and surgery rooms), diagnostic laboratory, the North Dakota Behavioral Research Core Facility (see below), barrier rooms, semi-barrier rooms, infectious disease rooms, isotope rooms, behavioral testing rooms, autopsy room, receiving area, two cage cleaning areas and numerous other conventional animal rooms. Each room has an anteroom to prevent cross-contamination. The facility also is equipped with self-watering cages, a water purification system, a water acidification system and water flushing system, as well as a bedding and changing area within a hood in each room. Excellent part-time and 24hr on-call veterinary supervision and care is assured.

Center for Biomedical Research 2:

The Satellite vivarium at the University of North Dakota is designed to act as a complement to the main vivarium on campus. A garage space adjacent to the Satellite vivarium is available for animal transfer between the facilities. All food and water provided to the animals comes from the main vivarium to ensure continuity of care to the animals. All main doors into the Satellite Vivarium are secure card access only. It consists of two general holding rooms for mice, one general holding room for rats, two procedure rooms, a behavioral suite and an infection suite. Support spaces in the Satellite Vivarium include an office area for records, a rest room, an autoclave, a utility room, and several storage rooms for food, clean supplies, vivarium waste, and dirty cages waiting for pick up. Every sink in the satellite vivarium has an eye wash. There is an eye wash safety shower and fire extinguisher in the common corridor for emergency use.

Computer:

Insert your lab specific computer information here. All computers are connected to the State University Systems mainframe allowing nucleic acid and protein sequence analysis through EMBL, Genbank and Protein Data Banks, E-mail, library search, and electronic journal accession. Computers for some major equipment are networked via the server at the UND School of Medicine & Health Sciences. Data is backed up nightly from all laboratory computers through an in-lab RAID drive as well as through the School of Medicine server.

Other:

Imaging Core

The Imaging Core is a 3350 sq. ft. facility housed in the UND School of Medicine and Health Sciences that provides investigators on the UND campus and within the surrounding region with access to both light and electron microscopy. Instrumentation available for light microscopy includes a Leica Stellaris 5 confocal microscope, an Olympus FV1000MPE basic multiphoton/single photon system on an upright microscope, an Olympus cellTIRF system on an IX83 fluorescence microscope and a Leica DMI8 Thunder Imager system for 3D imaging of fluorescently labeled cellular material. A Dell workstation equipped with imaging analysis tools is also available. The Leica Stellaris 5 system is a 4 laser, multichannel system equipped for superresolution and capable of imaging a wide variety of fluorochromes in fixed and live tissues and cells. The Olympus FV1000MPE system is configured for confocal and multiphoton microscopy of fixed samples, live cells and intravital microscopy using animal models. The Olympus cellTIRF microscope is a four laser system configured for multicolored TIRF microscopy, ratiometric imaging of Fura2 and FRET biosensors, SRRF superresolution microscopy, and long term live cell imaging. Instrumentation in the electron microscopy suite includes a Hitachi 7500 TEM equipped with a high resolution SIA digital camera and a Hitachi 4700 field emission SEM. Additional instrumentation for sample preparation includes an ultramicrotome, a Denton sputter coater and a vacuum evaporator for SEM sample preparation. Applications supported by the imaging Core include multi-label fluorescence imaging of fixed and live material, FRET, FRAP, FLIP, 3D imaging, channel separation using spectral fingerprinting, ratiometric fluorescent imaging, TIRF microscopy, thin section transmission electron microscopy, and scanning electron microscopy. The Core director, Dr. Bryon Grove, and two Core staff maintain the facility, provide microscopy services, training on the equipment, and assistance with sample preparation and

image analysis. (<https://med.und.edu/imaging/index.html>).

ND INBRE Microscopy Core Facility

The mission of the ND INBRE Microscopy Core is to enhance research productivity, research funding, and STEM efforts for the partners of ND INBRE by providing instrumentation, expertise, and training in microscopy. The core is equipped for the microscopic examination of cells and tissues and includes the following instrumentation: a Leica LMD6 Laser Microdissection Microscope System, a Leica Personal Confocal TCS SPE Microscope, an Olympus BX63 Upright Fluorescence Microscope, an Olympus FV3000 Laser Scanning Confocal Microscope with Live Cell Imaging capabilities. The facility is under the direction of Dr. Van Doze (van.doze@und.edu) with assistance from Dr. Swojani Shrestha (swojani.shrestha@und.edu).

North Dakota Flow Cytometry and Cell Sorting (ND-FCCS) Core

The North Dakota Flow Cytometry and Cell Sorting (ND-FCCS) core, located in the UND SMHS in the Janice I. Schuh Suite and is joint effort between the departments of Biomedical Sciences and Pathology, and the Host Pathogen COBRE (P20GM113123) and the North Dakota INBRE (P20GM103442) and the SMHS. The core staff, consisting of Dr. David Bradley (Director) who has 30+ years of flow cytometry experience, Dr. Suba Nookala (Assistant Director) who has 20 years of flow cytometry experience, and Steven Atkins (Core Technical Advisor) with 15 years of flow cytometry experience, provides training on the instrumentation and software as well as consultation for experimental design and data analysis. The ND-FCCS core contains 3 major instruments: a) BD FACS Aria II flow cytometer which has 3 lasers (UV (355 nm), Blue (488 nm), and Red (640 nm)) with simultaneous analysis of 9 colors in addition to FSC and SSC, first pass 4-way sorting, aseptic sorting, automated cell deposition, temperature control, and aerosol management capabilities; b) BD FACSymphony A3 equipped with 4 lasers [Blue (488nm), Violet (405 nm), and Yellow Green (561 nm), and Red (638 nm)], and filter sets to increase multicolor panel possibilities and enable the simultaneous measurement of more than 27 different markers on a single cell for phenotyping, apoptosis, proliferation or cell-cycle analysis, with capability to run a reliable high throughput acquisition platform; and c) Sony MA900 Cell Sorter that is equipped with 4 excitation lasers [Blue (488nm), Violet (405 nm), and Yellow Green (561 nm), and Red (638 nm) that is split into two laser beams]), a temperature controlled 4-way sorting with adjustable speeds into multiple tube types including multi-well and 96 well plate deposition system, with capabilities for automation, microfluidics chip-based design, and a user-friendly software for easy compensation of up to 12 fluorescence parameters. The ND-FCCS core also maintains the current release of BD FACS Diva and twelve licensed copies of FlowJo analytical software, all of which are available to all users for analysis. The ND-FCCS core is open to all users within the state of North Dakota, with the core providing both full service and self-service flowcytometric data and/or cell collection on for fee basis, as well as training, initial support and oversight of panel design, data analysis, and multiparameter aseptic for downstream applications.

Genomics Core

The University of North Dakota Genomics Core has provided laboratory services and bioinformatics analysis since 2014. Its creation aimed to offer technical laboratory support to investigators in the form of nucleic acid extraction, quality control testing, library preparation, and next-generation sequencing services for various types of samples, from tissues to isolated RNA/DNA. The Genomics Core specializes in library preparation for a wide range of applications, such as RNA-Seq, single-cell 10x, whole-genome sequencing, and microbiome analysis. Additionally, the Core employs sequencing platforms from Illumina for short reads, Nanopore for long reads, and NanoString for spatial transcriptomics. The Core also offers bioinformatics analysis services for RNA-seq, CHIP-seq, ATAC-seq, PRO-seq, CoPRO, Nanopore and single-cell data. Notably, the Core has developed a novice-oriented platform called *genomEX*, which, among many things, offers a cloud service where one-click pipelines for standard analysis can be run in fully personalized and dedicated high-performance computing environments. Lastly, the Core provides educational sessions to help investigators effectively utilize its various resources. The full list of Core and user-accessible equipment is available at the Core and *genomEX* websites.

Computational Resources in the Genomics Core. The Genomics Core has two high performance workstations buddy and Bart for data analysis. Each of these servers are equipped with Intel Xeon E5-2687W v2 processors (8 HT Cores, 3.4GHz), 256 GB 1866MHz DDR3 RAM, a NVIDIA Tesla K20c GPU, and 24 TB of storage space. Data is backed up in raid5 configuration. Additional data backed up in tapes at University of Oklahoma. Data is stored on a 50 TB shared network drive administered jointly by the core and UND IT. Data

collected by the core and UND investigators is stored redundantly on a Dell SC4020 (with 50 TB usable space with weekly backups, located at the UND–CEC) and on a set of Dell PowerEdge FC630 server blades located inside multiple Dell FX2 chassis. Each FC630 server node contains two 10 core Intel Xeon processors and 256GB of RAM. Each server node has dual 10GB nics which connect to the Dell SC4020 for extremely fast and reliable access to the storage.

Mass Spectrometry Core

The Mass Spectrometry Core facility is a state-of-the art 1,500 sq. ft. facility and very well equipped to perform mass spectral analysis of small molecules and proteins, including accurate mass high resolution analysis and targeted quantification. The high-resolution analyzers include Q-TOF G2S (Waters) with UPLC inlet, and QExactive orbitrap (Thermo Scientific) with nano-UPLC inlet. A high sensitivity targeted analysis is performed on Xevo triple quad UPLC-MS system (Waters), API 3000 triple quad HPLC-MS system, and a Thermo Scientific TSQ 9000 triple quadrupole GC-MS/MS system. The ion sources include ESI, nano-ESI, APPI, APCI, and solid probe ion sources, EI, ECI. Waters UPLC and nano-UPLC, and Agilent and Backman HPLC systems connected to MS analyzers consist of binary pumps, autosamplers, column heaters, and DDA detectors. Processing workstations include MarketLynx, MetaboLynx, Progenesis for small molecules and proteins, Lipid Search, and PLGS processing software. In addition, the MS Core is equipped with Beckman 2-D HPLC system to allow for protein fractionation. The core director, Dr. Mikhail Golovko, and full-time staff are available for help with project design, sample preparation, data analysis and interpretation, as well as data presentation.

Histology Core

Established in 2016 within the School of Medical and Health Sciences, the Histology Core provides routine histology, including tissue processing, embedding, sectioning, and slide digitization services to support clinical and basic science research at the University of North Dakota. The objective of the Core is to collaborate with, train, advise, and provide technical support for individuals in need of histology services for research, teaching, or clinical interests. The Core is designed for 24/7 access to instrumentation critical to high-quality preparation of tissue samples, and to assist with experimental design, specifically with application-specific sample preparation techniques, to identify appropriate analytical tools available, resolution restrictions, and quantitative morphological data analysis. The Core boasts an impressive array of conventional and state-of-the-art equipment: automatic tissue processor, Barnstead Smart2Pure Water Purification System, microtome, cryostats, antigen retrieval processor, Leica Autostainer XL, Leica automated cover-slipper, 48 Dako Autostainer IHC & PT Link, and high-resolution NanoZoomer Digital Pathology scanner. Under the directorship of Dr. Colin Combs, the Core is managed by Donna Laturnus, a full-time histology technician. The Core is supported by funding from the NIH/NIGMS and the UND SMHS.

Computational Data Analysis Core

The Computational Data Analysis Core (CDAC) at the University of North Dakota is newly established in 2021 with support from the Host-Pathogen Interactions COBRE Phase II grant to support bioinformatics and statistical data analysis, focusing on the advanced analysis of various high-throughput sequencing data, including but not limited to RNA-Seq, ChIP-Seq, metabolomics, lipidomics, and metagenomics. Collaborating with the Genomics Core, CDAC provides services, training, and genomics resources to the scientific research community at UND, NDSU, USDA, and nearby colleges. The Core director, Dr. Junguk Hur (junguk.hur@med.und.edu), and full-time staff are available to help design, analyze, and visualize sequencing data based on the needs of individual investigators and research projects. The CDAC currently maintains one Dell PowerEdge FC830 blade server for computational analysis. This server has a 10Gb network capacity with 4x Intel Xeon E5-4669 v4 2.2GHz (174 HT Cores), 1 TB RAM, and 16 TB of SSD storage space. This server is connected to the SMHS storage server providing over 80 TB of additional storage space.

Behavioral Research Core Facility (BRCF)

This facility was established in 2015 to facilitate and strengthen behavioral research in North Dakota. The BRCF is designed to promote research productivity and improve STEM training in behavioral science by providing 1) well-managed and maintained equipment; 2) methodological and technical support; 3) training in behavioral testing and analysis; and 4) interface for interaction of researchers to facilitate collaborations. The 5-room facility houses a sensory-motor skills assessment room, a cognitive function assessment room, and a neurostimulation

laboratory, a procedure room, and a temporary housing room. The sensory-motor and cognitive function assessment rooms are equipped with a variety of specialized equipment for assessment and monitoring of animal behavior, complete with laptops installed with ANYmaze software (ANY-maze, Stoelting). These devices include open-field activity monitoring enclosures, grip-strength gauges, startle-response instruments, freeze monitor chambers, passive- and active-avoidance systems, place-preference chambers, rotarods (balance and coordination), rotometer (rotational behavior), and a variety of mazes to test memory, cognition, and anxiety- and depression-like behavior (San Diego Instruments, Stoelting). The neurostimulation laboratory is equipped with a Pinnacle optogenetics and sleep-deprivation systems for the analysis of animal behavior resulting from precisely controlled activation of targeted neuronal populations with light or sleep deprivation. These systems are used for *in vivo* monitoring of electrophysiological activities as well as neurochemical fluctuations. The facility is conveniently located within the CBR and dedicated for behavioral assessments, tissue collection and housing for mice.

The BRCF was recently expanded to increase its capacity for the assessment of rat behavior. Dedicated rooms and equipment are now available, including open-field arenas, light-dark boxes, elevated-zero maze, radial-arm maze, Y-maze, and Morris water maze. These rooms are readily available to authorized BRCF users. In addition to the infrastructure, the BRCF provides training and networking opportunities for IDeA state investigators to interact and collaborate with other researchers. The BRCF is supported by the North Dakota INBRE (P.I., Dr. Donald Sens) and collaboratively operated and managed by the CBR staff, the Attending Veterinarian, the BRCF Director, and Department of Pathology.

DaCCoTA Biostatistics, Epidemiology, and Research Design Core

The mission of the Biostatistics, Epidemiology, and Research Design Core (BERDC) is to effectively leverage existing expertise and resources across regional academic and healthcare institutions in North and South Dakota to create a nationally recognized center of excellence, supporting cancer research through innovation, interdisciplinary collaboration, and public and private partnerships. Strong biostatistics leadership and participation in all aspects of biomedical research are considered essential to the mission of the DaCCoTA.