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RESOURCES

Northwestern currently supports approximately 60 core facilities on its Evanston and Chicago campuses. Core facilities provide research equipment, products, services and technical support for faculty, students, post-docs, and staff. These facilities enable sharing of University resources that individual researchers would not otherwise be able to afford.

Directors Teng-Leong Chew and Phil Hockberger work with Office for Research

All articles in this publication were written by Roger Anderson and adapted from the Office for Research Newsletter.
In the past few years, interest in proteomics – the large-scale studies of proteins – has exploded in the field of biological research. Recently, a leader in the field of proteomics, Neil Kelleher, joined Northwestern in the departments of molecular biosciences, chemistry and medicine. Kelleher serves as director of the new Proteomics Center of Excellence (PCE). Now the newest development is the Proteomics Core Facility, directed by Dhaval Nanavati, for which Kelleher will serve as the faculty advisor.

Housed in Silverman Hall and set to open in May, the new facility will have a close relationship with Kelleher’s research group and the PCE, which will share staff and resources with the core.

“We are independent units but have a fluid cross-relationship,” says Nanavati. “Some research groups might work with both of us, while projects involving deeper collaboration might be better suited for the Center, and we’ll pass those along. The relationship will solidify over time. The short-term focus of the core facility is to provide robust protein identifications.”

In the era of systems biology, the study of subjects that end in -omics, such as transcriptomics, proteomics, and metabolomics, has become a major discovery engine to understand different cellular states in biology and translational biomedical research.

The adoption of proteomics by biologists is uneven due to technological challenges and lack of high-end facilities capable of delivering quality data and their interpretations. The arrival of Kelleher’s research group paired with the establishment of the Proteomics Center and Core will begin to fill this strategic gap at Northwestern.

The core will have an LTQ orbitrap velos, a state-of-the-art mass spectrometer for protein identification. Installment and initial testing of equipment will be completed in January and February this year. With a combination of high-resolving power, mass accuracy, and superior scanning speed, the orbitrap allows larger numbers of protein identification with high confidence. The high-scanning speed makes it possible to identify proteins present at low molecular concentration, enabling researchers to dig deeper into the proteome. Often, identification of proteins present at low concentration is important for hypothesis creation and confirmation.

“The importance is not only the quantity of data but the quality,” Nanavati says. “We want to give high confidence data to our users.”

To give high confidence data, there will be an emphasis on “precision proteomics,” as described by Mattias Mann and Kelleher in an article published in the Proceedings of the National Academy of Science (PNAS, September 25, 2008).

In addition to directing the Core, Nanavati will provide no-cost consultations on proteomics research. He has already consulted with several research groups across both campuses. Before the establishment of the Core and Center, many researchers had to send their protein samples to institutions outside of Northwestern, which could be inconvenient and expensive.

“Many biologists work with proteins or desire to,” Nanavati says. “If DNA is the blueprint, then protein molecules are the functional and structural components of a cell. We are now on a path not only to catch up to peer institutions but, with a dynamic reserve of talent on campus, we will enjoy next-generation proteomics on the campus in the years to come.”

Nanavati says he looks forward to working on diverse projects with Northwestern researchers in Evanston and Chicago and to becoming a more competitive institution in the field. “The evolution of the Core will be user defined,” he says. “We’re starting with a small seed and will see how it grows.”

For more information about Northwestern’s new Proteomics Core Facility, please visit http://www.clp.northwestern.edu/research-facilities/proteomics-core.
Quantitative Bioelemental Imaging Center (QBIC)

Mapping the Inorganic Signatures of Life

As the old saying goes, sometimes the cure is worse than the disease. This statement rings particularly true when it comes to cancer. Chemotherapy often causes patients to experience fatigue, nausea, and cognitive impairment, among various other adverse side effects. What if researchers could create a method that delivers the chemicals straight to the tumor cells? Hitting specific targets would leave other tissues undamaged with less toxicity being released into the body.

Research being explored at the Quantitative Bioelemental Imaging Center (QBIC) at Northwestern has potential to do just that. The mission of QBIC is to map the “inorganic signatures of life,” transition metal atoms that are found in all living cells and conserved during evolutionary processes. Because platinum, gold, and other metals are used at the interfaces of nanotechnology and chemotherapy, instruments at the facility can be used to examine how the treatment works.

“Using a laser ablation microscope interfaced with inductively coupled plasma mass spectrometry, we can spatially resolve elemental concentration of solid samples,” says Rebecca Marvin, manager of the facility. “So we can take a tissue sample that has a tumor within it and treat the entire tissue with metallo-chemotherapy. Then we can see how the chemo is absorbed into the tumor as opposed to the rest of the tissue.”

This is one facet of the work being done by Thomas O’Halloran, chemistry, molecular biosciences, and director of QBIC. His work involves filling artificial fat droplets, known as liposomes, with chemotherapy drugs. The environment is different in tumors than regular tissues, so the liposome could be programmed to open and release drugs when sensing a certain environment. This would target the tumor while leaving the surrounding tissues untouched.

While Marvin says that most of the work done in QBIC has its greatest potential in the medical world, the facility serves 14 different departments from Feinberg, Weinberg, and McCormick. This includes 30 principal investigators from materials science, biology, chemistry, nanotechnology, and more. The staff trains users, helps design experiments, and prepares samples. It also offers full-service lab work for researchers from outside institutions who ship samples to the facility. In addition to identifying and quantifying elements, QBIC has equipment for two-dimensional elemental mapping. “We like to think of ourselves as a bridge between imaging and elemental quantification,” says Marvin who studies the abundance of zinc in malaria cells.
The facility has assembled a unique scanning transmission electron microscope (STEM) for extremely high-resolution elemental mapping. The microscope was funded by the W.M. Keck Foundation and the Chicago Biomedical Consortium in collaboration with Teresa Woodruff, obstetrics and gynecology, and Vinayak Dravid, materials science.

QBIC and NUANCE (Northwestern University Atomic and Nanoscale Characterization and Experimental Center) jointly run the instrument, which is the only commercial cryo-electron microscope in the nation that is equipped with dual energy dispersive x-ray spectroscopy (EDS) detectors. “Metals like zinc have very weak signals,” Marvin explains. “Our STEM has two EDS detectors, and this custom-designed Hitachi HD-2300 gives more than fourfold greater sensitivity. With this, we can detect elements like zinc when we couldn’t before.”

Currently, QBIC’s equipment is spread between the Pancoe Building, Silverman Hall, and Cook Hall, but Marvin says the goal is eventually to centralize the instruments to one location to make it easier for users.

For more information, visit www.qbic.northwestern.edu. QBIC is a part of the Chemistry of Life Processes Institute, for which O’Halloran serves as director. Center for Advanced Magnetic Resonance Imaging (CAMRI).

Outcomes Measurement and Survey Core (OMSC)

Improving Outcomes

The waiting time in a doctor’s office ends when the physician enters and opens with the usual line, “Tell me how you’re doing today?” Often, the patient might respond with something generic like “fine,” “all right,” or “could be better.”

While this patient-physician communication is valuable, it’s not a complete measure of the patient’s health status. Because of this, physicians tend to over-estimate and more optimistically report the current status of a patient’s physical and emotional condition. Self-reported outcomes for quality of life and treatment satisfaction offer a more reliable insight into monitoring patients.

Northwestern’s Outcomes Measurement and Survey Core (OMSC) Facility supports any research that involves self-reported data. Situated within the Department of Medical Social Sciences, the core is a shared resource of the Robert H. Lurie Comprehensive Cancer Center and also works with various research groups internationally. OSMC staff help researchers select the most appropriate questionnaires or surveys for a wide range of studies and provide assistance to develop and validate new ones.

“Patient-reported outcomes provide comprehensive information about a patient’s physical, mental, and social well-being,” says Elizabeth Hahn, director of the facility. “They can be used to monitor responses to treatment or disease progression. People can answer questionnaires over time to report how things are developing. And the responses can help in medical decision making, as patients and clinicians work together to determine the next step to take.”

Members of the OSMC also have expertise in diverse populations. They help facilitate the translation of questionnaires and surveys into various languages and ensure that the concepts are appropriate for different cultures. Hahn has a specific interest in giving voices to patients with limited literacy skills.

“If a person cannot read, then an interviewer typically reads the questions out loud,” Hahn says. “That could be a potential source of bias, especially if the questions are about something that’s sensitive. The interviewer might not get the same answer as if the person were answering the questions by themselves.”

To allow those with low literacy skills to self-administer surveys and questionnaires, Hahn developed the Talking Touchscreen. It provides one question at a time on a computer screen, and each component of text is accompanied by a sound file. The questionnaires let doctors know how patients are doing in day-to-day life.

“People might have a really good response to treatment based on physical measurements,” Hahn says. “Yet they might not be able to do their jobs or take care of their families or function well enough to do the things they want to do. The only way to measure that is to ask the person to tell you themselves.”
Hahn says the OSMC facility is working with researchers to figure out the best ways to incorporate patient-reported outcomes into clinical encounters. She hopes that having patients sit down at a kiosk and take a survey will become as routine as being weighed or having blood pressure taken at each visit.

“There are so many things that can affect a patient achieving the best outcome,” she says. “Culture and background, access to health care, and literacy skills can all act as barriers. We’re interested in overcoming those barriers.”

For more information about the Outcomes Measurement and Surveys Core Facility, visit http://www.cancer.northwestern.edu/research/shared_resources/outcomes_measurement/index.cfm.

Central Laboratory for Materials Mechanical Properties (CLaMMP)

Taking a Break at the CLaMMP Facility

Just two-and-a-half weeks ago, Southwest Airlines flight 812 lifted off from Phoenix with the planned destination of San Francisco. When the plane reached 34,400 feet, a five-foot long tear ripped open the fuselage above the cabin. The Boeing 737-300 made an emergency landing in Yuma. The incident was a result of metal fatigue, one of the properties that is studied in Northwestern’s Central Laboratory for Materials Mechanical Properties (CLaMMP).

“When an airplane’s cabin is pressurized, it stretches the aluminum skin,” says Mark Seniw, manager of the facility. “When it lands, it depressurizes and the skin goes back to its original shape. So it gets stretched and relaxed. This is called the ‘fatigue cycle,’ and we can test that here.”

In addition to fatigue testing, the facility contains mechanical testing machines for tension, compression, impact, repeated stress, and bending for a variety of materials including metals, polymers, ceramics, composites, and even biological materials. Undergraduates studying engineering design at the Segal Design Institute also visit CLaMMP, bringing materials to test for their projects.

“We like to break stuff here,” Seniw says with a laugh. “Then we can see how strong or weak it is.”

In the example of the airplane, sometimes lives depend on the strength of the material. But other times it’s more mundane. Every manufactured material is tested for its properties at some point during its life cycle. Even samples of paper are tested to see if they can withstand the conditions of the printing press.

One material being tested at CLaMMP is a metallic foam created in the laboratory of David Dunand, who directs the facility with Katherine Faber, both from materials science and engineering. Various forms of the foam underwent the compression test to see how well they would absorb impact.

“After the U.S.S. Cole was bombed in Yemen in 2000, there was a push to develop energy-absorbing materials,” Seniw says. “The hull of the ship was thick, but it could not withstand the blast. You can make a strong material, but it can still be brittle and crack.”
Seniw has managed the facility since 1984. And while the equipment hasn’t changed too much over the years, the researched materials have changed a great deal. Only recently did he start seeing biological materials come through the facility’s door. Members from the laboratory of Guillermo Ameer, biomedical materials, have brought in biomaterials with medical applications for bending strength and tension tests.

Ameer’s PhD student Eunji Chung is developing a biodegradable scaffold, which will be used for tendon tears. The scaffold will be placed over the tendon to create a platform for new cells to grow. After the cells repopulate, the scaffold is designed to be absorbed by the body.

“They grafted the scaffold onto rabbit bones,” Seniw explains. “We pulled the joint apart to test the strength of the scaffold material. The results turned out well.”

Other than testing materials, researchers use the instruments at CLaMMP to create new testing techniques. Graduate student Aurora Zinck, who is advised by Morris E. Fine, materials science and engineering, and Sridhar Krishnaswamy, mechanical engineering, is working on a mechanized technique to predict when metals will fail.

“The current testing can only predict failure very close to when it will actually happen,” she says. “The technique I’m working on should predict much sooner when something will fail.”

The technique works by using acoustics. A soundwave is sent into a metal material at varying frequencies. If it is solid, the wave continues through the material. If the material has a crack, the wave is reflected back. The acoustics can detect small cracks before they reach their failure points.

Being able to predict the failure of materials is especially important in the airline industry and could potentially be used to prevent another Southwest Airlines flight 812 mishap from occurring again.

For more information about CLaMMP, visit http://www.matsci.northwestern.edu/clammp/index.html.

### Mouse Histology and Phenotyping Laboratory (MHPL)

#### The Science of Precision

The length of a fully developed mouse embryo from crown to tail is less than 4 millimeters. If a researcher wants to study a specific part of the embryo, such as the brain or kidney, then those areas need to be sectioned with extreme skill and precision in order to isolate the area of interest and avoid damage to the specimen. And if the embryo sits out in the open for just a few minutes too long, then it may start to dry or degenerate, which will permanently change the cellular detail.

The study of the microscopic anatomy of cells and tissues, or histology, requires a high level of ability and expertise to perform. It’s something for which investigators may not have the time or skill. In 2008, members of the Robert H. Lurie Comprehensive Cancer Center founded the Mouse Histology and Phenotyping Laboratory (MHPL), which is now a shared core facility also supported by the Feinberg School of Medicine. The laboratory provides comprehensive histology services for mice and rats, including frozen and paraffin sectioning and histopathological analysis.

“Whether it’s a study that looks at cancer or the function of genes, at some point or another, you have to look at tissues and try to understand how the biology might be altered in those tissues,” says Warren Tourtellotte, MD, PhD, pathologist, co-director of the Medical Scientist Training Program, and director of MHPL. “That is just part of the analysis to find out
if the structure of cells or tissues may be altered in an organism such as a mouse."

Histology is an essential tool in medicine and can be used for the diagnosis of cancer, to better understand disease and gene functions, or to test the development of drugs.

“If you are screening a new drug as a potential new therapy for a disease, then you have to look at the tissues and ask questions like ‘Does this drug cause toxicity?’” Tourtellotte says. “If it does, then it’s probably not the best drug.”

The facility serves more than 100 Northwestern laboratories from 50 different departments as well as a few other institutions such as Children’s Memorial Hospital and Loyola and Rush Universities.

“Partly why we exist is to help investigators handle their tissue samples before they even bring them to us,” says Donna Emge, histology technician and manager of the lab. “The tissue has to be handled in such a specific way. The way it is initially handled in the investigator’s own lab will have a large impact in determining the histology results.”

One of the more sensitive aspects of the process is fixing the tissue. Chemical fixatives are used to preserve the tissue from decomposition and maintain the initial structure. The most common fixative is formalin, a mixture of formaldehyde and buffer solution, but there are various others from which to choose. The type of fixative used, time the fixative was applied, and how long the tissue was left in the fixative are delicate and important steps in the process.

From there, histologists process, paraffin embed, and then section the sample into thin slices that can be placed on slides for examination by a microscope. Stains are used to give contrast among the elements within the tissue and highlight features of interest.

“We have one group that wants to study a specific part of the brain, like the cerebellum or hippocampus,” Emge explains. “We can find that area, map it, and cut to get only that specific area. It gets quite nerve-wracking for some of the technicians. Then everything is checked before it leaves the lab for quality control.”

As pathologists, Tourtellotte and the lab’s associate director Lin Li can interpret data and analyze models. They are trained to understand what changes in tissues look like and what they might mean. Then they communicate the information to the investigator.

The Mouse Histology and Phenotyping Lab partners with Northwestern’s Pathology Core. Both facilities are housed in Olson Pavilion on the Chicago campus. Before MPHL was founded, investigators sent their samples to the Pathology Core, which now focuses mainly on human pathology.

For immunohistochemistry (IHC) services, MPHL staff members still send samples to the Pathology Core but plan to implement their own IHC equipment in the summer. IHC is the process of finding antigens, such as proteins, in a section of biological tissue. It can be used to assess how tumors will respond to various therapies or find the presence of enzymes and hormones.

The laboratory also provides training opportunities for learning histology techniques and phenotyping analysis. The first workshop will be offered on June 2. Sponsored by Leica Microsystems, the seminar will include tissue freezing and handling as well as brain and bone sectioning.

For more information about MHPL, visit http://www.feinberg.northwestern.edu/research/cores/units/mouse-histology.html.
Behavioral Phenotyping Core (BPC)

The First Step to Translation

Bench-to-bedside. Those are currently the most common buzzwords used to describe the process of translational research. But the progression from basic science to the treatment of patients is not nearly as direct as it may sound. Instead, it is full of complicated and crucial steps.

One of the most important stages of the translational process is to test newly developed therapeutics on animal models. This valuable and potentially life-saving step is work that’s done every day in Northwestern’s Behavioral Phenotyping Core (BPC) facility.

“The BPC can put the translation into many cellular, molecular, and genetic research projects,” says Craig Weiss, physiology and director of the facility. “In some sense, translation starts with BPC.”

BPC moved from the Lurie Building to the 15th floor of Ward in April. The four-year-old facility has equipment and staff to conduct behavioral screens on small rodent models. The BPC staff can test changes in cognition, motor behavior, anxiety, and sensory behavior. This research could lead to new therapies to treat Alzheimer’s disease, depression, memory loss, and learning disabilities, among other illnesses.

Weiss and John Disterhoft, physiology and executive director of the core, led the effort to establish the BPC after noticing a growing demand from faculty members from both campuses. John Linardakis, senior research technician and educator, was brought on board to train users to property collect data from the core’s computerized systems.

“We’re fairly well-known as experts in behavioral testing at Feinberg,” Weiss says. “So we kept getting asked to test animals for other researchers.”

Part of the core’s mission is to train users to conduct the tests by themselves. Training is often focused on graduate students and postdocs so they can understand the significance of certain behaviors, what those behaviors mean, and how to interpret the data. In four years, the facility has grown rapidly from serving just two labs to nearly 20.

Joseph Moskal, biomedical engineering, is one of the more frequent users of the facility. Jeff Burgdorf, biomedical engineering, visits the Chicago campus from Moskal’s laboratory in Evanston to run tests for novel molecular therapeutics that could improve cognition and depression. This work requires the swim test, which is one of the many behavioral assays that the BPC is equipped to conduct. Moskal’s study shows that rats tread water longer after they are given an anti-depressant developed in his lab. Rats without the anti-depressant tend to give up faster. This change in behavior indicates that the drug is successful.

Weiss’s personal research program is NIH-funded and uses rabbit eye blink conditioning as a model to test prefrontal cortex mechanisms of learning and memory.

A neutral stimulus, like a tone or vibration of the whiskers, is followed by a slight puff of air to the eye. Initially, the animal will blink during the air puff, but eventually it blinks after the tone and before the puff. The conditioned reaction involves the cerebellum and brain stem. By simply increasing the time...
between the two stimuli, the reaction also depends on the forebrain, particularly the hippocampus and prefrontal cortex, which are affected by aging and Alzheimer’s.

“With this test, we can compare forebrain-dependent learning to cerebellum-dependent learning,” Weiss says. “We can see what parts of the brain are active throughout the learning process.”

While approval from the University’s Animal Care and Use Committee (ACUC) is required for all tests carried out on animal subjects, the BPC provides several prepared protocols that have already received ACUC approval and that can be added easily into a principal investigator’s existing animal study protocol. Instructions can be found here.

For a list of all services, information required for NIH applications, and equipment available at BPC, visit www.bpc.northwestern.edu.

ChemCore

Northwestern’s “Chemical Gunslingers”

Karl Scheidt, chemistry, enjoys asking “What if?” questions.

“What if you could take tumor cells and keep them from migrating?” he asks. “What if we could make a molecule that would keep tumor cells from undergoing metastasis?”

The list of questions that Scheidt asks himself on a daily basis is endless. Finding an answer to one that could impact society and medicine is his ultimate reward. But the pathway from a biological question to its answer sometimes hits a dead end after the development of an idea and the screening of a compound library or enzyme assay.

“Researchers have access to very advanced biological screening technologies,” Scheidt says. “But where do you go from there? The next stop is at ChemCore.”

Scheidt founded ChemCore just two years ago as a part of the Center for Molecular Innovation and Drug Discovery (CMIDD), which he co-directs with Raymond Bergan, medicine: hematology-oncology.

ChemCore is located in Silverman Hall on the Evanston campus and is a key component of the Chemistry of Life Processes Institute’s suite of cutting-edge facilities. Supported in part by a Lever Award from the Chicago Biomedical Consortium, this one-of-a-kind resource provides synthetic and medicinal chemistry, compound purification, and molecular modeling services to researchers inside and outside of Northwestern.

Three of the four research scientists on staff at ChemCore — Chris Holmquist, Rama Mishra, and Gary Schlitz — are veterans of the pharmaceutical industry. Scheidt affectionately refers to them as “chemical gunslingers” due to their adventurous ability to plow into any and every “What if?” question presented to them.

“These guys don’t just make molecules, they guide the small molecule discovery process,” says Scheidt who directs the core. “They look at compounds and design new routes. They can really take investigators in new, high impact directions because they don’t just buy what’s commercially available, which is the typical approach. They create tailor-made compounds to answer specific hypotheses. It’s opening new doors and generating new funding opportunities rather than being limited to what’s already on the shelf.”

In the laboratory, researchers often have to screen tens of thousands of compounds in order to find a handful that have potential. At ChemCore, Mishra uses computational software that allows him to screen compounds virtually, narrowing the field down to the compounds that have the most potential while saving resources in the real world. The team can also recreate compounds that were expended in experiments, giving...
researchers a cost-effective alternative to ordering supplies from outside pharmaceutical companies.

Scheidt believes that the resources at ChemCore will help open the channel to drug discovery. ChemCore has users from both the Evanston and Chicago campuses with researchers working to find new approaches to treating cancer and Alzheimer's disease as well as those exploring basic sciences and advancing the biology and chemistry fields.

“It’s exciting to see that, combined with the High Throughput Analysis Laboratory and the new Tumor Biology Core, we have established a pipeline of small molecule discovery at Northwestern to make compounds that people one day might use in the clinic,” Scheidt says. “ChemCore works with researchers to help move the drug discovery process forward.”

While the ChemCore facility is on the third floor, the purification arm of the core is housed in the Silverman East basement. For more information about ChemCore and CMIDD, visit http://www.cmidd.northwestern.edu/chemcore.

### Biostatistics Core Facility

**Northwestern Research, Biostatistically Speaking**

When it comes to testing a new treatment on patients, the success of the clinical trial hinges on more than just the effectiveness of the medicine or the intervention. The number of patients enrolled, length of the study, and inclusion of a placebo or other control group are three examples of the numerous important factors that come into play. Finding the right combination of factors to ensure a quality trial can be complicated.

However, Northwestern has a team to address these issues. Faculty members in the Biostatistics Core Facility (BCF) of the Robert H. Lurie Comprehensive Cancer Center and the Biostatistics Collaboration Center (BCC) of the Feinberg School of Medicine specialize in biomedical study designs, including those specific to randomized clinical trials.

“There are many different kinds of design,” says Alfred Rademaker, preventive medicine, who directs both the BCF and the BCC. “When collaborating on medical research projects, study design is often the first thing we deal with.”

But the biostatistics work does not end there. After setting up a study, members of the BCF and BCC direct data summarization, statistical analysis, interpretation of results, and publication of the findings. The statistical information is paramount to secure funding and grants, support findings in scientific presentations and papers, and prepare progress reports.

The Cancer Center’s Biostatistics Core Facility was established in 1979 and the BCC in 2004. While both united are physically housed in the Department of Preventive Medicine on the 14th floor of 680 N. Lake Shore Drive, their collaborators are from different departments and centers throughout the medical school. The BCF and BCC offer similar expertise, but they collaborate with different investigators. The BCF works specifically with members of the Cancer Center, and the BCC serves non-cancer researchers.

One project currently active in the Biostatistics Core Facility is Kenzie Cameron’s National Cancer Institute-supported research into colorectal cancer (CRC) screening. Cameron, general medicine, and her research group noted that limited literacy is associated with decreased use of cancer-prevention services, such as CRC screening.

“She looks at different strategies for increasing colorectal cancer screening in community clinics,” Rademaker says. “She collects data on screening rates by way of a randomized clinical trial, and we analyze the screening rates and determine which strategy is better.”

Biostatisticians also engage in risk factor analyses to understand how patient, disease, and treatment factors may be related to their various outcomes, such as treatment response or survival. For longitudinal studies, some participants inevitably will improve, worsen, or even die. Statistical methods evaluate factors related to such heterogeneity in outcomes and take into account the fact that not all patients are followed for the intended length of time.
Rademaker says one thing that’s changed since he became director of the BCF 1999 is the amount of data attained by faster, more powerful technology. “You can’t imagine how much data you can extract, store, and automatically pull off machines,” he says. “Over the years, we’ve made adjustments to some of the traditional statistical methods because there is just so much data.”

For example, Thomas Hope, cell and molecular biology, studies HIV transmission in women by observing the movement of individual virions in cervical mucus. “He looks at 60 seconds worth of data for each sample,” Rademaker says. “In those 60 seconds of data from one person, he is tracking hundreds of virions and taking ten pictures every second.”

Other areas where data collection has expanded are studies of methylation patterns, gene expression, and protein-protein interaction.

Members of the Northwestern community are encouraged to explore options for collaboration with biostatistics faculty. The facilities also direct educational seminars, data management and programming support, and workshops for departments, students, and residents.

For more information, visit http://www.feinberg.northwestern.edu/depts/bcc or http://www.cancer.northwestern.edu/research/shared_resources/biostatics_core/index.cfm.

**Metabolic Hormone Core**

**Weighty Research**

The number of adults with diabetes worldwide has more than doubled since 1980 to 347 million. According to the Center for Disease Control, if the current trend continues, then one-third of US adults will have diabetes by 2050. While these numbers look bleak, there are researchers at Northwestern whose work creates hope for the epidemic. A main source of support for them is the Metabolic Hormone Core in the Feinberg School of Medicine.

The mission of the core is to advance research across Northwestern in metabolic diseases, including diabetes, obesity, thrombosis, and cardiovascular disease by establishing validated high-throughput hormone analyses and creating a consolidated reference center for efficient testing for the community.

“Our facility does the day-to-day work that needs to be done for research,” says Joe Bass, medicine: endocrinology, neurobiology, and director of the core. “That allows individual labs to focus on exploratory experimental work.”

An example of that experimental work includes Bass’s own research. Although lifestyle habits and poor diets are the most that is capable of measuring specific coenzymes involved in metabolic function, insulin levels, glucose, lipids, and cholesterol in blood samples as well as identify and examine genetic markers related to disease.

The Metabolic Hormone Core was founded in 2009 as a part of the Department of Neurobiology and Physiology on the Evanston campus. In April of this year, the facility moved to the seventh floor of the Lurie Building on the Chicago campus. Moving to the Chicago campus allowed Bass to expand the core to include behavioral testing that requires more animal handling. This behavioral component of the core is located on the 15th floor of the Ward Building.

Despite its move downtown, the core still has several users from the Evanston campus. For example, Fred Turek, neurobiology, has an ongoing program sponsored by the Defense Advanced Research Projects Agency (DARPA) that looks into stress responses and the genetics that control cytokine and endocrine
systems that are affected by stress. He uses the facility to analyze stress and genetic modifiers in animals. The core has also performed leptin analyses for a research group in anthropology that studies diabetes and obesity from a population standpoint.

Bass says that having the Metabolic Hormone Core places Northwestern in competition with top research institutions around the globe. It could also potentially discover the end of the ever-growing epidemic of diabetes.

For more information about the core, visit http://www.feinberg.northwestern.edu/research/cores/units/met-hormone.html.

Skin Disease Research Center (SDRC)

Center Gets Under the Skin

Whether it's something as simple as a rash or as serious as melanoma, skin diseases can cause discomfort, pain, disfigurement, embarrassment, and even death. They are common in people of all ages and can be fleeting or frustratingly chronic. Northwestern's Skin Disease Research Center (SDRC) supports skin-related research, education, and communication at the University to improve patient care.

While one might typically assume that only dermatologists do skin research, the SDRC is an interdisciplinary center that supports researchers across several fields.

"Research is at its best when it's a community of individuals from different disciplines who share ideas and resources," says Amy S. Paller, dermatology, pediatrics, and founding director of the SDRC. "That's what we've achieved here."

Funded by the National Institutes of Health (NIH), the SDRC is one of only six of its kind in the country. It actively works to urge scientists to research skin biology. One way it does this is through the Pilot and Feasibility Program, which supports junior researchers and encourages senior investigators to pursue skin-related research initiatives that are natural outgrowths to their ongoing projects by awarding grants.

For example, Chad A. Mirkin, chemistry and director of the International Institute for Nanotechnology, received one of the first SDRC pilot grants in 2009. He took genetic material, arrayed it around a nanoparticle, and introduced it into the skin to regulate gene expression in keratinocytes, cells of the outer most layer of human skin. This work has led to both R01 and R21 funding from the NIH.

Navdeep Chandel, medicine: pulmonary, also received a pilot grant from the SDRC to look at oxygen sensors in the outer layers of skin. His project also resulted in an R21 grant and will be published soon.
staining, analysis, and phenotyping. It also provides tissue acquisition for researchers needing tissue samples to complete their research. The last core is the Administrative Core, which is responsible for coordinating all SDRC activities and educational programs. These programs are open to researchers from any department and are listed on the SDRC website.

Currently at 59 members, the SDRC offers applications for membership online here. Members receive a 20 percent discount on all core facility services.

For more information about the Center, core facilities, and services, visit http://skinresearch.northwestern.edu.

Nanoscale Integrated Fabrication, Testing, and Instrumentation Center (NIFTI)

NIFTI Allows Users to See the Invisible

Researchers at the Nanoscale Integrated Fabrication, Testing, and Instrumentation (NIFTI) Center can peer inside living cells without harming them. While most types of biological imaging require the cell to be quick-frozen and then sectioned to see inside, NIFTI has a rare instrument that allows researchers to probe inside of living samples, moving through them nanometer by nanometer, without damaging or killing them.

This type of technology is called Scanning Near-Field Ultrasound Holography (SNFUH), and it was created right on campus at NIFTI by the facility’s manager Gajendra S. Shekhawat and director Vinayak P. Dravid, both materials science and engineering. A part of the Northwestern University Atomic and Nanoscale Characterization Experimental (NUANCE) Center, NIFTI offers an impressive array of scanning probe microscopy-based tools and techniques for imaging, manipulations, patterning, and analysis of nanostructures of soft, hard, and hybrid materials.

SNFUH is one of the three types of equipment that Shekhawat and Dravid have developed at NIFTI to give the facility’s users the best resources to advance research. It allows researchers to image buried nanostructures, defects, delamination, and related “metrology,” or the science and technology of measurement.

“We want to move the pace of metrology technology,” says Shekhawat, who has managed NIFTI since it opened in 2002. “We develop our own technology here, collaborate with our industrial partners, and push the field ourselves.”

The primary role of NIFTI is to provide hands-on training.
education, and assistance for research collaborations to the Northwestern community and external customers. NIFTI’s resources are also used in various undergraduate and graduate courses in McCormick and Weinberg.

Northwestern licensed SNFUH and the related portfolio of intellectual property to the startup company NanoSonix, Inc., which was cofounded by Shekhawat, Dravid, and CEO Sean Murdock in 2009. The instrument works by integrating three approaches to nanoscale subsurface imaging: the scanning probe microscope platform, microscale ultrasound source and detection, and novel holography. Moreover, NanoSonix is developing SNFUH as an add-on module for already existing atomic force microscopy systems. That way, all applications will be available in one device.

“Users should have all options available in one system,” Shekhawat says. “Otherwise they have to go all over to use different instruments for their research. That ends up costing more time and money.”

NIFTI uses this all-in-one approach for all of its instrumentation. The facility has seven instruments and all have various capabilities integrated into them by Dravid and Shekhawat, who has a background in physics and engineering. Shekhawat says integration makes the equipment more user friendly.

“Our goal is to help Northwestern faculty and students advance their research,” Shekhawat says. “But after developing technology here, we can give it to other academic institutions and national labs.”

NIFTI also actively participates with international collaborators. The facility has often served as a hub for numerous global partnerships, particularly with Singapore and India. The collaborations, both domestic and abroad, have resulted in inventions, patents, and high-impact papers in journals such as Nature, Science, and Applied Physics Letters, to name just a few.

Having grown from 20 users in its first year to more than 120 annual users from across various fields, NIFTI refers to these past years as its “decade of excellence.” During this decade, NIFTI also provided numerous open-house events and instrument demonstrations to local schools, museums, and the general public. It also participated in Science Chicago to help instill excitement in young minds for science and technology.”

Funded by the Northwestern Nanoscale Science and Engineering Center (NSEC), the International Institute for Nanotechnology (IIN), and the Office for Research, NIFTI is open 24 hours a day, 7 days a week. For more information, visit www.nuance.northwestern.edu/nifti.

Developmental Therapeutics Core (DTC)

DTC Gets Research Closer to the Clinic

As more and more pharmaceutical companies drop the early testing stages for new drugs, it is becoming increasingly important for academic institutions to participate in early-stage drug development. To foster this process, Northwestern established the Developmental Therapeutics Core (DTC) one year ago. Under the umbrella of the Center for Developmental Therapeutics, which is part of the Chemistry of Life Processes Institute, the core provides services focused on supporting the translation of new therapies.

“The name is a bit limiting because we do more than tumor biology models,” says Andrew Mazar, molecular biosciences and director of the core. “The majority of the work we do is in drug development, in general. We do the exploratory work that’s required to decide if the drug should be taken to the next step.”

After basic research is completed in the investigator’s lab, experienced staff members in the DTC can set up disease models, turn the drug into a solution that can be injected,
run toxicology tests to see how well the drug is tolerated in the body, and complete various other in vivo and in vitro studies.

For example, Teri Odom, chemistry, developed new particles that bind to specific parts of a DNA construct to target disease. The DTC is helping her learn where the drug is distributed in the organs to make sure it is activating within the tumor.

The DTC is also testing gold nanoparticles that were developed in the laboratory of Chad Mirkin, chemistry. Mazar suspects that the nanoparticles will enter clinical trials this year to treat patients with brain cancer.

“We can fit our services into whatever the faculty member’s needs are,” says Angki Kandela, assistant director of the DTC. “We can run all the tests from start to finish or we can train them to run everything on their own. Sometimes investigators just need us to do partial work because their lab does not have that specific expertise.”

Located in the basement of Silverman Hall, the DTC works closely with Northwestern’s Innovation and New Ventures Office (INVO) to partner with faculty investigators from the beginning. The DTC already serves 30 principal investigators and is actively growing.

“The core is a completely new model for academia,” Mazar says. “No one else has a core where they take compounds or targets invented in a basic research lab and figure out how to get them into the clinic. It’s the model that biotech and pharma use, so it’s a common model. But it hasn’t been applied before in an academic setting.”

Mazar spent 20 years working for pharmaceutical companies where he developed oncology drugs. Based on his own experience, he says that it is more productive for universities to handle the early stages of drug development. Otherwise, members of the companies tend to take the drug from the investigator who knows it best and try to get up to speed on the research by themselves.

“The better investment is to take that researcher who has the knowledge and partner him or her internally with people like us who can fill in the pieces in order to take it to the next step,” Mazar says. “Then you reach a critical point where you can now hand it off the drug to a company, and they can take it the rest of the way.”

In addition to partnering with INVO, the DTC also actively works with the Center for Molecular Innovation and Drug Discovery, the Center for Cancer Nanotechnology Excellence, NUCATS, the DNA/RNA Delivery Core, and the Clinical Pharmacology Core.

“People don’t realize that drug development needs to bring together many disciplines,” Mazar says. “You have to be able to work in collaborative teams; you have to be risk taking.”

For more information about the Developmental Therapeutics Core, visit http://www.clp.northwestern.edu/research-facilities/dtc.
Recombinant Protein Production Core (rPPC)

Producing Proteins

As more and more people are diagnosed with diabetes, the word “insulin” pops up more frequently in the news and in casual conversations. You might know that insulin is a hormone needed for regulating blood sugar in the body, and you might know that people with type-1 diabetes require insulin injections for survival. But do you know where the insulin for these injections comes from?

“Up until the early 1980s, the only way to get insulin was from the pancreas of a pig or other animal,” says Michael Jewett, chemical and biological engineering. “While this worked well for most patients, some developed adverse reactions or allergies.”

This challenge was addressed by the development of recombinant DNA (rDNA) technology. Researchers discovered that they could take the gene that encodes for the insulin protein and then cut and paste that gene into a plasmid vehicle that allows it to express, or be synthesized, in another organism. In the case of insulin, the first biosynthetic human insulin was produced in E. coli bacteria. Now, most insulin used across the globe is recombinant insulin.

rDNA technology is now widely used for biotechnology and medical research and applications. Recombinant proteins are still expressed in bacteria but can also be produced in yeast, insect cells, and mammalian cells, among others. As of the summer of 2011, this research found a new home at Northwestern in the Recombinant Protein Production Core (rPPC), which is located in the basement of Silverman Hall.

“Proteins are these very functionally diverse molecules that participate in just about every biological process within cells,” says Jewett, co-director of the rPPC. “People can drop off DNA samples, and we make proteins as reagents for them to study and understand their functions.”

Co-directed by Andreas Matouschek, molecular biosciences, and Keith Tyo, chemical and biological engineering, the core does protein expression and purification of recombinant or synthetic biologics.

Proteins are responsible for the regulation and functions of virtually all biological systems. However, a large number of proteins are left with no known function. As a production facility, rPPC facilitates the expression of proteins for a broad spectrum of research activities at Northwestern, ranging from producing potential therapeutics to structure and function studies.

For example, the rPPC successfully produced a large quantity of several proteins that are typically difficult to express by using well-controlled fermenters. The protein was then used for a crystallization study for bacterial pathogens in the laboratory of Wayne Anderson, molecular pharmacology and biological chemistry. This work could potentially aid drug discovery for antimicrobials.
Before the rPPC was established, researchers produced the recombinant proteins in his own lab. They would add DNA to a microbial system and put it in a shake flask, which was then shook inside of an incubator to allow the cells to grow.

Not only can the core create large quantities of inexpensive protein reagents but the proteins are also produced in well-controlled fermenters (from 1 to 5 liters) where the pH level and temperatures are stable.

“We’re not just meeting a need of throughput,” Jewett says. “We’re also meeting a need of quality.”

In addition to producing proteins for customers, the facility also trains researchers and students on how to use the instruments in the facility. Students in Keith Tyo’s lab are already using the parallel bioreactor system in the core to run their own experiments.

“This provides a unique opportunity for a lot of students,” Jewett says. “We want them to learn techniques and technologies that are going to be applied in their own professional careers down the road.”

For more information about the rPPC, visit http://rppc.mccormick.northwestern.edu.

Microsurgery Core

Surgery Under the Microscope

Before transplant surgeries can be tested with humans, the proof of concept must be established in the animal model. However, connecting the small organs and tiny blood vessels in the body of a mouse takes extensive training and tremendous skill. This is exactly the type of work supported by Northwestern’s Microsurgery Core.

“We work on tiny animals, so we can’t perform surgery with the naked eye,” says Jenny Zhang, transplant surgery and director of the core. “We have to perform the surgery under the microscope using very fine instruments. The suture we use is finer than a strand of hair. It’s technically demanding.”

Located on the 11th floor of the Tarry Building on the Chicago campus, the Microsurgery Core is a part of the Comprehensive Transplant Center (CTC) at the Feinberg School of Medicine. Staffed with five microsurgery experts, the core is a central resource for creating rodent models of organ transplantation and other microsurgical procedures that can be used to study human diseases.

The core is currently working on 10 major, ongoing projects. One of the projects uses a kidney transplant model to study the cytomegalovirus (CMV), a virus that typically goes unnoticed in healthy people but can be life-threatening for the immunocompromised. Because transplant patients take immunosuppressing drugs after surgery to avoid organ rejection, they are particularly vulnerable to the virus.

After initial exposure, the virus can remain latent in the body for a long period of time. However, after transplant surgery the virus can become activated and lead to an infection. “We want to know how this virus becomes activated,” Zhang says. “If we can understand that, then we can prevent it.”

Led by principal investigator Michael Abecassis, transplant surgery and director of the CTC, the project is funded by the National Institutes of Health.

Researchers at the Microsurgery Core also study organ rejection, which is one of the biggest hurdles for transplant recipients. One way to do this is to transplant a kidney or a heart from a black mouse into the body of a white mouse. These two mice have mismatched major histocompatibility complex (MHC), antigens on the cell surface of donated organs that give an immunological response in organ transplants. After the transplant surgery, researchers can study the immunological response and see if specific drugs have an effect on it.

Zhang is also working on her own research to study both acute and chronic rejection by examining molecular pathways and biomarkers in kidney transplants. “My goal is to find a biological signature for rejection,” she says. “We want to know what biological process is turned on when there’s a rejection.”

In addition to providing a service to principle investigators and creating new models for research, the Microsurgery Core is also a center for training residents, fellows, and students in
microsurgery techniques. The core has three microsurgery workstations, each with dual binocular heads, so one person can observe while the other person performs the surgery. Two large-screen monitors are available in the lab space, so visitors can watch the surgeries from nearby. The monitors can also record the surgeries in order to be played back in the future for educational purposes.

Although the core started just three years ago, it already has experienced much success. Studies in the facility have helped investigators secure funding support from various funding agencies and have generated multiple publications in a variety of peer-reviewed journals.

For more information or to initiate a project with the core, visit [http://www.feinberg.northwestern.edu/sites/transplant/research/research-cores/microsurgery-core.html](http://www.feinberg.northwestern.edu/sites/transplant/research/research-cores/microsurgery-core.html).

### Magnet, Low Temperature, and Optical Facility

#### Core Facility Is a Research Magnet

Magnets. They affix coupons and photos to our refrigerators. They encode digital information onto compact discs. And they guide the particles that whirl around the Large Hadron Collider at CERN. Things that display the physical property of magnetism are studied at Northwestern’s Magnet, Low Temperature, and Optical Facility on the Evanston campus.

“Anybody who wants to measure something in a high-magnetic field can come to this facility,” says John Ketterson, physics and astronomy, and director of the core. “We can measure temperature dependence of magnetization, electric response, and resistance to electrical current transport, and other things that depend on the magnetic field strength.”

A part of Northwestern’s Materials Research Center, the core facility’s history stretches back to 1959 when the University purchased the largest electromagnet that was commercially available at the time. The electromagnet was a centerpiece of the facility until a stronger magnet was acquired shortly after the recent renovation of the Technological Institute where the core facility is housed.

The electromagnet is held inside a copper-screened room to keep out electromagnetic inferences, such as those emitted by the University’s radio station WNUR and cell phone transmissions, from disturbing sensitive measurements.

The facility eventually gained a second electromagnet that is able to measure high-frequency magnetic responses.

Researchers studying a wide range of subjects, including materials science, physics, and chemistry, use the Magnet and Low Temperature Facility. In addition to having two powerful electromagnets, the core also has cryogenic systems to measure magnetization in temperatures from 1.9 Kelvin to 390 Kelvin. The types of measurements that are routinely performed are magnetization and magnetic susceptibility, acoustic propagation, microwave absorption, and electrical transport.

“The magnetism itself is a property that changes with temperature,” says Ketterson, who uses the facility to make magnetic measurements of a nanostructured material formed from permalloy. “If you have a magnet in your hand and you heat it, you will eventually reach a magic temperature. And boom! The magnetization disappears.”

This phenomenon is known as a phase transition and is widely studied in solid-state physics. A goal of many of the researchers is to find out how the tiny atomic magnets within some materials order themselves and why that order disappears above a certain temperature.
According to Ketterson, the instruments in the facility are very easy to use as all of the machinery is computer controlled. After loading a sample, researchers simply dial up the temperatures and magnetic fields on a computer. The computer runs the experiment and outputs the data. Facility technician Oleksandr Chernyashevskyy trains users to run their own experiments with the machinery.

The systems are designed to be as flexible as possible. When they require upgrades or new functions, Ketterson and Chernyashevskyy do it themselves, tailoring the equipment to the needs of the researchers.

"Much of the science we do can’t be done with things you buy off the shelf," Ketterson says. “We figure out what folks want to measure and build machinery to measure it.”

The Magnet, Low Temperature, and Optical Facility is located on the first and ground levels of the Technological Institute.

For more information visit http://www.mrsec.northwestern.edu/content/facilities/magnetlowtemp.htm.

Mary Beth Donnelley Clinical Pharmacology Core Facility

The Fine Line Between Poison and Remedy

After the 1941 attack on Pearl Harbor, scores of wounded were taken to a triage area to treat their injuries. They were given a normal dose of a short-acting barbiturate general anesthetic known as sodium pentothal. While healthy patients would have tolerated the dose, it had tragic consequences on those in shock from blood loss.

“The standard dose killed so many people that when the results of the experience at Pearl Harbor were reported in the journal Anesthesiology in 1943, the author called intravenous anesthesia an ideal form of euthanasia,” says Michael Avram, anesthesiology. “Fortunately, a case report and editorial accompanying this report concluded it was not the drug that was at fault, but the way it was administered.”

That fatal lesson is at the center of the Mary Beth Donnelley Clinical Pharmacology Core Facility, of which Avram is director. The core facility studies the effects of the body on drugs (pharmacokinetics) and the effects of drugs on the body (pharmacodynamics). Researchers do this by studying drug absorption into the blood stream, distribution throughout the body, and elimination by various means, including metabolism and renal excretion.

The core is also interested in the relationship between drug concentration and effect and the time for the drug to reach the sites of action or receptors.

In addition, they look at how disease can interfere with this process. For example, if a drug enters the blood stream and is later filtered by the kidneys, then what happens if the person has poorly functioning kidneys? Drug concentrations are likely to stay elevated for longer than predicted, so the dose needs to be adjusted accordingly.

“'The physician Paracelsus is one of our heroes,” says Tom Krejcie, associate director of the core. "In the early 1500s, Paracelsus said ‘All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy.’”

“When we lecture to medical students, we tell them that if they don’t remember anything else, remember that,” Avram adds.

The Clinical Pharmacology Core had its origins in the Department of Anesthesiology 30 years ago when Avram and Krejcie learned the discipline by working with Arthur J. Atkinson Jr., who had established the Clinical Pharmacology Laboratory at Northwestern in 1970. Avram says that anesthesiology was a natural home for clinical pharmacology because anesthetics are so powerful and potentially toxic that it’s important to understand how the body handles them in order to administer them safely and effectively. Ten years ago, the focus of the facility changed after Avram received a phone call from Steven Rosen who at the time was expanding resources for the Lurie Comprehensive Cancer Center.

“Dr. Rosen wondered if we’d be interested in collaborating with oncologists,” Avram recalls. “I had waited for that phone call for 20 years. I was delighted.”

In order to study state-of-the-art therapeutics for oncology, the facility required a whole new state-of-the-art laboratory,
which is now located on the 13th floor of the Ward Building in Chicago. With a generous donation from the Donnelley family, Northwestern was able to purchase a triple quadrupole mass spectrometer. The equipment enables researchers to detect small quantities (less than a nanogram) of drugs in biological matrices, such as plasma, cerebral spinal fluid, and breast milk.

In 2008 Judith Paice, medicine: hematology/oncology, approached Avram and his colleagues at the core with a serious concern. Paice, who directs the Cancer Pain Program at Northwestern Memorial Hospital, had a strong suspicion that the topical morphine gel they were administering to hospice patients was not working. For patients who were unable to swallow medicine, a topical solution was ideal as it was supposed to be absorbed through the skin. After the Donnelley Clinical Pharmacology Core completed a randomized, placebo-controlled crossover comparison of the topical gel with subcutaneous injection in volunteers, Paice’s suspicions were confirmed.

"Using the mass spectrometer, we measured plasma morphine concentrations in the volunteers at multiple times after the gel was applied to their skin," Avram says. "It showed that the topical gel didn’t work because none of the morphine was being absorbed. This study completely changed the practice of providing pain relief in hospice.”

In addition to testing drug effectiveness, the core is an integral part of drug development. The core provides support for preclinical and clinical studies of cancer chemotherapeutic agents, analgesics, and other small molecules. Members of the core work closely with Northwestern’s entrepreneur-in-residence, Andrew Mazar, to make connections with drug development researchers at the University.

Krejcie says some drugs never reach their potential in clinical trials because they are tested at the wrong dose and concentration. The core facility can develop mathematical models using data from classical pharmacokinetic studies that can guide investigators in the design of efficient concentration-controlled pre-clinical or clinical trials.

“You can’t give healthy people and wounded people the same dose,” Krejcie says. “Likewise, you shouldn’t give me the same dose as Shaquille O’Neal. You could test different doses on volunteers and hopefully not kill anybody or you can approach it the smart way and come up with a mathematical model to see what happens in healthy people. Then make adjustments in the model to compensate for physiological changes. We don’t want to throw promising drugs into the trash because we didn’t take the time with modeling.”

“Or worse than that,” Avram adds, “we don’t want to advance drugs that don’t belong in clinical trials.”

For more information about the Mary Beth Donnelley Clinical Pharmacology Core, click here.

Integrated Molecular Structure Education and Research Center (IMSERC)

As of August 1, the Integrated Molecular Structure Education and Research Center (IMSERC) and Biological Nuclear Magnetic Resonance (NMR) Center are combining to form one organization that will continue to operate as IMSERC. This combination has already resulted in the purchase of a new 14.1-Tesla magnet and will pave the way for future NMR proposals.

NMR manager Yongbo Zhang will join the IMSERC staff and report to Andrew Ott, director of IMSERC. Over the next several months, the Biological NMR Center’s infrastructure will be incorporated into IMSERC’s existing infrastructure. Researchers can expect little change to the daily operations of the biological nuclear magnetic resonance research activities.

For more information about IMSERC, visit: http://imserc.facilities.northwestern.edu/
Optical Microscopy and Metallography Facility (OMM)

Polished Work

In January 1959, Northwestern’s department of metallurgy underwent a groundbreaking name change. Recognizing that the interdisciplinary faculty was broader than metals—drawing from chemistry, mechanical engineering, and nuclear engineering—Northwestern renamed the unit “materials science,” forming the first materials science department in the world. Five decades later, Northwestern continues to lead the field. However, over the years, new materials have been developed and older materials have been improved. As these new and improved materials arise, the technology of sample preparation also needs to keep pace. Much of this material sample preparation occurs in one of the University’s oldest core facilities—the Optical Microscopy and Metallography Facility (OMM).

Originally founded as a shared facility within the metallurgy department, the OMM is a laboratory equipped to prepare specimens not only for examination by optical microscopy in the facility but also for other observation and testing techniques which require careful surface preparation. It is directed by Kenneth Shull, materials science and engineering.

“The core of materials science is studying the relationship between a material’s properties and its structure and the processing parameters which affect that structure,” says Carla Shute, manager of the facility. “As a material scientist myself, I work with my users to help them with sample preparation and even sometimes to discuss details of their experimental procedures. Many testing procedures also require careful sample preparation, so the OMM Facility does not only prepare samples for optical microscopy.”

Shute recently met with a research group from mechanical engineering that studies the interface between a thin, 80-micron polymethyl methacrylate (PMMA) layer and a silicon substrate. While PMMA is soft like plastic, silicon is hard and brittle. Hard materials polish at a different rate than a soft material component making hybrid materials challenging to work with. For situations like this, the facility recently acquired a triple beam ion milling machine (Leica TIC3X), which is able to prepare samples that are difficult to polish, such as porous, multi-component, water sensitive, heat sensitive, or composite samples.

In addition to preparing samples, the OMM facility serves as a learning facility for undergraduate and graduate students at Northwestern and for many visiting students, especially through the Research Experience for Undergraduates (REU) program which is administered through the Materials Research...
Center. Shute works with students for the laboratory component of several materials science classes and with students enrolled in the Engineering Design Course each year. Students learn how to prepare samples, perform hardness testing, heat treat samples, and examine materials with optical microscopy.

"Materials research is very equipment heavy," Shute says. "You have to be hands on. You have to work with instruments and understand your results and errors. The way you learn that is to gain experience by working in the lab. It’s a very important part of education."

Located on the second floor of Cook Hall in Evanston, the Optical Microscopy and Metallography Facility is used by researchers in materials science and engineering, civil and environmental engineering, mechanical engineering, electrical engineering and computer science, and applied physics. For more information about the facility, visit http://omm.facilities.northwestern.edu/.

Materials Processing and Microfabrication Facility (MPMF)

Big Ideas, Micro Structures

Since their conception in 1958, integrated circuits, or microchips, have transformed much of human society. They permit the manufacture of small electronic devices containing millions of components that are essential to computers, aircraft, cell phones, automobiles, and more. As chip complexity increases and size decreases, new applications for integrated circuits are continually being found. A lot of new work in this area is being completed right on campus at Northwestern’s Materials Processing and Microfabrication Facility (MPMF) in the Materials Research Center.

“When the facility opened, it was called the Materials Processing Facility,” says Bruce Wessels, materials science and engineering and director of the facility. “Then in 1984 I started adding microfabrication equipment as faculty members became more involved with micro- and nanomaterials.”

Located in Cook Hall, the facility is devoted to processing, growth, device fabrication, and electronic and photonic materials. The facility is used by faculty members from various disciplines, including physics, chemistry, materials science, mechanical engineering, biomedical engineering, and computer science.

Wessels uses the facility for his own research in the development of switches for optical communications, which use light to transfer information. Optical switches enable signals in optical fibers to be selectively switched from one circuit to another.

“It’s the basis for the Internet,” Wessels says. "We're working on photonic crystals for high-speed optical switches for the next generation of the Internet."

At MPMF Teri Odom, chemistry, has created nanoscale patterns with arbitrarily large rotational symmetries over large areas, which is advantageous for photovoltaic, optoelectronic, and sensing applications. (See blue image and caption at the lower right.)

The MPMF includes class 100 and 1,000 cleanrooms, meaning that they have fewer than 100 or 1,000 particles (≥0.5 microns in size) per one cubic foot respectively. Cleanrooms are imperative when working with such tiny devices. “A dust particle could be of the order of a micron or more,” Wessels says. “So dust particles can interfere with your samples. That can lead to device failures through broken lines and short circuits."

The facility activities grow every year as Wessels and facility manager Anil Dhote, materials science and engineering, work to attain newer state-of-the-art equipment for materials preparation and microfabrication. “We want to have all the essential microfabrication equipment here, so people don’t have to make extended trips off campus,” Dhote says. “It’s important to finish one microfabricated device in the same cleanroom space.”

The newest piece of equipment now housed at the MPMF is for atomic layer deposition (ALD). Microfabricated devices...
typically are constructed using one or more layers of thin films. For example, electronic devices may have thin films that are metallic conductors, insulators, or semiconductors. Optical devices may have films that are transparent, reflective, or scattering. Atomic layer deposition allows researchers to deposit layers of film that are as thin as one nanometer. According to Wessels, the thinner layers allow for smaller devices and higher levels of device integration.

As new equipment is added and the number of users grows, the facility has nearly outgrown its space. Because of this, the University recently opened the Northwestern University Micro/Nano Fabrication (NUFAB) Facility in the lower level of Tech. (Read more about NUFAB in the April 2010 issue of the Northwestern Research Newsletter.)

“We’re complementary facilities,” Wessels says. “We look at compounds, semiconductors, and advanced materials. NUFAB will greatly expand our capabilities in silicon-based materials and devices.”

Not only does the MPMF provide equipment, but Dhote also trains all the users to work with the instruments. The facility hosts users from the Northwestern community as well as those from government and industry. “I believe in making our users independent,” he says. “Then they can do the work that meets their specific needs.”

For more information about the Materials Processing and Microfabrication Facility, visit http://www.matsci.northwestern.edu/research/facilities/materials-processing-crystal-growth.html.

Cryogenics Facility

Northwestern’s Gas Station

In the early 1980s, several researchers at Northwestern were interested in pushing the boundaries of science to lower and lower temperatures to explore new materials and new phenomena. As researchers began experimenting with cryogenics, it became clear that Northwestern lacked the infrastructure to support this work. The need for having readily available liquid nitrogen and liquid helium was obvious. To meet this need, the University opened the Cryogenics Facility in the basement of Tech in 1984.

“Our service is very simple,” says Bill Halperin, physics and astronomy and founding director of the facility. “We provide liquid nitrogen and liquid helium. This service to the University is the heart and soul of our facility. We make low-temperature science possible.”

While liquid nitrogen can cool experiments down to 63 Kelvin, liquid helium can, in principle, cool experiments arbitrarily close to absolute zero. Having these liquefied gases right on campus is important for addressing immediate and spontaneous research needs. Sometimes researchers might create sensitive samples that do not age well and need to be frozen. Other times they might use more nitrogen or helium than expected and need more right away before the experiment warms up.

Halperin, who uses helium for basic research and discovery at low temperatures, understands how these needs can arise unpredictably.

“In my lab, our experiments last up to a year, continuously requiring helium every second day,” he says. “If something goes
wrong, then they need helium right away. If you warm up an experiment that requires six to 12 months of running, then you have to start over again. The loss of so much time and money is fantastic."

Due to a worldwide helium shortage, many universities struggle to meet the helium needs of their cryogenics labs. While Halperin says the future of helium appears grim, Northwestern has a special certification to use the gas for academic use and its supply remains steady. "We look to the short-term and plan for the long term," he says.

In order to obtain liquid helium, researchers just have to contact facility manager Yongjia Qian and can pick up a tank as early as the next day. A cryogenics expert, Qian joined Northwestern in 2005.

"In 1978 Qian was with the first group of scholars from China recognized to travel to the United States," Halperin says. "Then he was lured back to Hong Kong University of Science and Technology to lead the cryogenics group there. I was very well aware of his expertise going back to 1978. I worked on him for several years to come join us."

Obtaining liquid nitrogen from the Cryogenics Facility is an even easier process with no intermediaries. Liquid nitrogen is readily available for pick-up 24 hours a day, seven days a week.

"Liquid nitrogen is widely used in the sciences throughout the University, and we can deliver it on demand," Halperin says. "It's like going to a gas station where you drive up to a pump, open your tank, and fill up. Gas stations are open 24/7, and so is our liquid nitrogen gas station. It's a straightforward operation."

In addition to serving daily users, the Cryogenics Facility is on board to help with the Tech renovation project. As the Integrated Molecular Structure Education and Research Center (IMSERC)—directed by Andrew Ott—plans to move to the infill on the north side of Tech between the B and C wings, some of the transferred instruments will require significant amounts of liquid helium. IMSERC’s superconducting magnets, for example, need to stay at liquid helium temperatures in order to maintain the electrical current that supplies the magnetic field in the superconducting state. If the temperature warms up too much, then the superconductive currents stop flowing and the magnet becomes resistive.

"At the very least, once the magnets have been moved, they will need to be refilled," Halperin says. "We won't know when they'll need to be refilled until right before the move."

Because helium is a finite resource, losing it can be a costly disaster. To prevent this loss, the facility operates with a closed system to recapture the gas that boils from the liquid. Beneath the floors of Tech are large pipes that connect the laboratories of helium users back to the facility. Halperin refers to this network of pipes as "the veins and arteries of science." When the liquid evaporates and goes into the gas phase, the pressure drives the gas into the pipes. From there, it travels into one of several giant balloons in Tech's sub-basement. As the balloons fill up, compressors are triggered and automatically compress the gas. The Cryogenics Facility can then reliquefy the gas as a rate of up to 25 liquid liters per hour. The closed system recycles gas that may become released in an accident or during a power outage.

The Cryogenics Facility has 20-30 principal investigators using the helium and nitrogen liquids at any time. To learn more about the facility, visit http://cryogenics.facilities.northwestern.edu.
**Evanston Campus**

- Biological Imaging Facility (BIF)
- Biological NMR Center
- Center for Advanced Molecular Imaging (CAMI)
- Central Laboratory for Materials Mechanical Properties (CLaMMP)
- Clean Catalysis Core (CleanCat)
- Computation, Modeling & Bioinformatics Center
- CryoEM Facility
- Cryogenics Facility
- Developmental Therapeutics Core (DTC)
- Electron Probe Instrumentation Center (EPIC)
- High Resolution Electron Microscopy & Surface Structure Facility
- High Throughput Analysis Laboratory (HTAL)
- Instrument Shop
- Integrated Molecular Structure Education and Research Center (IMSERC)
- Jerome B. Cohen X-ray Diffraction Facility
- Keck Biophysics Facility
- Keck Interdisciplinary Surface Science Center (Keck-II)
- Magnet, Low Temperature, and Optical Facility
- Materials Processing & Microfabrication Facility - Cleanroom
- Medicinal and Synthetic Chemistry Core (ChemCore)
- Nanoscale Integrated Fabrication, Testing and Instrumentation Center (NIFTI)
- NU Center for Atom Probe Tomography
- NUFAB Cleanroom
- Optical Microscopy & Metallography Facility (OMM)
- Proteomics Center of Excellence
- Proteomics Core
- Quantitative Bioelemental Imaging Center (QBIC)
- Recombinant Protein Production Core (rPPC)
- Sleep, Circadian and Other Rhythm Experiments Core (SCORE)
- Surface Science Facility

**Chicago Campus**

- Behavioral Intervention Technology Development Core (BIT Core)
- Behavioral Phenotyping Core Facility (BPC)
- Bioinformatics Research Collaboratory (BIRC)
- Biostatistics Collaboration Center
- Biostatistics Core Facility
- CCM Rodent (Preclinical) Technical Services Unit
- Center for Advanced Microscopy & Nikon Imaging Center
- Center for Translational Imaging (CTI)
- Clinical Research Office-RHLCCC
- Comprehensive Metabolic Core
- Flow Cytometry Core Facility - Cancer Center
- Flow Cytometry Facility - Interdepartmental Immunobiology Center
- Genomics Core Facility
- Human Embryonic and Induced Pluripotent Stem Cell Facility
- IBNAM Equipment Core
- IBNAM Nanomedicine Cleanroom
- IBNAM Peptide Synthesis Core
- Instrument Shop - Chicago
- Mary Beth Donnelley Clinical Pharmacology Core Facility
- Mathews Center for Cellular Therapy (MCCT)
- Microsurgery Core
- Mouse Histology and Phenotyping Laboratory (MHPL)
- Next Generation Sequencing Facility
- Northwestern Medicine Enterprise Data Warehouse
- NUCATS-Center for Clinical Research
- NUCATS-Clinical Research Unit (Lurie Children’s Hospital)
- NUCATS-Clinical Research Unit (NMH)
- NUCATS-Research Bionutrition Services (NMH)
- NUCATS-Research Laboratory Services (NMH)
- NUCATS-Research Nursing Services (Lurie Children’s Hospital)
- NUCATS-Research Nursing Services (NMH)
- NUgene
- Outcomes Measurement & Survey Core (OMM)
- Pathology Core Facility
- Skin Disease Research Center (SDRC)
- Structural Biology Facility
- Transgenic and Targeted Mutagenesis Laboratory (TTML)

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Please Note: The use of data in a grant application, progress report or publication that was generated in a core facility contains the implicit understanding that the PI or authors will acknowledge the use of the core facility. Since many of our facilities are supported by federal agencies, such acknowledgment is mandatory.