Next-generation DNA and RNA sequencing have made it possible not only to look at individual genomes but also to rapidly compare genetic sequences among multiple genomes. These approaches can be used to determine differences in genomes and gene transcripts from person to person, among population groups, and between normal and diseased cells.

To take advantage of this groundbreaking technology, Northwestern opened the Next-Generation Sequencing (NGS) Core facility in December 2012.

“There was a significant need for additional next-generation sequencing options for researchers on both campuses,” says Matthew Schipma, director of the NGS core. “Researchers were relying on other institutions all over the country to get their sequencing done.”

Over the past few years, technological advances in sequencing have ushered rapid changes in sequencing instrumentation. After considering instrument costs and current sequencing demands, the University decided to partner with BGI Americas, the largest sequencing company in the world. “The cost is significant for just one instrument and a new model comes out nearly every year,” Schipma says. “So we would always be chasing the next model.”

“Because you need a certain number of samples to run the machine efficiently, there could be long wait times to fill a sequencing flow cell,” adds Grant Barish, endocrinology, who serves as scientific advisor to the NGS core along with John Crispino, hematology/oncology.

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Chromatin immunoprecipitation sequencing (ChIP-seq) is a technique to locate the genome-wide binding sites of specific proteins along DNA. When an organism's genetic sequence is unknown, de novo assembly enables bioinformaticists to stitch together DNA sequences to unravel a genome.

Through BGI, the NGS core can access a wide variety of state-of-the-art equipment, including the Illumina HiSeq2000 and Roche 454 FLX. Core services include:

- RNA-seq, or “whole transcriptome shotgun sequencing.” This technique involves using high-throughput sequencing to look at the expression of genes in samples, to determine, for example, what is turned on or off in specific conditions or disease states.
- Chromatin immunoprecipitation sequencing (ChIP-seq). ChIP-seq is a technique to locate the genome-wide binding sites of specific proteins along DNA.
- De novo assembly. Used when an organism’s genetic sequence is unknown, de novo assembly enables bioinformaticists to stitch together DNA sequences to unravel a genome.

The NGS core has a wet lab in the Lurie Building to assess the quality and quantity of RNA, DNA, or sequencing libraries prior to sending samples to BGI for sequencing. The core also handles all sample shipments and returns of sequencing data, uploading the sequencing reads directly onto Northwestern servers.

After the sample is sequenced, the biggest challenge is analyzing it. A typical instrument run will generate hundreds of millions of reads, or short stretches of DNA. For investigators who are not familiar with analysis, it can be overwhelming. Schipma and his bioinformatics team meet with investigators to find out what questions they would like answered in their experiments. Then the team performs analysis that is tailored to the project.

Barish has used the core facility for his own research examining hormone receptors. He uses RNA-seq to explore the changes in gene expression incurred by gain or loss of function of a particular transcription factor and its role in the macrophages. He then uses ChIP-seq to see where the transcription factor is occurring along the genome in the macrophages.

“Next-generation sequencing is becoming more of a necessity in some biological research,” Schipma says. “Grant review boards expect to see NGS on proposals because the benefits are so widely recognized.”

Funding for the NGS is provided by Feinberg and the Office for Research. For more information, email ngs@northwestern.edu.

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Developing Treatments for Macular Degeneration

Northwestern is a part of a multi-institution interdisciplinary consortium that has been awarded a $6.2 million grant over five years from the National Eye Institute. The consortium will develop new treatments for exudative age-related macular degeneration (AMD).

Exudative AMD is the leading cause of blindness among aging Americans, and the global rate of AMD is expected to double in the next decade due to an aging population.

The severe vision loss from AMD is caused by the overgrowth of blood vessels between the outer membrane of the eye and the retina. New therapeutic approaches are needed to restore eye function lost to the disease.

Led by the University of Wisconsin School of Medicine and Public Health, the consortium includes investigators from Northwestern’s Center for Developmental Therapeutics, Feinberg, and McCormick, and the University of Nebraska Center for Drug Delivery and Nanomedicine.

Northwestern is expected to receive approximately $3.9 million in funding over the five-year grant period. Olga V. Volpert, urology, is the Northwestern principal investigator. Other Northwestern researchers who will be involved are: Jack Henkin, chemistry; Hao F. Zhang, biomedical engineering; Sergei Revskoy, medicine; and Andrew Mazar, director of the Center for Developmental Therapeutics.

The Searle Center for Teaching Excellence is now known as the Searle Center for Advanced Learning and Teaching.

In its more than 20 years at Northwestern, the Searle Center has expanded in size and in the variety of activities in which it is engaged. Once a training center for a select group of faculty, Searle now engages a wide array of faculty, administrators, graduate students, and undergraduates. Research in the center has resulted in more than 100 publications in peer-reviewed journals and several books contributing to the scholarly conversation.

“While the new name is not vastly different, we feel it more fully reflects our mission within the University and within the academic community, nationally and globally,” Gregory Light, director of the Center, said in a press release.

The Center’s new name reflects its expansion from solely promoting teaching to enhancing learning and investigating how learning and teaching practices can be enriched.

Click here for more information.