The Center for Inherited Disease Research at Twenty

Scientific collaboration on a large scale has been a hallmark of genomics since the beginning of the field. NHGRI has been fortunate to be at the center of many large collaborative projects, such as the Human Genome Project (HGP). While the HGP represents one incredible milestone in the path to understanding human biology, it also resulted in new technologies and resources that are now foundational for many areas of biological research. This progression is nicely illustrated by an NIH-wide collaboration that has given researchers access to key genomic resources for the past 20 years – the Center for Inherited Disease Research (CIDR).

Emerging genomic technologies are not always available to all researchers, as instruments can be too expensive for small laboratories to purchase and only specialists might have the ability to perform appropriate data analyses. That such expertise was rare and hard to find was particularly apparent in the early days of the HGP, so in 1996, seven NIH Institutes and Centers (ICs) joined forces to establish CIDR, which aimed to gather the expertise and build the necessary infrastructure to provide large-scale genotyping services to investigators funded by those ICs.

The main goal of the CIDR service has been to fill the essential 'middle part' of the typical research path used for identifying disease genes. Investigators recruit study participants and collect their DNA. Then, a team of CIDR experts produces genome-wide genotype data for each sample, in essence determining the presence of specific genomic variants present in each DNA sample. After careful quality control, these data are returned to the original investigators. Under this model, the ICs benefit from CIDR's economies-of-scale and also share in the cost of evaluating new technologies. The investigators receive high-quality data, avoid having to keep up with technologic advances, and perhaps best of all, do not pay for the genotyping service (since the funding comes directly from the ICs).

CIDR also provides investigators with statistical expertise and analytical support. This includes playing a role in the design of the research projects, and later, the deposition of data into central databases.

At present, CIDR is one of the largest genotyping facilities in the world. The number of participating ICs has risen to 11. In the last five years, next-generation DNA sequencing was added to the menu of available technologies. Currently, Dr. Lawrence Brody of NHGRI

USA Science and Engineering Festival

NHGRI's Dr. Carla Easter (on left) explains genetic traits to students at the USA Science and Engineering Festival.

The Education and Community Involvement Branch and over 30 Institute volunteers led NHGRI's involvement at this year's USA Science and Engineering Festival (USASEF), which took place on April 15-17 at the Walter E. Washington Convention Center in Washington, DC. This behemoth of an event attracted over 350,000 visitors and showcased over 1,000 leading science, technology, engineering, and math (STEM) organizations. The NHGRI booth was visited by nearly 2,000 of those visitors, who had the chance to extract DNA from strawberries and to walk through the genetic trait tree. The USASEF is currently the only national science festival in the United States, and we are excited to have been part of it for the past six years. The festival included the collective efforts of universities, public and private organizations, and government agencies – all of which are investing in promoting interest and interaction with STEM activities.

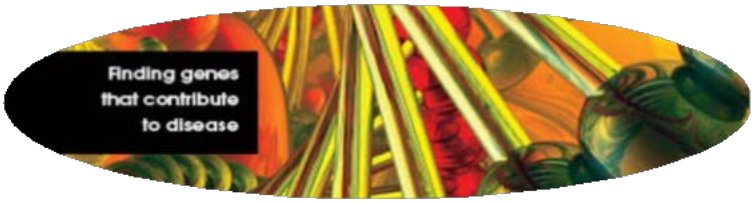
Future Directions for Undiagnosed Diseases Research: The UDN and Beyond

In March, experts and stakeholders gathered at a meeting to discuss the future of the NIH Undiagnosed Diseases Network (UDN). The UDN's goal is to improve the level of diagnosis and care for patients with conditions that even skilled experts have been unable to diagnose, despite extensive clinical investigation. The UDN grew out of the success of the Intramural NIH Undiagnosed Diseases Program (UDP), which began in 2008. Meeting participants discussed numerous key aspects of the UDN, including clinical evaluation, transition of

manages the CIDR program under a contract with the McKusick-Nathans Institute of Genetic Medicine at the Johns Hopkins University. Dr. Kimberly Doheny directs the CIDR program for Johns Hopkins University.

The genotyping and DNA-sequencing approaches used by CIDR over the years nicely illustrate the evolution of genomic technologies. In the beginning, CIDR scientists used methods to detect several hundred microsatellite markers (i.e., stretches of DNA where short sequences are repeated). As the technology advanced, they began analyzing single-nucleotide polymorphisms (SNPs, pronounced "snips"). Most recently, CIDR is using next-generation DNA sequencing to conduct whole-genome and whole-exome sequencing. The former analyzes the entire genome, while the latter analyzes just the protein-coding regions.

The accomplishments of CIDR in its first 20 years are indeed impressive. To date, CIDR's work includes ~850 published papers, ~400 completed projects, ~900,000 analyzed samples, ~600 billion genotypes and 30 trillion bases of DNA sequence generated. Even more impressive is the increasing size of projects. Early projects often involved generating data for a small number of families. Taking advantage of the decreasing costs of genotyping and genome sequencing, CIDR generated data on over 100,000 people for a single study last year.



While NHGRI supports many valuable resource projects, CIDR is distinguished by its trans-NIH nature. The cooperative spirit of all the participating ICs has been instrumental to CIDR's success, as has the consistent focus on providing researchers access to the cutting-edge genomic tools for conducting their disease-oriented research. To access the CIDR website, see cidr.jhmi.edu.

care, patient and family partnership, training, collaboration, fostering interactions, and integrating data. A report and video recording from the meeting are available at genome.gov/27564304.

Atlas of Human Malformation Syndromes in Diverse Populations

A new medical genetics resource is now available on the NHGRI website – a catalog of genetic and dysmorphologic syndromes that includes photographs of affected patients of various ethnicities (see genome.gov/atlas). NHGRI's Dr. Max Muenke and colleagues developed this resource, which is searchable by phenotype, syndrome, ethnicity, and genetic/molecular diagnosis. It is a unique collection due to its inclusion of many different ethnic groups, which will aid in the diagnosis of genetic malformations across different world populations. Now in its beginning stages, the resource will become increasingly populated with data in the coming months and years. For additional details, see genome.gov/27564852. Two relevant publications, a commentary and a review, are also available in *Genetics in Medicine*.

ASHG Global Virtual Meeting – Genetics in Your Clinic: What You Can and Should Do Now

Last month, NHGRI co-sponsored an American Society of Human Genetics (ASHG) global virtual meeting, along with several other organizations, for primary care physicians and other healthcare professionals entitled "Genetics in Your Clinic: What You Can and Should Do Now." This free virtual meeting focused on the need for clinicians to understand available genetic tests and how to use them in practice. Featured speakers shared information on genetic technologies currently available for clinical use; the limitations of these technologies; information in personal and family histories that indicates a need for genetic testing; how to interpret results in ways most useful to the patient; and when to use specialized genetic services. For more information, or to register for the 'On Demand' version of the event, visit engage.vevent.com/index.jsp?eid=782&seid=1617