Medical Xpress

North Carolina-based genetic resources fuel big scientific progress

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A series of 15 scientific papers published this week in the journals of the Genetics Society of America (*Genetics* and *G3: Genes|Genomes|Genetics*) put North Carolina at the epicenter of a scientific resource called the Collaborative Cross – a "library" of genetic diversity that scientists believe can help fast-track important discoveries about genetics and disease into new discoveries, tests, and treatments that impact human health.

Researchers have long been frustrated by promising lab results that hit obstacles on the road to human application. Sometimes this is because research in other living organisms is very limited in terms of what conclusions scientists can safely extrapolate to the human population as a whole. One reason for this problem is that organisms studied in the laboratory lack the genetic diversity of humans.

To overcome this obstacle, scientists have begun to create libraries of genetic material. These libraries – called Genetic Resource Panels (GRPs) – enable researchers to look at how genetic variation impacts living systems in a careful and systematic manner – an approach that they think will help draw more robust conclusions, often more quickly.

The Collaborative Cross, a project aimed at mirroring the diversity of human genetics in the laboratory mouse population, is one such GRP. The Collaborative Cross contains ten times the genetic diversity of a typical laboratory mouse population — a level equivalent to the natural genetic variation in humans. Furthermore, the genetic diversity is spread out across the genome of the Collaborative Cross, while the limited ancestry of typical laboratory mice means that about half of the genome lacks good data for geneticists. The Collaborative Cross fills in those gaps, and the result for scientists is a fast track to understanding and testing new treatment and prevention approaches for numerous human diseases with an underlying genetic component.

The project is led by Fernando Pardo-Manuel de Villena, PhD, in the UNC Department of Genetics and a member of UNC Lineberger Comprehensive Cancer Center, David Threadgill, PhD, a geneticist at North Carolina State University and UNC Lineberger member, and Gary Churchill, PhD, at The Jackson Laboratory. The mice are housed and 'curated' at UNC-Chapel Hill.

Pardo-Manuel de Villena is the lead author on the paper featured on the cover of Genetics, which provides the first comprehensive description of the mouse genome library, which is being shared with scientists across the country through an online resource called a genome browser.

He says, "It is important that all scientists have free access to this resource, which is a census of every genetic line we have and consolidates the work of researchers in the U.S., Israel and Australia in one central place."

The Collaborative Cross is a resource that is offered free to all scientists. The editors of *Genetics* and *G3* note in an editorial accompanying the papers, "Data sharing is particularly crucial for GRPs like the Collaborative Cross. If some pieces of the puzzle have been taken off the board . . . then the puzzle is unlikely to be completed and the community resource is compromised."

This is a big responsibility, notes Terry Magnuson, PhD, Chair of Genetics at UNC-Chapel Hill and Vice Dean for Research at the UNC

School of Medicine. "Just as a museum curator is responsible for the heritage of art in their facility, our colleagues at UNC and N.C. State University are responsible for the heritage of the mice in the Collaborative Cross. As scientists use this resource to find ways to prevent and address the genetic changes that cause disease, findings in laboratory experiments should be much easier to translate to humans."

Norman E. Sharpless, MD, UNC Lineberger's associate director for translational research, is collaborating with Charles Perou, PhD, co-director of the center's breast cancer research program, on studies of breast cancer using the Collaborative Cross. He says, "I expect that the results of this work will help human breast cancer patients. Huge consortia are successfully identifying regions of the genome associated with important human diseases like cancer and diabetes, but there are limitations in working with the human genome. The Collaborative Cross provides the best means to understand why certain genes are linked to certain diseases."

Pardo-Manuel de Villena notes that the Collaborative Cross would not be possible without the efforts of the collaborative cross consortium, a global group of scientists that includes National Institutes of Health Director Francis S. Collins, MD, PhD, and National Human Genome Research Institute scientist Samir Kelada, PhD, MPH.

Provided by University of North Carolina School of Medicine

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