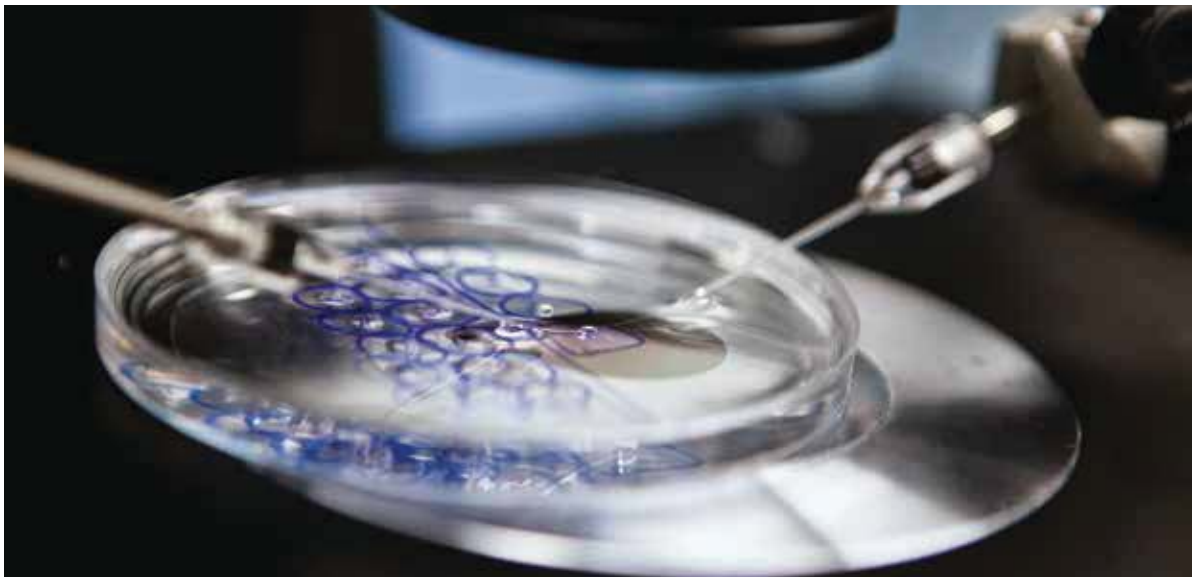
Made-to-Order Mice

Transgenic Animal And Genome Editing (TAGE) Core Lab Ushers in a Research Revolution



By knocking in a gene here, knocking out a gene there, Yueh-Chiang Hu, PhD, and colleagues are opening the door to a medical revolution that may soon produce made-to-order treatments for genetic diseases.

Hu directs the Transgenic Animal and Genome Editing (TAGE) Core at Cincinnati Children's, where a team of scientists use a new technology called CRISPR to rapidly produce gene-edited mice for research, and increasingly, for customized treatment.

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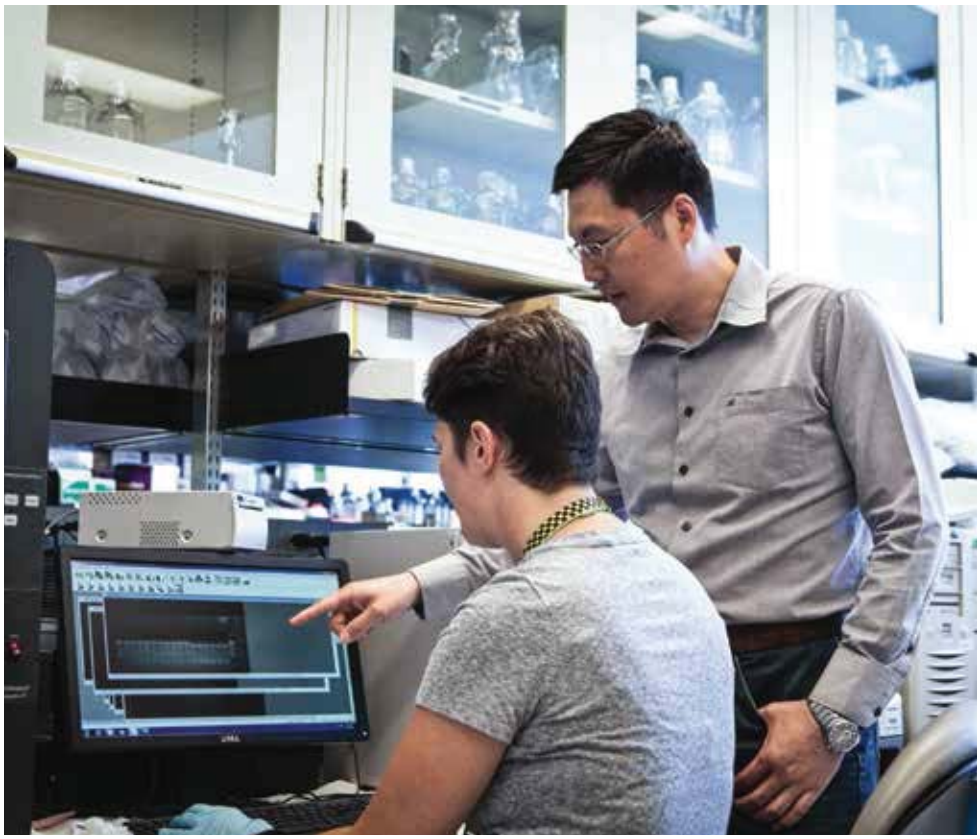
The TAGE core is among the first of its kind in the nation. Hu learned how to use CRISPR technology from one of its pioneers, while completing a post-doctoral fellowship at the MIT-affiliated Whitehead Institute. The technology allows editing, adding or removing any gene in a one-cell (fertilized egg) embryo, dramatically reducing the time it takes to produce biological models expressing specific gene combinations.

"CRISPR is changing the way we do genetic study. You can manipulate the genome in any cell type or organism you want at a previously unimaginable speed," Hu says.

With CRISPR, mouse lines can be developed in a matter of weeks instead of years, and costs have dropped from upwards of $25,000 to as low as $6,000. Since its inception, the core has created 60 new mouse lines, averaging one line a week.



Yueh-Chiang Hu, PhD, and colleagues use CRISPR technology to "edit" mouse genomes by adding or removing genes, allowing mouse lines to be developed within weeks.

The TAGE Core is critical to Cincinnati Children's success in bringing genomics to the bedside, says John Harley, MD, PhD, Director of the Center for Autoimmune Genomics and Etiology. "The facile ability to manipulate chromatin constitution in cells and whole animals opens powerful technologies for genetic insight into normal physiology and the pathophysiology of virtually any disease state," Harley says.

For knock-out mouse lines, in the past six months, 92 percent of mice developed by TAGE were born with the desired mutation. For more challenging knock-in mutations (inserting tags or changing nucleotides), about 50 percent of mice were born with the desired mutation.

Already, TAGE is making a difference for children with rare genetic diseases. Earlier this year, clinical geneticist Taosheng Huang, MD, PhD, was treating three children who suffered a set of identical symptoms including ataxia and seizures. Huang screened the children and found that they shared an otherwise unknown gene mutation.

Within two months, TAGE had developed a line of mice with the children's disease, which has allowed the team to understand disease pathogenesis and test potential treatments. If an off-label treatment can be found, the core lab will have dramatically reduced the cost and time involved in diagnosing and treating a rare disease.

"Usually it takes years to confirm novel genetic variants to be the cause of a disease, but now it is just a matter of few months," Hu says.