

New Agreements on Mice

HHMI aims to help manage the logistics and allay the cost of the ever more refined yet ubiquitous laboratory mouse.

WITH THE USE OF LABORATORY MICE skyrocketing, it's no surprise that scientists across the country face a murine housing crunch—and that's just for starters. Not only do the mice represent a significant investment of time and laboratory resources but requirements by organizations like HHMI and the National Institutes of Health (NIH) mean that researchers also have to find cost-effective ways to share mouse stocks with their colleagues and preserve them for future experiments.

“Because most institutions’ facilities are bursting at the seams, any way that you can more effectively maintain your mouse colonies will be a big benefit to the community,” says Nathaniel Heintz, an HHMI investigator at the Rockefeller University. He ought to know: Heintz has created hundreds of transgenic mice in studying the development of the mammalian brain and deposited many of them in an NIH-supported facility that makes them available at nominal cost.

More than one-third of HHMI's 321 investigators now use laboratory mice in their research, and that percentage is likely to increase. With spending on animal breeding and maintenance hitting an estimated \$47 million between 2002 and 2004, an Institute-wide initiative was required.

Enter Philip Perlman, one of HHMI's senior scientific officers, whose own research focused on mitochondrial genes in yeast—a more manageable model organism. Perlman has spent the past 18 months identifying approaches to improve the management of mouse colonies in HHMI laboratories so that resources could be freed for more research.

After consulting with HHMI investigators, several NIH scientists, and experts in mouse genetics and animal care, the Institute has taken two steps. First, it has entered into a new agreement with the

Jackson Laboratory (TJL), the leading independent center for mouse genetics in the United States, as well as one of three NIH-supported mouse repositories and home to two HHMI investigators. The agreement focuses on improving ways to archive and distribute valuable strains of mice and develop better tools for managing mouse colonies. Second, HHMI is running a short-term trial program with Transnetyx, a Memphis-based company, to outsource genotyping, the important task of determining the genetics of a mouse.

“This gives us an opportunity to invigorate our historic relationship with the Jackson Lab by funding projects that are relevant to the aims of both TJL and HHMI and are also cutting-edge,” says David Clayton, HHMI's chief scientific officer, noting that HHMI has collaborated with TJL since the 1980s.

About 75 percent of the nearly 3,000 mouse strains at TJL are stored as frozen embryos or sperm. Cryopreservation is efficient, but recovering live mice requires techniques not widely used in HHMI labs. So part of the initiative focuses on training lab staff and developing better cryopreservation approaches. Other goals include creating more effective ways to tag individual mice and enhancing mouse colony management software that was largely developed by HHMI investigator Simon W.M. John.

Perlman says the Institute is planning another project to help defray the costs of archiving mutant mice developed in HHMI labs. With HHMI partially covering the expenses, Perlman expects the labs to break even in the first year. “We're always looking for ways we can improve how research is being done,” he notes.

Because many mutant mice do not look any different from wild-type mice or from other mutant mice, DNA genotyping of every mouse born in a mouse



“We're always looking for ways we can improve how research is being done.”

PHILIP PERLMAN

facility is a necessary part of mouse research. This genotyping determines which individual mice have certain mutant and wild-type genes. It is a time-consuming and costly activity, which is why HHMI is funding the pilot program with Transnetyx. More than 70 HHMI investigators are now trying out the company's automated approach to mouse genotyping.

“This is the kind of work that is repetitious and not very interesting for a researcher to do, but we have to know the answer,” says Richard A. Flavell, an HHMI investigator at Yale University School of Medicine and one of the scientists participating in the program.

Each of these initiatives can make mouse research in HHMI laboratories a little more efficient and can potentially reduce the cost of mouse breeding for research. Notes Perlman, “Whichever projects prove to be effective for HHMI researchers will also be useful for the wider community of mouse researchers.” ■