OPINION

Hundreds of mouse mutants added to virtual 'catalog'

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More than a decade ago, I chose to do my Ph.D. project using yeast as a model organism. Yeast falls trillions of cells short of modeling the complex dynamics of the human body. On the other hand, yeast is easy to manipulate genetically, making it a powerful and appealing tool: Just about any yeast mutant I could imagine was listed in a convenient catalog.

The same may soon be said of mice — a much more relevant species in which to study human health. In 2011, researchers announced an ambitious international venture to engineer thousands of mice, **each lacking a single gene** in the mouse genome[1]. The researchers had created 17,000 stem cell lines — the starting point for genetically engineered mice. In each mouse, they would be able to switch a single gene on, or off, at will.

The consortium, now called the **International Mouse Phenotyping Consortium** (IMPC), is creating these mice and carefully detailing their features. They plan to release data from the first 300 mice by mid-June and to complete 15,000 by 2021.

The researchers are putting the mice through a battery of behavioral tests, including measures of anxiety and their startle response — often used to test mouse models of schizophrenia and autism.

One of the goals of the project is to standardize mouse studies, which have been beset by **inconsistent data**. For example, mutant mice that show social deficits when made by one team may seem happy to interact with their peers when made by another. The researchers invariably conclude each time that the mice's **different genetic backgrounds** are to blame for the inconsistent results.

According to an editorial published 22 May in *Nature*, researchers are also worried about the

impact of new technologies that make it easy to make mutant mice[2]. If each lab were to engineer its own mouse mutants, the field would be flooded with inconsistent models (not to mention wasting valuable research time and money).

The consortium proposes a simple solution: It plans to make each mouse from the same strain and provide a baseline analysis of the model. The mice will live in repositories in 12 countries. This instant access to every model should speed up the pace of research.

Not surprisingly, the solution also creates problems of its own. Because each individual carries his or her own unique combinations of genetic variants, creating mice that all have the same background would miss the interactions between variants that can alter a mutation's impact.

"The more combinations [of mutations] you have, the better you can represent how your gene may interact with other genes," says **Valerie Bolivar**, director of the Mouse Behavioral Phenotype Analysis Core at the New York State Department of Health in Albany. "[This] is a great way to start. But as humans, we're so outbred that it may not give us the complexities we need."

References:

1: Skarnes W.C. *et al. Nature* **474**, 337-342 (2011) **PubMed**

2: *Nature* **509**, 399 (2014) **PubMed**