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New lab mice cut search for genetic links to disease by more than a decade

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With a 95 percent genomic similarity to humans, mice have long been used to learn about the genetic causes of human disease. Once researchers can shine a light on the genetic factors that cause disease in mice, they can start to develop prevention and treatment options to protect the human population.

But this process, called genetic mapping, is a long and difficult road, made more challenging by the 5% difference between the humans and lab mice. Now Prof. Fuad Iraqi of Tel Aviv University's Sackler Faculty of Medicine is closing the gap with an international project called Collaborative Cross. The project is developing lab mice with increased genetic diversity, making them more advantageous for genetic research related to human health.

The new population will offer 1,000 genetic strains within a fixed genotype — the composite of the entire genetic makeup of an organism. This is a marked improvement on the previously existing 450 genetic strains of lab mice with varying genotypes, making Prof. Iraqi's new strain ideal for genetic mapping. And with these mice, researchers will be able to identify a gene associated with a particular disease within two to three years instead of the 10 to 15 years it takes now, says Prof. Iraqi.

The research has been published in the journals *Nature*, *Nature Genetics*, and *Genome Research*, and receives its primary funding from the Wellcome Trust in the UK. The project itself is a collaboration among Tel Aviv University, Oxford University in the UK, North Carolina State

University in the US, and Perth University in Australia.

Expanding the family tree

Genetic determinants play an important role in a variety of conditions from diabetes and obesity to different types of cancers. For example, mutated forms of the genes BRCA1 and BRCA2, which can be genetically inherited, are associated with higher rates of breast and ovarian cancers. This kind of genetic diversity in humans influences diseases and helps researchers track their genetic causes. According to Prof. Iraqi, the fact that humans have many genetic variances for the same gene means that they are "outbred" among individuals from different families. To best identify the genes that cause a disease, scientists require a test population with these same variances.

But standard strains of lab mice are inbred. Their genetic similarities make it difficult to identify the connection between particular traits and the specific genes responsible. The Collaborative Cross project answers this deficiency in lab mice by increasing genetic variation as much as possible — a powerful and unique resource for research.

In order to develop a genetically enriched population of lab mice, the researchers took five classic inbred strains of mice and mixed them with three wild-derived strains, mating brothers and sisters for generations in order to reshuffle the genetic deck but keep the genotype consistent. With an increased range of traits, including differences in appearance such as fur color and tail length, this new mouse population more closely mimics the genetic diversity of humans, says Prof. Iraqi.

Building a better mouse

The various genetic strains are housed within participating universities

across the world, notes Prof. Iraqi, and are already available for order by researchers. Within Tel Aviv University's laboratories, there are currently genetic mapping projects for a variety of diseases, including diabetes, various types of cancers, dental infections, bacterial infections, and fungal infections — all making use of these genetically enriched mice.

Prof. Iraqi has already used the new mouse population to identify a group of genes that are crucial to susceptibility to infection when exposed to Aspergillus fumigatus, a soil fungus that causes respiratory infections in humans. Getting to this point took only a year — compared to the 15 years it might have taken using standard lab mice, he calculates.

Provided by Tel Aviv University

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