Major mouse study reveals the role of genes in disease

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The functions of around 150 genes have been discovered by scientists across Europe in a major initiative to try to understand the part they play in disease and biology.

Since mice share 90 per cent of their genes with humans they are one of the best organisms to help us understand human genetics. The European Mouse Disease Clinic (EUMODIC) brought together scientists from across Europe to investigate the functions of 320 genes in mice. Over half of these genes had no previously known function, and the remaining genes were poorly understood.

Over 80 per cent of the mouse lines assessed had a characteristic that provided a clue to what the missing gene's role might be. If the mouse fails a hearing test, for example, it suggests the missing gene might have a role in hearing. In total, they carried out over 150 different tests on each mouse line.

The researchers classified 94 genes linked to disease into three categories: bone and skeleton, metabolism, and neurological and behavioural disorders.

One of the genes discovered, Elmod1, belongs to a large group of genes active in the brain for which there was no information about its function. This work revealed that mice with a faulty Elmod1 gene had lower blood glucose levels and lower body weight. It also revealed that this gene was involved in gait and the animals had a lower grip strength.

In order to study gene function, the EUMODIC consortium produced mouse lines which each had a single gene removed. These mouse lines were then analysed in mouse clinics, where each mouse was assessed by a series of tests and investigations, allowing the researchers to establish the functions of the missing genes.

EUMODIC was the first step towards the creation of a database of mouse gene functions, a vision now being realised by the International Mouse Phenotyping Consortium (IMPC).

The IMPC incorporates 18 centres from across the globe with the aim over the next ten years of uncovering the functions of all 20,000 genes in the mouse genome. IMPC builds on the groundwork and achievements of EUMODIC in establishing the procedures and processes to identify and catalogue the functions of genes.

Professor Steve Brown, Director of the MRC Mammalian Genetics Unit

at Harwell and the coordinator of the EUMODIC consortium, said: "EUMODIC leaves a powerful legacy that will live on in the IMPC and the data and resources it has provided for scientists. EUMODIC and IMPC will be truly transformative for medical research by revealing the roles that different genes play in disease."

"The standardised practices that have been developed through this research allow multiple centres to work in concert to generate robust, reproducible data," says Dr David Adams, Experimental Cancer Genetics Group Leader at the Wellcome Trust Sanger Institute, a major contributor to the EUDOMIC Consortium. "In the long term, this streamlined approach and the availability of the data from these studies will significantly reduce the number of animals used in research."

This was the first time such a project has been attempted on this scale with multiple centres cooperating together from different countries. The consortium had to establish new standardised procedures to generate and assess the mouse lines and a central European database to store all the data.

The aim of the project was to understand more about genes we currently know very little about, and open up new avenues for research into the genetics of human disease. All the findings have been made publically available, allowing other scientists to use them in their own research.

More information: "Analysis of mammalian gene function through broad based phenotypic screens across a consortium of mouse clinics." *Nature Genetics* (2015) DOI: 10.1038/ng.3360

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