

## Mouse Genetics Programme

Karen Steel, Niels Adams, Jacqui White,  
Gordon Dougan, Bill Skarnes, Seth Grant,  
Pentao Liu, David Tannahill, Lorraine Everett,  
David Adams and Allan Bradley

### Introduction

As we discover more about the role of genes in disease, it is becoming clear that we cannot easily predict the function of a gene by its sequence alone, but that we need to examine each gene in the context of a whole living organism. The Mouse Genetics Programme aims to make a significant impact on our understanding of the function of genes and their role in disease by generating large numbers of mutant mice and screening them for characteristic features of disease.

We are exploiting the growing resource of targeted mouse ES cells produced by the ES mutagenesis program at the Sanger Institute and plan to select at least 250 (up to 500) each year to generate new mouse mutants. Age-matched cohorts of these mutants will be subjected to a standard battery of phenotyping tests. Both mice and data will be made freely available to the scientific community.

### Programme collaborations

We are actively soliciting suggestions from the academic community for genes to add to our list and phenotypic screens to include in our battery of tests. More than 500 genes have been requested by 50 individual

researchers, and each request is considered only if the proposer is willing to study the mutant if we are able to construct it. We have established collaborations with several outside groups with diverse areas of expertise to carry out focused screens. We are one of the four main phenotyping centres in the EUMODIC programme, with funds from the EC to study a wide range of phenotypic measures in around 40 new mutant lines each year.

However, the philosophy of the core-funded phenotyping battery is to include only tests where we have a collaborator who is willing to take on for further definitive study the mutants with the feature of interest, and to reduce the number of mice required to a minimum consistent with detecting a robust phenotype. We also aim to include as many challenges as possible to maximize our chances of finding new phenotypes.

### Recent achievements

In addition to building up the network of collaborators, our recent focus has been on piloting the phenotyping tests in control cohorts of wildtype mice and existing mutants, and establishing the informatics structure for managing the workflow and data. The first

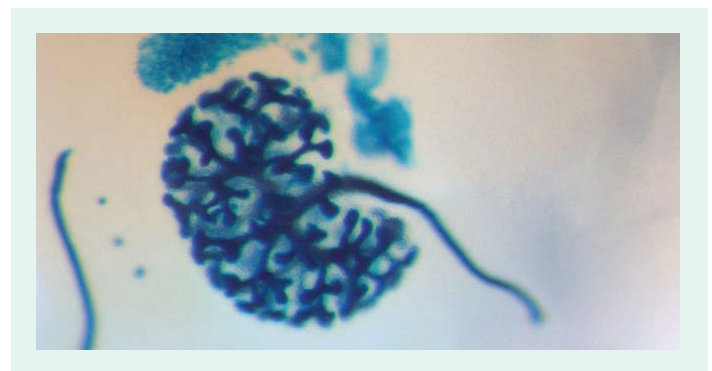
mutants from the targeted ES cells are just beginning to emerge. We have some early findings of skeletal malformations and a significantly increased rate of bacterial clearance by shedding from the gut in the infectious challenge amongst the first handful of mutants studied.

### Publication

**The Mouse Phenotype Database Integration Consortium (2007) Integration of mouse phenome data resources. *Mammalian Genome* 18: 157–63**



*Expression of Gata3 in an early-stage mouse embryo, showing a distinctive pattern (in blue) in specific tissues.*



*Expression of Gata3 in an embryonic kidney.*