Abstract
I will review the methods for identifying the genetic basis of behaviour in mice. Starting from crosses between inbred strains I will cover the methodologies that have been used to map the location of sequence variants that differentiate laboratory strains of mice. Factors that determine our ability to find genes will be emphasized, including problems surrounding the identification of loci, establishing correct significance thresholds and the more intractable problem of modelling the correct genetic architecture of complex traits. I will review the new resources that are being developed, including the collaborative cross and outcross, and consider their advantages, again in the light of the need for gene identification. I will compare these quantitative genetic approaches to methods that use engineered mutations, either by mutagenesis or by homologous recombination of ES cells, to identify genes involved in behaviour. My review aims to teach students how to weigh up the available strategies and decide which is most suitable for their purpose.

Biography
For the last ten years, my laboratory has been investigating the genetic basis of common psychiatric disorders, in particular the determination of the genetic basis of anxiety and depression in animal models and in humans. I was the first to show that the genetic basis of an animal model of human anxiety is amenable to mapping and that the genetic basis is relatively simple. Since then I have developed novel strategies for fine-mapping the genetic loci using outbred animals. I was the first to propose the use of outbred heterogeneous stocks for genetic mapping, and have gone on to develop the methodology that makes the identification of susceptibility genes possible using this approach. My method has the potential to become a general tool for finding genes of biomedical importance in mouse models of disease. Most recently I have shown that heterogeneous stocks can be used to map multiple phenotypes, opening up new possibilities for a systems level approach to complex traits. I have also investigated the genetic basis of personality traits in humans that predispose to depression and anxiety. I have already shown that it is possible to identify susceptibility loci by selecting genetically informative families from extremely large samples, and my work indicates that some of the same loci are likely to act in both rodents and humans in regulating levels of fearfulness. In the last four years I have set up the largest study of the genetics of depression which is recruiting 12,000 women in China. The initial aim is to identify susceptibility loci using genome wide association. In the longer term this unique resource will be used to explore the biological and environmental causes of one the commonest psychiatric diseases.