

Year of the Rat

The usefulness of the rat as a genetic model of complex traits and disease is increasing, with the development of a number of genome-wide resources enabling high-resolution genetic analysis. This special focus on rat genetics surveys the landscape and highlights the range of discoveries that are now possible.

The laboratory rat was the first mammalian species domesticated for scientific research and has been a well-studied animal model across the biomedical sciences. Inbred strains of rats, first established by Helen Dean King nearly a century ago, are used for research into a broad array of human conditions and diseases, including addiction, aging, autoimmunity, cardiovascular disease, hypertension, metabolic disorders and cancer, to name just a few. The rat is also widely used in the pharmaceutical industry to assess the efficacy and toxicity of drugs, owing to its well-studied physiology and the relative ease of experimental intervention. Despite this history, the rat has lagged behind the mouse as a model in which to pinpoint the genetic contributions to disease.

Although the mouse is still the mammalian genetic model of choice, the gap may be closing. Dedicated funding from government agencies in the United States (Rat Genome Project), the European Union (EURATools Consortium) and Japan (National Bio Resource Project for the Rat) has spurred the development of a suite of new genetic and genomic resources that are available to investigators. These include a high-quality sequence of the rat genome, high-resolution maps of genetic variation and the integration of rat genomics with comparable resources associated with the human and mouse genomes. As such, it is now possible to map the genetic variants and mutations that underlie complex disease-related phenotypes in the rat in a much more efficient manner.

As the pace of discovery quickens—and in light of the fortuitous alignment of the Chinese calendar in 2008—the time seemed right for a special focus that would showcase the increasing power of rat genetics for a broad readership. This focus is something of a departure for the journal, as it features not only commentaries, but primary research as well. This view of the field is not meant to be exhaustive, but should provide the interested reader with a better sense of what it is now possible to achieve in the study of complex traits in the rat. Two introductory commentaries set the stage. The first,

entitled “Progress and prospects in rat genetics: a community view,” represents the community’s overview of the field, as well as its vision for the future, and is informed by comments from more than 250 geneticists. This ‘white paper’ should serve as a starting point for anyone interested in an introduction to rat genetics for the foreseeable future. The second, from Simon Twigger and colleagues, discusses the status of the sequence of the rat genome and the variety of online bioinformatics resources that are available. A short correspondence from Tadao Serikawa and colleagues describes the Kyoto University Rat Mutant Archive, an increasingly important repository that houses cryopreserved ENU-mutagenized sperm.

The primary research encompasses papers that present both new biology and new resources for genetic analysis of the rat. In particular, three papers associate genetic variants with complex traits or diseases. Norbert Hubner and colleagues show that differential regulation of *Ephx2*, encoding soluble epoxide hydrolase, is associated with susceptibility to heart failure. Osteoglycin is implicated in the regulation of left ventricular mass in a paper by Stuart Cook and colleagues. Timothy Aitman and colleagues report that *Jund* is a determinant of macrophage activation and is associated with susceptibility to glomerulonephritis. New resources are presented in two papers: the first, by Edward Cuppen and colleagues, describes regions of copy number variation and their non-random distribution throughout the rat genome. Finally, the STAR Consortium reports the identification of nearly 3 million newly identified SNPs, as well as accurate and complete genotypes for more than 20,000 SNPs in 167 inbred strains. The importance of this resource for fine mapping genetic variants underlying complex traits is readily apparent, and, along with the two commentaries, it will be freely available to all.

We thank the authors for their excellent contributions to this special focus, as well as the referees, whose thoughtful reviews improved each submission. We trust that the pieces featured herein will serve as a helpful guide to the genetics of this increasingly important model organism. ■