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## GENOMICS

# Year of the rat

The world's first laboratory mammal has become the second, after the mouse, to have its genome sequenced.

As a genetic model, the rat has been running second to the mouse for a long time, but it remains the pre-eminent model species for a swathe of other biomedical research areas, including physiology and drug development. In sequencing the 2.7-Gb rat genome, the Rat Genome Sequencing Project Consortium (RGSPC), led by the Human Genome Sequencing Center at Baylor College of Medicine, has provided an explicitly genetic framework that will be invaluable for interpreting the experimental data that are generated in such research areas.

The RGSPC combined whole-genome shotgun sequencing and bacterial artificial chromosome (BAC) sequencing in assembling the draft rat genome: a strategy that paid off both in terms of speed (<2 years) and quality of the draft sequence (mostly close to 'finished' quality).

This third mammalian genome sequence provides a window on genome evolution over a much shorter time

frame than was previously possible because the rat and mouse lineages split much more recently (12–24 million years ago (mya)) than the human lineage diverged from rodents (75 mya).

Although the rat genome encodes a similar number of genes to the mouse and human genomes, there have been some notable changes since it diverged from the mouse. In particular, some gene families that are involved in immunity, chemosensation, detoxification and proteolysis have expanded, almost certainly reflecting the adaptive importance of these processes during the evolution of the rat lineage.

Having the rat genome sequenced also allows insights into the characteristics and evolution of mammalian genomes in general. For example, we now have a much better idea of what constitutes the 'core' eutherian mammal genome: this corresponds to ~40% of the euchromatic rat genome. Moreover, the RGSPC was able to disentangle which differences among the three sequenced mammalian genomes occurred in the human lineage, which were rodent-specific and which were characteristic of more exclusive rodent groups that are represented by the rat and the mouse. In general, it seems that there has been much more action (such as rearrangements

or base substitutions) in the rodent lineages than in the primate.

However, in terms of genomics as a field, perhaps the most notable difference between the draft of the rat genome compared with those of the human and mouse genomes is that it is unlikely to be upgraded or finished anytime soon. As the RGSPC explicitly acknowledges, this decision reflects the lack of funding support for the increased effort that finishing requires, as well as the pressing need to prioritize new genomes. Until the vision of very low-cost sequencing is realized, we should expect many more eukaryotic genomes to be sequenced to a 'good enough' standard rather than the finished standard that allows difficult and often interesting regions to be resolved.

Nick Campbell

## References and links

**ORIGINAL RESEARCH PAPER** Rat Genome Sequencing Project Consortium. Genome sequence of the brown rat yields insights into mammalian evolution. *Nature* 1 Apr 2004 (doi:10.1038/nature02426)

**FURTHER READING** Jacob, H. J. & Kwitek, A. E. Rat genetics: attaching physiology and pharmacology to the genome. *Nature Rev. Genet.* 3, 33–42 (2002) | Mouse Genome Sequencing Consortium. Initial sequencing and comparative analysis of the mouse genome. *Nature* 420, 520–562 (2002) | Rat genome issue. *Genome Res.* 14, 493–786 (2004)

## WEB SITE

Rat Genome Project:  
<http://www.hgsc.bcm.tmc.edu/projects/rat>

