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Sequencers come together

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An international collaboration of genome sequencing teams previously at odds over strategy puts aside its differences this week in Nature to publish the third complete mammalian genome sequence. The Rat Genome Sequencing Project Consortium combined whole genome shotgun (WGS) methodology with a clone-by-clone approach to produce a high-quality draft covering over 90% of the brown Norway rat (*Rattus norvegicus*) genome.

The team sequenced bacterial artificial chromosome (BAC) clones to produce a 1x-coverage of the rat genome and used data from each BAC to identify the matching sequences from the WGS data using its own purpose-built software. "It was a real combined strategy, bringing the two things together in real time," said Richard A. Gibbs, director of Baylor College of Medicine Human Genome Sequencing Center and principal author of the paper.

Sequencing teams have been engaged in a robust debate over the merits of WGS. Despite the success of the rat sequence project - and the consortium say there are no plans to improve the quality of the draft, because of the high cost - the jury is still out on the best way to obtain mammalian sequences.

"I would say what they've done is opt for a kind of half-and-half approach, where they used not only the WGS - because they knew they weren't going to finish it - but also used skimmed BAC sequences to give them the mapping information they know was so important for the human sequence," said Ian Dunham, senior investigator at the Sanger Institute, who was not involved in the study.

The collaboration has produced a wide range of publicly available resources. Gibbs said that the rat sequence in the database is the strongest product of the study, along with the collection of BAC clones themselves that are now available. "The next thing that's been generated is what I call the level of knowledge that's been advanced by the rat being compared to the other species and the analysis that's been performed," said Gibbs. "In terms of evolution, the third species has really allowed us to triangulate what's going on between all the mammals."

Rudolf A. Raff, professor in the Department of Biology, Indiana University, said he would not want to stop at only three mammalian genomes because he thought it only gave the barest phylogenetic sampling. "There are many other orders of mammals from bats to elephants where we don't have any sampling like this." Raff, an evolutionary biologist not involved in the study, said, "I think there is a lot going on in genomic evolution, and you see it even in these particular samples."

Given that in the next round of genomes to be sequenced the dog and cow have been afforded high priority but other organisms remain to be decided, Raff urged that scientists consider candidates' phylogenetic position so that a good sense of the nature and evolution of vertebrate and mammalian genomes can be achieved.

The rodent-human genomic comparison reveals that all but a handful of human disease gene orthologs are present, underscoring the importance of the rat as a model organism of human disease, according to Christopher P. Ponting, professor of bioinformatics at the University Of Oxford and a member of the team. "I think this gives us an idea of how to handle the primate genomes that are going to come online

soon, so the observations provide a foretaste of the fruits of comparing our genome - the human genome - with those of other primates," he said.

"It's only when you take several organisms and consider their evolutionary histories and look at the common elements [that] you can really understand some of the general rules," Gibbs said.

References

1. *Nature*, [http://www.nature.com/]

2. *Rattus norvegicus* (Norway rat and brown rat), [http://www.bbc.co.uk/nature/wildfacts/factfiles/273.shtml]

3. Richard A. Gibbs, [http://www.bcm.tmc.edu/pa/gibbs.htm]

4. Holding C: Celera defends human sequence *Genome Biology*, February 20, 2004., [http://genomebiology.com/researchnews/default.asp?arx_id=gb-spotlight-20040220-01]

5. Team 62: Molecular Genetics and Proteomics, [http://www.sanger.ac.uk/Teams/Team62/]

6. Rudolf A. Raff, [http://www.bio.indiana.edu/facultyresearch/faculty/RaffR.html]

7. Powledge TM: How many genomes are enough? *Genome Biology*, November 18, 2003., [http://genomebiology.com/researchnews/default.asp?arx_id=gb-spotlight-20031118-01]

8. Powledge TM: High-priority genomes announced *Genome Biology*, September 13, 2002., [http://genomebiology.com/researchnews/default.asp?arx_id=gb-spotlight-20020913-02]

9. Christopher P. Ponting, [http://www.mrcfgu.ox.ac.uk/ponting.htm]