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Recount slashes number of human genes

18:00 20 October 2004
NewScientist.com news service
Andy Coghlan

Humans have just 20,000 to 25,000 genes - well down on previous estimates of 27,000 to 40,000, says the latest analysis of the gene-containing portion of the human genome.

And a separate study has found detailed flaws in "shotgun" sequencing, the more rapid of the two methods used to sequence genomes.

The latest gene count reveals that researchers overestimated the number of genes lurking in heavily-duplicated regions of the human genome, which are extremely tricky to sequence because they are repeated DNA sequences.

"Finding the genes is hard, even in a finished sequence," says Bob Waterston of the University of Washington in Seattle, US, and a lead author of the latest genome analysis.

"But the main point is that we have the genome correct now," he says. "We've got through the many hard parts of the genome, and these included recently duplicated segments which were impossible to study in the earlier drafts."

Evolution and disease

By analysing these "difficult" duplicated regions, Waterston and his colleagues in the International Human Genome Sequencing Consortium discovered that 1183 of the genes had recently been acquired through duplication and the evolution of pre-existing genes.

"These segments are rapidly evolving and appear to be particularly prominent in primate and great ape genomes," says Waterston. "We can at last begin to learn about these and find out how they've contributed to evolution and disease."

A second study has identified shortcomings in shotgun sequencing, the quick fire method of sequencing invented by Craig Venter, founder of Celera Genomics in Rockville, Maryland, US.

Instead of painstakingly amplifying and sequencing each segment of human DNA in cloned bacteria - the traditional method of sequencing - Venter found a way to sequence an entire genome in one go. He did this by smashing it into fragments then reassembling it into the correct order with powerful computer algorithms.

Venter's accelerated method of sequencing precipitated a race between his team at Celera and an international team of publicly funded scientists. But the teams drew in February 2001.

Method of choice

However, the latest analysis - a comparison of Venter's original shotgun sequence with a recent

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public draft - has revealed flaws in shotgun sequencing. It failed to pick up many duplicated regions, which have now been deciphered.

“We found that duplicated regions were not properly assembled by the [shotgun] approach,” says Evan Eichler, whose team at the University of Washington School of Medicine in Seattle identified the flaws. “These regions are important for human genetic disease.”

But Eichler says that the errors do not invalidate the shotgun sequencing method, currently the method of choice for rapid sequencing. The key is to identify regions where shotgun sequencing does not work well, and to use the slower, cloning approach to tidy up those particular regions.

Eichler’s colleagues included Granger Sutton and Aaron Halpern, two co-pioneers of shotgun sequencing with Venter, now working with him at the Venter Institute, also in Rockville, Maryland.

Halpern says their new work highlights problems in the 3% to 5% of the gene-coding regions which contain duplications. “We’ve known for a long time that long duplicated repeats are the Achilles heel,” he says.

“Every technique has its limitations, and it’s good to know what they are,” says Sutton. “Now, we know how much to revisit and tidy up.”

Journal reference: *Nature* (vol 431, p 927 and 931)

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