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The man within: enthusiasts will be able to examine the genetic make-up of Craig Venter.

ations between the two sequences, including single nucleotide differences, sequence insertions and deletions, and differences in the number of copies of a given gene. Some 44% of Venter's genes contained a genetic difference between copies found on each chromosome. Venter's two sets of chromosomes differed by 0.5%, suggesting that there may be seven times more DNA variation than previously expected, says Levy.

This approach provides a clearer picture of the human genome, says Edward Rubin, director of the Joint Genome Institute in Walnut Creek, California. Before, the sequence gave a "statistical view" of the genome, Rubin says. "And in fact the genome is not statistical, it's really a linear array of bases."

Venter notes that single genetic changes are unlikely to seal his fate. "I take it very seriously," he says. "But most diseases are going to be some huge compilation of human factors and environmental factors." Witkowski agrees, but says that reading about someone's genome can strike an emotional chord. "Somehow there's a sense that when you tell people that sequence, you're telling them in a very deep way about yourself," he says. "It's like looking at their medical records." ■

Heidi Ledford

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DNA probe finds hints of human

A groundbreaking analysis of Neanderthal DNA that suggested they interbred with humans was based on samples contaminated with human DNA, a new study suggests.

The study¹, published on 28 August in *PLoS Genetics*, reanalysed about one million base pairs of fossilized Neanderthal DNA that had been analysed in a paper published last November in *Nature*². The *Nature* paper and a paper in *Science*³ published the same week on 65,000 base pairs were the first reports on Neanderthal nuclear DNA.

But around 80% of the sequences in the *Nature* paper are modern human DNA, not Neanderthal, claims Jeffrey Wall, an evolutionary geneticist at the University of California, San Francisco, who led the *PLoS Genetics* study. This indicates that human genetic material was somehow introduced into the samples. This known risk is increased by the closeness of the two species — the 3-billion-base-pair genomes of a human and a Neanderthal differ by less than 0.5%.

The results in the *Nature* paper suggested that there was interbreeding among Neanderthals and humans in their common European home ground before Neanderthals became extinct 30,000 years ago. The *Science* article found no genetic evidence of interbreeding.

Svante Pääbo, senior author of the *Nature* paper, concedes that his group at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, had problems with contamination. These



Neanderthal DNA has been reanalysed, leading to suggestions of human DNA contamination.

prompted him to change laboratory procedures and to add controls late in 2006, after the paper was published. "I agree with [Wall's] analysis," Pääbo says. "Their observations are formally correct."

Pääbo's co-author Michael Egholm, who is research vice-president at 454 Life Sciences in Branford, Connecticut, adds: "There is no denying contamination. It was one of the dangers of doing this." But ongoing analysis indicates that human contamination in their study was just 30%, Egholm adds.

There had been intense debate over the contrasting results in the *Nature* and *Science* papers, which analysed the same 38,000-year-old Neanderthal bones from Croatia using different sequencing methods. Pääbo's group used 454's rapid 'direct sequencing' approach, whereas the *Science* team, led by Edward Rubin of the Joint Genome Institute in Walnut Creek, California, used a traditional method using cloned DNA and bacteria to generate the base pairs.

The studies gave different estimates for the time Neanderthals diverged from humans — the *Science* article pegged it at 706,000 years ago, whereas the *Nature* paper set it at 516,000 years ago. Wall's study confirms the 706,000-year divergence date. The probable human DNA contamination led to the more recent date and may have led to the suggestion of later interbreeding, Wall says.

The *Nature* paper also found more similarities between genetic variations called SNPs (single nucleotide polymorphisms) in Neanderthal and human DNA than the *Science* paper, even after allowing for the *Nature* group's larger number of base pairs. Pääbo's team reported that about 30% of the SNPs in the Neanderthal DNA are derived — that is, the mutations occurred — in today's humans.

Pääbo acknowledges there is "a potential problem" with the presence of these human SNPs in the Neanderthal sequence. These same discrepancies were noted by Rubin's group. "We had concerns," says Rubin. "We suspected some of the issues raised by Wall."

Both Pääbo's and Rubin's groups expect to publish further Neanderthal sequences from other specimens that each group is studying. Pääbo and Egholm say their analysis will address the anomalies in their *Nature* paper. ■

Rex Dalton

1. Wall, J. D. & Kim, S. K. *PLoS Genet.* doi:10.1371/journal.pgen.0030175.eor (2007).
2. Green, R. E. *et al. Nature* **444**, 330–336 (2006).
3. Noonan, J. P. *et al. Science* **314**, 1113–1118 (2006).