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Human genome project completed

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It's not completely complete, and perhaps never will be. But the version of the human genome sequence that opened for business yesterday (April 14) at the University of California-Santa Cruz is so accurate that scientists will be consulting it for the next several centuries, Francis Collins, who heads the US National Human Genome Research Institute (NHGRI), told us.

"You can think of this as the end of the high-throughput phase of human sequencing. The fact that it's yielded up 99% of the gene-containing DNA at this level of accuracy means that almost everybody who is looking for answers from the genome will find it in the most final form that they ever could have dreamed of," Collins said.

The remaining gaps, numbering about 400, comprise about 1% of the gene-containing euchromatin. "We've known for a long time that there are parts of the human genome that cannot be reliably sequenced, or even in most instances cloned, because they're unstable in all known vectors." Collins said. The unclonable bits include the long, monotonous repeats in the centromeres, plus islands of material scattered across the euchromatin on the 46 human chromosomes. "People feared those might involve a significant proportion of the euchromatin. But we banged away and have basically gotten down to the ones that are just absolutely recalcitrant."

NHGRI would still like to rescue those bits if somebody can come up with the right technology. "We've been funding efforts to do that for several years. So far they have not yielded up a method that works," Collins said.

But nitpicking about the missing human DNA was itself missing from the celebratory press conference in Washington DC yesterday. Millions of people might not be watching the announcement on television, noted Mark Walport, director designate of the UK's Wellcome Trust. But the Human Genome Project is a leap forward for mankind infinitely more complex than any lunar landscape, he said. The project was an international collaboration among 18 institutions, but the largest contributor was the Wellcome Trust Sanger Institute, which carried out nearly one third of the work.

How long it will take to translate the human genome sequence into health care is unpredictable, but the process has begun, Walport noted. Drugs are already being designed to target the BRAF protein; mutations in the *BRAF* gene were revealed by Sanger Institute researchers last June to be involved in 70% of malignant melanomas.

Sanger researchers also made another critical contribution, Walport pointed out. They argued that data generated by sequencers should be posted on the web immediately and be available to anyone free of charge. That principle of open access to genome data may be extended to other large projects, such as the International HapMap Project.

Wellcome also underwrote Ensembl, which presents the free genome data in a user-friendly gene browser. An annotated assembly will be released on the main Ensembl site in July, and researchers there say they are working on a fully-featured Ensembl build with cross-references to other datasets (including microarrays) and a data mining interface.

Robert Waterston, who heads the Genome Sequencing Center at Washington University in St. Louis, recalled the original announcement that a working draft of the genome was complete, a huge media event orchestrated by the White House in June 2000. The final 10% has been the biggest challenge, he said, but in the past three years, researchers have closed 99.5% of the gaps in the working draft, he said. The error rate is down to 1 per 100,000 bases, and we now have the full sequence of almost every gene. "Press conferences may come and go, but the sequence will remain," he said.

In one sense, the Human Genome Project can never be complete, as there are billions of people, each with a different genome. "Completing the Human Genome Project requires attention to that, and recognition of all the genetic variation that's responsible for physiological differences among people, as well as susceptibility to various diseases," said Bert Vogelstein, the prominent cancer geneticist, who is at Johns Hopkins University in Baltimore.

"But," Vogelstein told us laughingly, "it's certainly more finished than it was when it was first finished!"

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