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LETTERS

E. coli Sequencing

Rachel Nowak (Research News, 13 Jan., p. 172) describes the current status of the *Escherichia coli* genome sequencing project and the possible termination of funding for Fred Blattner's program. While it is true that from the beginning (1989) I have been critical of the manual sequencing method used by Blattner's group for large-scale genome sequencing, this is not the time to abandon his effort. According to the article, Blattner has completed 1.4 megabases of the *E. coli* genome, with most (1.0 megabase) being completed in the last year. If the National Institutes of Health (NIH) cuts off funding to the existing *E. coli* project in the hopes of funding someone else, it could take up to 6 months for NIH to issue a Request for Proposals and have proposals written and submitted, and an additional 9 months for proposals to be reviewed and funded. During that same interval Blattner's group could sequence another 1.5 megabases of the *E. coli* genome with continued funding. This would provide partial coverage over the whole *E. coli* genome and high-quality sequence for more than 2.9 megabases.

The *E. coli* genome sequence is a key needed reference for the biology community. It is not clear, however, that our current federal system of funding science promotes good decision-making. If the *E. coli* genome project was to be redirected, it should have happened 2 to 3 years ago. If Blattner is not funded now, it will only impede progress to complete the genome. If Blattner is to be faulted for the current progress on *E. coli*, then he should be faulted for striving for higher quality data than most and for introducing biology into his annotation instead of exclusively focusing on base pair counts. Let's get *E. coli* finished!

J. Craig Venter
President/Director,
Institute for Genomic Research,
932 Clopper Road,
Gaithersburg, MD 20878, USA

Nowak's article emphasizes that *E. coli* may not be the first free-living organism to have its genome fully sequenced. That may not be true. Its correctness depends on a definition of "fully sequenced." The Wisconsin group deposits sequence data when they are certain that they contain less than one frame-shift in 50,000 residues, a standard not matched for most of the sequences deposited in GenBank already. Even if *E. coli* is not first, so what? Is there some kind of molecular genetics Olympics? And if there is, what about weight categories? Blattner's critics, quoted in the article, have themselves not deposited a fraction of his finished sequence.

In the article, several people are quoted as being impatient with the rate of progress in Wisconsin. Such people appear to be ill-informed. The project has been slower to produce finished sequence than originally projected. But how many of us fulfill all the goals of our research projects in the time stated in our grant applications? Could it have been anticipated that the bits of *E. coli* sequence deposited by others would have so many discrepancies, requiring re-sequencing to determine the cause? And who anticipated the technical problem of G compressions, which took many months to solve?

Quotes by Ken Rudd at NIH and George Church at Harvard, who support Blattner's efforts, are immediately followed by what amounts to a premature press release from Craig Venter, who states that his team has sequenced 99% of the *Haemophilus influenzae* chromosome and that the finished sequence will be deposited with GenBank early this year. Where is the evidence to support such a claim? Will the sequence be annotated? With what accuracy? And what is the relevance? The *H. influenzae* genome is less than half the size of the *E. coli* genome. Indeed, comparison of the two would provide important clues to the evolution of bacterial chromosomes.

Science is supposed to be a cooperative effort. A few individuals appear to have forgotten that.

Robert Haselkorn
Department of Molecular Genetics and Cell Biology,
University of Chicago,
920 East 58 Street,
Chicago, IL 60637, USA

NSF FastLane Goals

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