How Frequently Should Genomic Results be Updated?

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Continuous new discoveries about the genome make updates important.
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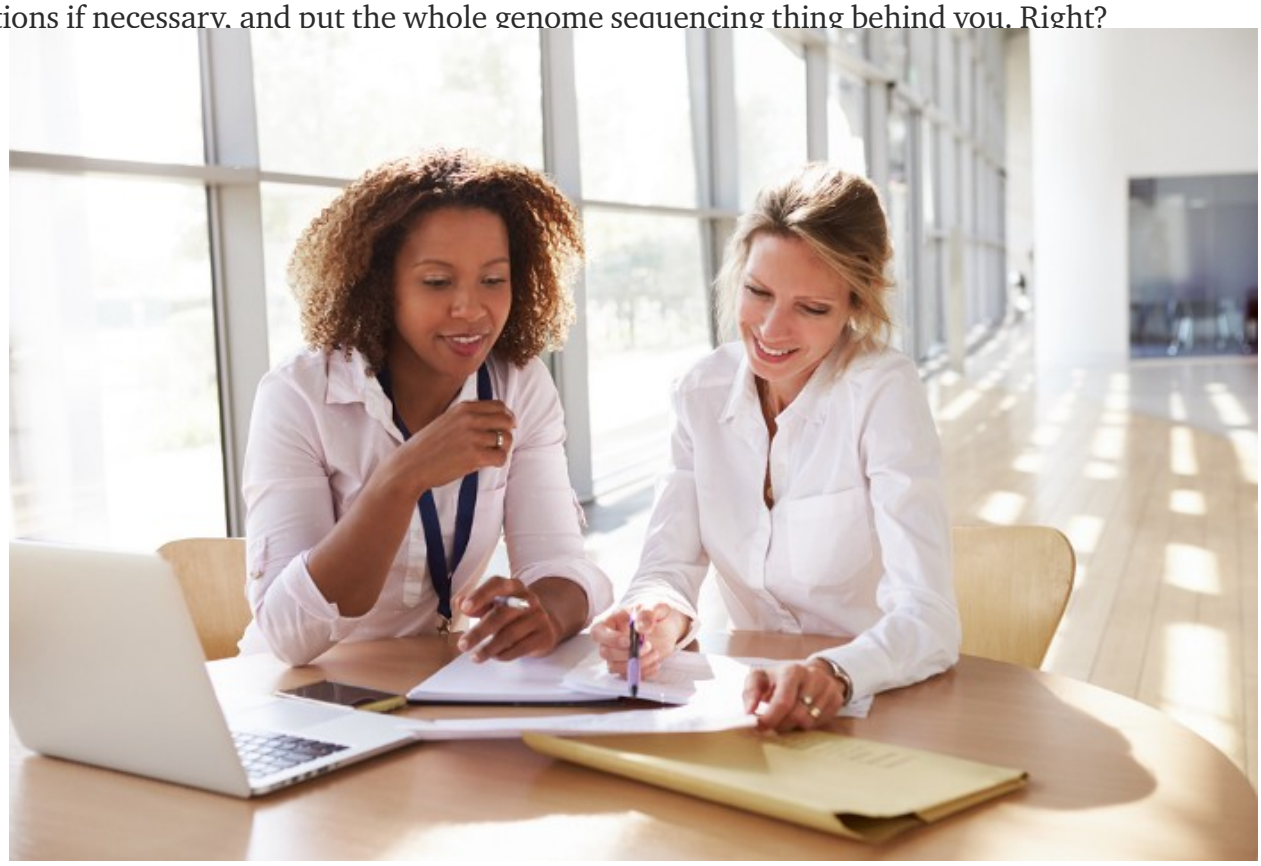
by Robert C. Green

The doctor hands you a report. Your genome has just been sequenced and analyzed, and this report tells you about several potential medical issues you should be paying attention to, based on what variants turned up in your genome. Now you can move forward with this knowledge, taking actions if necessary, and put the whole genome sequencing thing behind you. Right?



Not exactly. If those same genome sequencing results are re-analyzed in two years, or even in six months, it is surprisingly likely that something in your original results will have to be corrected.

A new paper published this week in the *American Journal of Human Genetics* underlines just how quickly our knowledge about the genome is changing. The paper reports findings from our NIH-funded MedSeq Project, the first randomized trial of whole genome sequencing in apparently healthy adults, which I lead at Brigham and Women's Hospital, Broad Institute and Massachusetts General Hospital.

After returning comprehensive medical genome sequencing results to 100 individuals, MedSeq Project investigators re-analyzed the participants' original genome sequencing information

What could explain that?

First, both the original analysis as well as the re-analysis looked at an unprecedented number of genes that were associated monogenic conditions. When you examine more than 5,000 genes, a lot of discoveries can take place in two years. And in fact, this was the explanation! For the most part, researchers had identified many new associations between variants and diseases over that time period. In addition, a few previously reported variants had been removed from the reports because new research revealed that they were no longer considered pathogenic.

The need to revisit genome sequencing results isn't an indictment of the current processes or technology; it's a credit to the speed at which we are learning about the human genome, and to the vastness of information we have yet to discover.

Indeed, lead author Kalotina Machini, PhD, a research scientist in Pathology at Brigham and Women's Hospital, suggested, "These results suggest there is a critical need for periodic reinterpretation of secondary findings results from genomic sequencing data, since it is likely to yield new findings or updated interpretations for many individuals."

The study is also notable for its comprehensive approach to medical genome sequencing interpretation, and for the approaches and resources shared in the paper.

Evaluating more than 5,000 genes, we found monogenic disease risks (diseases connected to a single gene) in 21 percent of patients. Considering that the participants were apparently healthy and had not reported symptoms of the indicated diseases during study enrollment, finding a monogenic disease risk in one of every five participants was a remarkable outcome.

The study also identified carrier status for recessive diseases in 94 percent of participants and non-standard drug dosing recommendations in 95 percent. In fact, all participants had a medically significant finding from genome sequencing using this comprehensive approach.

The study shows that it is possible to carry out a broad interpretation of genomic sequencing data, that this analysis can reveal a plethora of potentially actionable information — and that this information needs to be frequently re-examined.

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