Ethics in Whole Genome Sequencing

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How much information is too much information?

The use of whole-genome sequencing (WGS) in diagnostic testing brings up the topic of secondary findings or incidental findings for many clinicians. Secondary findings are variants associated with a condition other than the one for which the patient is tested. For instance, if a newborn baby has a suspected illness detected on prenatal ultrasound and the infant is tested – would it be ethical for a clinician to disclose other medical conditions that the child may experience as an adult? The patient may not currently have any symptoms associated with the condition but may be at risk of developing it in the future.

Another example would be a three-year-old girl tested to identify the cause of her seizures and developmental delays. At the same time, through WGS, it is found that she has a BRCA1 variant that puts her at a higher risk of developing breast cancer years down the line. This information is not relevant to her current condition, but is it relevant for her future health?

This topic is particularly relevant for WGS because the entire DNA is sequenced, providing access to the individual's complete genomic information. This same level of access is not possible with more targeted single gene or panel tests.

The American College of Medical Genetics published recommendations to labs performing whole-exome and whole-genome sequencing. (1) They identified a list of 59 genes with known disease associations, for which there is some actionability. Labs commonly refer to this as ACMG59. Most of the genes are involved with cancer or cardiac conditions.

It is typical for labs to provide patients undergoing WES or WGS testing to opt into receiving findings in these genes. But other variants may also provide valuable, actionable information. An example is variants in the HFE gene, which can cause hereditary hemochromatosis, a disorder that causes the body to absorb too much iron from food. Excess iron is stored in organs like the liver, heart, and pancreas; it can lead to life-threatening conditions like liver disease, heart problems, and diabetes. If individuals know that they have hereditary hemochromatosis, these conditions can be avoided, but symptoms often do not appear until they are in their 40s.

Ethically, it is also a challenge, as some patients will want to know about conditions that they are at risk of developing, and others will not. This situation is why most labs provide the ability to opt-in or out of these types of findings. Explaining the types of findings that may be reported is an essential part of the consent process for genetic testing, which often involves a genetic counselor. But with what genes do you draw the line?

As a bigger picture, WGS provides a resource for life. Since the patient's entire DNA has been sequenced, it is possible to look at it for any number of reasons throughout the individual's lifetime. Initial testing may be done to address a specific set of symptoms. If the individual develops different symptoms later in life, the sequence can be revisited to extract the information needed at that time.

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References:

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727274/

Disclosure: Toni Lewis, MS, is a Field Genetic Counselor at Variantyx, a provider of highly specialized genetic testing to clinicians and their patients. Christine is responsible for overseeing clinical genomic interpretations and regulatory compliance for the clinical laboratory.

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