Whole Exome Sequencing: The Next Phase of Genetics Care

Suzanne M. Mahon, RN, DNSc, AOCN®, APNG

Mahon is a professor in the Department of Internal Medicine, Division of Hematology/Oncology, and a professor of adult nursing in the School of Nursing at Saint Louis University in Missouri.

No financial relationships to disclose.

Mahon can be reached at mahonsm@slu.edu, with copy to editor at ONFEditor@ons.org.

Key words: genetics; genetic testing; exome sequencing; hereditary cancer syndromes

ONF, 43(2), 249–252.

doi: 10.1188/16.ONF.249-252

Exome sequencing is a technique for sequencing all of the genes that code for functioning proteins in the genome. It is now being used to identify mutations in families with suspected hereditary cancer syndromes where single-gene testing or testing for a panel of genes has not been able to detect a mutation. Oncology nurses need to anticipate that more patients and families will be undergoing this testing and be prepared to explain basic concepts about this new technology. Challenges exist with this testing. For example, testing must often be done on several family members to yield useful results, many variants of unknown clinical significance may be detected, and unexpected gene variants associated with known diseases unrelated to the primary purpose of the test may be incidentally discovered. Families need support and information throughout the genetic testing process for whole exome sequencing.

The identification of mutations associated with an increased risk for developing cancer have implications for better long-term follow-up of cancer survivors, the prevention or detection of second malignancies, and the ability to identify which other close family members might be at risk, so they can make good decisions about cancer prevention and early detection. Oncology nurses routinely identify families with suspected hereditary risk because of family history and clinical characteristics (e.g., early onset cancers) and refer these families for genetic counseling and, when appropriate, genetic testing services.

Next-generation sequencing (NGS) allows for rapid analysis of multiple genes at a considerably lower cost compared to traditional genetic sequencing techniques. Patients with cancer undergoing genetic testing for hereditary cancer syndromes typically undergo a panel of 10–40 genes using NGS rather than single-gene testing with Sanger sequencing. The standard only a few years ago, Sanger sequencing uses short pieces of DNA to sequence a gene by separating fragments of DNA by size and then sequencing them with capillary electrophoresis to detect the order of base pairs on each fragment. NGS technology has paved the way to bring the next phase of genetic care, whole exome sequencing (WES), to the clinical setting (Levenson, 2015).

Data from the Human Genome Project suggest that the human genome consists of 3 billion nucleotides of DNA. However, only 1%–1.5% of those nucleotides are actually translated into proteins that have functional significance. This part of the genome is known as the exome. WES has the potential to sequence 20,000 genes simultaneously (Biesecker & Green, 2014). Research suggests that WES may be able to routinely identify genetic mutations in 25%–31% of