Published on *American Council on Science and Health* (https://www.acsh.org)

Whole genome sequencing: potential for the clinic still not available today

By ACSH Staff — March 12, 2014

For years, academic scientists have used whole genome sequencing (WGS) technology to isolate specific genes associated with disease. These days, researchers and clinicians are working to expand its application into routine patient care, where WGS can elucidate known and unknown variations in about 95% of the patient s genome. According to Dr. William Ferro of the Maine Dartmouth Family Medicine Residency in Fairfield, ME: [U]ncertainty in medical decision making would be reduced and clinical outcomes improved by making interpreted genome-sequence information available to patients, physicians, and other healthcare practitioners. Moreover, cost and time efficiency have made the technology accessible to more people, even outside the medical realm.

However, a study published in the current *JAMA* [1]cautions clinicians and commercial users about flaws involved with unjustified reliance on WGS. The study, led by Dr. Frederick Dewey from Stanford University School of Medicine, sequenced the genomes of 12 people, five men and seven women, with two different commercial WGS systems. Professionals in genetics interpreted data and results using gene data banks, and asked medical doctors to recommend further clinical testing based on initial genetic results.

For each individual, the Stanford researcher s found two to six disease-risk associated variations. One study participant had a genomic variant that required medical action: [An unexpected abnormality] in the BRCA1 gene implicated in hereditary breast and ovarian cancer, according to Dr. Michael Smith from *MedPage Today*. The finding was potentially lifesaving because the woman did not have a family history that would have warranted referral for testing. She elected to have her ovaries removed and begin intensive breast cancer screening.

Aside from the one clinically significant and life-saving genomic recovery, the study reported many problems, as summarized by *MedPage Today* [2]:

-Results from the two sequencing approaches did not completely agree.

-Some regions of the genome -- including some with known variants associated with disease risk -- were not well covered.

-The genetics professionals were not in complete agreement on how to interpret the results, and the medical professionals did not always agree on what to do with them.

-Genetics databases were incomplete; for each participant about 100,000 previously unidentified variants were found.

Therefore, improvements in this revolutionary technology are needed before expanding to clinical settings. In an editorial accompanying the study [3], Dr. Ferro points out why premature use of WGS is possibly of little value at this time, and may even be misleading and counterproductive: Early adopters of the technology run the risk of being snowed under by data that can't be easily used in making clinical decisions. This begs the question, whether the technology will enhance clinical decision-making or merely exponentially increase the complexity of clinical care. Indeed, experts are wary of instituting this technology because it can lead to doctors ordering expensive and unnecessary tests for their patients.

ACSH s Anisha Contractor had this perspective: Fortunately, current difficulties with WGS technology can be fixed, leaving hope for a future applications in clinical care. Not only will WGS accurately recover disease risk variants, but it is also expected to be able to find genetic variations that might influence and direct drug choice and dosing.

Links

[1] http://jama.jamanetwork.com/article.aspx?articleID=1840236&utm_source=Silverchair%20Information%20System

[2] http://www.medpagetoday.com/Genetics/GeneticTesting/44721

[3] http://jama.jamanetwork.com/article.aspx?articleID=1840218&utm_source=Silverchair+Information+Systems&amp