Podcast interview: C. Thomas Caskey & Amy McGuire

PNAS: I’m your host, Paul Gabrielsen, and welcome to Science Sessions. In the United States, shortly after a baby is born, a small sample of its blood is collected for screening against diseases that may require early intervention. Could genetic screening for adults help them take steps to prevent adult-onset disease before they ever feel sick? In a recent paper in PNAS, Baylor College of Medicine internist C. Thomas Caskey attempted to answer that question. Caskey and his colleagues carried out whole-genome sequencing on 81 adults and searched for known disease-causing genes among the results. They found that while there are limitations to genetic screening methods, the volunteers who were screened subsequently used what they learned from their genetic data to take preventative action against disease. I spoke with Caskey, a member of the National Academy of Sciences, at the Institute of Medicine 2013 Annual Meeting in Washington, D.C.

Caskey: This was a study that was devoted to education of our community in the area of predictive genome science. So we were very interested in seeing how this technology could be introduced into the community and how well would it be understood and perceived.

PNAS: Volunteers for this study came from the Houston-area chapter of the Young Presidents’ Organization, a worldwide community of chief executives in business under age 45. Each volunteer provided personal and family medical histories as part of their genetic screening. For 24 of the 81 volunteers, Caskey and his colleagues were able to link disease-causing genes with known diseases in their histories. The team found, on average, five genetic variations possibly linked to disease, per volunteer. Caskey met with each volunteer individually to present the report of their results.

Caskey: The motivation for these individuals to be sequenced was they either had illness themselves, or they recognized illness in their family, and they were seeking answers. It played to a maximum return on the effort to be able to provide them with risk information and a lot of diagnosis. We made 24 diagnoses out of 81 people. That was remarkable, in my opinion.

PNAS: In the course of the study, the researchers repeatedly turned to the scientific literature to make sense of the genetic markers they discovered.

Caskey: So, you can examine the mutation you find and ask the question, has this ever been seen in patients? We went back to the original papers and looked at whether it had been something highly validated, or casually associated. And we found many examples of the databases not being correct.

PNAS: The authors followed up with a survey of the volunteers within a year after the study. 72% of those who responded had spoken with their doctors about their genetic results, and 25% were already changing their lifestyle to reduce their risk of disease.

Caskey: The YPO group is a group of CEOs, self-made individuals, they are very aware of risk-taking and what a risk is, and what a benefit is. They do that in their business daily. We would work with them to modify the risk to a favorable outcome. They understood this beautifully.
**PNAS:** Study co-author Amy McGuire is an expert on policy and ethics issues surrounding personal genomics.

**McGuire:** One of the biggest policy issues around genomics is when and under what circumstances is it medically indicated to order a whole genome sequencing test or a whole exome test. There's a real onus on both the physician and the patient to have a thorough conversation about the meaning of the results to that individual, because oftentimes the results that you get back really need to be contextualized, not just based on the individual's family history but also based on other lifestyle factors in order for that individual to understand what those results mean for them.

**PNAS:** Caskey believes genetic screening may become a larger part of future healthcare.

**Caskey:** We already have in place newborn screening, screening for pre-natal diagnosis, panels of genes that we use for children that have genetic disorders at the time of birth. There's not anything that is devoted at the present time to adult-onset screening, and it's time that we implement adult-onset screening trying to intervene on the pathology of the diseases that we are at risk for. It will be a routine part of medical care as we move forward. What are the barriers? The databases need to be strengthened, the speed with which we can do the analysis, and then how do we deliver the information to the patient. Those are the challenges for making it generally acceptable.

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