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New test can screen all deafness genes simultaneously

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Pinpointing the exact genetic cause of inherited deafness has always involved sequencing one gene at a time, a process that can take up to a year and cost roughly $1,000 per gene. It would cost around $75,000 to test all known deafness causing genes using this approach.

Now University of Iowa researchers working with colleagues at Baylor College of Medicine have developed a test that can screen all of the genes known to cause deafness in a single run, in one to three months and for about $2,000. It means quicker answers for families anxious to determine treatment options or learn the likelihood that future children will have hearing loss.

The new test, called OtoSCOPE, will be available through the UI's Molecular Otolaryngology and Renal Research Laboratory (MORL) by spring 2011 to clinicians and patients within the U.S. and potentially in other countries.

The team, including co-lead study author Eliot Shearer, an UI M.D./Ph.D. student, and Michael Hildebrand, Ph.D., UI postdoctoral fellow, published the research online the week of Nov. 15 in the Proceedings of the National Academy of Sciences Early Edition.

Senior study author is Richard Smith, M.D., the Sterba Hearing Research Professor and vice-chair of otolaryngology. Smith also is a pediatric otolaryngologist with UI Children's Hospital and director of MORL, which is a not-for-profit lab.

"There has been genetic testing for hearing loss for over a decade and our laboratory was one of the first in the country to offer it," Shearer said. "But traditional gene sequencing can only look at one gene at a time, which can be prohibitively expensive and time consuming. We will be the first laboratory in the world to offer genetic testing for all known hearing loss genes simultaneously, which will significantly increase efficiency and decrease cost."

Hearing loss is a very common problem. It affects 1 in 500 newborns and an estimated 278 million people worldwide have moderate to severe hearing loss. About two thirds of hearing loss is inherited and can be caused by mutations in many different genes.

"Genetic testing can provide information on whether the hearing loss will be severe, moderate or mild and whether it will progress," Shearer said. "It can also give information on the chances that another child born in the family will also be affected by hearing loss. Finally, genetic information can help determine the best options for treatment. We often know, based on what gene is affected, whether cochlear implants or hearing aids are the best treatment to improve hearing."

The new method uses the latest DNA sequencing technology to simultaneously screen all 54 genes known to cause non-syndromic deafness –- hearing loss that is not associated with other medical problems -- along with a dozen additional genes that cause syndromic deafness -- hearing loss that occurs with other complications such as blindness.

The test covers two of the most common types of syndromic deafness - Usher syndrome and Pendred syndrome. Usher is the most common cause of deaf-blindness in the U.S., but while the deafness occurs early, blindness does not develop until the child is around 10 years old.

"Using our genetic screen we can test for the Usher gene and that early diagnosis allows the patient to take preventative measures to slow the progression of the blindness. It also helps the patient and their family prepare for the vision loss," Hildebrand said.

Working with Steven Scherer, Ph.D., associate professor of molecular and human genetics at the Human Genome Sequencing Center at Baylor College of Medicine, and colleagues from the UI College of Engineering and Center for Bioinformatics and Computational Biology, the team developed the OtoSCOPE method, which captures and sequences all the portions of a patient's DNA that coincide with areas of the human genome known to contain deafness mutations.

OtoSCOPE was tested with DNA from ten patients -- three samples were positive controls where the mutation was already known, one sample known to have no deafness mutations was the negative control and six samples were "unknowns," meaning the team didn't know the hearing loss mutation.

The screening test was able to identify the genetic cause of hearing loss in five of the six unknowns. In fact, in addition to finding two known hearing loss mutations, the test also uncovered three new mutations within known genes.

The results proved that the new technology can provide similar sensitivity and resolution as the current gold standard sequencing test, but because OtoSCOPE can screen all the genes in one run, it is faster and less expensive to identify the mutation causing the hearing loss. In addition, as more gene mutations are found to cause deafness, they can easily be included in the screening test.

The researchers note that this screening test can be applied to other genetic diseases to decrease cost and give more comprehensive results,

and it will also be useful for gene discovery.

More information: For more information, visit www.healthcare.uiowa.edu/labs/morl

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