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Genetic Test Now Available – But is it Ready for Prime Time?

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Independent Forensics, an Illinois-based company specializing in paternity testing and DNA evidence used in criminal investigations, has begun marketing a genetic assay intended for HIV-positive people. The test, called Basepair, looks for genetic variations in human DNA that can affect the function of CCR5, a receptor on CD4+ cells (also known as T4 cells) that is needed by HIV to enter cells, reproduce, and eventually damage the immune system. Knowing which genetic variations are present, the company suggests, may help HIV-positive people determine if they may progress to AIDS more slowly or quickly than usual and assist them in making important treatment decisions. In fact, one of the genetic variations that the test looks for has been associated with "immunity" to HIV, meaning that the assay may be of significant interest to people who aren't infected with the virus. But some experts question the value of such testing, in light of the fact that the study of human genetics – as it applies to HIV susceptibility and disease progression – is still fragmented and hardly complete.

The study of human genetics as it relates to medicine is a rapidly expanding research field. While genes play a role in obvious physical characteristics, such as eye or hair color, they also play a major role in biological processes, including the body's susceptibility to certain diseases and the way it responds to infections.

In recent years, a great deal of research funded by the U.S. National Institutes of Health (NIH) has found that specific genetic variations, or haplotypes, can affect people's susceptibility to HIV infection and, among those already infected with the virus, the rate of progression to AIDS. The CCR5 receptor on CD4+ cells, for example, is regulated by a gene. Some variations in this gene can render the receptor ineffective, meaning that it can't be used by HIV to infect cells. Other variations have more subtle effects on CCR5, but may have a significant impact on the way HIV uses it to enters cells, potentially resulting in slower or more rapid disease progression.

Independent Forensics' assay identifies the nucleotides – building blocks of DNA – at seven different positions near the CCR5 gene. Other genetic variations examined by the test include those involving CCR2, believed to be important among HIV-positive African Americans. It also looks for the delta-32 form of the CCR5 gene, believed to be a genetic factor resulting in resistance to HIV infection.

As explained by Karl Reich, PhD, Chief Scientific Officer for Independent Forensics, all human beings are made up of two complete copies of their genes: one copy from their

mother, the other copy from their father. "Our test does not determine the origin of the gene, such as which copy came from mom or dad, but it does determine the actual DNA sequence of both copies," he said. "This is important, as each copy can affect the function of CCR5 and therefore the progression of HIV infection."

For example, people who inherit the delta-32 form of the CCR5 gene from one parent can be infected with HIV, but may experience slower disease progression. Conversely, people who inherit the delta-32 form from both parents often have near-complete protection against infection with the virus.

While the Independent Forensic test looks for this delta-32 form, Dr. Reich stressed that the existence of the delta-32 gene variant – inherited from both parents – is very rare. "It is not a genetic 'free pass' for immunity from HIV infection," he says. "In fact, delta-32 individuals can still become infected with other HIV variants and progress to AIDS," referring to transmissible viruses that use another receptor on CD4+ cells, called CXCR4, instead of CCR5.

The real benefit of the test, Dr. Reich argued, is the evaluation of haplotypes that have been found to be associated with slower or rapid disease progression. For example, HIV-positive Caucasians who have inherited an "HHE" CCR5 variant from both parents may progress quickly to AIDS, whereas HIV-positive African Americans who inherit the "HHA" CCR5 variant from one parent and the "HHF*2" variant from the other parent may experience much slower disease progression. Slower and more rapid disease progression CCR5 haplotypes have been defined for people of both races.

"Our goal is to provide information to clinicians and patients in order to help them better manage their disease," he said. "HIV-positive patients who are slow progressors may benefit from decreased drug dosages to reduce side-effects. This information may also influence choices of anti-HIV medications in order to decrease the rate of viral resistance. Fast progressors may benefit from more aggressive treatment, more tests of viral load, more frequent monitoring or similar interventions."

The test costs approximately $250, but is currently priced at $179 to mark the launch of the assay in June. Independent Forensics hasn't yet made an effort to push for insurance coverage, although it is interested in doing so. The test can be ordered by doctors, or independently and anonymously by patients, notably through the company's website. A test packet is sent by the company, involving a cotton swab that is rubbed around the inside of the cheek, and then shipped to the Independent Forensics laboratory in Hillside, Illinois. DNA is extracted from the swab and then analyzed for variations in the CCR5 gene. A report indicating the results is then sent back to the patient or doctor.

Dr. Reich noted that the test is not approved by the FDA, nor does it require FDA oversight, as it is not a diagnostic test. He also confirmed that Basepair has not been evaluated in clinical trials. The information used to analyze test results come from the NIH-funded studies. "We are simply taking these important results and making them available for a competitive price to the public," he says.

Not all experts believe that CCR5 haplotype testing is useful, at least not outside the realm of scientific research. John Moore, PhD, Professor of Microbiology and Immunology at Weill Cornell Medical College in New York and an active researcher in the field of human (host) genetics as it relates to the entry of HIV into cells, does not recommend that the test be used by healthcare providers or patients. The use of this test in the medical management of HIV, he said, "is a mistake, given the present state of the science. CCR5 genetics are but one contribution to disease progression rates, and information on CCR5 genetics, taken in isolation, could be highly misleading."

Dr. Moore also indicated that he is unaware of any data indicating how this information could be used to influence treatment options. "I would think drinking a cup of tea, pouring the dregs away and looking at the pattern of the tea leaves would be just as valuable right now," he wryly commented.

For Dr. Reich, the time is right to begin using genetic information to help personalize medicine and to address the individual needs of patients. "There are many good examples where knowing the genetics of the host improves outcomes, including reduced costs, decreased errors, improved diagnostics, and sometimes all four," he said. "However over hyped ‘personalized medicine' may be in the media, the tide of genetic information is in fact, irrevocable." At the same time, he conceded that, "CCR5 genetics are one contribution among many and should not be taken in isolation or as the entire story of host-HIV interaction."