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Technique traces origins of disease genes in mixed human populations

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A team of researchers from Washington University in St. Louis and the Israeli Institute of Technology (Technion) in Haifa has developed a technique to detect the ancestry of disease genes in hybrid, or mixed, human populations.

The technique, called expected mutual information (EMI), determines how a set of DNA markers is likely to show the ancestral origin of locations on each chromosome. The team constructed an algorithm for the technique that selects panels of DNA markers that render the best picture of ancestral origin of disease genes. They then tested the algorithm to show that it is more powerful and accurate than standard algorithms that currently select for markers.

The impact is on identifying inherited genes that cause diseases in people of mixed races, which researchers call population admixture. Nephrologists, for instance, have noted that African Americans are far more likely than Europeans to die rapidly of end-stage, progressive kidney failure. Many African Americans also have genes that originated in Europe due to ethnic mixing. The technique helps researchers isolate the genetic causes of disease by detecting from which continent the recurrent disease genes originated.

It is hoped, then, that through gene therapy or perhaps drugs the disease can be prevented or treated.

“This technique will allow researchers to analyze which regions of the

genome are associated with end-stage, progressive renal failure," said Alan R. Templeton, Ph.D., Washington University Charles Rebstock Professor of Biology, and co-author of a paper on the technique and the algorithm published in the current issue of *Genome Research* 18, 661-667. "Once the regions are identified, then you look at the individual genes and ask: Are there genetic factors involved with this, and if so, what are the candidates?"

It's a good bet, Templeton said, that the disease genes are highly likely to have emerged from Africa, as African –Americans have shown the tendency to die more quickly of the disease.

The technique and algorithm apply beyond this particular disease, Templeton added.

"We can look at many different hybrid human populations with this algorithm and use it on a diversity of diseases," he said.

"Our novel approach extends previous methods by incorporating knowledge on population admixture, drawing a more precise picture of the mosaic of ancestries along an individual's genome," said Sivan Bercovici, Templeton's colleague at Technion and primary author of the Genome Research paper.

The researchers analyzed DNA from 575 cases of African-Americans with end-stage progressive renal failure and compared them to controls that did not have the disease. They came up with a panel of approximately 2,000 genetic markers, enough, Templeton said, "to cover the whole genome."

To tease out the origins of disease-causing genes, researchers use a technique called mapping by admixture linkage disequilibrium (MALD), a powerful approach to identify regions of the genome that have genes

associated with disease. It takes advantage of differences in disease prevalence between populations to look for variation patterns that are over-represented in groups with high susceptibility to a certain disorder.

Both EMI and the algorithm make MALD more accurate and efficient.

Source: Washington University in St. Louis