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Scientists create new technique to study how disease is inherited

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(Medical Xpress)—Human reproduction is simple. A sperm cell carries the man's genome into the egg. There, during fertilization, male and female genomes comingle in a way that fuses different traits from each parent into the DNA blueprint for a new human being.

Parents aren't perfect; their genomes may contain disease-causing mutations. Nature tries to protect offspring by gene-mixing. This way if one parent passes on a defective mutation, the other has a chance to contribute a working copy.

Until now, however, there hasn't been an easy way to determine whether an offspring inherited a good working copy of a gene or two defective mutations, a scenario that could cause disease.

In a recent paper in *Nature Biotechnology*, a research team led by Stanford scientists describes a new process for analyzing an offspring's DNA to reveal which specific genes they inherited from each parent.

"If you sequence the child, you can now tell what traits they inherited from their parents," said Michael Snyder, PhD, professor and chair of genetics, and senior author of the study.

DNA is made up of four chemicals—abbreviated A, T, G and C—strung in a particular order. A person has 6 billion of these chemicals assembled into 46 chromosomes: 23 from the mother and 23 from the father.

When scientists sequence a person's genome, they break the DNA into small pieces to determine the order of the A, T, G and Cs.

The problem is that the process now used doesn't reveal all the information needed to ascertain which parts of our genome come from which parent. Important variants could come from either the mother's or the father's chromosomes.

The Stanford scientists used several innovations to provide this missing information on parental inheritance.

First they chopped the DNA into blocks that were 10,000-letters long. Since modern sequencers can't directly read blocks that long, they then cut these segments into shorter snippets of 100 letters, tagging each snippet to know which mega-block it came from.

Using a computer analysis, the researchers determined which genetic variants from the offspring's DNA were linked together in 10,000-letter blocks. Finally, their algorithms reassembled these longer blocks into two complete sequences, one for each parent's chromosomes.

The Stanford process can reveal whether individuals have one good copy of a gene or two bad copies—without sequencing the DNA of parents. Knowing this inheritance information is crucial to determine which DNA changes may cause disease. The new process also allows scientists and treating physicians to collect this genetic information more quickly and accurately than previous methods, according to the study.

Because of its speed, precision and utility, the Stanford approach is being marketed as a commercial process by the biotechnology firm Illumina.