MedicalXpress

Most mutations come from dad

August 24 2012

Humans inherit more than three times as many mutations from their fathers as from their mothers, and mutation rates increase with the father's age but not the mother's, researchers have found in the largest study of human genetic mutations to date.

The study, based on the DNA of around 85,000 Icelanders, also calculates the rate of human mutation at high resolution, providing estimates of when human ancestors diverged from nonhuman primates. It is one of two papers published this week by the journal *Nature Genetics* as well as one published at *Nature* that shed dramatic new light on human evolution.

"Most mutations come from dad," said David Reich, professor of genetics at Harvard Medical School and a co-leader of the study. In addition to finding 3.3 paternal germline mutations for each maternal mutation, the study also found that the mutation rate in fathers doubles from age 20 to 58 but that there is no association with age in mothers—a finding that may shed light on conditions, such as autism, that correlate with the father's age.

The study's first author is James Sun, a graduate student in Reich's lab who worked with researchers from deCODE Genetics, a biopharma company based in Reykjavik, Iceland, to analyze about 2,500 short sequences of DNA taken from 85,289 Icelanders in 24,832 father-mother-child trios. The sequences, called microsatellites, vary in the number of times that they repeat, and are known to mutate at a higher rate than average places in the genome.

Reich's team identified 2,058 mutational changes, yielding a rate of mutation that suggests human and chimpanzee ancestral populations diverged between 3.7 million and 6.6 million years ago.

A second team, also based at deCODE Genetics (but not involving HMS researchers), published a paper this week in *Nature* on a large-scale direct estimate of the rate of single nucleotide substitutions in human genomes (a different type of mutation process), and came to largely consistent findings.

The finding complicates theories drawn from the fossil evidence. The upper bound, 6.6 million years, is less than the published date of Sahelanthropus tchadensis, a fossil that has been interpreted to be a human ancestor since the separation of chimpanzees, but is dated to around 7 million years old. The new study suggests that this fossil may be incorrectly interpreted.

Great Heights

A second study led by HMS researchers, also published in *Nature Genetics* this week, adds to the picture of human evolution, describing a newly observable form of recent genetic adaptation.

The team led by Joel Hirschhorn, Concordia Professor of Pediatrics and professor of genetics at Boston Children's Hospital and HMS, first asked why closely-related populations can have noticeably different average heights. David Reich also contributed to this study.

They examined genome-wide association data and found that average differences in height across Europe are partly due to genetic factors. They then showed that these genetic differences are the result of an evolutionary process that acts on variation in many genes at once. This type of evolution had been proposed to exist but had not previously been

detected in humans.

Although recent human evolution is difficult to observe directly, some of its impact can be inferred by studying the human genome. In recent years, genetic studies have uncovered many examples where recent evolution has left a distinctive signature on the human genome. The clearest "footprints" of evolution have been seen in regions of DNA surrounding mutations that occurred fairly recently (typically in the last several thousand years) and confer an advantageous trait, such as resistance to malaria. Hirschhorn's team observed, for the first time in humans, a different signature of recent evolution: widespread small but consistent changes at many different places in the genome, all affecting the same trait, adult height.

"This paper offers the first proof and clear example of a new kind of human evolution for a specific trait," said Hirschhorn, who is also a senior associate member of the Broad Institute. "We provide a demonstration of how humans have been able to adapt rapidly without needing to wait for new mutations to happen, by drawing instead on the existing genetic diversity within the human population."

Average heights can differ between populations, even populations that are genetically very similar, which suggests that human height might have been evolving differently across these populations. Hirschhorn's team studied variants in the genome that are known to have small but consistent effects on height: people inheriting the "tall" version of these variants are known to be slightly taller on average than people inheriting the "short" versions of the same variants.

The researchers discovered that, in northern Europe, the "tall" versions of these variants are consistently a little more common than they are in southern Europe. The combined effects of the "tall" versions being more common can partly explain why northern Europeans are on average taller

than southern Europeans. The researchers then showed that these slight differences have arisen as a result of evolution acting at many variants, and acting differently in northern than in southern Europe.

"This paper explains—at least in part—why some European populations, such as people from Sweden, are taller on average than others, such as people from Italy," Hirschhorn said.

The researchers were only able to detect this signature of evolution by using the results of recent genome-wide association studies by the GIANT consortium, which identified hundreds of different genetic variants that influence height.

Provided by Harvard Medical School

Citation: Most mutations come from dad (2012, August 24) retrieved 27 April 2024 from https://medicalxpress.com/news/2012-08-mutations-dad.html