60 new mutations in each of us: Speed of human mutation revealed in new family genetic research

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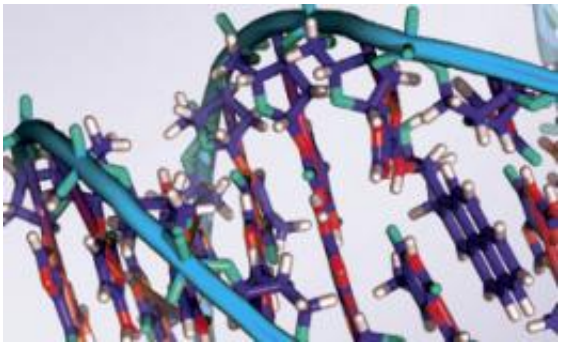

(Medical Xpress) -- Each one of us receives approximately 60 new mutations in our genome from our parents. This striking value is reported in the first-ever direct measure of new mutations coming from mother and father in whole human genomes published today.

For the first time, researchers have been able to answer the questions: how many new mutations does a child have and did most of them come from mum or dad? The researchers measured directly the numbers of mutations in two families, using whole genome sequences from the 1000 Genomes Project. The results also reveal that human genomes, like all genomes, are changed by the forces of mutation: our DNA is altered by differences in its code from that of our parents. Mutations that occur in

sperm or egg cells will be 'new' mutations not seen in our parents.

Although most of our variety comes from reshuffling of genes from our parents, new mutations are the ultimate source from which new variation is drawn. Finding new mutations is extremely technically challenging as, on average, only 1 in every 100 million letters of DNA is altered each generation.

Previous measures of the mutation rate in humans has either averaged across both sexes or measured over several generations. There has been no measure of the new mutations passed from a specific parent to a child among multiple individuals or families.

"We human geneticists have theorised that mutation rates might be different between the sexes or between people," explains Dr Matt Hurles, Senior Group Leader at the Wellcome Trust Sanger Institute, who co-led the study with scientists at Montreal and Boston, "We know now that, in some families, most mutations might arise from the mother, in others most will arise from the father. This is a surprise: many people expected that in all families most mutations would come from the father, due to the additional number of times that the genome needs to be copied to make a sperm, as opposed to an egg."

Professor Philip Awadalla,who also co-led the project and is at University of Montreal explained: "Today, we have been able to test previous theories through new developments in experimental technologies and our analytical algorithms. This has allowed us to find these new mutations, which are like very small needles in a very large haystack."

The unexpected findings came from a careful study of two families consisting of both parents and one child. The researchers looked for new mutations present in the DNA from the children that were absent from

their parents' genomes. They looked at almost 6000 possible mutations in the genome sequences.

They sorted the mutations into those that occurred during the production of sperm or eggs of the parents and those that may have occurred during the life of the child: it is the mutation rate in sperm or eggs that is important in evolution. Remarkably, in one family 92 per cent of the mutations derived from the father, whereas in the other family only 36 per cent were from the father.

This fascinating result had not been anticipated, and it raises as many questions as it answers. In each case, the team looked at a single child and so cannot tell from this first study whether the variation in numbers of new mutations is the result of differences in mutation processes between parents, or differences between individual sperm and eggs within a parent.

Using the new techniques and algorithms, the team can look at more families to answer these new riddles, and address such issues as the impact of parental age and different environment exposures on rates of new mutations, which might concern any would-be parent.

Equally remarkably, the number of mutations passed on from a parent to a child varied between parents by as much as tenfold. A person with a high natural mutation rate might be at greater risk of misdiagnosis of a genetic disease because the samples used for diagnosis might contain mutations that are not present in other cells in their body: most of their cells would be unaffected.

More information: Conrad DF et al. (2011) Variation in genome-wide mutation rates within and between human families. *Nature Genetics*, published online 12 June 2011. doi:1038/ng.856

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