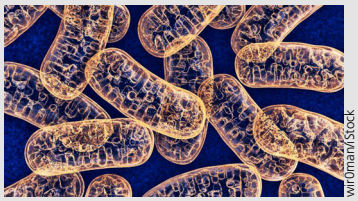
NEWS

Persistence of paternal mitochondrial DNA in human offspring



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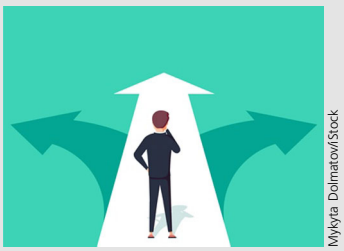
Children inherit mitochondrial DNA (mtDNA) solely from their mothers, right? Assumptions about the exclusively matrilineal inheritance of mtDNA are so entrenched in medical genetics and the study of human genetic history that they are generally accepted without question or controversy. Prior cases purporting to show biparental inheritance of mtDNA have largely been dismissed as artifact. But a recent report by Luo et al. in *PNAS* (https://doi.org/10.1073/pnas.1810946115) once again puts our long-standing suppositions about the inheritance of mtDNA to the test. In their article, the authors present compelling evidence for the persistence of paternal mtDNA in offspring of three unrelated families. For the first family ascertained, the research team evaluated a child for suspicion of mitochondrial disease. Sequencing of the child's mtDNA failed to identify any pathogenic or likely pathogenic mtDNA variants but detected an unusually high level of heteroplasmy. Sequencing of mtDNA from the proband's two siblings and mother revealed the same pattern of heteroplasmy. mtDNA sequencing of additional family members showed biparental inheritance of mtDNA in the proband's mother, maternal grandfather, and two other family members. To determine whether the findings in this family were unique, the research team studied two additional families with probands suspected of having a mitochondrial disease. As with the first family, mtDNA sequencing of these probands had not yielded pathogenic or likely pathogenic mtDNA variants but had revealed high levels of heteroplasmy. Persistence of paternal mtDNA in offspring was observed for five individuals in these two families. To rule out the possibility that their observations were due to contamination or sample mix-ups, the authors used two independent, accredited genetics laboratories to corroborate their findings, all of which were verified. Across all three families evaluated in this study, the authors documented levels of mtDNA heteroplasmy that ranged from 24% to 76%. Pedigree analysis revealed that the persistence of paternal mtDNA in offspring occurs in a manner consistent with autosomal dominant inheritance. The authors propose that pathogenic variation of a single nuclear gene could explain the inheritance pattern seen in these families and speculate that the phenomenon could result from defects in the processes that eliminate paternal mitochondria from early embryos or from dysregulation of mtDNA replication or copy number during early embryonic development. From these investigations, the authors conclude that biparental inheritance of mtDNA does occur in humans and, while no assessment of the potential frequency of this phenomenon was performed, note that the phenomenon is likely rare. They suggest that elucidation of the mechanism behind the persistence of paternal mtDNA in offspring might inform new approaches to the treatment of mitochondrial diseases caused by pathogenic variants in the maternal mtDNA. —*Raye Alford, News Editor*

How do scientists pick which genes to study?



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With only about 20,000 protein-coding genes in the human genome—and so much effort and money being put toward biomedical research—one might reasonably assume researchers have the human genomic landscape pretty well covered; but apparently this is not the case. In a study recently reported in *PLOS Biology* (https://doi.org/10.1371/journal.pbio.2006643), Stoeger et al. sought to understand why some potentially important genes just don't seem to get much attention. First, the research team compiled a database that included various features of genes and proteins such as intrinsic biochemical and physical properties; bibliographic, scientific, and technological information; and data related to funding. Using the number of publications about a gene as a measure of how much attention the gene has received, the authors queried the database to identify which features best explained the volume of research on any given gene. Of the 430 intrinsic biochemical and physical characteristics of genes and proteins included in the database, the authors found 15 that correlated highly with the number of publications. The inclusion of additional characteristics did not substantially improve predictions, suggesting that the most widely studied genes share a small set of characteristics. The authors note that these 15 characteristics are suspected of making the genes easy to study with conventional methodologies. The research team then evaluated whether past research predicted current research. They found that the number of prior publications per gene and the date of initial publication of a gene or its protein correlated with the number of current publications. They also found that the date of initial publication of homologous genes from model organisms and the number of publications on homologous genes correlated with the number of current publications. Finally, the authors found that combination of the 15 previously identified key characteristics with the existence of model organisms correlated with levels of funding and the availability of drugs, regardless of the biological relevance of the genes. The authors argue that career pressures and the need to obtain funding may deter scientists, especially junior scientists, from pursuing research on less studied genes. They suggest that funding earmarked for innovative, exploratory research on little-studied genes is needed, as are mechanisms for the ongoing support of scientists interested in pursuing such speculative research. The authors predict that the resulting broadening of the scope of genes that are active targets of research would yield substantial dividends and suggest that their observations may also apply to other scientific disciplines. Although noncoding genes are not included in the database developed by Stoeger et al., it is interesting to speculate whether a similar bias also exists for noncoding genes. —*Raye Alford, News Editor*