New advances in the study of human mitochondrial DNA

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A study concerning the evolution of mitochondrial DNA, performed by researchers from the Universitat Autònoma de Barcelona (UAB), has allowed to determine the frequency and pattern of heteroplasmy in the complete mitochondrial genome using a representative sample of the European population. This phenomenon, which indicates the presence of different mitochondrial DNA types in a cell or an individual, can be found in more than half of the population. The data obtained indicates that many of the newly arising mutations found never reach fixation at the population level due to the effect of evolutionary mechanisms such as genetic drift or selection. The study, published in *PLOS ONE*, may open a new perspective on medical, evolutionary and forensic research.

The mitochondrial DNA copies of an individual are not necessarily identical. The presence of different types of mitochondrial DNA is known as heteroplasmy. This is an obligatory phase in the evolution of the mitochondrial DNA, an intermediate stage between the mutation origin and its fixation at cellular and individual level. The study of heteroplasmy is proving to be useful in the study of mutation patterns, the role of selection and the mitochondrial DNA recombination in mammals.

In this study, researchers Amanda Ramos, Cristina Santos and Maria Pilar Aluja, from the Unit of Biological Anthropology of the UAB, determined the frequency and pattern of heteroplasmy in the complete mitochondrial genome of 101 unrelated healthy individuals, which are representative of the European population. The results demonstrate a

high frequency of mitochondrial heteroplasmy, being heteroplasmic a 61% of the individuals analysed.

"This is an important data. Until now no one had established these frequencies, probably due to methodological reasons - we detected, with a sensitivity of 100%, mitochondrial DNA mixtures in which minority variants were present with a frequency of only 10% – but also because for a long time the research carried out on heteroplasmy was associated with the study of mitochondrial diseases. Given the high frequency of heteroplasmy at population level, the research demonstrates that the presence of heteroplasmy is not necessarily associated with specific diseases; in fact, it is likely that most of us are heteroplasmic without affecting our health negatively", states Amanda Ramos, lead author of the article and the PhD thesis on which the research was based on.

Researchers determined how many heteroplasmic positions presented each analysed individual and in which positions of their mitochondrial genome were located. as well as the percentage of each of the genetic variants. With this information, they detected that several of these mutations in heteroplasmy had not been previously described at population level.

"Many of these mutations will probably not be fixed at population level. We detected the presence of heteroplasmy at highly stable positions of the mitochondrial genome. This suggest that some evolutionary forces may be acting to lower them at population level. Especially, those stable heteroplasmic positions that could have a negative effect on the individual, which suggest that purifying selection could be operating to prevent their fixation within individuals", says Cristina Santos, co-author of the article.

The present study represents an important advance in the research of the mitochondrial DNA. "By taking into account the large amount of data

presented and the scarce information available up to date, we are convinced that it will open a new perspective in the research of mitochondrial DNA-related diseases, as well as in population studies, and evolutionary and forensic field", concludes research director Maria Pilar Aluja.

More information: Ramos, A. et al. Frequency and Pattern of Heteroplasmy in the Complete Human Mitochondrial Genome, *PLOS ONE*. www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0074636

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