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Rare mitochondrial mutations—maybe not so rare?

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French scientists have discovered that supposedly rare mutations in the mitochondria, the 'power plants' of human cells responsible for creating energy, account for more than 7% of patients with a mitochondrial disease manifesting itself as a respiratory deficiency. Their data emphasise the need for comprehensive analysis of all the mitochondrial DNA (mtDNA) in patients suspected as having a mitochondrial disease, and this should include children, a researcher will tell the annual conference of the European Society of Human Genetics today (Sunday).

Dr. Sylvie Bannwarth and Professor Véronique Paquis, from the Hôpital Archet 2, Nice, France, together with colleagues from the ten diagnostic centres that make up the French Mitochondrial Disease Network, investigated 743 patients who were suspected of having a respiratory chain disorder caused by defective mitochondria, but who did not carry a common mtDNA mutation. Mitochondrial diseases, which can be very severe, are estimated to affect one child in every 5000, and are usually untreatable. However, prompt diagnosis can help clinicians to prescribe treatment to alleviate secondary symptoms.

"We examined the relationship between clinical presentation of disease, age at onset, and the localisations of mutations. Our results showed that, in the French population, clinical presentations that are not associated with common mtDA mutations begin mainly before adulthood, and that neuromuscular problems are the most common manifestation of such mutations", says Dr. Bannwarth.

"We found that early onset disease was significantly associated with mutations in genes that code for proteins, while late onset disorder were associated with mutations in tRNA genes, and that two genes represent 'hotspots' for disease-causing mutations. Knowing the prevalence of these rare mutations is essential if we are to be able to improve the diagnosis of these diseases."

There are very many mitochondrial diseases, and they manifest themselves in a large number of different ways. They can involve muscle weakness, neurological disease, respiratory, gastrointestinal and cardiac problems, and strokes. Many are degenerative, while some are relatively static.

One of the two techniques used for screening the entirety of an individual's mtDNA was developed by Dr. Bannwarth. The use of such techniques can aid not just in diagnosis, but also in genetic counselling and prenatal diagnosis for mitochondrial disease. Up to now the study of mtDNA mutations has usually been restricted to the detection of deletions and a few common mutations, but without any data about the prevalence of rare mutations and their associated phenotypes (characteristics or traits).

"With the advent of Next Generation Sequencing techniques, screening all mtDNA is now feasible, and this means that we can detect both common and rare mutations as well as deletions. For example, in the patients we studied we found that Leigh syndrome – a rare disorder that affects the central nervous system – was found in 41% of patients with rare mtDNA mutations. Had we not screened all of the mtDNA, including the rare mutations, we would not have known this", says Dr. Bannwarth. "This is clearly a big aid to accurate diagnosis and we hope that our results will underline the importance of comprehensive mtDNA screening."

Provided by European Society of Human Genetics