

Discovery : The gene of Friedreich's ataxia

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Eight years of exhausting work have come to conclusion with the identification of the gene of Friedreich's ataxia.

In an article published in the journal Science of this week, scientists working in Houston, Strasbourg, Naples and Valençia, unveil the nature of the genetic fault responsible for Friedreich's disease. Their discovery of a genetic mutation, in this case the expansion of a trinucleotide, GAA, associated with a recessive genetic disease, is a first. Although the repetition of triplets, in limited numbers, prove to be common in normal individuals, their presence in a number several tens of times greater than normal have only been found until now in association with dominant diseases or linked to chromosome X, among others Steinert's myotonic dystrophy, type 1 spinocerebellar ataxia and the mental retardation linked to a weak X.

One single copy of the expansion of the repeated triplets is apparently required to provoke the appearance of a dominant disease. In the case of Friedreich's ataxia, they found in most of the ill, a very limited number presenting only a very great expansion of triplets in association with another more conventional mutation. In the parents who were not afflicted, they confirmed the presence either of a dynamic mutation or of an isolated mutation in association with a copy of the normal gene.

It is in a gene called X25 that the researchers identified these mutations. The abnormal expansion of the GAA triplet is inserted between the two first encoding sequences (exons) of the gene attaining up to 200 to 900 repetitions, with 7 to 22 normally. They do not know the cause of this expansion but they realize that it represents more than 97% of the mutations met in Friedreich's disease in the populations where it was researched. As for isolated mutations, they have only been found up until now in three (3/184) families of French, Spanish and Italian origin, and always in a heterozygous state, therefore in association with a dynamic mutation.

Among the organs where the gene is expressed, let us emphasize those where Friedreich's disease plays the most havoc, the spinal chord (neuronal degeneration), the heart (cardiomyopathy) and the pancreas (intolerance to glucose and diabetes).

The gene encompasses only 7 exons and its role is not yet known. A computerized prediction of the virtual structure of the protein called frataxine suggests that it concerns a secreted protein, related to similar proteins found in yeast and in the C elegans worm. The preservation of the DNA sequence starting from organisms that far back in evolution confers on this protein a role of primary importance.

This discovery allows us to reach a new phase of research which is drawn from tissue banks and experimental models in order to study the physiopathology of Friedreich's disease and the mode of action of frataxine in a normal person and in the disease. The benefits expected by the ill and by their families will come from a better understanding of the action of the gene and of its product. The prospect of developing a treatment has never been so close as now, with the identification of frataxine of which the nature predicts an eventual multisystemic role and consequently a therapeutic avenue.

All those among us who work for the cause of hereditary ataxias will rejoice for the success of our scientific colleagues who have just identified the gene of Friedreich's disease. This discovery would not have been possible without the constant support and participation of the ill, their families and support groups like the Canadian Association of Friedreich's Ataxia. We must master the new scientific knowledge pertaining to the exact nature and function of the Friedreich gene without delay and intensify our efforts to reach the goal which we are set on, to know the cause and the treatment of Friedreich's ataxia !

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