title

NOVEL LDLR VARIANTS IN IBERO-AMERICA: PRELIMINARY MOLECULAR RESULTS OF FAMILIAL HYPERCHOLESTEROLAEMIA IN IBERO-AMERICA

Abstract:

Aim: Familial hypercholesterolaemia (FH) is an autossomal dominant disorder with increased cardiovascular risk. The study of the molecular basis of FH in Ibero-american countries, which have an historical link, can contribute for phenotype/genotype clarification and improve patient prognosis.

The aim of this study is to promote, at early age, an accurate identification and diagnosis of FH in Ibero-american countries, so preventive measures/treatment can be implemented in order to give these patients a longer and better life.

Methods: Since July of the present year, 32 samples were received in our lab from Mexico (1), Argentina (12) and Portugal (19). The molecular diagnosis was performed by analysis of *LDLR* and *APOB* (2 fragments), by PCR and Sanger Sequencing. *PCSK9* will be studied in negative patients.

Results: In these 32 samples, 16 variants were found in *LDLR* in 15 index patients until now (positive rate of 47%) but the molecular studies are still ongoing. From these, 12 alterations were already reported although 6 require functional studies in order to determine their pathogenicity. Furthermore, 3 novel *LDLR* variants were found: p.Glu267Lys (Portugal), p.Asp307Gly and c.-135C>A (Argentina) that also need functional validation as mutation causing disease. Among all patients, 2 were compound heterozygous (Mexico and Argentina) and 1 true homozygous (Argentina).

Conclusions: Although more than 1300 variants have been described in the *LDLR* there are still novel variants being found, proving the heterogeneity of FH. These results will contribute for the elucidation of the molecular basis of FH in Ibero-america.

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