

Poster

Study of the genotype-phenotype correlation in fibroblasts of patients with mutations in COQ4.



Verónica Astillero López (1), Guillermo López Lluch (1,2), Gloria Brea-Calvo (1,2), María Alcázar Fabra (1), Plácido Navas Lloret (1,2), Daniel José Moreno Fernández-Ayala (1,2).

(1) Centro Andaluz de Biología del Desarrollo (CABD-CSIC), Universidad Pablo de Olavide, Seville, Spain.

(2) CIBERER, Instituto de Salud Carlos III, Seville, Spain.

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ABSTRACT

Motivation: Coenzyme Q10 (CoQ10), or ubiquinone, has a crucial role in the energetic metabolism due to its redox capacity in the electron transport chain (ETC), where it shuttles electrons from complex I or II to complex III. Lack of this essential component leads to mitochondrial disorders characterized by a rare condition with a huge spectrum of different phenotypes and different genetic mutations. To date, specific genotype-phenotype correlations do not exist because the link between specific genetic defects and phenotypes is unclear. In this way, the diagnosis and treatment of these patients is so complicated. The diagnosis on time is extremely important to start the treatment in order to avoid the fulminant course of the disease with an irreversible damage and a fatal outcome.

In a previous study reported in our lab it was described that CoQ10-deficient fibroblasts (independently from the etiology) showed a common transcriptomic profile. The expression of certain genes was modified in the same way, that is to say, they were always increased or decreased. COQ4 is one of the genes involved in CoQ10 biosynthesis. It has been also demonstrated that COQ4 mutations are responsible for early-onset mitochondrial diseases with heterogeneous clinical presentations and associated with CoQ10 deficiency. The aim of this work is to find a possible correlation between different COQ4 mutations, the pathological phenotype, the clinical severity of the disease and the level of markers genes expression.

Methods: To achieve this goal, we have used two fibroblast cell lines as control, and four mutant fibroblast cell lines from patients with different COQ4 mutations. We have performed different genetic and biochemical assays such as analysis of the expression profile by microarray, Seahorse or flow cytometry.

Results: Fibroblasts from subjects with COQ4 mutations show similar profiles between them, and at the same time, they show a different profile when we compared them to control fibroblasts. In addition, a more differentiated profile is observed according as the severity of the symptoms increases. Taken together, these results suggest a correlation between the phenotype and the clinical severity.

Conclusions: Cells with COQ4 mutations look for an adaptive biological response to face the mitochondrial damage due to the CoQ10 deficiency. And interestingly, our results suggest an association between genotype and phenotype in these patients.

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