STUDIES ABOUT THE NEW VARIANT OF TRANSTHYRETIN A19D INVOLVED IN THE FAMILIAL AMYLOIDOTIC CARDIOMYOPATHY

Andrade, C.A.; Ferreira, P. S.; Antonio Pereira-Neves; Foguel, D.

1Instituto de Bioquímica Médica, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil.

2Fiocruz Pernambuco, Research Center Aggeu Magalhães, Department of Microbiology, Brazil.

Introduction: Mutations in the transthyretin (TTR) gene are known to destabilize the structure of protein and facilitate the aggregation process causing an amyloidosis which can be characterized by the involvement of peripheral nerves and cardiac function. We reported a patient from the south region of Brazil, and his family from Swedish/German origin, with a rare mutation in exon 2 of TTR gene where we have a substitution of an Ala for an Asp at the codon 19, causing a severe compromise of cardiac function characterizing the Familial Amyloidotic Cardiomyopathy (FAC).

Objective: The objective of this work was to available the toxicity of aggregates formed by this mutant in primary culture of mice Swiss cardiomyocytes and others cell lines in order to validate the toxicity of the mutant to these tissues.

Materials and Methods: For this study, we cloned and expressed the mutant. The aggregates were prepared by acidification. The primary cardiomyocytes culture was characterized by immunohistochemistry with antibody anti desmin. The viability assay was performed with Live/Dead, MTT and LDH assay.

Results: The primary culture of mice Swiss cardiomyocytes and cardiac fibroblasts were incubated with the mutants A19D or V122I in the oligomeric state or with the fiber fraction for 24h or 48h. We have noticed in morphological analysis that the cells, which were incubated with the mutants A19D or V122I in the oligomeric state, showed pyknotic nuclei. The cells that were incubated with the oligomeric state of the protein showed a reduction of the viability cellular, whereas the cells that were incubated with fiber fraction haven’t had a decrease in the cell viability. Conclusions: Our data suggests that the mutant A19D in the oligomeric state is more toxicity than the fibril form for primary culture of mice Swiss cardiomyocytes and cardiac fibroblasts.

Key Words: FAC; Transthyretin; cardiomyocytes