IJAE
Vol. 123, n. 1 (Supplement): 161, 2018
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Cell damage due to amyloid aggregation process on cell membrane involves membrane ganglioside GM1

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The term amyloidosis describes a wide group of pathologies occurring in various tissues, and characterized by the presence of proteinaceous deposits grown from different peptides/proteins, yet sharing similar structural features, the cross-beta structure. Amyloid aggregates may interact with a wide variety of lipid or protein molecules on cell surface, thus inducing membrane destabilization and cell damage. Such surface molecules may interact with monomeric or oligomeric amyloid species, enhancing aggregate nucleation. It is known that the amphipathic structure of amyloid peptides may prompt them to aggregate and eventually to interact with different molecules to gain structural stability in the fibrillar form. Therefore, the cytotoxic properties of fibrillar assemblies may differ on the basis of the physicochemical properties of the interacting molecules. Among the membrane molecules that interact with amyloid fibrils, the GM1 ganglioside raised great interest and contradictory data emerge from literature. In fact, cytotoxic effects of the interaction between amyloid aggregates and GM1 on cell membranes have been demonstrated [1]. On the other hand GM1 appears to contrast amyloid toxicity [2]. In this study, GM1 interaction with various amyloid intermediates at the cellular level were analyzed. To this purpose, amyloid aggregation process of Sup35 was studied by using confocal microscopy, transmission electron microscopy, and spectroscopy techniques. Sup35 is a yeast translation termination factor that has no homologous endogenous proteins in mammalian cells, and therefore allows to analyze structural and molecular basis of amyloid cytotoxicity in the absence of any physiological interference with cell elements. In vitro- experiments were performed on a murine endothelioma (H-END) cell line using the same amyloid peptides.

This work was supported by grants from MIUR FIRB 2010 and MIUR PRIN-2009.

References

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Key words

Amyloidosis, aggregation, GM1, Sup35.

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