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Role of GM1 in the Interaction between Amyloid Prefibrillar Oligomers of Salmon Calcitonin and Model Membranes

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Abstract : We investigated induced functional effects by evaluating Ca2+-influx in liposomes and cell viability in HT22-DIFF neurons. Only solutions rich in unstructured Prefibrillar-Oligomers (PFOs) were able, in the presence of Monosialoganglioside-GM1 (GM1), to induce Ca2+-influx and were also neurotoxic, suggesting a correlation between the two phenomena. Thus, in the presence of GM1, we investigated the protein conformation and liposome modification due to the interaction. Circular Dichroism showed that GM1 fostered the formation of β-structures and Energy Filtered-Transmission Electron Microscopy that PFOs formed “amyloid-channels” as reported for Aβ. We speculate that electrostatic forces occurring between the positive PFOs and negative GM1 drive the initial binding, while the hydrophobic profile of the flexible PFO is responsible for the subsequent pore formation. Conversely, the rigid β-structured mature/fibers (MFs) and proto-fibers (PFs) were unable to induce membrane damage and Ca2+- influx.

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