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Membranes as modulators of amyloid protein misfolding and target of toxicity

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ABSTRACT

Abnormal protein aggregation is a hallmark of various human diseases. α-Synuclein, a protein implicated in Parkinson's disease, is found in aggregated form within Lewy bodies that are characteristically observed in the brains of PD patients. Similarly, deposits of aggregated human islet amyloid polypeptide (IAPP) are found in the pancreatic islets in individuals with type 2 diabetes mellitus. Significant number of studies have focused on how monomeric, disaggregated proteins transition into various amyloid structures leading to identification of a vast number of aggregation promoting molecules and processes over the years. Inasmuch as these factors likely enhance the formation of toxic, misfolded species, they might act as risk factors in disease. Cellular membranes, and particularly certain lipids, are considered to be among the major players for aggregation of α-synuclein and IAPP, and membranes might also be the target of toxicity. Past studies have utilized an array of biophysical tools, both *in vitro* and *in vivo*, to expound the membrane-mediated aggregation. Here, we focus on membrane interaction of α-synuclein and IAPP, and how various kinds of membranes catalyze or modulate the aggregation of these proteins and how, in turn, these proteins disrupt membrane integrity, both *in vitro* and *in vivo*. The membrane interaction and subsequent aggregation has been briefly contrasted to aggregation of α-synuclein and IAPP in solution.

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