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The Formation of Alzheimer's Plaques in Synthetic Membranes

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Alzheimer's disease is a type of dementia that affects memory, thinking, and behaviour. One of the hallmarks of the disease is the formation of neurotoxic senile plaques, primarily consisting of amyloid-β peptides. Despite their importance for the pathogenesis of the disease, little is known about the properties of these plaques and the process by which they form.

We developed a model system to study the formation and properties of Alzheimer's plaques in-vitro. Synthetic anionic lipid membranes with brain-like composition were prepared that included different concentrations of the amyloid-β(25-35), the transmembrane segment of the full 42 amino acid long peptide. The systems were prepared as multi-lamellar membranes supported on silicon chips. We investigated size, density and molecular properties of these plaques using optical microscopy and X-ray diffraction. At concentrations of 3mol%, the peptides were dispersed in the membranes, but at concentrations of 10mol% and 20mol%, peptide aggregates were observed.

Plaques formed from amyloid-β aggregates were typically around 12 to 13 micrometers in diameter. With increasing peptide concentration, the density of small plaques increased, however, their size stayed approximately constant. The aggregates were found to form inside the membranes and to coexist with the membrane structure. We used X-ray diffraction to determine the molecular structure of the membranes and peptide structure. At concentrations of 3mol%, only the alpha-helix signal was detected whereas in the 10mol% and 20mol% samples, both alpha-helix and beta-sheet signals were detected.

The preparation of synthetic Alzheimer's tissue is a milestone for the in-vitro testing of anti-Alzheimer's drugs before they go into clinical studies. By preparing membranes of different composition, such as saturated and unsaturated lipids, cholesterol and hormones, quantitative information about plaque formation can be obtained.

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