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Oxidative Mapping of Alzheimer's Disease Amyloid Fibrils

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Alzheimer's disease amyloid fibrils are conglomerates of a large number of Abeta peptide molecules (40-43 residues). Because of their size, and rapid formation, conventional NMR and X-ray structural methods cannot be applied to the fibrils. Using X-ray radiolysis methodology amyloid fibril structure is being mapped. Carefully prepared fibril samples are radiolyzed, and then the oxidized Abeta is recovered via chemical solubilization. The oxidative pattern is then analyzed via liquid chromatography mass spectrometry using an ion-trap detector. Multiple rounds of mass spectrometry are necessary to fully map the sites of oxidation. Mapping data from these experiments is then combined with other chemical modification data, and will be used to construct atomistic models of amyloid fibril structure. This will set the stage to use the structure of the amyloid fibril as well as that of soluble Abeta as input structures for reaction path calculations.