

Enhanced Fibril Fragmentation of N-Terminally Truncated and Pyroglutamyl-Modified A β Peptides.

Wulff M, Baumann M, Thümmeler A, Yadav JK, Heinrich L, Knüpfer U, Schlenzig D, Schierhorn A, Rahfeld JU, Horn U, Balbach J, Demuth HU, Fändrich M (2016) Enhanced Fibril Fragmentation of N-Terminally Truncated and Pyroglutamyl-Modified A β Peptides. *Angew Chem Int Ed* 55(16), 5081-5084.

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Abstract

N-terminal truncation and pyroglutamyl (pE) formation are naturally occurring chemical modifications of the A β peptide in Alzheimer's disease. We show herein that these two modifications significantly reduce the fibril length and the transition midpoint of thermal unfolding of the fibrils, but they do not substantially perturb the fibrillary peptide conformation. This observation implies that the N terminus of the unmodified peptide protects A β fibrils against mechanical stress and fragmentation and explains the high propensity of pE-modified peptides to form small and particularly toxic aggregates.

Involved units

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