PLENARY SPEAKER II

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A cause of neurodegeneration? Structural interpretation of Cu binding in N-Truncated Amyloid-β Peptides from X-ray Absorption Spectroscopy

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by the presence of amyloid plaques composed mainly of amyloid-β peptides (Aβ). Soluble, diffusible Aβ oligomers of unknown structures may be involved in extensive redox chemical reactions possibly causing cellular toxicity. The first protein sequencing studies of the Aβ plaque core (APC) of AD patients identified NH_2-terminal heterogeneity; the majority (64%) of the APC-AD Aβ peptides begin with a F_4 residue. Novel X- ray Absorption Spectroscopy (XAS) of Cu-Aβ under in situ electrochemical control (XAS-SEC) with propagation of uncertainty for hypothesis testing has allowed elucidation of the relationship between the truncated peptide structures and the redox properties of the Cu II bound. XAS of Cu II :$Aß_{1-16}$ and Cu II :$Aß_{4-y}$ (y=9,12,16) frozen solutions (10 K) and XAS-SEC at room temperature under potentiostatic control have been measured. In two experiments at the Australian Synchrotron XAS beamline, the excellent performance is demonstrated by the structural uncertainty of the final results. Derivation of new structural models for binding of Cu I and Cu II with N- truncated Aβ peptides helps to explore the reduction properties in the peptide. We explain how this can be an explanation of the cause of neurodegeneration.