

**P028** Cu(II) and Zn(II) interaction with  $\beta$ -amyloid peptide fragments affect their oligomerization and toxicity  
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Different transition metals play a prominent role in Amyloid- $\beta$  peptide ( $A\beta$ ) conformational change and toxicity (Huang et al. 2004 Ann. NY Acad Sci. 1012, 153), particularly  $Cu^{2+}$  and  $Zn^{2+}$  due to their crowding in and around amyloid plaques of Alzheimer's disease (AD) (Barnham et al. 2004 Nature Rev. Drug Discovery, 3:205). Different  $A\beta$  peptides were incubated under different conditions in the presence of these metal ions. Circular Dichroism spectra in the UV region revealed characteristic changes toward the aggregation-prone  $\beta$ -sheet conformation, whereas Dot-Blot analysis indicated increased oligomerization. Moreover, an increase of peptide toxic activity was observed on cell cultures. Metal-peptides interaction was further characterized using a new  $A\beta(1-16)/PEG$  conjugate encompassing the amino acid residues involved in metal coordination.  $Zn^{2+}$  and  $Cu^{2+}$  metal complex speciation and spectroscopic characterization (CD, UV-Vis, EPR, ESI-MS, NMR), carried out at different metal to ligand ratios, revealed that  $A\beta(1-16)/PEG$  can bind up to three zinc ions or four copper ions at preferential binding sites. These results are in agreement with the notion that soluble  $A\beta$  oligomers and protofilaments are responsible of cell death and the presence of certain metal ions favor changes toward toxic activity.