Chem Sci J 2017, 8:3 (Suppl)
DOI: 10.4172/2150-3494-C1-012

Characterisation of metal-ligand interactions and the effect of metal ions on the gene expression of amyloid precursor protein

Gayani Petersingham, Narsimha Reddy, Allan Torres and **Ming J Wu**
Western Sydney University, Australia

Metal ions such as Al^{3+}, Zn^{2+}, Fe^{2+} and Cu^{2+} have been implicated in the aggregation of amyloid β peptide (Aβ). Various factors such as amyloid precursor protein (APP), Aβ and metal ions have been identified to play a role in Alzheimer's disease (AD), a progressive neurodegenerative condition. Aβ serves as a ligand for metal ions and such coordination can cause Aβ aggregation, a hallmark in AD. This research aims to first characterise interactions by nuclear magnetic resonance (NMR) between metal ions and histidine (a key coordinating residue in Aβ) as well as other biological and synthesised compounds, secondly to uncover the effects of metal ions on the expression of APP. ^{1}H NMR titrations demonstrated that histidine coordinates strongly to metal ions via binding sites in amide, carboxylic group and N1-imidazole nitrogen- which is free to coordinate in Aβ. The relative chemical shift deshielding and line broadening indicate Al^{3+} bind stronger, compared to the other metals tested. The cytotoxicity analysis indicates ligands such as histidine and glutathione prevent the toxicity of metals such as Al^{3+} and Cr^{6+} in mammalian cells more effectively than known metal-sequestering agents like maltol, citric and malic acids. The findings could benefit development of therapeutic drugs for metal-related health problems such as acute metal poisoning and chronic disorders such as AD. The effect of metal ions on the expression of APP is currently being investigated in mammalian cells by quantitative polymerase chain reaction (qPCR). The panel of ligands examined in the previous NMR analysis will then be screened for their interaction with the metal ions on APP expression. Because of the scant knowledge at the present on whether accumulation of metal ions can affect APP expression, the outcomes of this project could provide details to fill in the gap.

g.petersingham@westernsydney.edu.au