Prion Protein Aggregation Induced by Copper(II) and Heparan Sulfate. Pressure-dependent Switch of Reaction Pathways

Driss El Moustaine, Joan Torrent, and Reinhard Lange

Univ Montpellier 2, Montpellier, F-34095 France; Inserm, U710, Montpellier, F-34095 France; EPHE, Paris, F-75007 France

Reprint requests to Reinhard Lange. E-mail: reinhard.lange@inserm.fr


Dedicated to Professor Gérard Demazeau on the occasion of his 65th birthday

Copper ions (Cu^{2+}) and heparan sulfate (HS) are suspected to act as regulatory agents in the conversion of cellular prion protein (PrP^{C}) to its infectious isoform. However, the mechanism of this reaction is still largely unknown. Our previous report suggested multidimensional pathways for structural alterations of PrP, which may be modulated by high pressure (HP). Here we use HP to investigate the effects of Cu^{2+} and HS binding on PrP conformational changes and assembly. In the presence of Cu^{2+}, amyloid fibrils are formed only under HP. In contrast, in the presence of HS, fibrils are formed at atmospheric pressure, but not under HP. Both compounds appear to compete for the same binding site, since HS-supported fibril formation is quenched by Cu^{2+}. Inversely, Cu^{2+}-mediated fibril formation under HP is inhibited by HS.

Key words: Prion Protein, Copper, Heparan Sulfate, Amyloid Fibrils, High Pressure