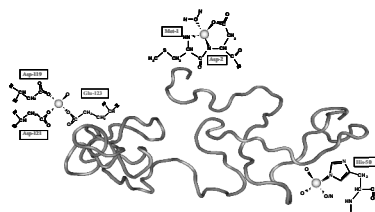


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INTERACTIONS OF METAL IONS AND METAL-BASED COMPOUNDS WITH ALPHA-SYNUCLEIN: FROM BASIC RESEARCH TO THERAPY

The aggregation of alpha-synuclein (AS) is a critical step in the etiology of Parkinson's disease (PD). Protein-metal interactions play an important role in AS aggregation and might represent the link between the pathological processes of protein aggregation, oxidative damage and neuronal cell loss. Our studies revealed a hierarchical effect of metal interactions on AS aggregation kinetics, dictated by structural factors corresponding to different protein domains [1-3]. These results constituted the basis to investigate the impact of metal ion occupancy on the binding and inhibitory capacity of anti-amyloidogenic small molecules [4,5]. The elucidation of molecular and structural determinants of these interactions serves as scaffold for on going structure-based drug discovery efforts targeting AS amyloid formation.



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