Abstract No.280

Homocysteinylation of Intrinsically Disordered Proteins (IDP) and their Tranformations

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Elevated homocysteine levels are resulting in N-homocysteinylation of lysyl residues in proteins and they correlate with a number of human pathologies. However, the role of homocysteinylation of lysyl residues is still poorly known. In order to study the structural impact of homocysteinylation of IUPs intrinsically unstructured proteins such as ovine PrP and bovine caseins were used. Besides ovine PrP, α_{S1}-, β- and κ-caseins, showing different aggregations and micelle formation, were modified with homocysteine-thiolactone. Intrinsic and extrinsic fluorescent markers such as Trp, thioflavin T, ANS and CD spectra, reveal structural changes of casein and PrP structures after homocysteinylation reflected by an increase in beta-sheet content characteristic of amyloid-like transformations. Homocysteinylation of studied IUPs leads in all cases to aggregation. The sizes of aggregates and aggregation rates were dependent on homocysteine thiolactone concentration and temperature. N-Hcy-PrP formed insoluble multimers. DLS and microscopic studies of modified caseins and PrP have revealed the formation of large aggregates of about 1-3 µm. Homocysteinylation of α_{S1}- and β-caseins results in formation of regular spheres. Homocysteinylated κ-casein forms thin unbranched fibrils about 400-800 nanometers long. In case of κ-casein amyloidogenic effect of homocysteinylation was confirmed by Congo red spectra. Taken together, data indicate that N-homocysteinylation provokes significant changes in properties of native caseins and PrP. A comparison of amyloidogenic transformation of 3 different casein types, belonging to the IUP protein family, shows that the efficiency of amyloidogenic transformation upon homocysteinylation depends on micellization capacity, additional disulphide bonds and other structural features.

Keywords: Homocysteinylation, Intrinsically Disordered Proteins, Aggregation, κ-caseins.

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MesoScopic Biophysics – The Foundations, Frontiers & The Challenges

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Physics at the interface of microscopic and nanoscopic scales, the so-called "Mesoscopic Scale", ranging from 0.1 to 1.0·m, has immense potential for the understanding of living systems, especially in cellular physiology. This is the regime where classical effects tend to drop off and the quantum mechanical effects begin to affect the dynamics of the system. This talk presents an acquaintance with the interesting biophysics at the mesoscopic scale. Starting with a quick orientation with underlying foundations of the subject, a discussion on various techniques and problems in mesoscopic biophysics is presented. The talk builds an argument by developing a rationale that how could physics at the mesoscopic scale be different from that at the nano and micro scales and the way it could possibly have significant repercussions on living systems. The possibilities of emergence of biophotons within the Infra-red spectral regions, photon evanescent tunneling and Quantum Mechanical Resonant Tunnelling (QMRT) of clusters of electrons within cells are cited as a few cases of mesoscopic biophysical phenomena. The theoretical treatment of these systems, especially in a biological environment, is a hard problem, however, computational methods could provide valuable insight. Since the dimensions are favorable at these scales, viable experimental methods and techniques could be developed to tap these interesting phenomena and effects. The talk concludes with an exhaustive introduction to the major challenges in developing techniques for probing living systems at the mesoscopic scale (under physiological conditions). If these challenges could be successfully circumvented, a whole new field of science could be opened, where novel theoretical ideas like possible electromagnetic channels for signal transduction and inter-cellular signaling via weak IR links could be appreciated.

Keywords: Mesoscopic Biophysics, Cell Signalling, Signal Transduction, Electromagnetic Channels.