Probing Protein Interaction with Proteins, Heavy Metal Ions and Nanoparticles

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Protein-protein interaction: Protein-protein interactions (PPIs) are crucial for numerous biological processes, including signal transduction, metabolism, inter-cellular interactions etc. One such PPI is found between pathogenic E.coli and human intestinal cells (enterocytes). The protein complex formed there is termed the Intimin-Tir complex, which is the main virulence factor behind the diseases caused by pathogenic E.coli[1]. We aim to probe the strength of this complex using AFM based Single-Molecule Force Spectroscopy (SMFS), which will provide new insights into the mechanism of adherence. We also aim to perform ensemble experiments to study the thermodynamics and kinetics of complex formation.

Protein-heavy metal ion interaction: Heavy metal ion toxicity at cellular level is widely studied, which includes cell membrane rupture, increase in ROS etc[2]. At the molecular level, how these heavy metal ions interact with biomolecules like proteins, lipids etc. to ultimately bring such cellular change is still not very well explored. To get a molecular insight of these interactions, we have studied the effect of Pt (II) ion on the native state of SUMO1 where we report the formation of a molten globule in an equimolar mixture of SUMO1 and Pt (II) salt.

Protein-nanoparticles interaction: Nanoparticles (NPs) are potential candidates in the field of medicine and are being developed for targeted drug delivery. The fate of these NPs inside the biological system is not predictable due to limited information available on the interaction of NPs with biomolecules. We aim to study NPs-Protein interaction using Gold NPs (AuNPs) and SUMO-1 and its mutant as our model system. We studied SUMO-1 interaction with AuNPs using fluorescence, DLS, UV-Vis Spectroscopy and HSQC NMR. HSQC-NMR studies resulted in negligible chemical shift perturbation of SUMO-1 residues in the presence of AuNPs while the rest of the techniques suggested that there are significant interactions and increment in the aggregation propensity of AuNPs. In the past, HSQC-NMR has been used to probe NP-Protein interaction[3]. However, our studies suggest that HSQC-NMR can't capture the residue level information of NP's-Protein interactions.

References:

1) Luo, Y., Frey, E., Pfuetzner, R. *et al.* Crystal structure of enteropathogenic *Escherichia coli* intimin–receptor complex. *Nature* 405, 1073–1077 (2000).
2) Beyersmann D, Hartwig A. Carcinogenic metal compounds: recent insight into molecular and cellular mechanisms. *Arch Toxicol.* 82, 493-512 (2008).
3) Calzolai L, Franchini F, Gilliland D, Rossi F. Protein-nanoparticle interaction: identification of the ubiquitin-gold nanoparticle interaction site. *Nano Lett*. 10, 3101-5 (2010).