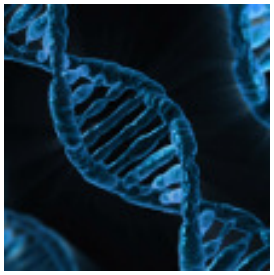

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KEYNOTE 3 - Characterization of intrinsically disordered proteins and their dynamic complexes by NMR spectroscopy

Monday 4 June 2018 15:45 (40 minutes)

Over the last two decades, the classical structure-function paradigm has gradually been revisited with the discovery and the increasingly recognized importance of intrinsically disordered proteins (IDPs). IDPs do not rely on a well-defined three-dimensional structure to be functional, but rather exploit their intrinsic conformational dynamics for carrying out a wide range of biological functions. It is estimated that around 40% of the human proteome is intrinsically disordered or contain disordered regions of significant length, and it has been shown that intrinsic disorder is particularly abundant in proteins implicated in human diseases underlining the importance of understanding the conformational properties and functional interactions of IDPs at the molecular level.
Nuclear magnetic resonance (NMR) spectroscopy is the most promising technique for visualizing the structure, dynamics and interactions of IDPs at atomic resolution. Here, our sample-and-select approach will be presented for obtaining representative ensemble descriptions of IDPs on the basis of experimental NMR data providing detailed insight into the conformational sampling of IDPs at amino acid resolution [1]. In addition, experimental NMR approaches will be presented for characterizing the structure, dynamics and kinetics of complexes involving IDPs. Examples will be given of functional protein disorder in important biological systems such as paramyxoviruses [2], the nuclear pore complex [3] and cell signaling cascades [4,5].

[1] Jensen et al, Chem. Rev. 114 (2014) 6632–6660.
[2] Schneider et al, J. Am. Chem. Soc. 137 (2015) 1220–1229.
[3] Milles et al, Cell 163 (2015) 734–745.
[4] Kragelj et al, Proc. Natl. Acad. Sci. U. S. A. 112 (2015) 3409–3414.
[5] Delaforge et al, J. Am. Chem. Soc. 140 (2018) 1148–1158.

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