

Understanding the functional role of the intrinsically disordered proteome

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Higher eukaryotic proteomes contain extensive unstructured intrinsically disordered regions. These regions often control the localisation, stability and modification state of a protein. Yet, the functional role of the vast majority of these regions is still unknown. Various estimates have suggested that there may be upwards of one hundred thousand interaction interfaces in these regions. However, to date, only a small portion of the functional elements predicted to reside within these regions have been characterised. The majority of known interfaces in disordered regions belong to a class of compact, degenerate and *ex nihilo* evolvable interaction modules known as short, linear motifs (SLiMs). In this talk, we introduce our recent work characterising the regulatory SLiM modules recognised by the two key enzymes, the Anaphase-Promoting Complex/Cyclosome (APC/C) and Protein Phosphatase 2A (PP2A). We discuss how the information encoded in the sequence of the disordered regions allow these proteins to alter their function in reaction to cell state changes, thereby allowing conditional decision-making. Finally, the growing consensus that the disordered regions of proteins are the key determinant of the post-translation regulation that controls the life of almost all proteins from their synthesis to their destruction will be discussed.