Poster Presentation

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Conformational plasticity in the regulation of nuclear receptor gene transcription

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Despite lacking of permanent secondary or tertiary structure, Intrinsically Disordered Proteins (IDPs) perform a large variety of functions that are crucial for signalling, regulation and maintenance. Functions performed by IDPs are complementary to these executed by globular ones indicating that the biophysical properties of disordered proteins dictate their functional mechanisms. Conformational plasticity, large solvent accessibility, and transient structuration are inherent characteristics of IDPs that are ideal to trigger signalling, and to precisely regulate biological processes. The relevance of IDPs has fostered an intense research to structurally and dynamically characterize these proteins and their functional complexes. This characterization requires the use of hybrid methods that integrate complementary information from multiple techniques.

Here, we will present our efforts to unveil the structural bases of the modulation of Retinoic Acid nuclear Receptor (RAR) gene transcription by its intrinsically disordered co-repressor. To achieve this aim we have used a hybrid approach integrating Nuclear Magnetic Resonance (NMR), Small-Angle X-ray Scattering (SAXS) and X-ray crystallography. Our results show that co-repressor protein contains partially structured regions that modulate the thermodynamics of the interaction. Moreover, the complex fluctuates between different conformational states that could orchestrate the transition between the repressive to the active state. We show that the presence of ligands or point mutations modulate the dynamics of the complex facilitating this transition.

Keywords: Nuclear Receptor, Intrinsically Disordered Protein, protein dynamics