Structural Analyses of PPAR Oligomeric States

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Nuclear receptors are members of a superfamily of ligand-inducible transcription factors involved in the regulation of biological processes as metabolism, development and reproduction. They are modular proteins that contain two main domains**:** the DNA binding domain (DBD) and the ligand biding domain (LBD). The peroxisome proliferator-activated receptors (PPAR) are members of this family**.** They are activated by natural fatty acids and hypolypidemic drugs of the fibrate class. The PPAR controls a variety of target genes involved in key steps of lipid metabolism, including fatty acid transport, intracellular binding and transcription activation, as well as catabolism (ß-oxidation) and storage.

The characterization of PPAR can unveil new mechanisms for the regulation of lipid metabolism and provide insights into possible molecular determinants of metabolic disorders like obesity and type II diabetes.

In this work we focus on the studies of PPARγ heterodimerization in the presence of retinoid X receptor (RXRa) and also on the studies of oligomers states of nuclear receptors in the absence of its binding partner of heterodimerization in solution with the use of small-angle X-ray scattering (SAXS), dynamic light scattering and native polyacrylamide gel electrophoresis.

As a result, we present a well defined purification protocols of PPARγ DBD-LBD and LBD and the first structural analyses of the oligomeric states of these nuclear receptors according to different protein concentration. The results clearly shown that PPARγ in complex with RXRa form heterodimers in solution and on the other hand the PPARγ itself, unlike the other members of this superfamily, appears as monomers in solution.

Keywords: Nuclear Receptor, Oligomeric States, Peroxisome Proliferator-activated Receptors, Small-angle X-ray Scattering, Transcriptional Regulation

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