Institut Européen de Chimie et Biologie

I E C B

Molecular mechanisms of DNA and coactivator recognition by nuclear receptor heterodimers.

Natacha ROCHEL
Institute of Genetics and of Molecular and Cellular Biology (IGBMC), UMR7104, Illkirch, FRANCE

Nuclear Retinoic Acid receptors (RARs) and the Vitamin D nuclear receptor (VDR) function as ligand-dependent transcriptional regulators, forming heterodimers with Retinoid X receptors (RXRs). RARs mediate the effects of retinoic acid, the active metabolite of Vitamin A, while VDR is regulated by the dihydroxy-vitamin D3. Both receptors regulate many biological functions such as embryonic development, organogenesis, homeostasis, vision, immune functions, and reproduction. Their activation function involves and is controlled by ligands and multiple cofactors (repressors, activators and bridging proteins). Further post-translational modifications resulting from the crosstalk between different signaling pathways provide additional regulations. The numerous players involved allow the sophisticated fine-tuning of transcriptional regulation.
By combining structural and biophysical approaches, we analyzed integral RAR-RXR and VDR-RXR receptors dimers in complex with DNA and coregulators. Our studies give insight into the importance of DNA sequences for binding selectivity and the role of promoter response elements in the spatial organization of the protein domains into functional complexes. These studies provide also data on the allosteric mechanisms controlling the sequential and ordered binding of nuclear receptors and the various protein effectors to target DNA.

Institut Européen de Chimie et Biologie
2, rue Robert Escarpit - 33607 Pessac, France
Tél. : +33(0)5 40 00 30 38 - Fax. : +33(0)5 40 00 22 15
www.iecb.u-bordeaux.fr