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Nuclear Receptors as targets in the treatment of atherosclerosis and related disorders

Nuclear receptors (NR) constitute a superfamily of ligand-activated transcription factors and play major roles in regulating gene expression related to development and homeostasis. NRs signaling pathways control many biological effects that are involved in many diseases such as cardiovascular diseases, obesity and diabetes. Therefore, NRs are targets of choice for drug-based therapeutic interventions. Over the past years, extensive investigations have been launched to delineate the complexity of signal transduction of this class of receptors. Pharmacology of nuclear receptors identify and allow the development of natural and synthetic high affinity ligands respectively. The availability of agonistic ligands for nuclear receptor is crucial to delineate molecular and biochemical mechanisms of biological effects of NR. Careful analysis of the overall regulatory action of NRs led to the emergence of the concept of selective NR modulators. Indeed, one set of NR target genes may be regulated by a any ligand of a given receptor whereas another set may be differentially regulated upon the nature of the ligand tested. This concept provides the basis of new therapeutic opportunities with the notion of several drugs for a common receptor but with distinct final effects. Peroxisome proliferator-activated receptor represents a typical member to illustrate current concepts on nuclear receptor research field.