Expression of APOE regulated by NR1H2 or NR1H3

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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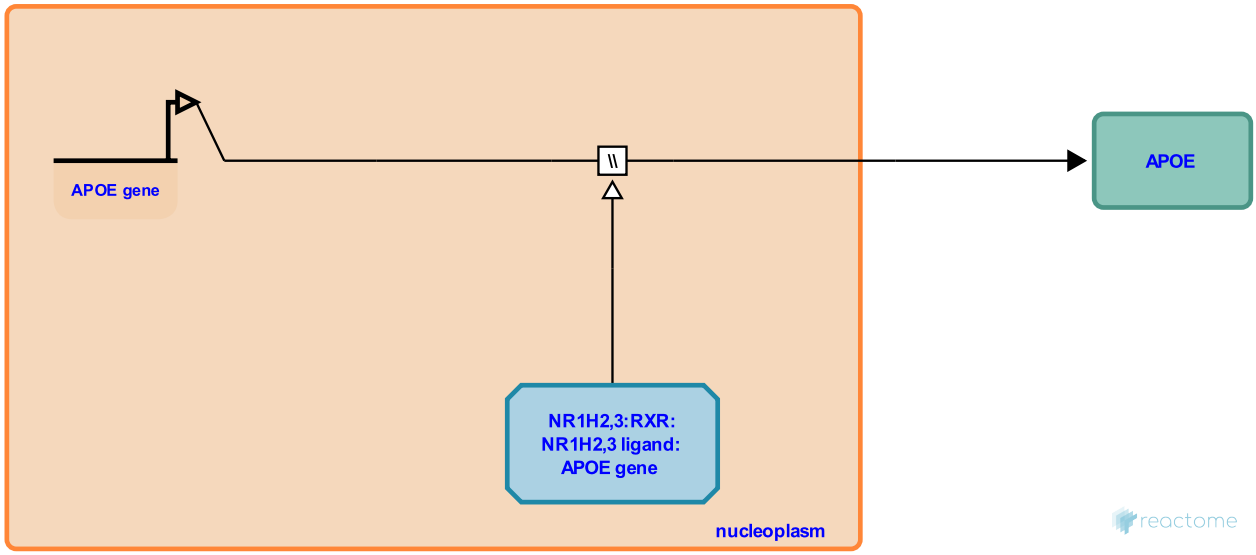
Stable identifier: R-HSA-9031512

Type: omitted

Compartments: nucleoplasm



The apolipoprotein E (APOE) gene is transcribed to yield mRNA and the mRNA is translated to yield protein. APOE, a 34-kD glycoprotein, is involved in lipoprotein clearance by serving as a ligand for the low-density lipoprotein (LDL) receptor family. APOE is primarily lipidated via the ATP-binding cassette transporter 1 (ABCA1), and both are under transcriptional regulation by the liver X receptor α (LXRα or NR1H3) and LXRβ (NR1H2) whose natural ligands are oxysterols such as 24(S),25-epoxycholesterol (24(S),25-epoxy) (Laffitte BA et al. 2001; Beyea MM et al. 2007). The endogenous and synthetic agonists of NR1H2 or NR1H3 increased expression of APOE in human and murine macrophages, and murine adipocytes but not in liver (Laffitte BA et al. 2001; Mak PA et al 2002; Beyea MM et al. 2006). This tissue-specific regulation is conferred by the presence of LXR response elements (LXREs) in multienhancer regions ME.1 and ME.2 downstream of the APOE gene that are revealed only in adipose tissue and macrophages (Shih SJ et al. 2000). In addition, ligand-activated NR1H2 and NR1H3 lead to a dramatic increase in APOE mRNA and protein expression as well as secretion of APOE in a human astrocytoma cell line (CCF-STTG1 cells) to impact cholesterol efflux (Liang Y et al. 2004; Abildayeva K et al. 2006). In the central nervous system, APOE is considered a major apoprotein acceptor for the efflux of cholesterol in the formation of high-density lipoprotein (HDL)-like particles necessary for intercellular lipid trafficking, and is implicated in various neurodegenerative diseases, such as Alzheimer's (reviewed in Hirsch-Reinshagen V & Wellington CL 2007).

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Editions

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