Retinoic acid activates HOXD4 chromatin

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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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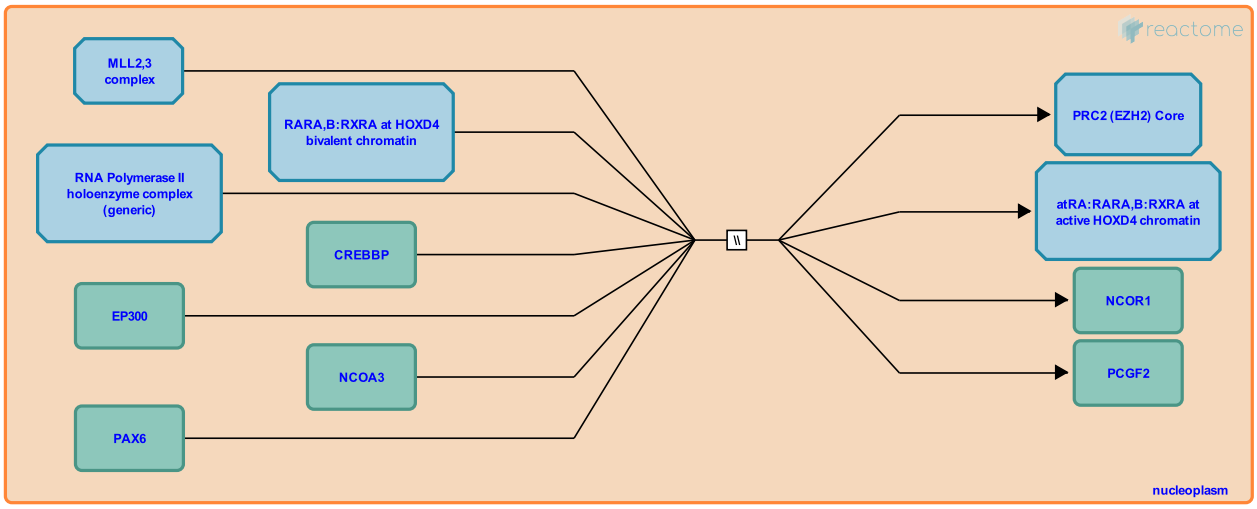
Stable identifier: R-HSA-5617896

Type: omitted

Compartments: nucleoplasm

Inferred from: Retinoic acid activates Hoxd4 chromatin (Mus musculus)



As inferred from mouse embryos, retinoic acid activates the HOXD4 gene in rhombomere 7 (r7) by binding RARB or RARA in RAR:RXR receptor dimers bound to a retinoic acid response element (RAREs) in the 5' flanking region of the gene. Ligand binding by retinoic acid receptors causes dismissal of corepressors such as NCOR1 and recruitment of coactivators such as NCOA3 (Klein et al. 2000). The response of HOXD4 to retinoic acid is also observed in human embryonal carcinoma cells (Moroni et al. 1993, Morrison et al. 1996, Morrison et al. 1997). PAX6 binds near the RARE and is required for maximal activation.

In human fibroblasts chromatin at HOXA genes is activated by loss of methylation at lysine-27 (H3K27me3), loss of Polycomb repressive complex 2 (PRC2), and gain of H3K4me3 (Lan et al. 2007). Similar changes occur at Hoxd4 in mouse embryos. The histone demethylase KDM6A (UTX) binds the HOXD4 gene in human lung fibroblasts and may participate in demethylating H3K27me3 (Lan et al. 2007). Other factors may also be involved in demethylation. KDM6A associates with the histone methyltransferases KMT2C,D (MLL2,3) which may participate in methylating H3K4 (Lee et al. 2007). As inferred from mouse homologs, PCGF2 (MEL18) dissociates from Hoxd4 during activation. After activation by retinoic acid, HOXD4 maintains its own expression by binding and activating its own promoter.

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Editions

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