Retinoic acid activates HOXB1 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-5617452

Type: omitted

Compartments: nucleoplasm

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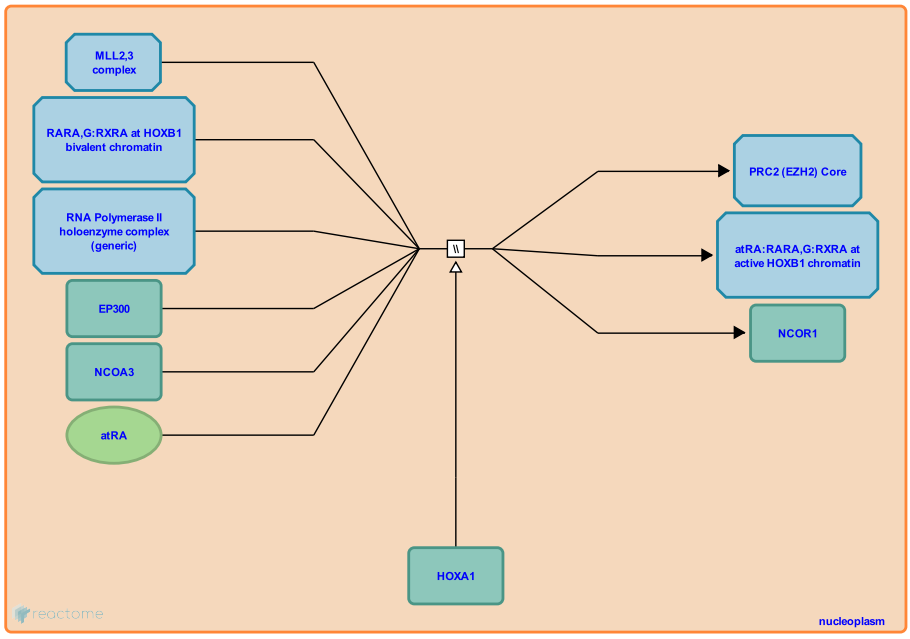

As inferred from mouse embryos and cell lines, retinoic acid binds receptors (RARA or RARG) at retinoic acid response elements (RAREs) located 3' to the HOXB1 gene, causing recruitment of coactivators such as NCOA3 and alteration of chromatin at the HOXB1 gene to an active conformation. Similar activation of the HOXB cluster by retinoic acid is observed in human embryonal carcinoma cells (Simeone et al. 1990). In human carcinoma cells and primary fibroblasts, KDM6A (UTX) binds the HOXB1 gene upon retinoic acid treatment (Agger et al. 2007, Lee et al. 2007) and may demethylate trimethylated lysine-27 of histone H3 (H3K27me3). Reduced H3K27me3 is also observed at HOXB1 in lung fibroblasts (Lan et al. 2007). Other demethylases may be redundant with KDM6A. Polycomb repressive complex 2 (PRC2), which binds H3K27me3, is also lost during activation (Lee et al. 2007). KDM6A forms complexes with the histone methyltransferase KMT2C,D (MLL2,3) which may participate in methylating histone H3 at lysine-4 (H3K4me3), an activating chromatin modification (Lee et al. 2007). After activation by retinoic acid HOXB1 maintains its own expression by binding elements in its own promoter and activating expression (Di Rocco et al. 1997).

In mouse embryos, Hoxb1 is expressed in mesoderm and neurectoderm of primitive streak stage embryos and then becomes restricted to rhombomeres of the hindbrain. Before rhombomere formation Hoxb1 is initially expressed in the region that becomes r3-7. After rhombomere formation Hoxb1 becomes restricted to r4 and is also observed in caudal mesoderm. Hoxb1 activates expression of Egr2 (Krox20), a transcription factor that subsequently activates Hoxa2, Hoxb2, and Hoxb3 and represses Hoxb1.

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Editions

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