RUNX2 regulates osteoblast differentiation

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Introduction

Reactome is an 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


Reactome database release: 80

This document contains 1 pathway and 24 reactions (see Table of Contents)
RUNX2 regulates osteoblast differentiation

Stable identifier: R-HSA-8940973

The complex of RUNX2 and CBFB regulates transcription of genes involved in differentiation of osteoblasts.

RUNX2 stimulates transcription of the BGLAP gene, encoding osteocalcin (Ducy and Karsenty 1995, Ducy et al. 1997). Binding of the RUNX2:CBFB complex to the BGLAP gene promoter is increased when RUNX2 is phosphorylated on serine residue S451 (Wee et al. 2002). Osteocalcin, a bone-derived hormone, is one of the most abundant non-collagenous proteins of the bone extracellular matrix (reviewed in Karsenty and Olson 2016). Association of the activated androgen receptor (AR) with RUNX2 prevents binding of RUNX2 to the BGLAP promoter (Baniwal et al. 2009). When YAP1, tyrosine phosphorylated by SRC and/or YES1, binds to RUNX2 at the BGLAP gene promoter, transcription of the BGLAP gene is inhibited (Zaidi et al. 2004). Signaling by SRC is known to inhibit osteoblast differentiation (Marzia et al. 2000).

Simultaneous binding of RUNX2 and SP7 (Osterix, also known as OSX) to adjacent RUNX2 and SP7 binding sites, respectively, in the UCMA promoter, synergistically activates UCMA transcription. UCMA stimulates osteoblast differentiation and formation of mineralized nodules (Lee et al. 2015).

The SCF(SKP2) E3 ubiquitin ligase complex inhibits differentiation of osteoblasts by polyubiquitinating RUNX2 and targeting it for proteasome-mediated degradation (Thacker et al. 2016). This process is inhibited by glucose uptake in osteoblasts (Wei et al. 2015).

Literature references


https://reactome.org


Editions

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Activated AR binds RUNX2

Location: RUNX2 regulates osteoblast differentiation

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