MMP2, MMP9 cleave SCUBE3

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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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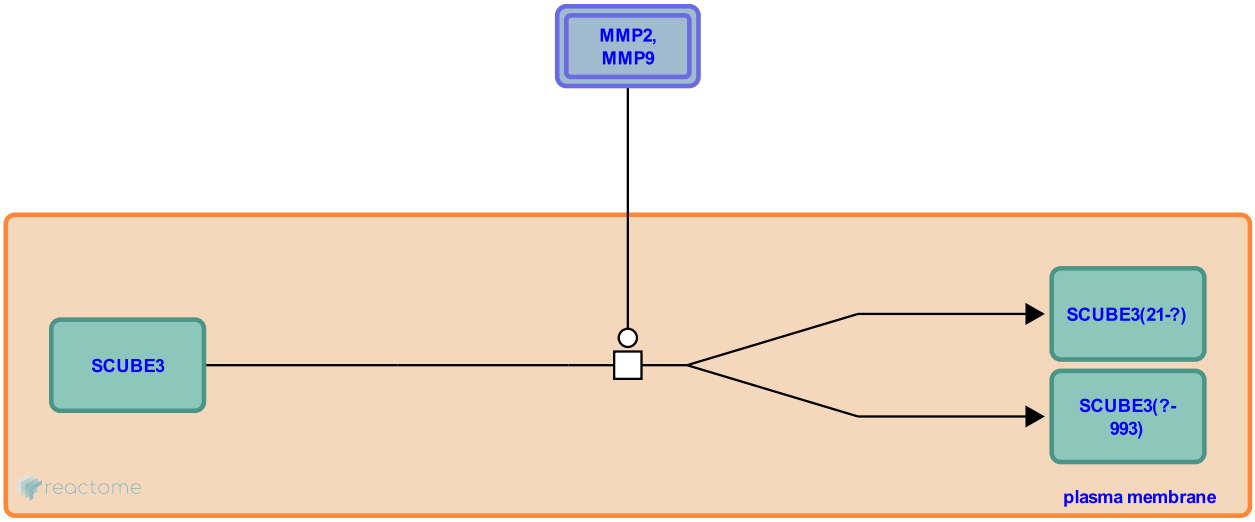
Stable identifier: R-HSA-8943959

Type: transition

Compartments: plasma membrane



Signal peptide-CUB-EGF-like domain-containing protein 3 (SCUBE3) is a secreted glycoprotein that is highly expressed in osteoblasts. It can form homooligomers and heterooligomers with SCUBE1, which stably associate with the peripheral cell surface. In normal lung it is mainly expressed in bronchial epithelial cells. Its expression is upregulated in some lung cancer tumors and correlates with invasive ability in a lung cancer cell line model (Wu et al. 2004, 2011). SCUBE3 knockdown is associated with lower tumor vascular permeability, inhibiting the metastatic potential of Non-small-cell lung carcinoma (Chou et al. 2013).

SCUBE3 can be cleaved by the gelatinases Matrix metalloprotease-2 (MMP2) and MMP9, releasing two major fragments. The C-terminal fragment contains a complement proteins C1r/C1s, Uegf and Bmp1 (CUB) domain. The secreted SCUBE3 protein and the C-terminal CUB domain fragment can bind the Transforming growth factor beta type II receptor (TGFBR2) and activate signaling (Wu et al. 2011). SCUBE3 may act as an FGF co-receptor, augmenting FGF8 signaling (Tu et al. 2014) . Overexpressesion of Scube3 has been linked to significant murine cardiac hypertrophy (Yang et al. 2007). The C-terminal portion of SCUBE3 can physically interact with Transforming growth factor beta-1 (TGFB1) and promote TGFB1-mediated transcriptional activation in vitro (Yang et al. 2007). Consistent with this, the phosphorylated and total protein levels of Smad2, a well-known TGFB1 downstream signaling molecule, are elevated in Scube3 transgenic mouse heart under pressure overload. SCUBE3 may be a component of the regulatory mechanisms for active TGFB1 bioavailability, either systemically or locally in cardiac tissues, under baseline conditions and during pathological stresses. A Scube3 mutant mouse line (carrying a missense mutation in exon 8) has phenotypic alterations that suggest a role of Scube3 in bone metabolism and morphology, hearing, and renal function. The observed morphological abnormalities of the skeleton, impaired bone metabolism and hearing impairments are comparable with the rare metabolic bone disorder Paget disease, which is associated with the chromosomal region that includes SCUBE3 (Fuchs et al. 2016).

Literature references

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Editions

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