SCUBE1, SCUBE3 oligomerize

Jupe, S., Xavier, X.
**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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

**Literature references**


Reactome database release: 78

This document contains 1 reaction (see Table of Contents)
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 (Wu et al. 2004).

Overexpression 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**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Author/Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016-11-01</td>
<td>Authored</td>
<td>Jupe, S.</td>
</tr>
<tr>
<td>2017-01-18</td>
<td>Edited</td>
<td>Jupe, S.</td>
</tr>
<tr>
<td>2017-01-20</td>
<td>Reviewed</td>
<td>Xavier, X.</td>
</tr>
</tbody>
</table>