Phosphorylated SMAD2 and SMAD3 form a complex with SMAD4

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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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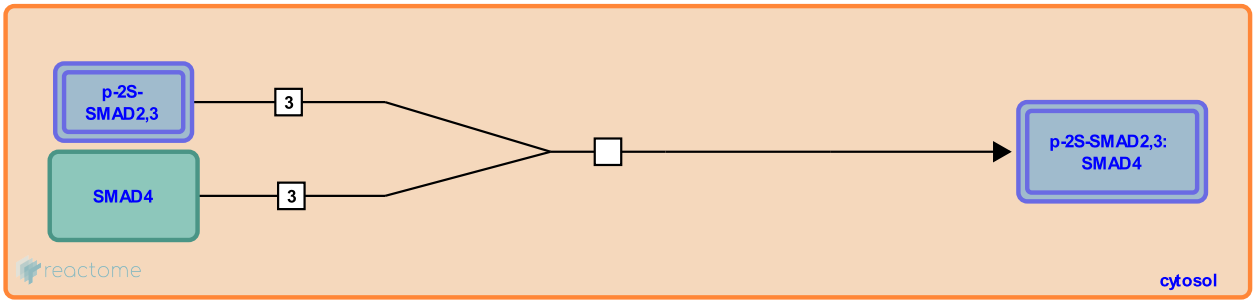
Stable identifier: R-HSA-170847

Type: transition

Compartments: cytosol



The phosphorylated C-terminal tail of R-SMAD induces a conformational change in the MH2 domain (Qin et al. 2001, Chacko et al. 2004), which now acquires high affinity towards Co-SMAD i.e. SMAD4 (common mediator of signal transduction in TGF-beta/BMP signaling). The R-SMAD:Co-SMAD complex (Nakao et al. 1997) most likely is a trimer of two R-SMADs with one Co-SMAD (Kawabata et al. 1998). It is important to note that the Co-SMAD itself cannot be phosphorylated as it lacks the C-terminal serine motif.

ZFYVE16 (endofin) promotes SMAD heterotrimer formation. ZFYVE16 can bind TGFBR1 and facilitate SMAD2 phosphorylation, and it can also bind SMAD4, but the exact mechanism of ZFYVE16 (endofin) action in the context of TGF-beta receptor signaling is not known (Chen et al. 2007).

SARS-CoV-1 nucleocapsid protein (N) associates with SMAD3 and this binding interferes with the complex formation between SMAD3 and SMAD4. By this mechanism N modulates TGF-beta signaling to block apoptosis of SARS-CoV-infected host cells (Zhao et al. 2008).

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