

## Phospho R-SMAD(SMAD2,3):CO-

# SMAD(SMAD4):FOXH1 binds Activin Re-

## sponse Element

Chen, YG., May, B., Peng, C.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of <u>Creative Commons Attribution 4.0 International (CC BY 4.0)</u> <u>License</u>. For more information see our <u>license</u>.

16/05/2024

### 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

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. 7
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. A
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, *14*, e1005968. *オ*

This document contains 1 reaction (see Table of Contents)

### Phospho R-SMAD(SMAD2,3):CO-SMAD(SMAD4):FOXH1 binds Activin Response Element 7

Stable identifier: R-HSA-1225919

Type: binding

Compartments: nucleoplasm

Inferred from: p-Smad2,3:Smad4:Foxh1 binds Activin Response Element (Mus musculus)



As inferred from mouse, DRAP1 binds FOXH1 and inhibits activation of gene expression in response to NODAL signaling.

SMAD2 and SMAD3 do not bind DNA efficiently. They must interact with DNA-binding proteins to activate transcription. FOXH1 interacts with phospho-SMAD2 and phospho-SMAD3 complexed with CO-SMAD (SMAD4) at promoters containing the Activin Response Element (Zhou et al. 1998, Yanagisawa et al. 2000, inferred from Xenopus in Chen et al. 1996, Chen et al. 1997, Yeo et al. 1999). Follicle-stimulating hormone beta subunit (FSHB) and the Lim1 homeobox gene (LXH1) are examples of genes regulated by Activin.

#### Literature references

- Yeo, CY., Chen, X., Whitman, M. (1999). The role of FAST-1 and Smads in transcriptional regulation by activin during early Xenopus embryogenesis. J. Biol. Chem., 274, 26584-90. *¬*
- Weisberg, E., Watanabe, M., Fridmacher, V., Naco, G., Chen, X., Whitman, M. (1997). Smad4 and FAST-1 in the assembly of activin-responsive factor. *Nature*, 389, 85-9. 7
- Sugiyama, M., Uchida, K., Takahashi, T., Masuda, A., Yamaki, K., Saito, T. et al. (2000). Heterogeneities in the biological and biochemical functions of Smad2 and Smad4 mutants naturally occurring in human lung cancers. Oncogene, 19, 2305-11. ↗
- Zawel, L., Zhou, S., Kinzler, KW., Vogelstein, B., Lengauer, C. (1998). Characterization of human FAST-1, a TGF beta and activin signal transducer. *Mol Cell*, *2*, 121-7.
- Rubock, MJ., Chen, X., Whitman, M. (1996). A transcriptional partner for MAD proteins in TGF-beta signalling. *Nature, 383*, 691-6. 7

#### Editions

| 2011-02-14 | Authored, Edited | May, B.   |
|------------|------------------|-----------|
| 2011-08-25 | Reviewed         | Peng, C.  |
| 2012-11-14 | Reviewed         | Chen, YG. |