

Activated FGFR1 binds FLRT1,2,3

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https://reactome.org

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

- 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.
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467.
- 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.

Reactome database release: 88

This document contains 1 reaction (see Table of Contents)

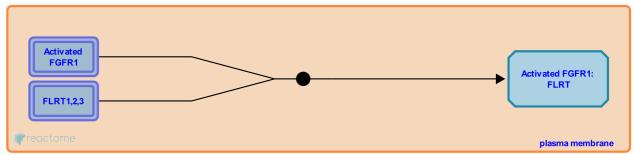
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Activated FGFR1 binds FLRT1,2,3

Stable identifier: R-HSA-5656064

Type: binding

Compartments: plasma membrane



The three fibronectin-leucine-rich transmembrane (FLRT) proteins were identified as positive regulators of FGFR signaling that enhance FGFR-dependent RAS/MAPK pathway activation. All three FLRT proteins have been shown to interact with FGFR1 by co-immunoprecipitation and, at least in the case of FLRT3, the interaction is mediated by the FLRT fibronectin-like domain (Bottcher et al, 2004; Haines et al, 2006). Each FLRT gene has a distinct expression pattern and the strength of the protein-protein interaction with the FGF receptor varies, allowing for cell-type specific modulation of signaling activity (Haines et al, 2006). How the FLRT proteins act to enhance FGFR-dependent MAPK pathway activation is not clear, however FLRT1 has recently been shown to be phosphorylated in an FGFR1- and Src family kinase (SFK)-dependent manner (Wheldon et al, 2010).

Literature references

Rigby, PW., Summerbell, D., Heath, JK., Haines, BP., Wheldon, LM. (2006). Regulated expression of FLRT genes implies a functional role in the regulation of FGF signalling during mouse development. *Dev. Biol.*, 297, 14-25.

Mason, I., Heath, JK., Haines, BP., Rajappa, R., Wheldon, LM., Rigby, PW. (2010). Critical role of FLRT1 phosphorylation in the interdependent regulation of FLRT1 function and FGF receptor signalling. *PLoS ONE*, 5, e10264.

Niehrs, C., Böttcher, RT., Delius, H., Pollet, N. (2004). The transmembrane protein XFLRT3 forms a complex with FGF receptors and promotes FGF signalling. *Nat. Cell Biol.*, *6*, 38-44.

Editions

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