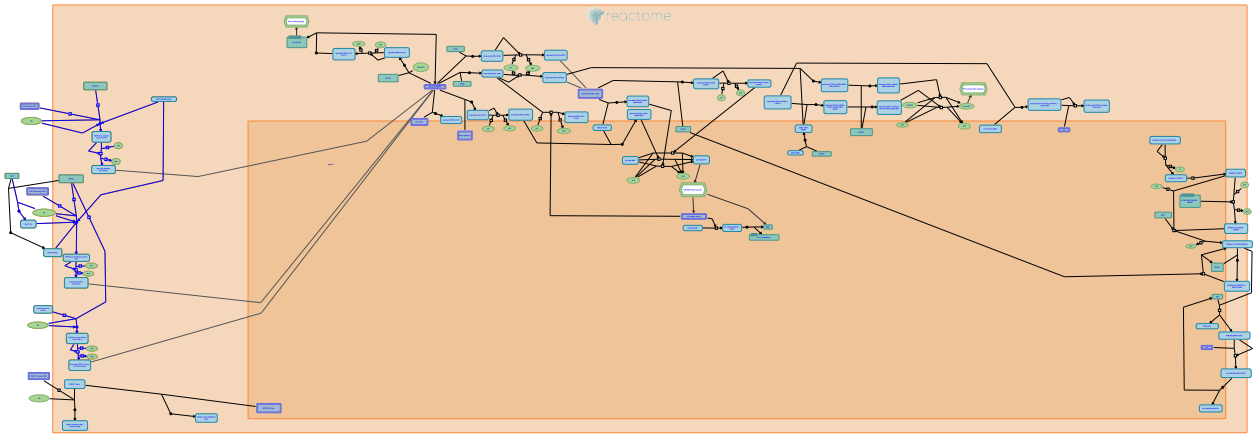
FGFR1 ligand binding and activation



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06/10/2024

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. ↗

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: 90

This document contains 4 pathways (see Table of Contents)

FGFR1 ligand binding and activation ↗

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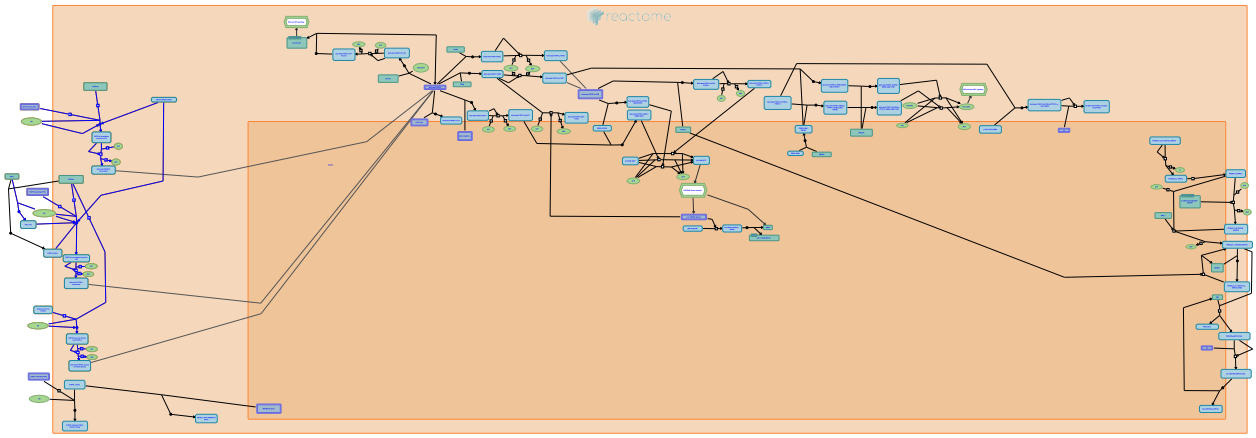


The vertebrate fibroblast growth factor receptor 1 (FGFR1) is alternatively spliced generating multiple variants that are differentially expressed during embryo development and in the adult body. The restricted expression patterns of FGFR1 isoforms, together with differential expression and binding of specific ligands, leads to activation of common FGFR1 signal transduction pathways, but may result in distinctively different biological responses as a result of differences in cellular context. FGFR1 isoforms are also present in the nucleus in complex with various fibroblast growth factors where they function to regulate transcription of target genes.

FGFR is probably activated by NCAM very differently from the way by which it is activated by FGFs, reflecting the different conditions for NCAM-FGFR and FGF-FGFR interactions. The affinity of FGF for FGFR is approximately 10e6 times higher than that of NCAM for FGFR. Moreover, in the brain NCAM is constantly present on the cell surface at a much higher (micromolar) concentration than FGFs, which only appear transiently in the extracellular environment in the nanomolar range.

Literature references

Ornitz, DM., Umemori, H., Mohammadi, M., Olsen, SK., Ibrahimi, OA., Zhang, X. (2006). Receptor specificity of the fibroblast growth factor family. The complete mammalian FGF family. *J Biol Chem, 281*, 15694-700. ↗

Kulahin, N., Soroka, V., Jensen, PH., Poulsen, FM., Tsetlin, V., Hinsby, AM. et al. (2003). Structural basis for a direct interaction between FGFR1 and NCAM and evidence for a regulatory role of ATP. *Structure, 11*, 691-701. ↗

Lardelli, M., Groth, C. (2002). The structure and function of vertebrate fibroblast growth factor receptor 1. *Int J Dev Biol, 46*, 393-400. ↗

Soroka, V., Kiselyov, VV., Berezin, V., Bock, E. (2005). Structural biology of NCAM homophilic binding and activation of FGFR. *J Neurochem, 94*, 1169-79. ↗

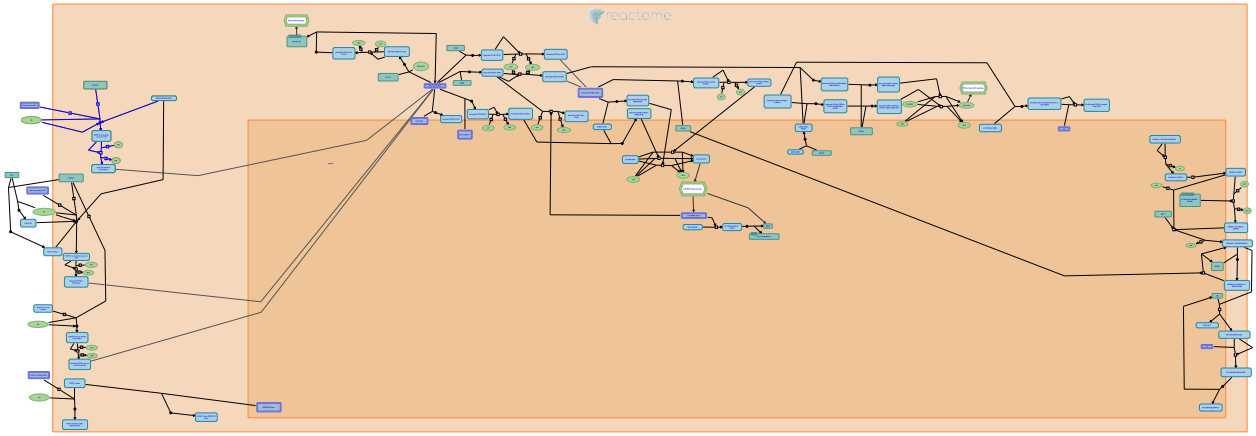
Editions

2007-01-10	Authored	de Bono, B.
2007-02-07	Reviewed	Mohammadi, M.
2007-02-11	Edited	de Bono, B., D'Eustachio, P.
2016-01-06	Reviewed	Grose, RP.

FGFR1b ligand binding and activation ↗

Location: FGFR1 ligand binding and activation

Stable identifier: R-HSA-190370



This pathway depicts the binding of an experimentally-verified range of ligands to FGFR1b. While binding affinities may vary considerably within this set, the ligands listed have been established to bring about receptor activation at their reported physiological concentrations.

Literature references

Ornitz, DM., Umemori, H., Mohammadi, M., Olsen, SK., Ibrahimi, OA., Zhang, X. (2006). Receptor specificity of the fibroblast growth factor family. The complete mammalian FGF family. *J Biol Chem, 281*, 15694-700. ↗

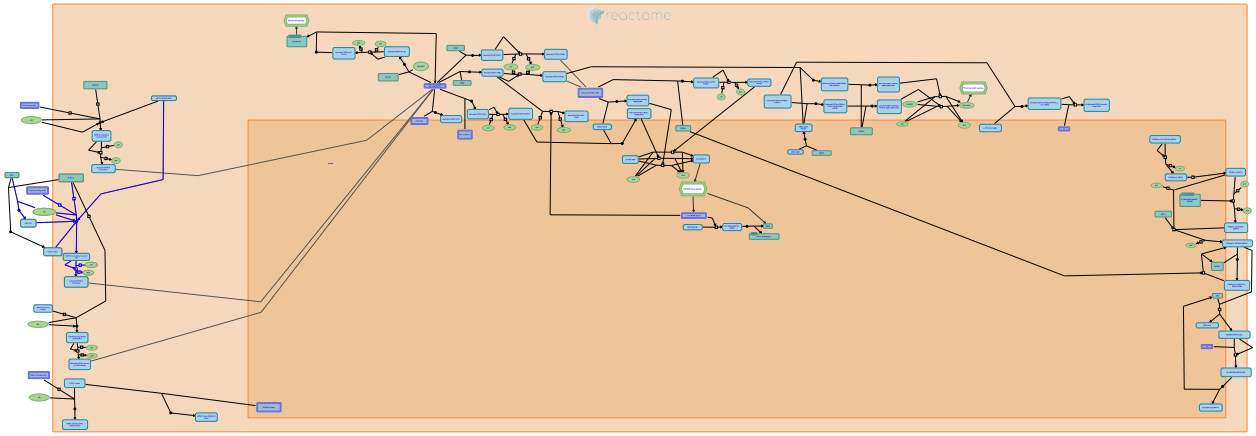
Editions

2007-01-10	Authored	de Bono, B.
2007-02-07	Reviewed	Mohammadi, M.

FGFR1c ligand binding and activation ↗

Location: FGFR1 ligand binding and activation

Stable identifier: R-HSA-190373



This pathway depicts the binding of an experimentally-verified range of ligands to FGFR1c. While binding affinities may vary considerably within this set, the ligands listed have been established to bring about receptor activation at their reported physiological concentrations.

Literature references

Ornitz, DM., Umemori, H., Mohammadi, M., Olsen, SK., Ibrahimi, OA., Zhang, X. (2006). Receptor specificity of the fibroblast growth factor family. The complete mammalian FGF family. *J Biol Chem, 281*, 15694-700. ↗

Editions

2007-01-10	Authored	de Bono, B.
2007-02-07	Reviewed	Mohammadi, M.
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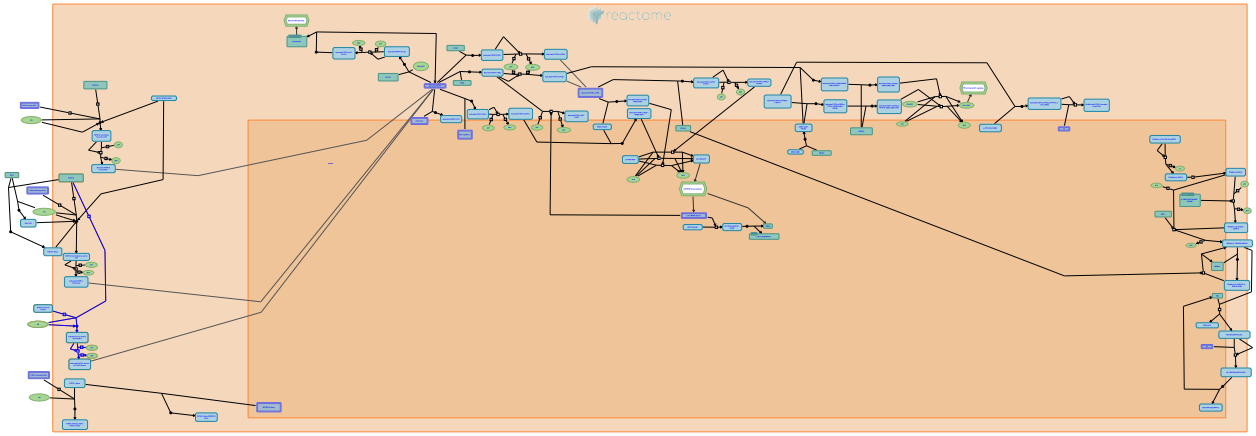
FGFR1c and Klotho ligand binding and activation ↗

Location: FGFR1 ligand binding and activation

Stable identifier: R-HSA-190374



FGF23 is a member of the endocrine subfamily of FGFs. It is produced in bone tissue and regulates kidney functions. Klotho is essential for endogenous FGF23 function as it converts FGFR1c into a specific FGF23 receptor.

Literature references

Yamazaki, Y., Fukumoto, S., Shimada, T., Iijima, K., Urakawa, I., Okawa, K. et al. (2006). Klotho converts canonical FGF receptor into a specific receptor for FGF23. *Nature.* ↗

Kuro-O, M., Baum, MG., Miyoshi, M., Ogawa, Y., Schiavi, S., Nandi, A. et al. (2006). Regulation of fibroblast growth factor-23 signaling by klotho. *J Biol Chem, 281*, 6120-3. ↗

Editions

2007-01-10	Authored	de Bono, B.
2007-02-07	Reviewed	Mohammadi, M.

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