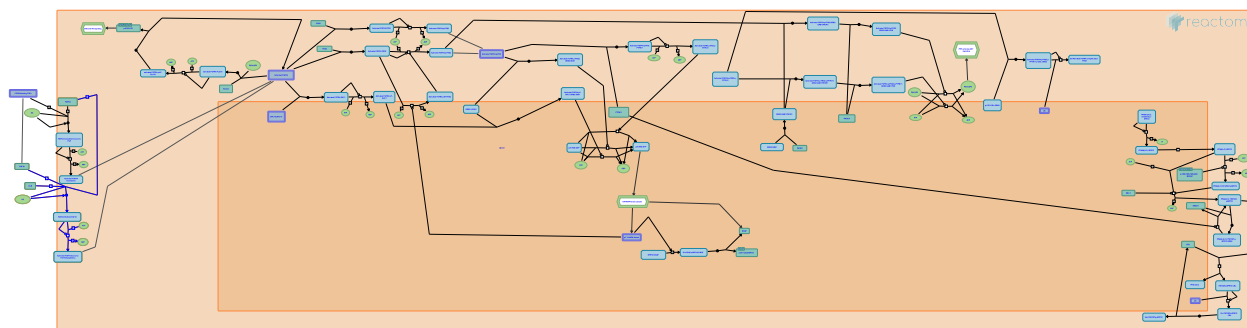


# betaKlotho-mediated ligand binding



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/textbook/).

08/05/2024

## 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).

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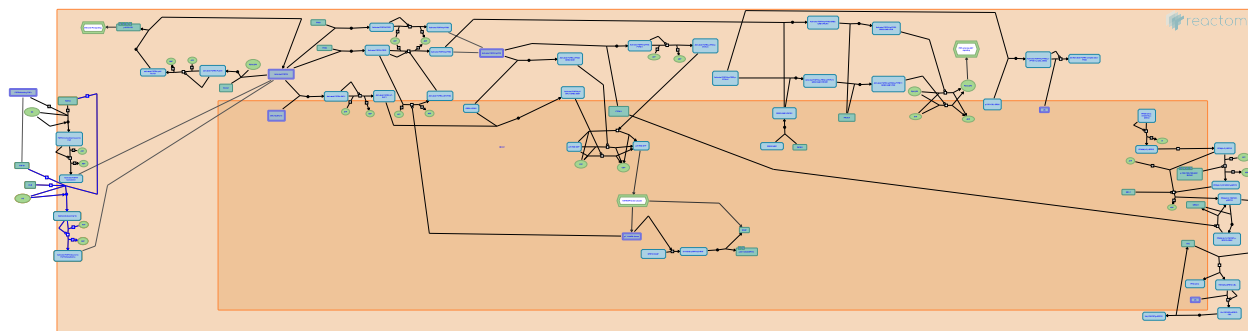
Reactome database release: 88

This document contains 1 pathway and 2 reactions ([see Table of Contents](#))

## betaKlotho-mediated ligand binding [↗](#)

**Stable identifier:** R-HSA-1307965

**Compartments:** cytosol, extracellular region, plasma membrane



FGF21 and FGF19 require betaKlotho for efficient signaling through FGFR1c and FGFR3c. betaKlotho does not interact with 'b' receptor isoforms, and only weakly with FGFR2c. In addition, FGF19, but not FGF21, signals through FGFR4 in a betaKlotho-dependent fashion

### Literature references

Kuro-O, M., Kurosu, H. (2009). The Klotho gene family as a regulator of endocrine fibroblast growth factors. *Mol Cell Endocrinol*, 299, 72-8. [↗](#)

Kuro-O, M., Eliseenkova, AV., Goetz, R., Kliewer, SA., Ogawa, Y., Dickson, AS. et al. (2007). Tissue-specific expression of betaKlotho and fibroblast growth factor (FGF) receptor isoforms determines metabolic activity of FGF19 and FGF21. *J Biol Chem*, 282, 26687-95. [↗](#)

### Editions

2011-08-15	Authored	Rothfels, K.
2011-08-26	Reviewed	Gotoh, N.

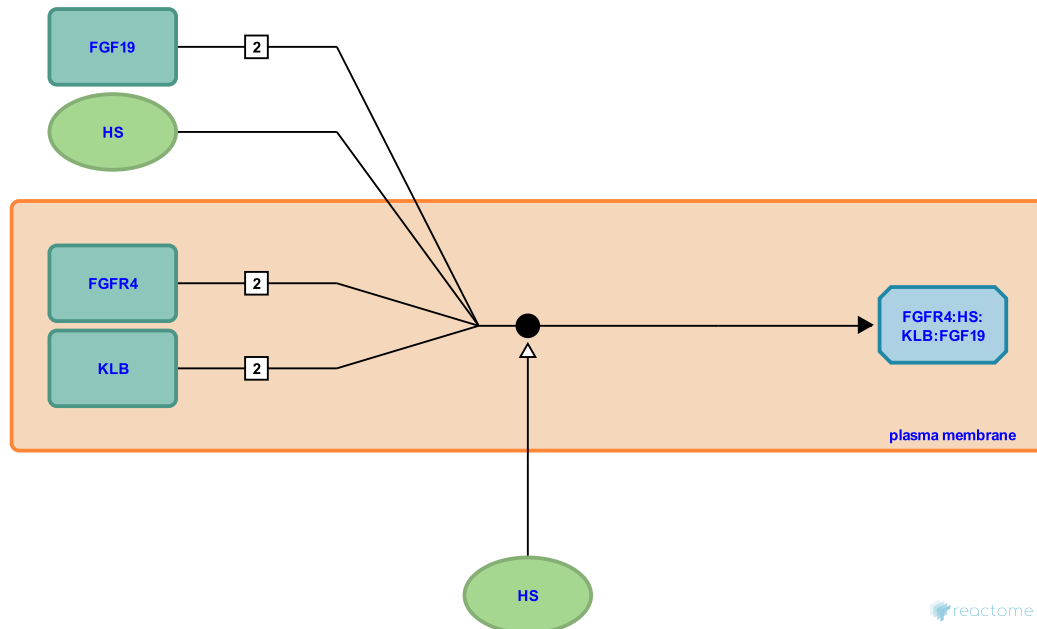
## FGFR4 binds HS:KLB:FGF19 ↗

**Location:** [betaKlotho-mediated ligand binding](#)

**Stable identifier:** R-HSA-1307955

**Type:** binding

**Compartments:** plasma membrane, extracellular region, cytosol



BetaKlotho (KLB) and heparan sulfate (HS) are required for fibroblast growth factor 19 (FGF19)-dependent signaling through fibroblast growth factor receptor 4 (FGFR4) .

**Followed by:** [Autocatalytic phosphorylation of BetaKlotho-bound FGFR4](#)

### Literature references

- Kuro-O, M., Kurosu, H. (2009). The Klotho gene family as a regulator of endocrine fibroblast growth factors. *Mol Cell Endocrinol*, 299, 72-8. ↗
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### Editions

2011-08-15	Authored	Rothfels, K.
2011-08-26	Reviewed	Gotoh, N.

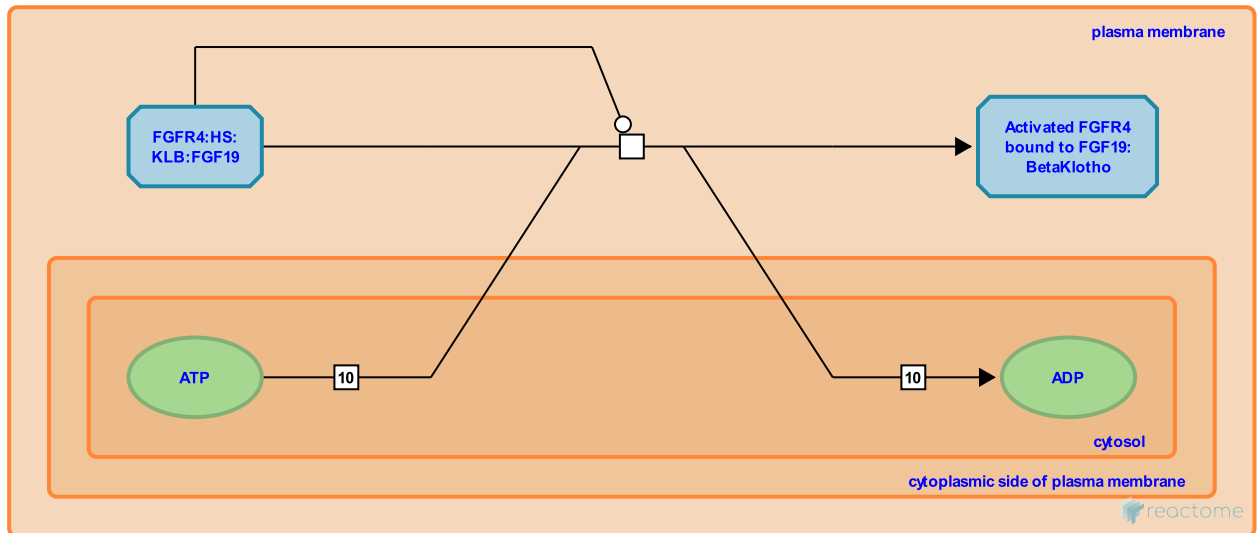
## Autocatalytic phosphorylation of BetaKlotho-bound FGFR4 [↗](#)

**Location:** [betaKlotho-mediated ligand binding](#)

**Stable identifier:** R-HSA-1307963

**Type:** transition

**Compartments:** plasma membrane, extracellular region, cytosol



After being bound by BetaKlotho and FGF19, FGFR4 undergoes autophosphorylation on tyrosine residues in the intracellular portion of the receptor. The phosphorylation sites on FGFR4 have not been accurately determined *in vitro* or *in vivo* but are predicted based on sequence comparison with the other FGF receptors.

**Preceded by:** [FGFR4 binds HS:KLB:FGF19](#)

### Literature references

- Kuro-O, M., Kurosu, H. (2009). The Klotho gene family as a regulator of endocrine fibroblast growth factors. *Mol Cell Endocrinol*, 299, 72-8. [↗](#)
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