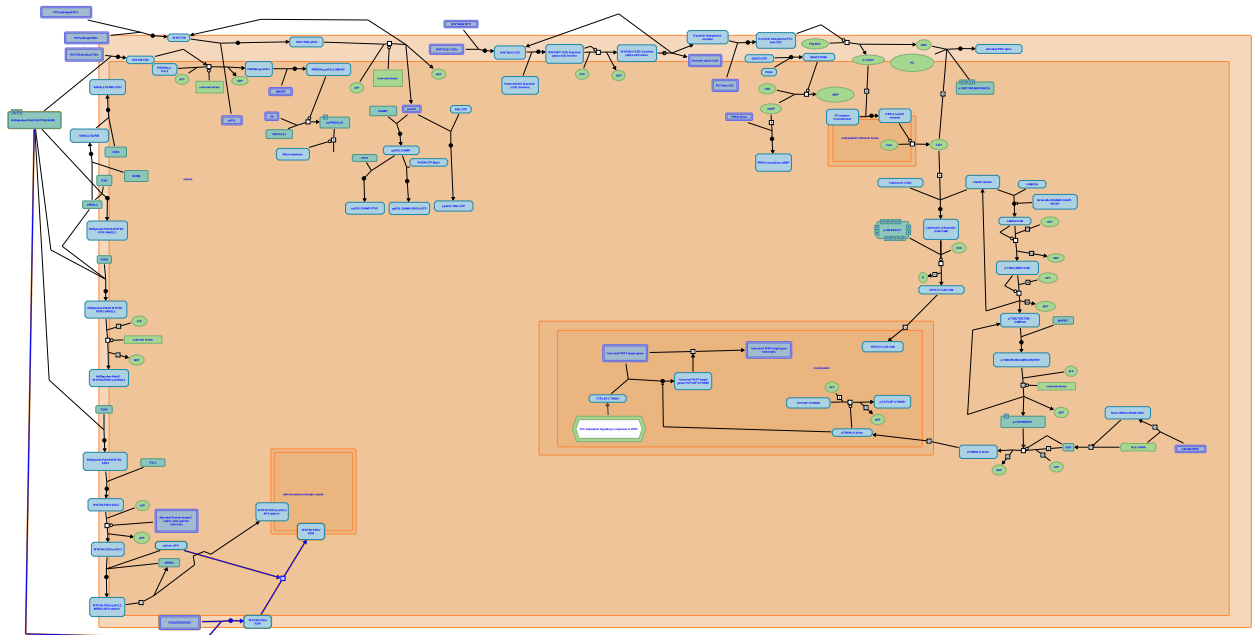


WNT5A-dependent internalization of FZD2, FZD5 and ROR2



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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/).

03/05/2024

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. [↗](#)
- 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. [↗](#)

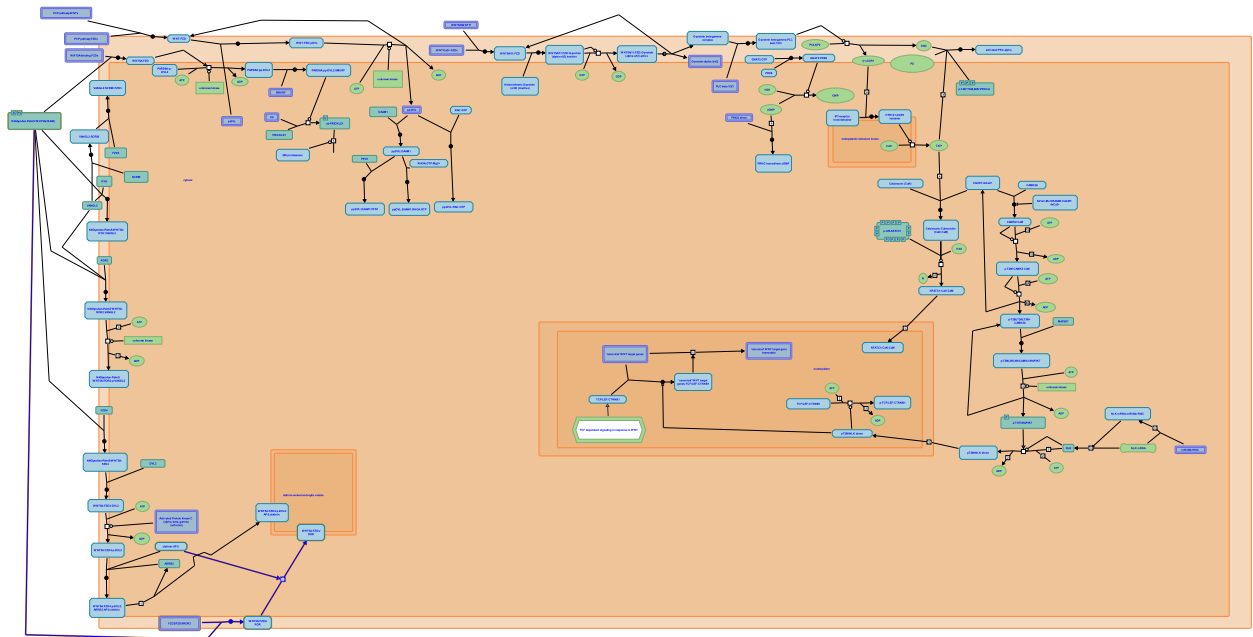
Reactome database release: 88

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

WNT5A-dependent internalization of FZD2, FZD5 and ROR2 ↗

Stable identifier: R-HSA-5140745

Compartments: plasma membrane, clathrin-coated endocytic vesicle, cytosol, extracellular region



reactome

Internalization of FZD2, FZD5 and ROR2 after WNT5A binding is thought to occur in a clathrin-dependent manner and is required for the activation of RAC signaling (Kurayoshi et al, 2007; Sato et al, 2010; Hanaki et al, 2012; Yamamoto et al, 2009).

Literature references

- Koyama, H., Kikuchi, A., Sato, A., Yamamoto, H., Sakane, H. (2010). Wnt5a regulates distinct signalling pathways by binding to Frizzled2. *EMBO J.*, 29, 41-54. ↗
- Izumi, S., Kurayoshi, M., Kikuchi, A., Yamamoto, H. (2007). Post-translational palmitoylation and glycosylation of Wnt-5a are necessary for its signalling. *Biochem. J.*, 402, 515-23. ↗
- Kikuchi, A., Matsumoto, S., Sato, A., Ohdan, H., Hanaki, H., Yamamoto, H. et al. (2012). An anti-Wnt5a antibody suppresses metastasis of gastric cancer cells in vivo by inhibiting receptor-mediated endocytosis. *Mol. Cancer Ther.*, 11, 298-307. ↗
- Kikuchi, A., Kitadai, Y., Ohdan, H., Oue, N., Yasui, W., Yamamoto, H. et al. (2009). Laminin gamma2 mediates Wnt5a-induced invasion of gastric cancer cells. *Gastroenterology*, 137, 242-52, 252.e1-6. ↗

Editions

2013-11-13	Authored	Kikuchi, A.
2013-11-16	Edited	Matthews, L.

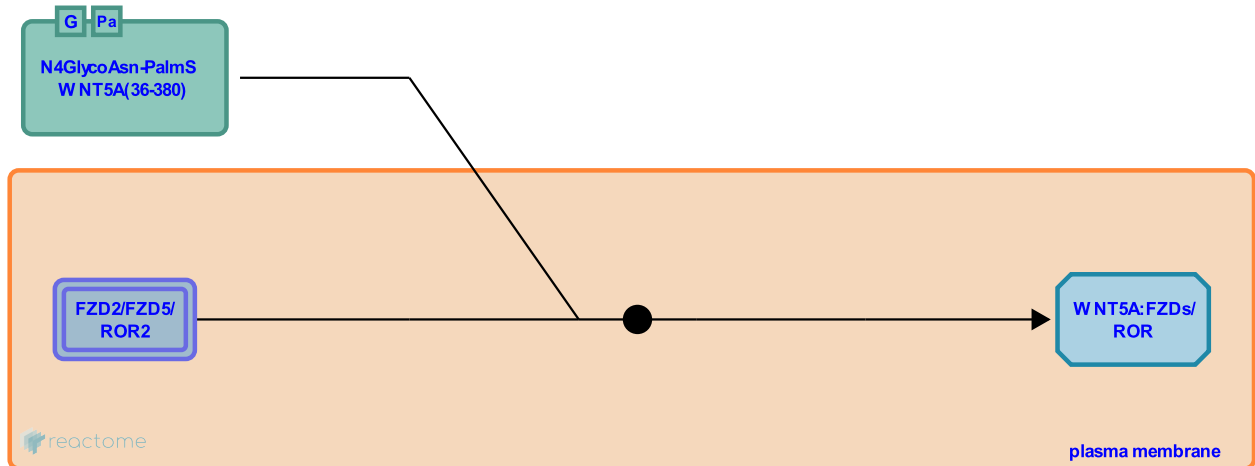
WNT5A binds FZD and ROR receptors ↗

Location: [WNT5A-dependent internalization of FZD2, FZD5 and ROR2](#)

Stable identifier: R-HSA-5140741

Type: binding

Compartments: plasma membrane, extracellular region



WNT5A induces the internalization of FZD2, FZD5 and ROR2 in a clathrin-mediated route, but the activation of PKC is not required (Kurayoshi et al, 2007; Sato et al, 2010; Hanaki et al, 2012).

Followed by: [FZD2, FZD5 and ROR2 are internalized in a WNT5A and clathrin-dependent manner](#)

Literature references

- Koyama, H., Kikuchi, A., Sato, A., Yamamoto, H., Sakane, H. (2010). Wnt5a regulates distinct signalling pathways by binding to Frizzled2. *EMBO J.*, 29, 41-54. ↗
- Izumi, S., Kurayoshi, M., Kikuchi, A., Yamamoto, H. (2007). Post-translational palmitoylation and glycosylation of Wnt-5a are necessary for its signalling. *Biochem. J.*, 402, 515-23. ↗
- Kikuchi, A., Matsumoto, S., Sato, A., Ohdan, H., Hanaki, H., Yamamoto, H. et al. (2012). An anti-Wnt5a antibody suppresses metastasis of gastric cancer cells in vivo by inhibiting receptor-mediated endocytosis. *Mol. Cancer Ther.*, 11, 298-307. ↗

Editions

2013-11-13	Authored	Kikuchi, A.
2013-11-16	Edited	Matthews, L.

FZD2, FZD5 and ROR2 are internalized in a WNT5A and clathrin-dependent manner

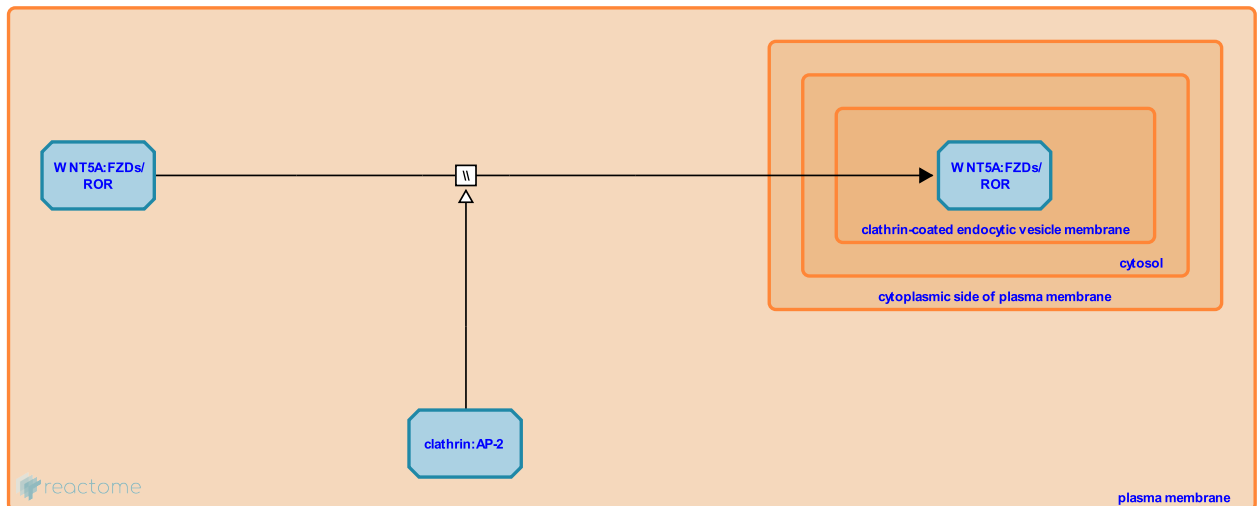


Location: WNT5A-dependent internalization of FZD2, FZD5 and ROR2

Stable identifier: R-HSA-5140747

Type: omitted

Compartments: plasma membrane, clathrin-coated endocytic vesicle



Stimulation of HEK293, HeLaS3 or KKLS gastric cancer cells with WNT5A promotes the internalization of FZD2, FZD5 and ROR2. Internalization is required for RAC activation downstream of WNT5A and subsequent activation of laminin gamma 2 gene expression which is associated with metastasis and invasion in gastric cancer (Sato et al, 2010; Hanaki et al, 2012; Yamamoto et al, 2009). Knockdown or inhibition of clathrin abrogates receptor internalization and RAC activation suggesting that clathrin-mediated endocytosis is required for this WNT5A-dependent signaling (Sato et al, 2010; Hanaki et al, 2012).

Preceded by: WNT5A binds FZD and ROR receptors

Literature references

Koyama, H., Kikuchi, A., Sato, A., Yamamoto, H., Sakane, H. (2010). Wnt5a regulates distinct signalling pathways by binding to Frizzled2. *EMBO J.*, 29, 41-54. [↗](#)

Kikuchi, A., Kitadai, Y., Ohdan, H., Oue, N., Yasui, W., Yamamoto, H. et al. (2009). Laminin gamma2 mediates Wnt5a-induced invasion of gastric cancer cells. *Gastroenterology*, 137, 242-52, 252.e1-6. [↗](#)

Editions

2013-11-13	Authored	Kikuchi, A.
2013-11-16	Edited	Matthews, L.

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