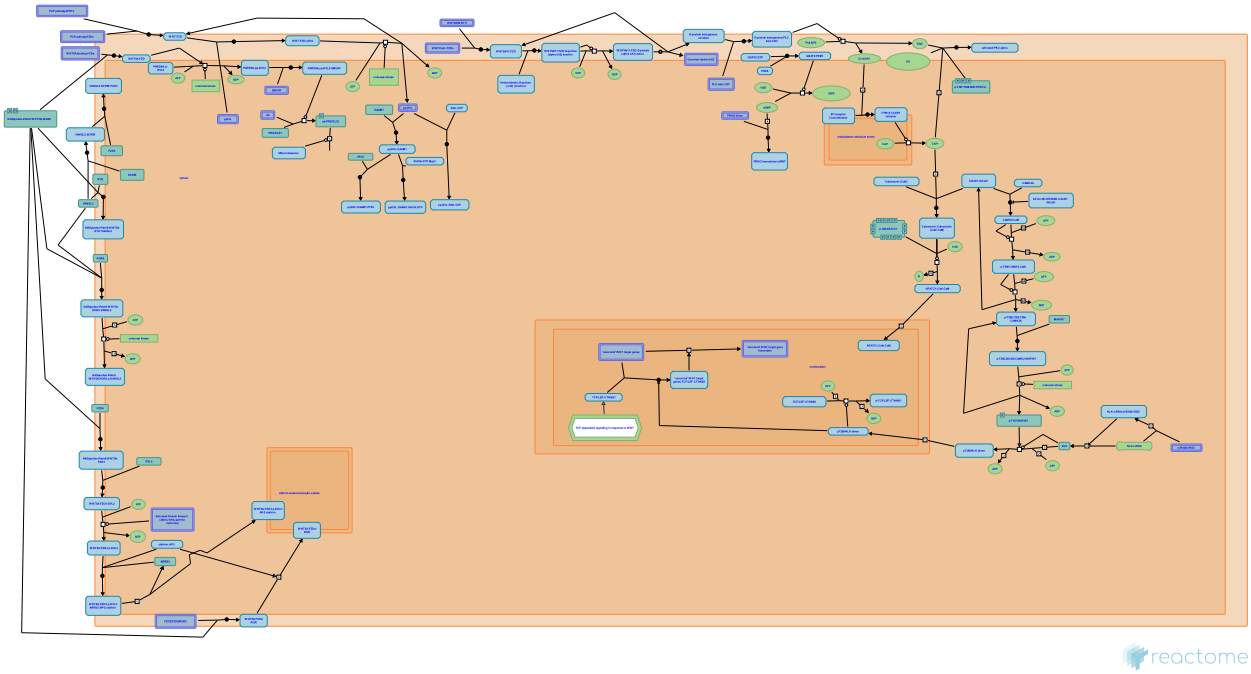
Beta-catenin independent WNT signaling



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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.

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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

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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. ↗

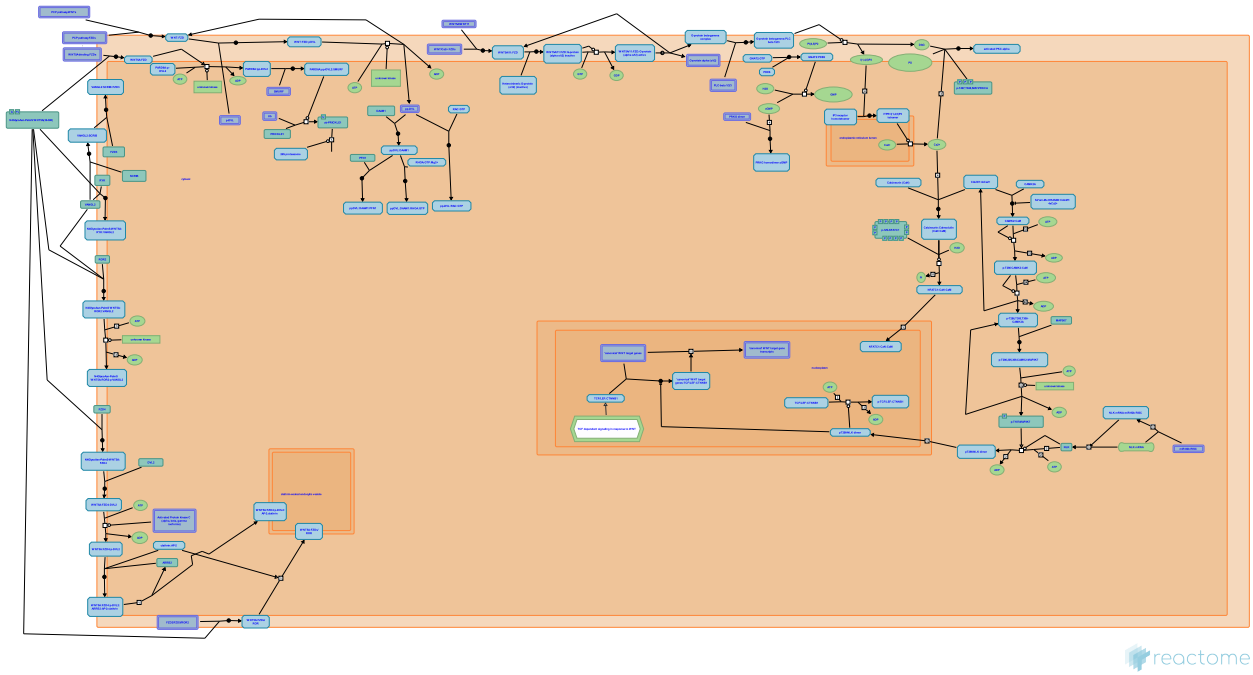
Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

Beta-catenin independent WNT signaling ↗

Stable identifier: R-HSA-3858494

Compartments: cytosol, plasma membrane



Humans and mice have 19 identified WNT proteins that were originally classified as either 'canonical' or 'non-canonical' depending upon whether they were able to transform the mouse mammary epithelial cell line C57MG and to induce secondary axis formation in Xenopus (Wong et al, 1994; Du et al, 1995). So-called canonical WNTs, including Wnt1, 3, 3a and 7, initiate signaling pathways that destabilize the destruction complex and allow beta-catenin to accumulate and translocate to the nucleus where it promotes transcription (reviewed in Saito-Diaz et al, 2013). Non-canonical WNTs, including Wnt 2, 4, 5a, 5b, 6, 7b, and Wnt11 activate beta-catenin-independent responses that regulate many aspects of morphogenesis and development, often by impinging on the cytoskeleton (reviewed in van Amerongen, 2012). Two of the main beta-catenin-independent pathways are the Planar Cell Polarity (PCP) pathway, which controls the establishment of polarity in the plane of a field of cells, and the WNT/Ca2+ pathway, which promotes the release of intracellular calcium and regulates numerous downstream effectors (reviewed in Gao, 2012; De, 2011).

Literature references

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Editions

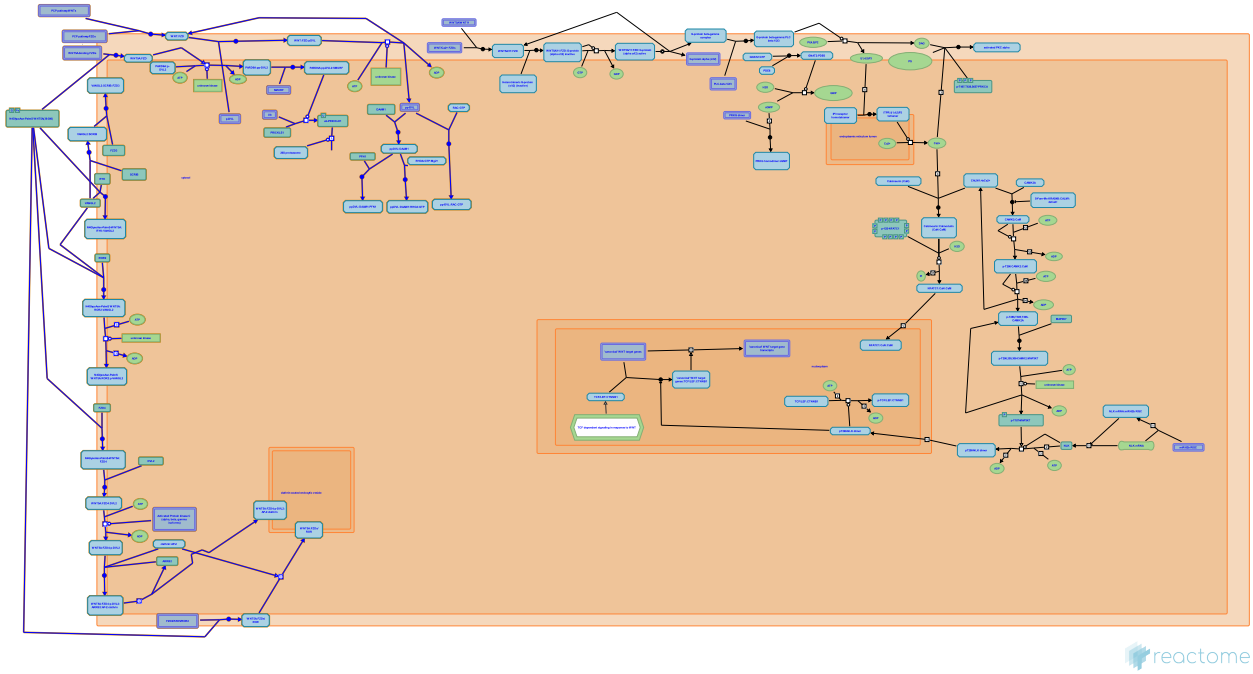
2013-07-10	Authored	Rothfels, K.
2013-10-07	Edited	Matthews, L.
2013-11-13	Reviewed	Kikuchi, A.

PCP/CE pathway ↗

Location: Beta-catenin independent WNT signaling

Stable identifier: R-HSA-4086400

Compartments: plasma membrane, cytosol



The planar cell polarity (PCP) pathway controls the establishment of polarity within the plane of a sheet of cells. PCP was initially characterized in Drosophila, where it controls the arrangement of hair bristles and photoreceptors in the eye (reviewed in Maung and Jenny, 2011). In vertebrates, PCP regulates convergent extension (CE, a process by which a tissue narrows along one axis and lengthens along a perpendicular one), closure of the neural tube, hair orientation and inner ear development, among others (reviewed in Seifert and Mlodzik, 2007). Studies in Drosophila identified a core group of PCP genes including Frizzled (Fz), Flamingo (Fmi), Van Gogh (Vang), Dishevelled (Dsh), Prickle (Pk) and Diego (Dgo), whose products become asymmetrically localized in the cell upon initiation of PCP (reviewed Maung and Jenny, 2011). Subsequent studies in vertebrates have shown that many of these PCP genes are conserved.
Unlike in Drosophila, where the upstream signal for the PCP pathway has not been defined, in vertebrates, a number of so-called 'non-canonical' WNTs have been shown to have roles in PCP processes. WNT5B and WNT11 are both required for CE during gastrulation, and WNT5A physically and genetically interacts with VANGL2 in the inner ear and the developing limb bud (Heisenberg et al, 2000; Rauch et al, 1997; Qian et al, 2007; Gao et al, 2011). WNT ligand can be bound by one of a number of FZD receptors or the single pass transmembrane proteins RYK or ROR, depending on context (reviewed in Green et al, 2008; Fradkin et al, 2010). Although the downstream pathway is not well established, vertebrate PCP signaling appears to work at least in part through DVL, DAAM1 and small GTPases to remodel the actin cytoskeleton (reviewed in Lai et al, 2009; Gao et al, 2012).

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Editions

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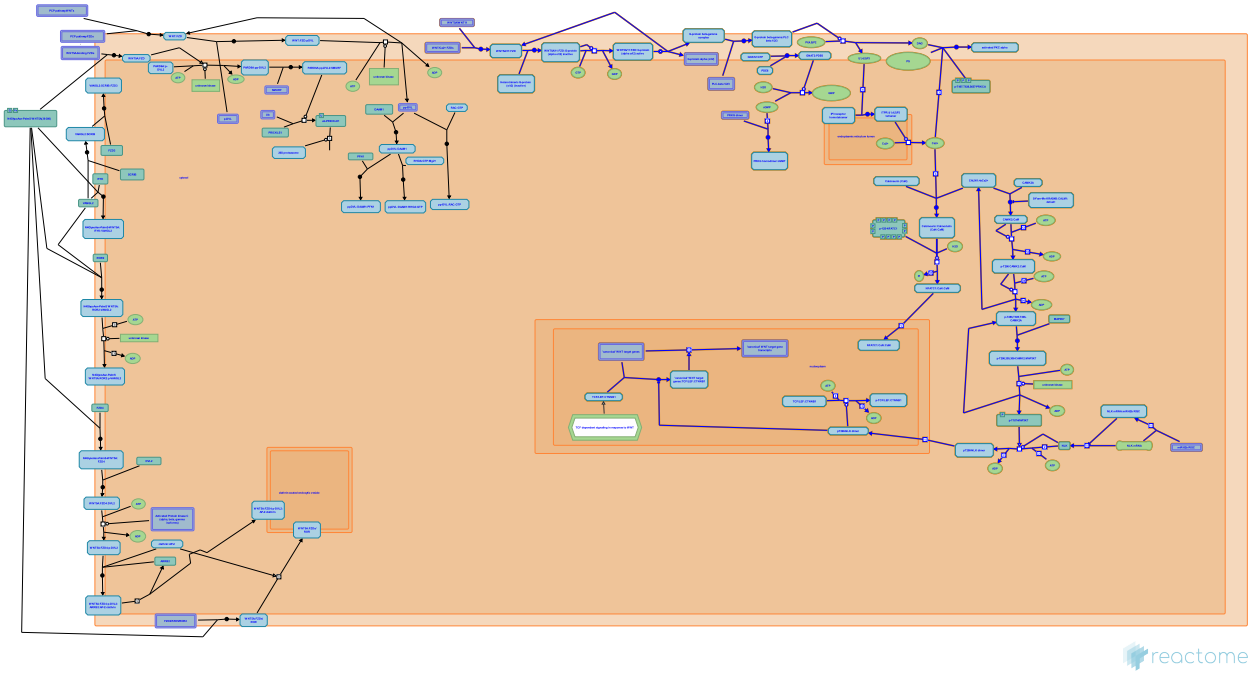
Ca2+ pathway ↗

Location: Beta-catenin independent WNT signaling

Stable identifier: R-HSA-4086398

Compartments: cytosol, plasma membrane



A number of so called non-canonical WNT ligands have been shown to promote intracellular calcium release upon FZD binding. This beta-catenin-independent WNT pathway acts through heterotrimeric G proteins and promotes calcium release through phophoinositol signaling and activation of phosphodiesterase (PDE). Downstream effectors include the calcium/calmodulin-dependent kinase II (CaMK2) and PKC (reviewed in De, 2011). The WNT Ca2+ pathway is important in dorsoventral polarity, convergent extension and organ formation in vertebrates and also has roles in negatively regulating 'canonical' beta-catenin-dependent transcription. Non-canonical WNT Ca2+ signaling is also implicated in inflammatory response and cancer (reviewed in Kohn and Moon, 2005; Sugimura and Li, 2010).

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