Wnt signaling

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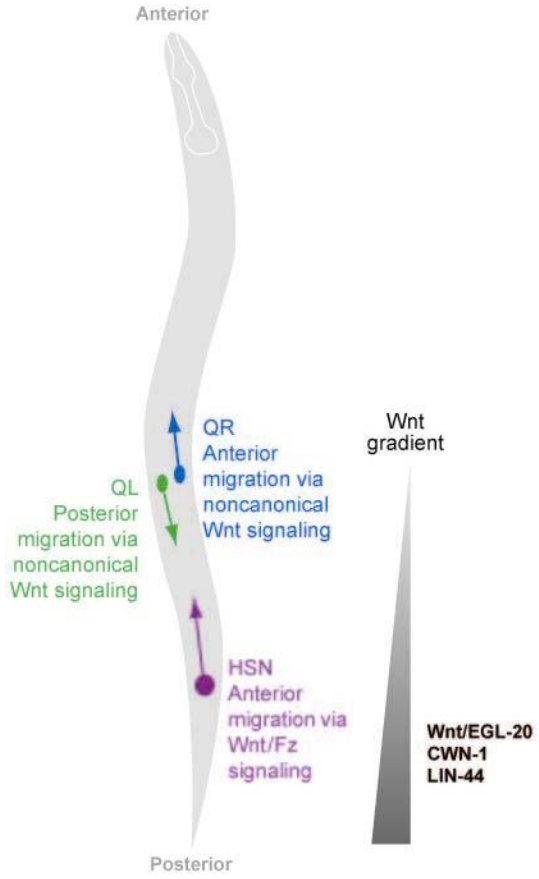
Wnt Signaling

- Wnt consists of a family of secretory glycoproteins (19 genes) with MW ~40Kd
- Wnt signaling was initially known for its roles in regulation of embryonic development and association with tumorigenesis.
- Wnt signaling has now been shown to be involved in a wide range of biological and pathophysiological processes, including neuronogenesis, organogenesis, adipogenesis, myogenesis, bone development, lipid and glucose metabolism, and stem cell biology.

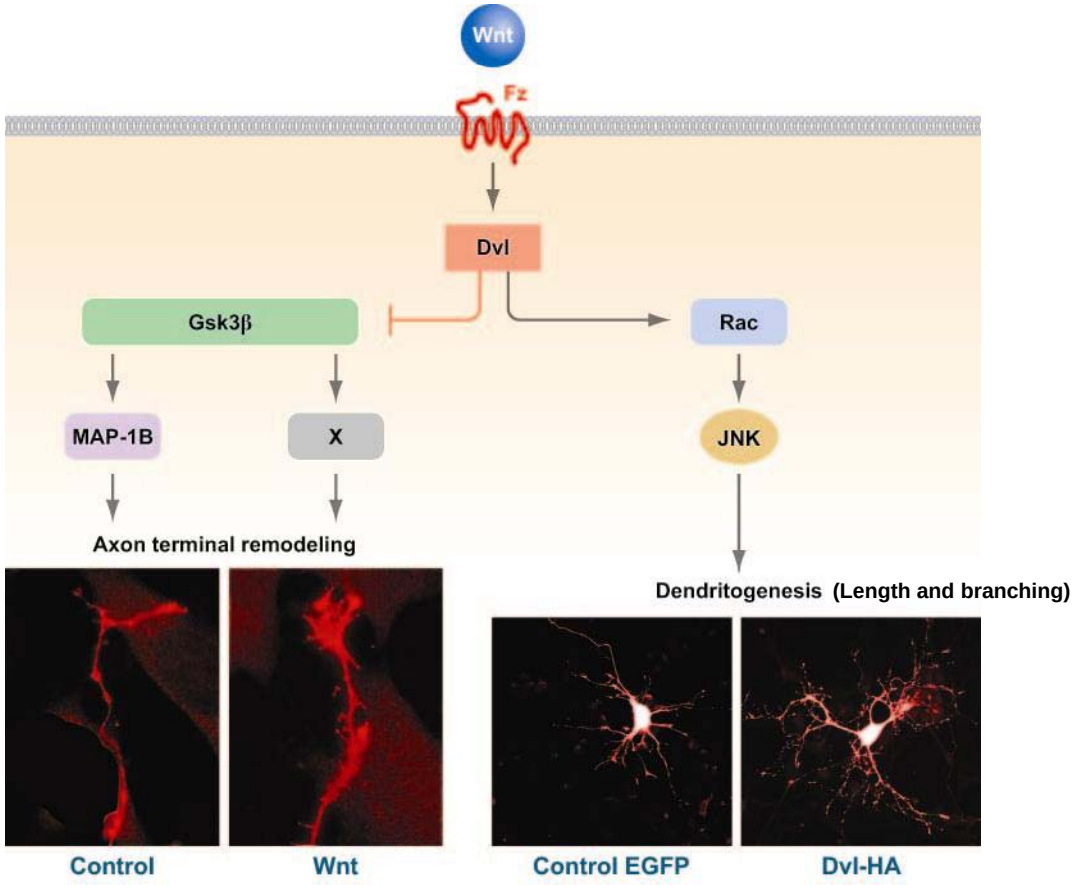
Wnt signaling regulates neuronal migration and positioning



Wnt signaling controls
Q cell and HSN migration
along the A-P axis in
C. elegans

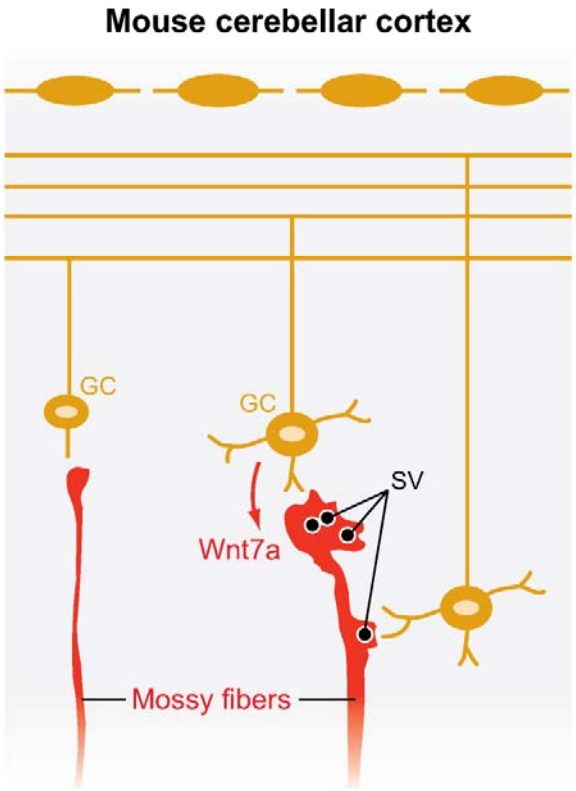
Salinas PC, Zou Y. 2008.
Annu. Rev. Neurosci. 31:339–58.

Wnts regulate the terminal arborization of axons and dendritic morphogenesis.



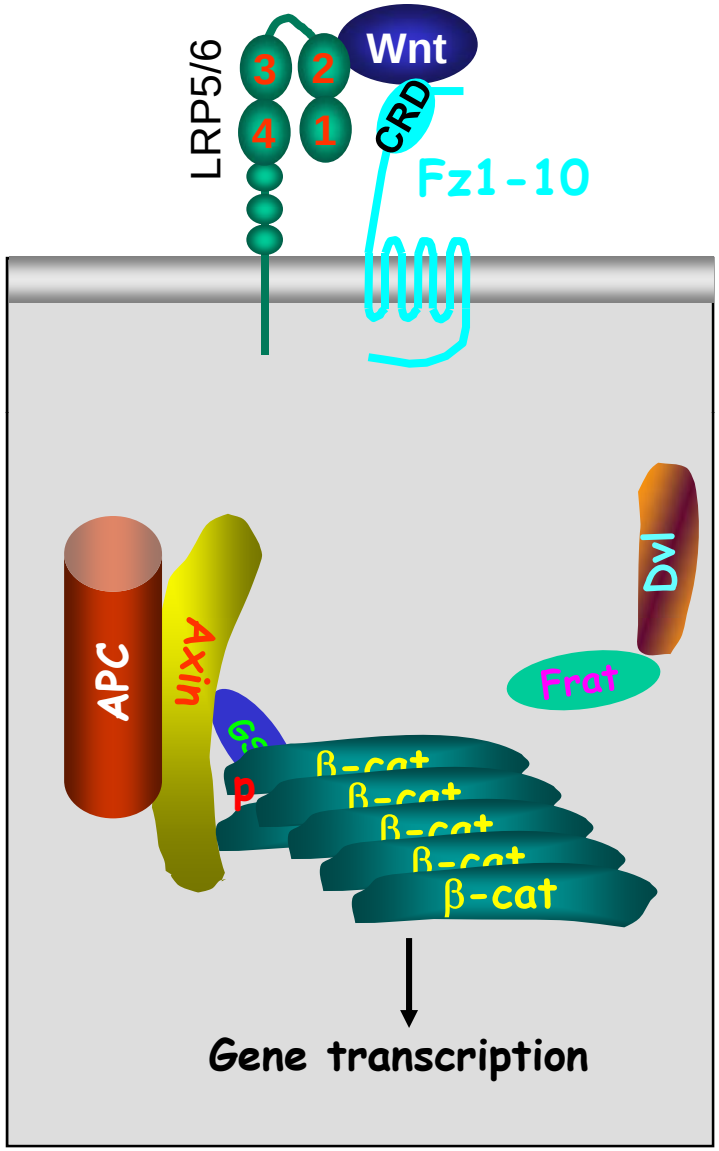
Salinas PC, Zou Y. 2008.
Annu. Rev. Neurosci. 31:339–58.

Wnts regulate the assembly of synapses

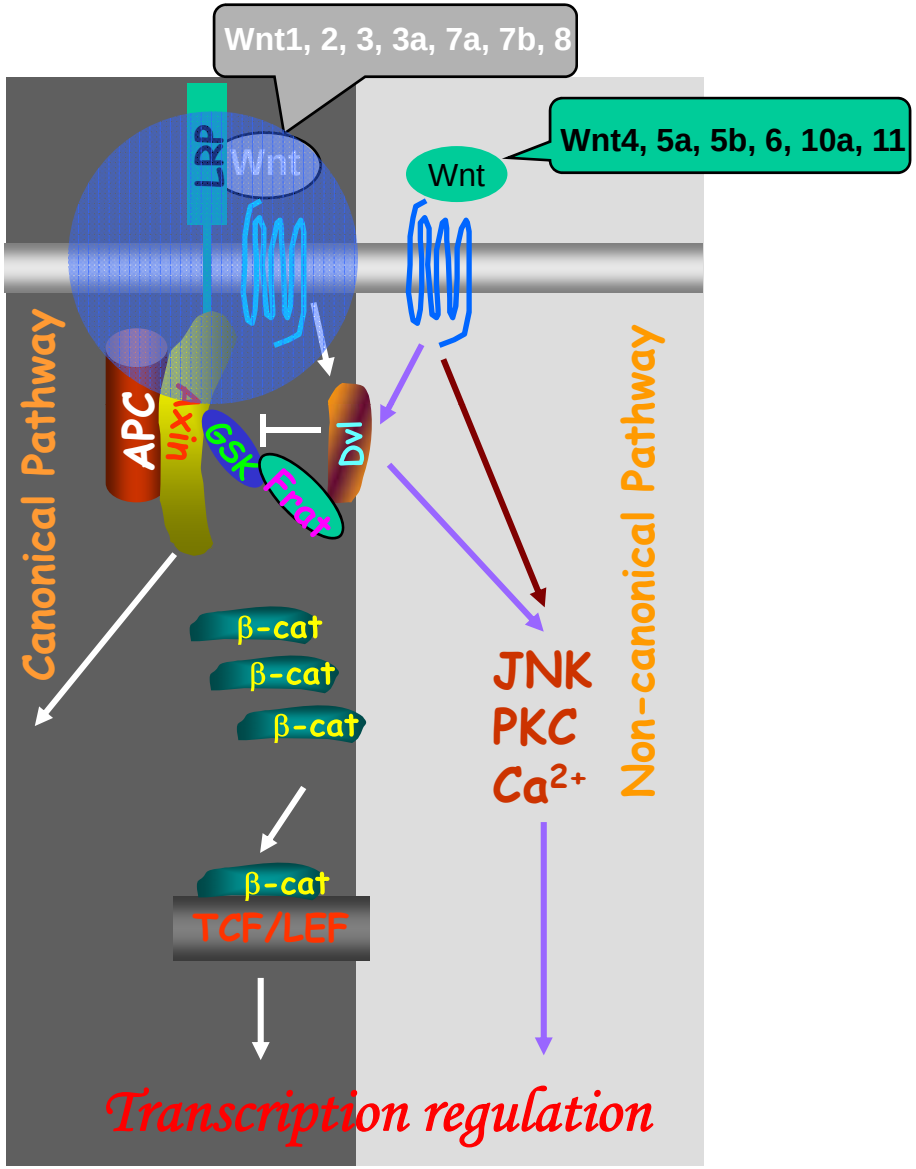


Salinas PC, Zou Y. 2008.
Annu. Rev. Neurosci. 31:339–58.

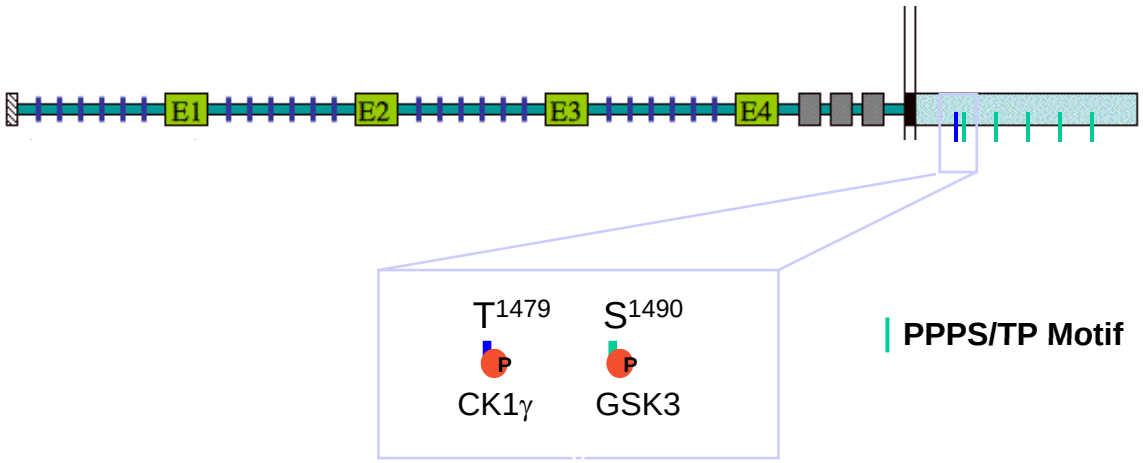
Canonical Wnt signaling



Wnt signaling pathways

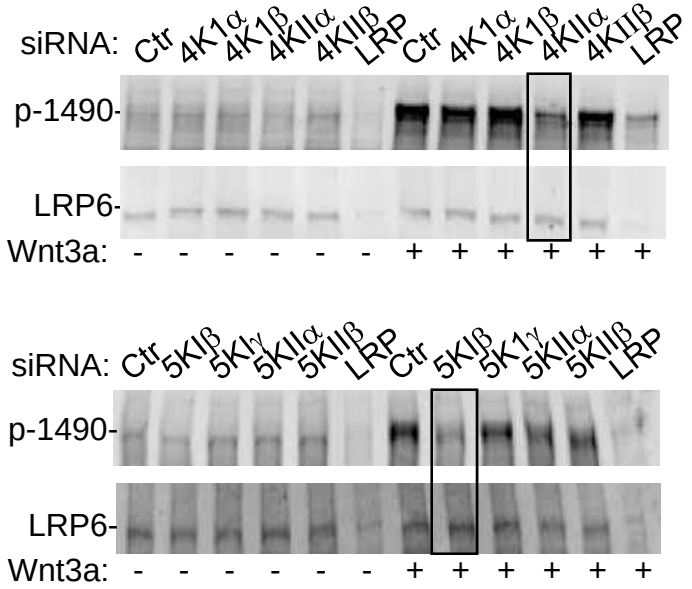


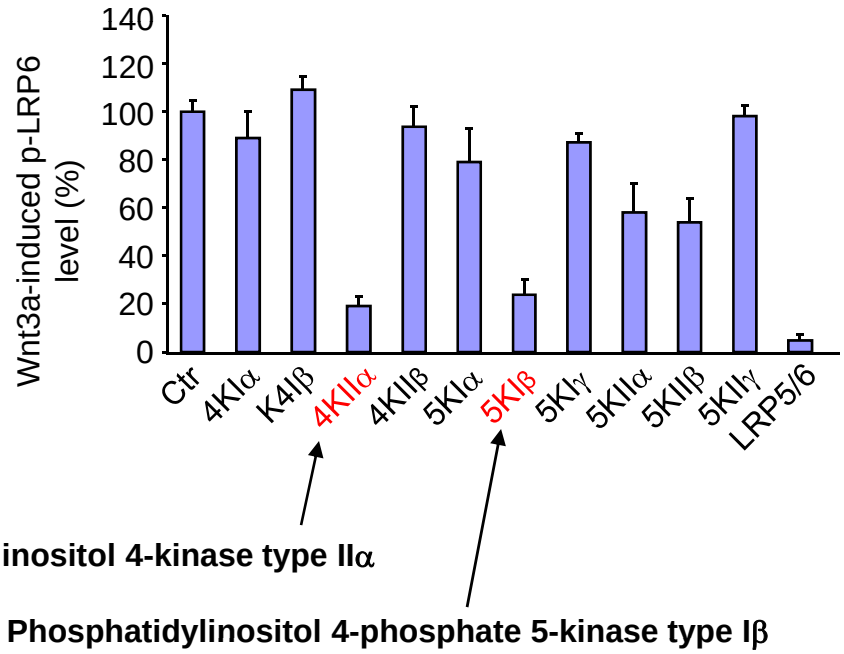
Wnt coreceptor LRP5/6



Nature. 2005 438(7069):873-77.
Nature. 2005 438(7069):867-72.

Effect of phosphatidylinositol lipid kinase siRNAs on the levels of pSer^{1490} of LRP6





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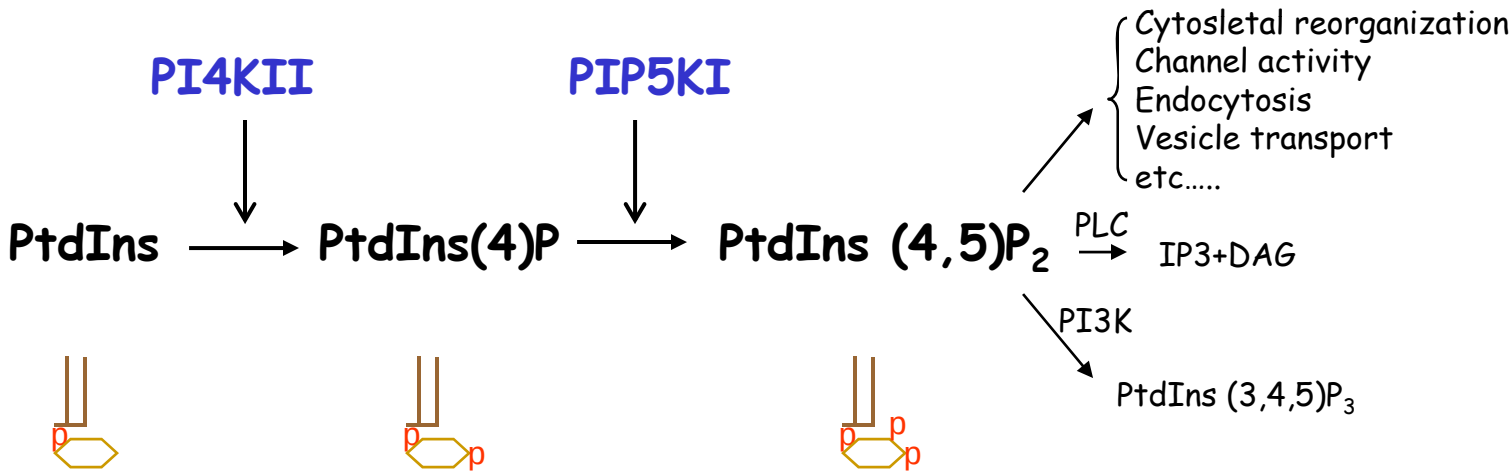
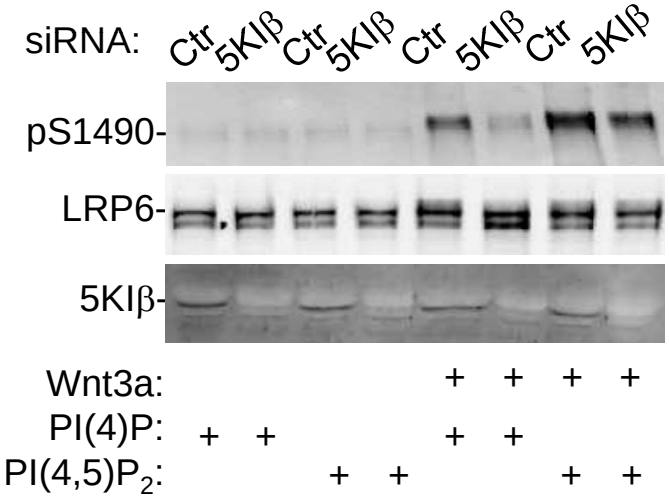
Phosphatidylinositol lipid metabolism



Effect of PI kinase siRNAs can be rescued by direct delivery of PIs



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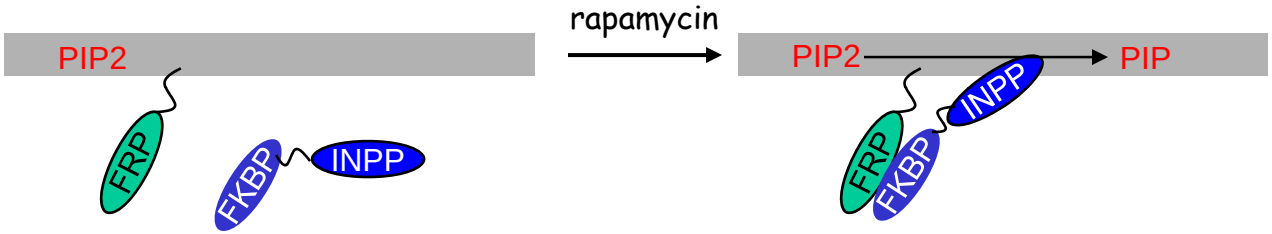
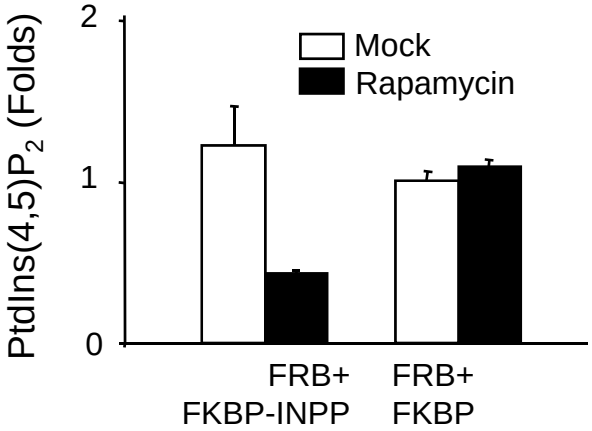
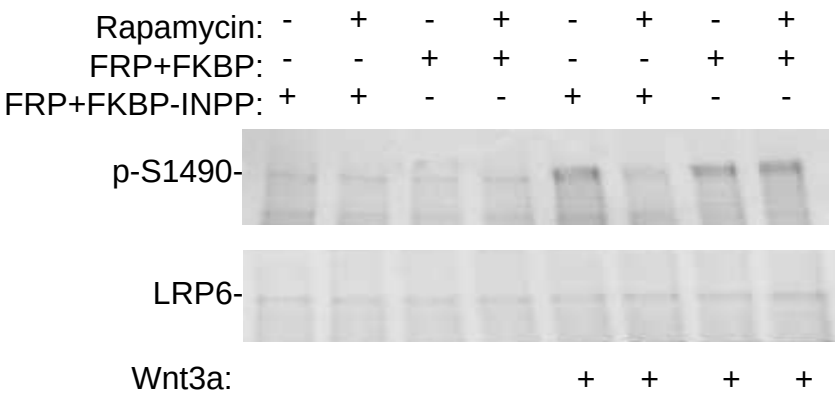
Reduction in PIP_2 levels leads to decrease in LRP6 phosphorylation



P. Varnai, T. Balla, et al. *J Cell Biol.* **175**, 377 (2006).





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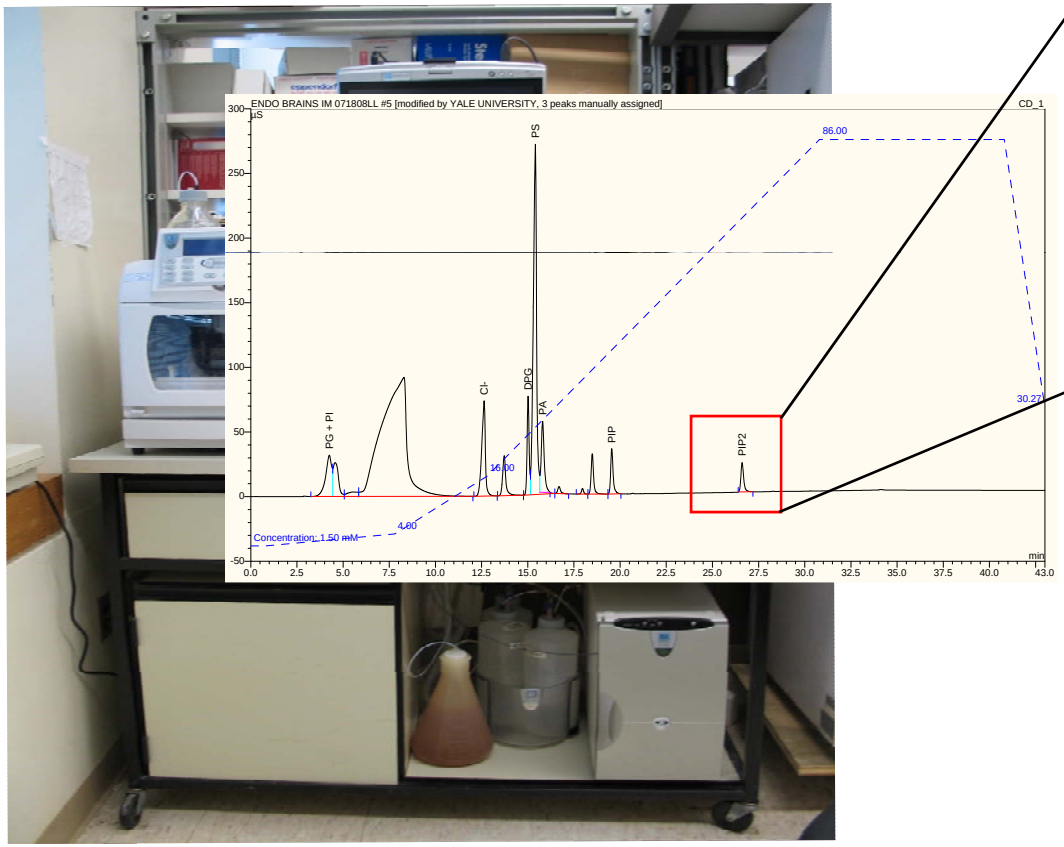
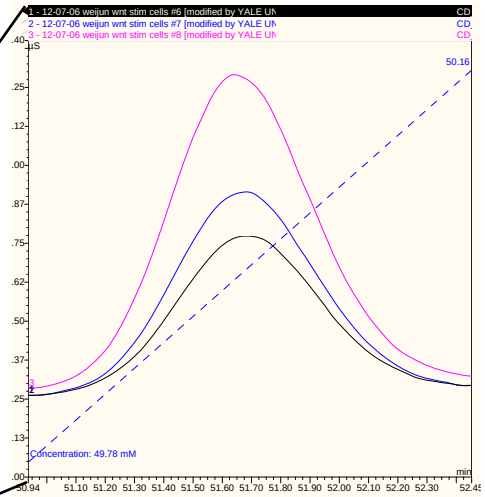
Wnt3a stimulates PIP_2 production

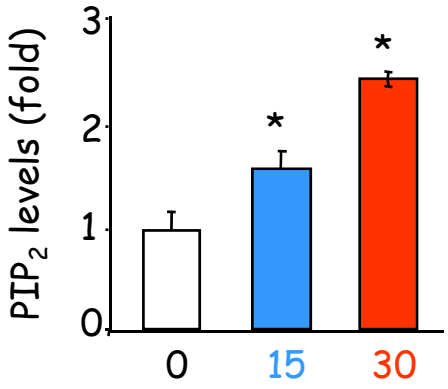
The Lipid Core



Dionex HPLC with the conductivity detector



Wnt3a treatment 0, 15, 30 mins



* P<0.05 vs. Time 0

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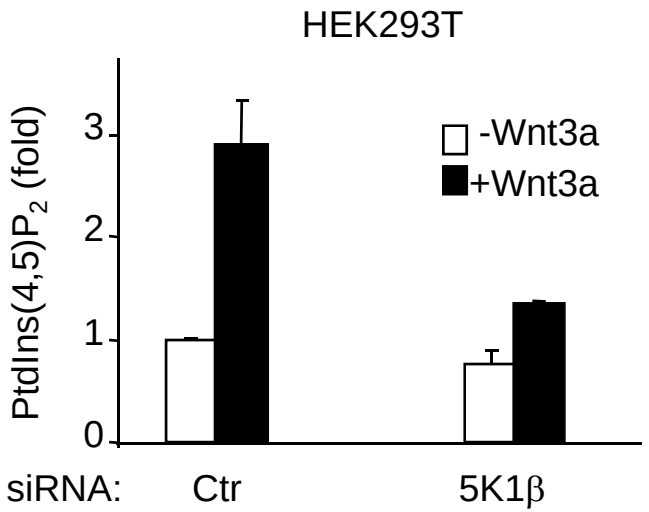
Wnt3a-stimulated PIP_2 production depends on PIP5KI



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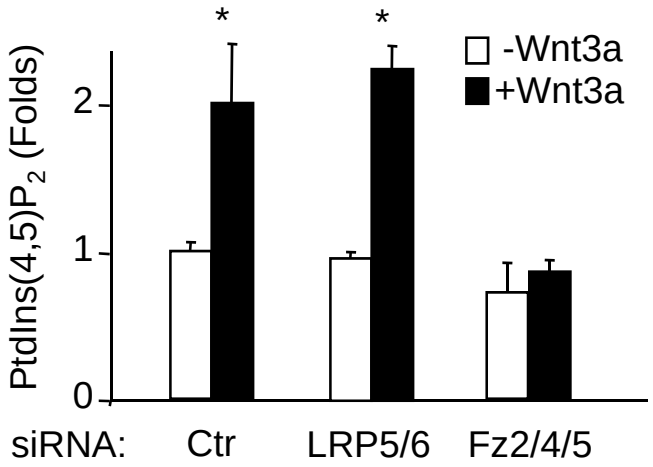
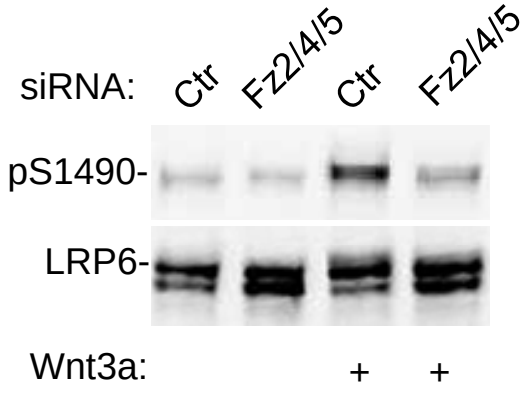
Wnt3a-stimulated PtdIns (4,5)P_2 production depends on Fz, but not LRP5/6





* P<0.05 vs. -Wnt3a

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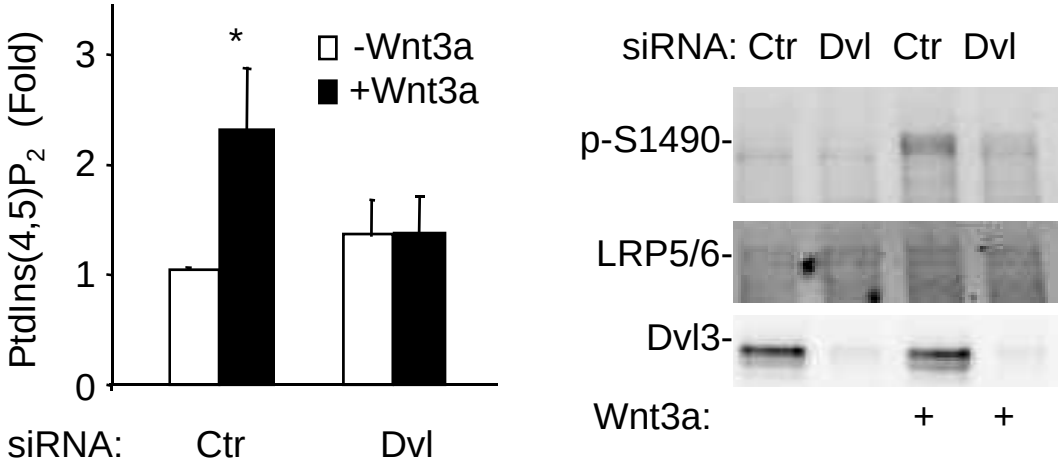
Wnt3a-stimulated PIP_2 production depends on Dvl



* P<0.05 vs. -Wnt3a

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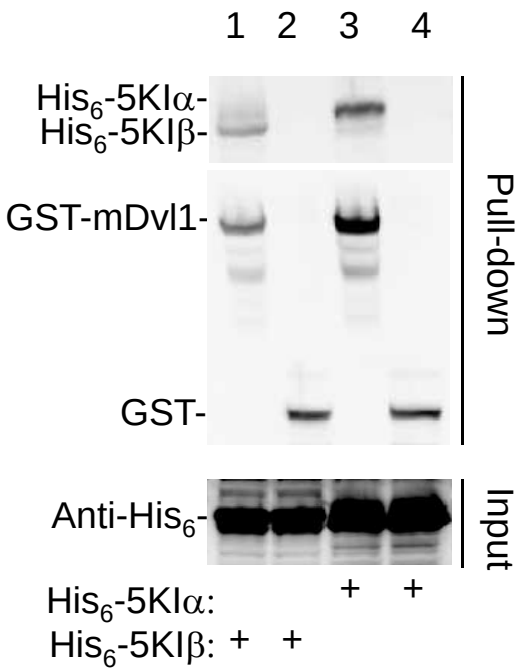
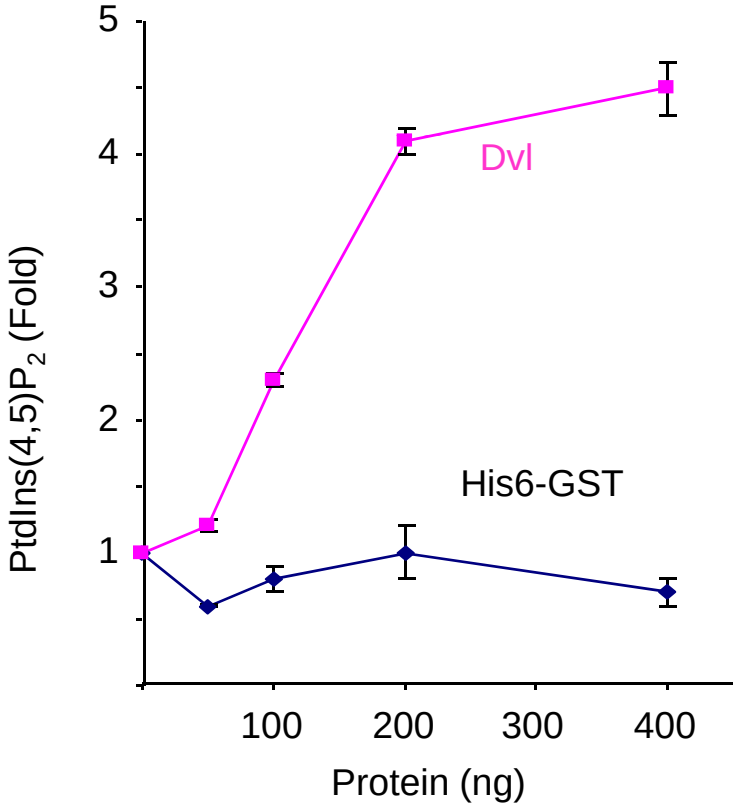
Dvl directly interacts with and stimulates PIP5KI





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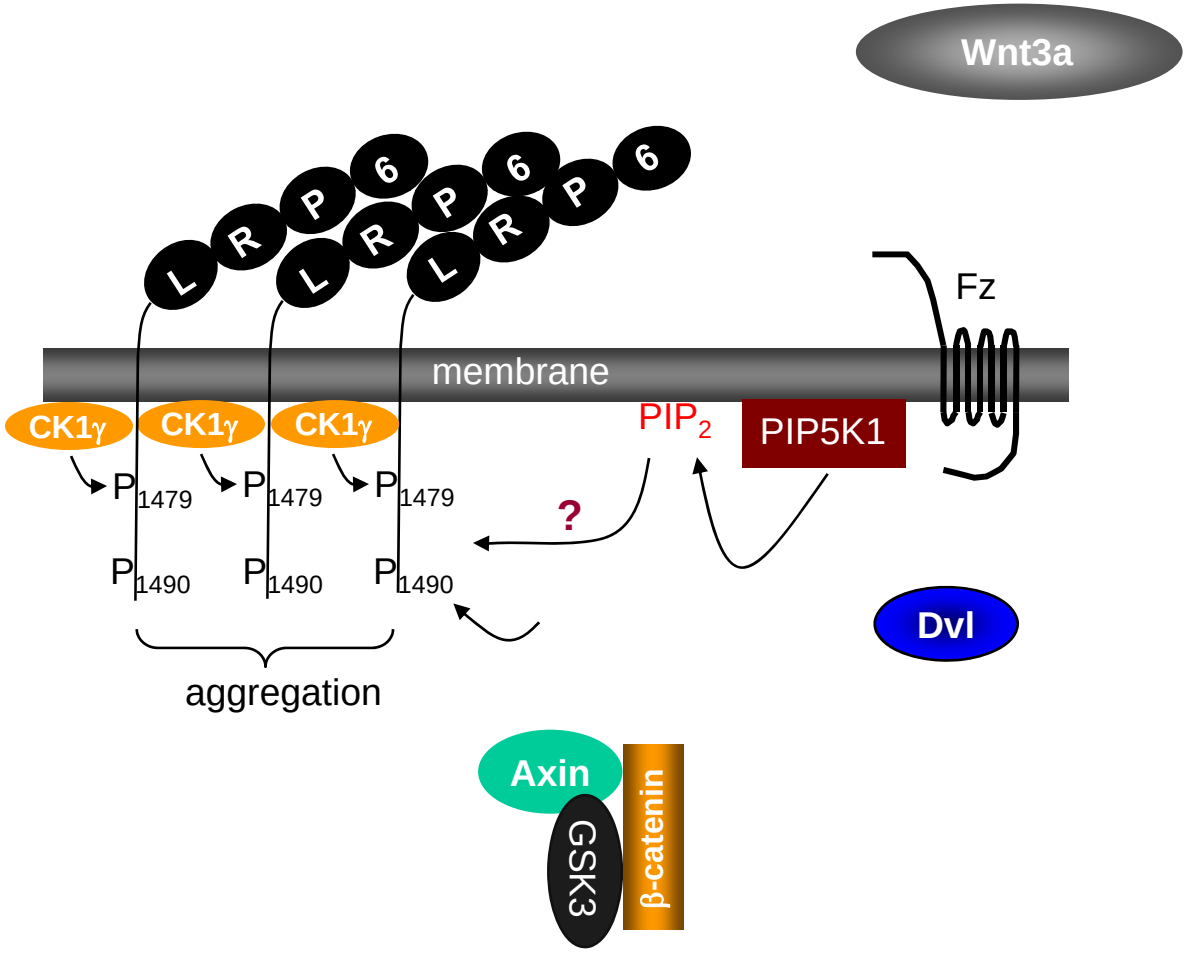
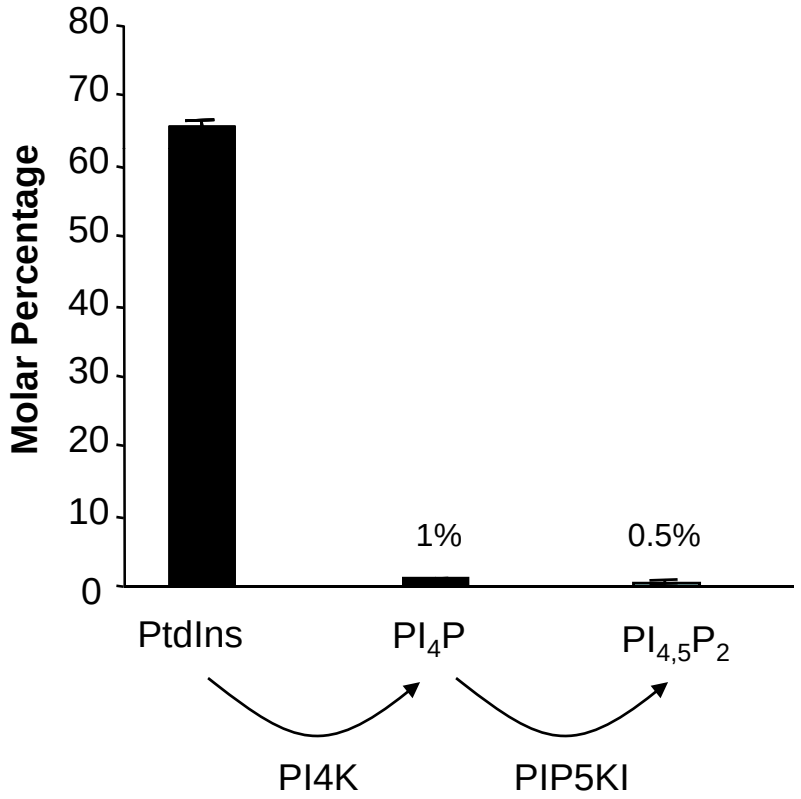
A model for Wnt cross-membrane signaling



Future direction 1: Regulation of PI4P fomration by Wnt



Laura Swan

Future direction 2: Phosphoproteomes of Wnt-treated cells

Wnt Signaling

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