

## **Zic2 abrogates an alternative Wnt signaling pathway to convert axon attraction into repulsion**

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Wnt signaling is involved in axon pathfinding during brain wiring but it is unknown how Wnt ligands promote attraction or repulsion. In addition, the participation of the canonical ( $\beta$ catenin-dependent transcription) versus non-canonical ( $\beta$ catenin-independent) Wnt pathways in this process remains controversial. Here we show that Wnt5a is expressed at the optic chiasm midline and promotes axon crossing by triggering an alternative Wnt pathway that depends on polarized accumulation of  $\beta$ catenin at the axon terminal but does not activate the canonical pathway. Remarkably, this alternative pathway is silenced by the transcription factor Zic2 in the small subset of ipsilaterally projecting neurons. Zic2 directly regulates genes related to Wnt and Eph signaling that lead to global accumulation of  $\beta$ catenin but triggers its asymmetric phosphorylation to facilitate the steering of the growth cone. This alternative Wnt pathway found in contralateral axons and its Zic2-mediated abrogation in ipsilateral neurons is likely operating in many other contexts requiring a two-way response to Wnt ligands.