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A WiNTers tale

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The secreted WNT proteins activate two distinct signalling pathways: the canonical WNT/β-catenin pathway and a WNT/Ca2+ pathway that interferes with the canonical pathway. In the May 16 Nature, Saneyoshi *et al.* define NF-AT as a downstream target of the WNT/Ca2+ pathway (*Nature* 2002, **417:**295-299). Members of the NF-AT (nuclear factor of activated T cells) family play a pivotal role in the regulation of gene expression in T lymphocytes. NF-AT is translocated to the nucleus following activation by calcineurin in response to Ca2+ signalling. Saneyoshi *et al.* reasoned that NF-AT might play a role in ventral cell signalling in the WNT/Ca2+ pathway. To demonstrate this they cloned the *Xenopus* homologue of NF-AT (XNF-AT). They found that XNF-AT showed Ca-dependent dephosphorylation during development, and that dephosphorylation lead to nuclear localization and transcriptional activation. Injection of an activated XNF-AT mutant lead to 'ventralized' *Xenopus* embryos, whereas a dominant-negative isoform induced a complete secondary dorsal axis. Saneyoshi *et al.* demonstrated that expression of Wnt5A and its receptor Frizzled led to the nuclear translocation of XNF-AT, and that activated XNF-AT inhibited the canonical WNT/β-catenin pathway. Thus, XNF-AT is an important regulator of ventral cell fate and regulates cross-talk between the different WNT signalling pathways.

References

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