(P13) The Wnt/Calcium pathway activates NF-AT and promotes ventral cell fate in *Xenopus* embryos

Takeo Saneyoshi, Shoen Kume, Yoshiharu Amasaki, Katsuhiko Mikoshiba

Institute of Medical Science, University of Tokyo, Calcium Oscillation Project, ICORP, Japan Science and Technology Agency, RIKEN BSI

We have proposed involvement of IP_3-Ca^{2+} signaling in dorsoventral axis formation in *Xenopus* embryo(Science 278 1940-1943, 1997), but the immediate target of free Ca^{2+} is not well understood. The secreted Wnt protein family comprises two functional groups, canonical Wnt and Wnt/Ca^{2+} pathways. Despite the finding that the Wnt/Ca^{2+} pathway interfered with the canonical Wnt pathway, the underlying molecular mechanism is poorly understood. We cloned the cDNA encoding *Xenopus* homolog of the nuclear factor of activated T-cell (XNF-AT). Gain-of-function XNF-AT mutant (CA XNF-AT) inhibited anterior development of the primary axis as well as Xwnt8-induced ectopic dorsal axis. Loss-of-function XNF-AT mutant (DN XNF-AT) induced an ectopic dorsal axis and expression of the canonical Wnt signaling target molecules, *siamois* and *Xnr3*. Xwnt5A induced translocation of XNF-AT from the cytosol to the nucleus. Our data strongly suggest that XNF-AT functions as a downstream target of Wnt/Ca^{2+} and IP_3-Ca^{2+} pathways and plays an essential role in mediating ventral signals in the *Xenopus* embryo by suppressing the canonical Wnt pathway (Nature 417 295-299, 2002).

Publications: Science 278 1940-1943 1997, Nature 417 295-299 2002