CDB SEMINAR

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MRC National Institute for Medical Research

Monday, November 11, 2013

14:00~15:00 A7F Seminar Room

Using genome engineering to reinvestigate the range of Wnt signalling

Summary

Wnts are evolutionarily conserved secreted signaling proteins that organize patterns and stimulate growth in various developmental contexts. Wnt proteins have been suggested to act as morphogens, spreading from the site of synthesis and activating target gene expression in a dose-dependent manner. This has been particularly well studied in wing imaginal discs of Drosophila. There, Wingless produced at the dorso-ventral boundary spreads into the prospective blade, where it controls growth and patterning. However, post-translational palmitoylation renders Wnts poorly soluble in aqueous media raising the question of how it spreads in the extracellular space. Various mechanisms have been suggested to help overcome this solubility paradox but so far, no genetic mutation has been shown specifically to prevent the spread of Wnts. To determine the phenotype of such hypothetical mutants, we used genome engineering to replace the endogenous wingless gene (encoding the main Drosophila Wnt) with one that expresses a membrane-tethered form. Surprisingly, the resulting flies, which only express non-diffusible Wingless,were viable and had normally patterned appendages of nearly the right size. We suggest that two processes contribute to obviating the need for Wingless to spread. First, prospective wing blade cells produce their own local supply of Wingless during the early period of growth and patterning. Later, after local expression terminates, target gene expression persists by a mechanism akin to cellular memory. Although imaginal discs achieve a near normal pattern and size without long range signaling from Wingless release, their growth rate and that of the whole larva are reduced. Using a novel method for tissue-specific allele switching, we found that organ-autonomous growth rate reduction and organismal delay occurs through independent mechanisms.

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