Organelle Network Biology Seminar Series

大阪大学 グローバルCOE

「オルガネラネットワーク医学創成プログラム」

Mechanisms of Wnt signalling: assembly of signalosomes and degradasomes

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Wnt signals through beta-catenin to control animal development and tissue homeostasis; if inappropriately activated, beta-catenin can cause cancer, notably colorectal cancer. This seminar is focussed on the role of the DIX domain in Wnt signalling, a remarkable domain only found in two Wnt pathway components – Axin and Dishevelled – with opposing roles in Wnt signal transduction. In the absence of a Wnt signal, the APC tumour suppressor promotes the assembly of Axin degradasomes through DIX-mediated homo-polymerisation; degradasomes keep the signalling OFF by earmarking the Wnt effector beta-catenin for proteasomal degradation. In the presence of Wnt, Dishevelled signalosomes are assembled at the plasma membrane, which recruit the degradasomes through DIX-mediated hetero-polymerisation between Dishevelled and Axin; signalosomes switch signalling ON by inactivating the degradasomes. The underlying principle in degradasome and signalosome assembly is a dynamic 'head-to-tail' polymerisation conferred by the DIX domain, which generates a high local concentration of weak protein-binding sites, allowing efficient interaction with low-affinity binding partners of Axin or Dishevelled.

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