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Drosophila Wnt-1/Wingless undergoes a hydrophobic modification and is targeted to lipid rafts for secretion, a process that requires Porcupine

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[Xiaoling Hill, University of Massachusetts - Amherst](#)

Abstract

Wnt ligands are a family of highly conserved glycoproteins that act as morphogens to regulate development in many organisms. *Drosophila* Wnt-1 (Wingless) is involved in directing cell fate decisions and pattern formation during differentiation. Wnt signaling are of high interest of many developmental biologists due to their important functions, yet little is known about how these ligands function on a biochemical level. Previously it was found that Porcupine, an ER-membrane-bound acyltransferase is required for Wingless secretion. But it is unclear how a secreted morphogen requires an acyltransferase to function. Studies reported here demonstrated that Wingless undergoes a hydrophobic modification, in which a lipid moiety containing a palmitate group is covalently attached to the polypeptide through an ester linkage. And it partitions with the specialized detergent insoluble lipid raft microdomains in the plasma membrane. Porcupine is required for the modification and the raft targeting of Wingless. Blocking Wingless modification with a specific inhibitor results in the loss of rafts-association as well as loss of protein secretion. Disrupting raft microstructures by cholesterol depletion reagents also impaired Wingless secretion, indicating that the ligand secretion is dependent on its specific association with the plasma membrane. This work provided the first insight on the function of Porcupine and the important biochemical evidence on the role of specialized membrane microdomains in Wnt signaling. ^

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