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Syndecan-assisted endocytic trafficking

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Guido David obtained his MD degree from the Catholic University of Leuven Medical School, Belgium (1972). He was resident in Internal Medicine at the University Hospital of Leuven (1972-1976), and board certified in Clinical Pathology-Hematology (1979). In 1976, he joined the laboratory of Merton Bernfield, at Stanford University Medical School, where he stayed for four years as post-doctoral research fellow, supported by Fogarty International and Damon Runyon-Walter Winchell Cancer Fund fellowships. Upon his return to Belgium, he became a Research Associate (1981) and later Research Director (1990) of the National Fund for Scientific Research of Belgium, in the Department of Human Genetics at the Catholic University of Leuven. In 1997, he was appointed as the Scientific Director of the Department of Human Genetics of the Flanders Interuniversity Institute for Biotechnology, and became full professor at the Catholic University of Leuven, Belgium.

While the best recognized role of endocytosis in signaling is to down-regulate the signal by sending the receptor and /or the ligand to degradative compartments such as lysosomes, it has now become clear that endocytosis also contributes to activation of signaling, modulating interactions between signaling molecules and their inhibitors, regulating receptor presentation at the cell surface, contributing to the formation of morphogen gradients and even providing localized endosomal environments where signaling takes place. Thus, the pathways of vesicular trafficking are emerging as extremely important for the spatial and temporal fine-tuning of developmental signaling, and there is circumstantial evidence that syndecans and glypicans have specific roles in this respect. Research addressing the functions of the syndecans in signaling has mostly centered on their presumptive roles as cell surface HS-acceptors/receptors of extracellular matrix proteins and soluble growth factors. It appears now that, side by side with integrins and tyrosine kinase receptors, the core proteins of the syndecans contribute significantly in signaling and are regulated by signaling. We have evidence that, via the PDZ-protein syntenin, the syndecans are connected with PIP2, a phosphoinositide that in concert with Arf6 regulates the organization of the actin cytoskeleton and vesicular transport. Cell surface recycling of syndecan and syndecan cargo, such as adhesion molecules, FGF and FGFR depend on syntenin and Arf6 (Zimmermann et al., 2005), potentially identifying a novel signalling function for these 'endocytic' receptors.

References : Zimmermann P, Zhang Z, Degeest G, Mortier E, Leenaerts I, Coomans C, Schulz J, N'Kuli F, Courtoy P and David G. (2005) Syndecan recycling is controlled by syntenin-PIP2 interaction and Arf6. *Dev Cell* 9:377-388.

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