



*Sci. STKE*, 11 May 2004  
Vol. **2004**, Issue 232, p. tw165  
[DOI: 10.1126/stke.2322004TW165]

## EDITORS' CHOICE

### DEVELOPMENT

## Pathways with Sugar

Extracellular proteoglycans present on cell surface molecules and components of the extracellular matrix can regulate the effect of secreted factors on developmental processes by altering their stability, transport, and interaction with receptors. Studies in *Drosophila* have revealed that loss of a gene encoding a heparan sulfate (HS)-synthesizing enzyme called *tout velu* (*ttv*) impairs the distribution and signaling activity by the Hedgehog (Hh) growth factor and morphogen. Bornemann *et al.* report that lack of HS synthesis in flies also affects two other major signaling pathways that control patterning and development--Wingless (Wg) and Decapentaplegic (DPP), arguing against a specific role for *ttv* in Hh signaling. Loss of either *ttv* or another gene that encodes a HS copolymerase called *sister of tout velu* (*sotv*) compromised signaling of all three signaling pathways in the wing imaginal disk. HS levels, protein levels and gradients of Hh, Wg, and DPP, as well as expression of target genes, decreased in the wing cells of either mutant larvae. Although Hh protein abundance was reduced in the posterior compartment of wing imaginal discs, Hh transcription levels were unaltered, indicating that lack of Hh signaling in mutants could be due in part to decreased Hh protein stability. It has been thought that heparan sulfate proteoglycans (HSPGs) enhance targeting of Hh to lipid rafts for subsequent transport from cell to cell. The authors propose that HSPGs could also stabilize Hh molecules by either direct binding or indirectly, by reducing activity of extracellular proteases. Both *ttv* and *sotv* have human homologs, which suggests that the mechanism of HS biosynthesis in fruit fly and vertebrates is conserved.

D. J. Bornemann, J. E. Duncan, W. Staatz, S. Selleck, R. Warrior, Abrogation of heparan sulfate synthesis in *Drosophila* disrupts the Wingless, Hedgehog, and Decapentaplegic signaling pathways. *Development* **131**, 1927-1938 (2004). [[Abstract](#)] [[Full Text](#)]

**Citation:** Pathways with Sugar. *Sci. STKE* **2004**, tw165 (2004).

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EDITORS' CHOICE

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Elizabeth M. Adler (4 March 2008)

*Sci. Signal.* **1** (9), ec80. [DOI: 10.1126/stke.19ec80]

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