



*Sci. Signal.*, 4 March 2008  
Vol. 1, Issue 9, p. ec80  
[DOI: 10.1126/stke.19ec80]

## EDITORS' CHOICE

Development

# Translating GAGs to Regulate Morphogens

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Heparan sulfate proteoglycans [HSPGs, widely distributed extracellular macromolecules that consist of a core protein modified by covalently linked glycosaminoglycan (GAG) chains] interact with and influence the signaling of Hedgehog, Wingless, and bone morphogenetic proteins (BMPs), all of which are critical to *Drosophila* embryonic development. Noting that HSPGs have been directly implicated in regulating Hedgehog and Wingless signaling in *Drosophila* embryos, Bornemann *et al.* investigated their role in BMP signaling. Surprisingly, embryos with mutations that interfered with GAG synthesis showed normal dorsal patterning, a process that depends on the establishment of a BMP signaling gradient. In contrast, exposure to exogenous heparin (which replaces some functions of endogenous HSPGs) disrupted dorsal patterning and inhibited expression of a reporter of signaling by the *Drosophila* BMP decapentaplegic (Dpp). Sequelae of Dpp signaling are evident earlier (2.5 hours after fertilization) than are sequelae of Hedgehog and Wingless signaling (more than 3 hours after fertilization), and Western analysis indicated that GAG modifications were not apparent in embryos less than 3 hours old. The glypican core proteins Dally and Dlp were present in early embryos, as were maternally derived transcripts encoding the GAG synthetic enzymes Ttv and Sfl. Substantial amounts of Ttv and Sfl proteins, however, were not apparent at these very early developmental stages. The *ttv* 5' UTR contained an internal ribosomal entry site (IRES); analysis of the expression of proteins derived from various constructs implicated this IRES in blocking Ttv translation during early embryogenesis and indicated that the *ttv* 3' UTR cooperated with the 5' UTR to block translation. Thus, BMP signaling early in embryogenesis is independent of HSPGs because of a translational block of GAG synthesis.

D. J. Bornemann, S. Park, S. Phin, R. Warrior, A translational block to HSPG synthesis permits BMP signaling in the early *Drosophila* embryo. *Development* 135, 1039–1047 (2008).

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**Citation:** E. M. Adler, Translating GAGs to Regulate Morphogens. *Sci. Signal.* 1, ec80 (2008).

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