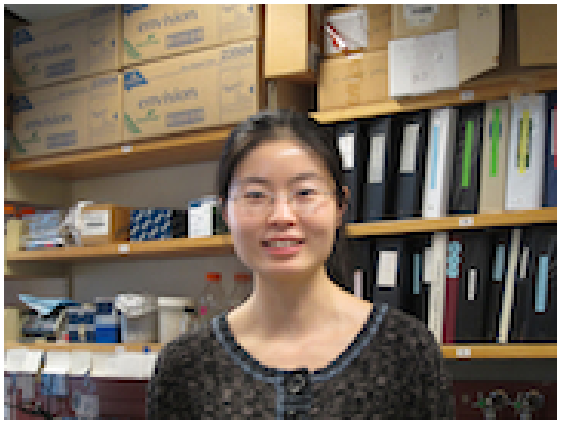
2014 LPS GGD Best Paper Award

Chenxi Tian



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The neogenin/DCC homolog UNC-40 promotes BMP signaling via the RGM protein DRAG-1 in *C. elegans*

Chenxi Tian[1,*], Herong Shi[1], Shan Xiong[2], Fenghua Hu[1,3], Wen-Cheng Xiong[2] and Jun Liu[1,‡]

SUMMARY

The deleted in colorectal cancer (DCC) homolog neogenin functions in both netrin- and repulsive guidance molecule (RGM)-mediated axon guidance and in bone morphogenetic protein (BMP) signaling. How neogenin functions in mediating BMP signaling is not well understood. We show that the sole *C. elegans* DCC/neogenin homolog UNC-40 positively modulates a BMP-like pathway by functioning in the signal-receiving cells at the ligand/receptor level. This function of UNC-40 is independent of its role in netrin-mediated axon guidance, but requires its association with the RGM protein DRAG-1. We have identified the key residues in the extracellular domain of UNC-40 that are crucial for UNC-40–DRAG-1 interaction and UNC-40 function. Surprisingly, the extracellular domain of UNC-40 is sufficient to promote BMP signaling, in clear contrast to the requirement of its intracellular domain in mediating axon guidance. Mouse neogenin lacking the intracellular domain is also capable of mediating BMP signaling. These findings reveal an unexpected mode of action for neogenin regulation of BMP signaling.

KEY WORDS: BMP signaling, Neogenin, DCC, UNC-40, RGM, DRAG-1, *Caenorhabditis elegans*