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Modulation of BMP Activity in Dorsal-Ventral Pattern Formation by the Chordin and Ogon Antagonists

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Abstract

We analyzed the interactions between mutations in antagonistic BMP pathway signaling components to examine the roles that the antagonists play in regulating BMP signaling activity. The dorsalized mutants *swirl/bmp2b*, *snailhouse/bmp7*, *lost-a-fin/alk8*, and *mini fin/tolloid* were each analyzed in double mutant combinations with the ventralized mutants *chordino/chordin* and *ogon,* whose molecular nature is not known. Similar to the BMP antagonist *chordino*, we found that the BMP ligand mutants *swirl/bmp2b* and *snailhouse/bmp7* are also epistatic to the putative BMP pathway antagonist, *ogon,* excluding a class of intracellular antagonists as candidates for *ogon*. In *ogon*;*mini fin* double mutants, we observed a mutual suppression of the *ogon* and *mini fin* mutant phenotypes, frequently to a wild type phenotype. Thus, the Tolloid/Mini fin metalloprotease that normally cleaves and inhibits Chordin activity is dispensable, when Ogon antagonism is reduced. These results suggest that Ogon encodes a Tolloid and Chordin-independent antagonistic function. By analyzing genes whose expression is very sensitive to BMP signaling levels, we found that the absence of Ogon or Chordin antagonism did not increase the BMP activity remaining in *swirl/bmp2b* or hypomorphic *snailhouse/bmp7* mutants. These results, together with other studies, suggest that additional molecules or mechanisms are essential in generating the presumptive gastrula BMP activity gradient that patterns the dorsal–ventral axis. Lastly we observed a striking increased penetrance of the *swirl/bmp2b* dominant dorsalized phenotype, when Chordin function is also absent. Loss of the BMP antagonist Chordin is expected to increase BMP signaling levels in a *swirl* heterozygote, but instead we observed an apparent decrease in BMP signaling levels and a loss of ventral tail tissue. As has been proposed for the fly orthologue of *chordin*, *short gastrulation*, our paradoxical results can be explained by a model whereby Chordin both antagonizes and promotes BMP activity.

Keywords

Zebrafish; *Danio rerio*; dorsal–ventral; BMP; BMP antagonist; Chordin; pattern formation

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