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ACCEPTED MANUSCRIPT

Contribution of Hedgehog signaling to the establishment of left-right asymmetry in the sea urchin

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Summary

Most bilaterians exhibit a left-right asymmetric distribution of their internal organs. The sea urchin larva is notable in this regard since most adult structures are generated from left sided embryonic structures. The gene regulatory network governing this larval asymmetry is still a work in progress but involves several conserved signaling pathways including Nodal, and BMP. Here we provide a comprehensive analysis of Hedgehog signaling and it's contribution to left-right asymmetry. We report that Hh signaling plays a conserved role to regulate late asymmetric expression of Nodal and that this regulation occurs after Nodal breaks left-right symmetry in the mesoderm. Thus, while Hh functions to maintain late Nodal expression, the molecular asymmetry of the future coelomic pouches is locked in. Furthermore we report that cilia play a role only insofar as to transduce Hh signaling and do not have an independent effect on the asymmetry of the mesoderm. From this, we are able to construct a more complete regulatory network governing the establishment of left-right asymmetry in the sea urchin.

Introduction

While the adult sea urchin exhibits secondary penta-radial symmetry it develops as a bilaterally symmetric larva prior to metamorphosis. In most species the juvenile forms from a specialized structure, termed the rudiment, that develops on the left side of the feeding larva. A cascade of morphological and cell communication events precedes this development. A maternal asymmetry in the sea urchin egg establishes the animal-vegetal

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