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The Mechanism To Establish Robust Left-Right Asymmetry

A development of animal body proceeds under the intrinsic noise (gene expression, protein interaction, cell migration etc.) and the extrinsic noise (environment). In spite of existence of so much noise, an animal development proceeds robustly and C.H.Waddington called a stability of a development, "Canalization". Of course, left and right determination in the mouse is not exception and canalization of L-R development attains 99.99 %.

Our body has many internal organs that show asymmetric morphologies about left-right axis and these morphologies play important roles in its function, such as the heart, liver, stomach and intestine. Recently, mechanisms to establish L-R asymmetry in the mouse embryo have been elucidated by using genetics and molecular approaches. In the mouse embryo, the small leftward fluid flow in the node produces first asymmetric information along L-R axis and the left-side specific genes are expressed in the left lateral plate mesoderm subsequently.

Although some cascades of gene expressions were studied, it is unknown how robust expressions of left side specific genes are established from the small asymmetric water flow in the node. Nodal and Lefty, two members of the transforming growth factor-β super family of proteins and are expressed in the lateral plate mesoderm, have been implicated in Turing system. Turing system is a mathematical model that consists of two diffusible molecules and may underlie pattern formation during development. We have now examined the potential role of Turing system in left-right patterning both by experimentally manipulating Nodal and Lefty gene expression in the mouse embryos and by constructing a mathematical model.

Our results suggest that an initial small difference in the level of an activating signal between the left and right sides of the embryo is amplified and converted into robust asymmetry by Turing system involving Nodal and Lefty.

References

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