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Mechanism uncovered for the establishment of vertebrate left-right asymmetry

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A research team at the Hubrecht Institute, Utrecht, demonstrates a mechanism by which left–right asymmetry in the body is established and maintained. The study, published in the open-access journal *PLoS Genetics* on September 29, offers a new model of how families of genes interact to promote and direct body asymmetry.

Although organisms appear bilaterally symmetrical when observed from the outside, internal organs are positioned asymmetrically along the left–right axis, and the organs themselves exhibit intrinsic left–right asymmetries. While complete organ reversal (situs inversus) rarely gives rise to medical complications, severe medical problems occur in infants with partial organ reversal (situs ambigious or heterotaxia), including improper connections of the major vessels to the heart. These heart defects are often lethal if not immediately corrected after birth by cardiac surgery, meaning that the establishment of correct left–right asymmetry is a critical process.

The researchers, led by Dr. Jeroen Bakkers, identified a receptor for bone morphogenetic proteins (BMP) as a regulator of left–right patterning in zebrafish using a forward genetic screen. Two growth factors, Nodal and BMP, have previously been shown to be important for orchestrating left–right asymmetry, but the mechanism and hierarchy for the regulation of this process had been unclear. The data presented in this study reveal a new mechanism by which these proteins pattern the embryo along the left–right axis, through the induction and maintenance of a genetic midline 'barrier'.

Dr. Bakkers and colleagues conclude that further studies are required to tease out whether there are species–specific differences during the development of embryonic left–right patterning, but this study and another by other researchers studying mouse development lend support for a conservation of this pathway in regulating organism left–right asymmetry.

More information: Smith KA, Noël E, Thurlings I, Rehmann H, Chocron S, et al. (2011) Bmp and Nodal Independently Regulate lefty1 Expression to Maintain Unilateral Nodal Activity during Left-Right Axis Specification in Zebrafish. PLoS Genet 7(9): e1002289. doi:10.1371/journal.pgen.1002289