Highlights in *DD*

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"Highlights" calls attention to exciting advances in developmental biology that have recently been reported in *Developmental Dynamics*. Development is a broad field encompassing many important areas. To reflect this fact, the section spotlights significant discoveries that occur across the entire spectrum of developmental events and problems: from new experimental approaches, to novel interpretations of results, to noteworthy findings utilizing different developmental organisms.

Calculating what's left (*Fluid dynamics of nodal flow and left-right patterning in development* by Julyan H.E. Cartwright, Nicolas Piro, Oreste Piro, Idan Tuval, *Dev Dyn* 237:3477–3490) Like it or not, most biological phenomena cannot be adequately explained without the help of physics. Luckily for the physics-phobe, there are gifted teachers such as Cartwright and colleagues who are exceptionally skilled at explaining biology's numerical roots. This review covers their and others' work modeling the fluid dynamics behind nodal flow–fluid flow induced by monocilia within the node, one of the earliest steps in establishing vertebrate left–right asymmetry. In the interest of examining models with predictive power, they discuss what happens when as of yet experimentally untested variables are included in fluid dynamical models. Biological concepts are nimbly intertwined with the derivation of models that can be used to understand them, giving even the most mathematically challenged something onto which they can grasp.

Change of heart (*Cellular nonmuscle myosins NMHC-IIA and NMHC-IIB and vertebrate heart looping* by Wenge Lu, Steven H. Seeholzer, Mingda Han, Anne-Sophie Arnold, Maria Serrano, Barbara Garita, Nancy J. Philp, Cassandra Farthing, Peter Steele, Jizhen Chen, Kersti K. Linask, *Dev Dyn* 237:3557–3564) Galanin is a neuropeptide, well known for regulating various nervous system functions, such as metabolism and regulation of food intake. Therefore, it is surprising that Schweickert and colleagues found that *Gal*, the gene that encodes Galanin, is asymmetrically expressed in the linear heart tube, and is later localized to the second pacemaker, the atrioventricular node and ring. Furthermore, like asymmetric expression of left–right (LR) patterning gene *Nodal*, and downstream genes *Lefty2* and *Pitx2c* in the lateral plate mesoderm (LPM) in the early embryo, left-sided heart *Gal* expression at later stages is dependent on leftward flow of cilia in the posterior notochord (commonly termed as node). This finding demonstrates that *Gal* is regulated by the LR pathway. Therefore, it is surprising that *Gal* heart expression remains unchanged in mutants for the Nodal co-receptor *cryptic*, even though expression of Nodal cascade genes disappears in the LPM. Also surprising is that asymmetric heart expression of *Pitx2c* also remains unchanged in half of *cryptic* homozygotes. This discovery led the authors to hypothesize that asymmetric gene expression in the heart is *cryptic* independent. Neither Galanin nor cryptic are behaving as expected—perhaps they had a change of heart.

MANning the barrier (*Man1, an inner nuclear membrane protein, regulates left-right axis formation by controlling nodal signaling in a node-independent manner* by Akihiko Ishimura, Shinsuke Chida, Shin-Ichi Osada, *Dev Dyn* 237:3565–3576) During specification of the left–right axis, the midline acts as a barrier that keeps asymmetrically expressed signals from becoming bilateral. Here, Ishimura et al., provide evidence for the first time that Man1, an inner nuclear membrane protein, regulates activity of a midline barrier. Transgenic mice bearing truncated MAN1 that lacks an R-SMAD interacting domain (R-SMADs are downstream effectors of TGFβ family signaling), show bilateral expression of the left–right determination gene *Nodal*, and downstream genes *Lefty2* and *Pitx2*. Of interest, ectopic expression of the three genes occurs despite that *Lefty1*, a marker for the midline barrier, is still present. How could this be? One possible answer lies in the discovery that expression of coreceptors for Nodal, *Cryptic* and *Cripto*, are up-regulated. The event may enhance competence for Nodal signaling. Another possibility stems from their finding that bilateral *Nodal* expression is maintained in *Man1* mutants crossed with *Nodal* hypomorphs, despite that these double mutants lack a node, and thus early node-derived *Nodal*. This means that, instead of under the control of node-derived *Nodal*, ectopic *Nodal* may be controlled by an unknown molecule that is derepressed in a *Man1* mutant background. One candidate is *Bmp2*, whose expression is also augmented in *Man1* mutants. The observation that *Man1* is transiently expressed in the posterior midline bolsters the idea that the gene also directly or indirectly regulates activity of a midline barrier.