LABORATORY FOR SPATIOTEMPORAL REGULATIONS

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Our laboratory is currently pursuing two paths of scientific inquiry of interest to developmental biology. One goal is to clarify the mechanism of left-right (L-R) determination. The other is to develop imaging technologies for developmental biology.

I. Initial step for left-right asymmetry

The first L-R asymmetry in mammalian development arises on the embryonic surface. A gastrulating mouse embryo has a shallow hollow on its ventral surface, called 'the node,' with hundreds of cilia moving in a clockwise rotational manner (Figure 1; Nonaka et al., 1998). The sum of the vortical motions of the cilia, however, generates a leftward flow of the surrounding fluid rather than a vortex. The cilia can generate L-R asymmetry *de novo*, i.e. without pre-existing left-right asymmetry, by their posteriorly tilted rotation axis (Nonaka et al., 2005).

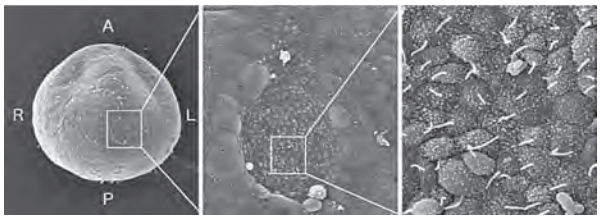

Figure 1. Left: ventral view of a 7.5-day mouse embryo. Middle: the node. Right: node cilia.

The leftward flow, called nodal flow, determines subsequent L-R development. This principle has been confirmed by our experiments, which demonstrated that embryos raised with an artificial rightward flow develop reversed L-R asymmetry (Nonaka et al., 2002).

While it is clear that nodal flow conveys asymmetric information along the L-R axis, the nature of the information remains unclear. We are now working to clarify how the direction of nodal flow is converted to the subsequent step, asymmetric gene expression.

II. Imaging technologies

Long-term live imaging of large specimens, such as embryos, is very useful in developmental biology but technically challenging, mainly because of phototoxicity and the limitations of deep imaging. The Digital Scanned Light-sheet Microscope (DSLM, Figure 2) developed by Dr. Ernst Stelzer's group at the European Molecular Biology Laboratory (EMBL) is extremely suitable for this purpose, and we have introduced a DSLM set and applied it to visualize cell movements in intact mouse embryos at gastrulating stages.

Additionally, we support researchers who are interested in using our DSLM and two-photon microscope (for example, Hashimoto et al. Nat. Cell Biol. 12, 170-186, 2010). Several collaborative projects are in progress.

Figure 2. Principle of light-sheet microscopy. Left: light path of conventional fluorescent microscopes using single objective lens for both illumination (Ex) and detection (Em). Right: light-sheet microscopes including DSLM, where illumination light is limited to the focal plane of the detection objective.

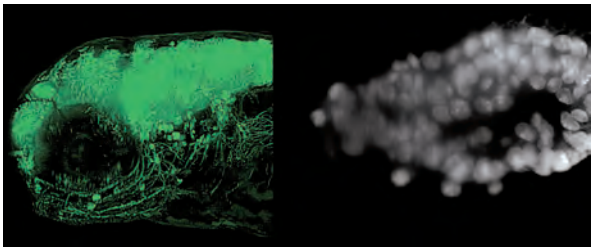

Figure 3. Images taken with DSLM. Left: optical section of a 6-day mouse embryo with fluorescent nuclei. Right: a juvenile zebrafish head expressing GFP in neurons.

Publication List

〔Review article〕

● Nonaka, S. (2009). Modification of Mouse Nodal Flow by Applying Artificial Flow. In Methods in Cell Biology, S. King, and G. Pazour, eds. (Academic Press), pp. 287-297.