DIVISION OF EMBYOLOGY

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This laboratory was started in August 2008. The aim of our research is to understand the events underlying early mammalian development during the period from the pre-implantation to establishment of the body axes.

An understanding of early events during embryogenesis in mammals, as compared to other animals, has been relatively delayed. This is mainly due to the difficulties in the approaches to the developing embryos in the uterus of the mother. The other characteristic of mammalian embryos is their highly regulative potential. The pattern of cell division and allocation of cells within an embryo during the early stages vary between embryos. The timing of the earliest specification events that control the future body axes is still under discussion. Functional proteins or other cellular components have not been found that localize asymmetrically in the fertilized egg. We want to provide basic and fundamental information about the specification of embryonic axes, behaviors of cells and the regulation of body shape in early mammalian development. Our specific research interests are as follows.

Ⅰ. Characterization of the earliest event in body axis formation

It is generally accepted that, of the three body axes, the anterior-posterior (AP) axis is actively specified earliest. This is initiated by the movement of visceral endoderm from the distally located position to the future anterior side. It is still an open question whether any differential information relating to the future body axes already exists within the embryo before the movement of distally located visceral endoderm. We are planning to observe the behaviors of cells and the changes of embryonic morphology to characterize the earliest event of axis formation. We will analyze the general behaviors of cells within embryos by utilizing live imaging techniques in addition to morphological observation of embryos within the uterus.

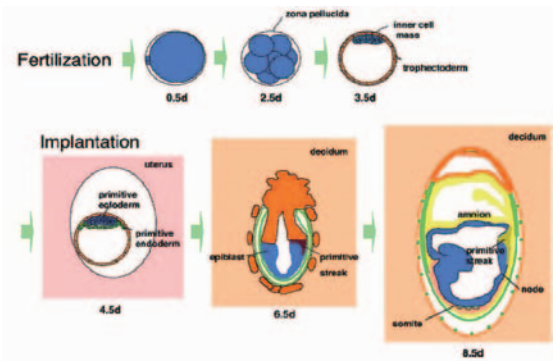

Figure 1. Summary of mouse early development.

Ⅱ. Molecular mechanisms regulating the cell differentiation in preimplantation development.

In early blastoycst, two types of cells - the cells of inner cell mass (ICM), and the cells of trophectoderm (TE) - can be distinguished. This is the earliest event of cell differentiation in mouse development. By the studies of genes expressed in the blastocyst and in the ES cells, several genes are known to play key roles in the regulation of cell differentiation during preimplantation stages. In the late blastocyst stage, expression of Oct4 is lost in TE and primitive endoderm (PE) cells. By contrast, Cdx2 is expressed in the TE lineage. Nanog is expressed in the ICM of early blastocyst and will be lost in PE lineage at a later stage. Continuous realtime analyses of the behaviors of these genes are unique, and will provide general basic ideas concerning the regulation of cell differentiation.

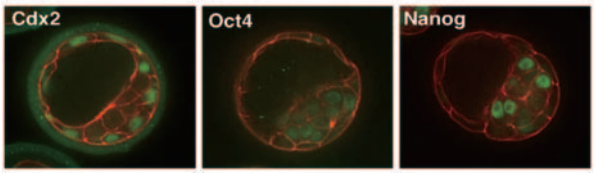

Figure 2. Expression of key genes in the mid blastocyst

Ⅲ. Analysis of mechanisms those regulate embryonic body shape

Mammalian early embryos change their total body size rapidly after the implantation, whereas the total shape of the embryo is well established. We will study the mechanisms regulating embryonic body shape by analyzing the behaviors of individual cells within the embryo.

Publication List

〔Original papers〕

- Ishii, Y., Matsumoto, Y., Watanabe, R., Elmi, M., Fujimori, T., Nissen, J., Cao, Y., Nabeshima, Y., Sasahara, M., and Funa, K. (2008). Characterization of neuroprogenitor cells expressing the PDGF beta-receptor within the subventricular zone of postnatal mice. Mol. Cell. Neurosci. *37*, 507-518.
- Katsuno, T., Umeda, K., Matsui, T., Hata, M., Tamura, A., Itoh, M., Takeuchi, K., Fujimori, T., Nabeshima, Y., Noda, T., Tsukita, S., and Tsukita, S. (2008). Deficiency of zonula occludens-1 causes embryonic lethal phenotype associated with defected yolk sac angiogenesis and apoptosis of embryonic cells. Mol. Biol. Cell *19*, 2465-2475.
- Tokunaga, A., Oya, T., Ishii, Y., Motomura, H., Nakamura, C., Ishizawa, S., Fujimori, T., Nabeshima, Y., Umezawa, A., Kanamori, M., Kimura, T., and Sasahara, M. (2008). PDGF receptor beta is a potent regulator of mesenchymal stromal cell function. J. Bone Miner. Res. *23*, 1519-1528.
- Toyooka, Y., Shimosato, D., Murakami, K., Takahashi, K., and Niwa, H. (2008). Identification and characterization of subpopulations in undifferentiated ES cell culture. Development *135*, 909-918.