SL 103 Control of organogenesis in undifferentiated and cultured cells in Xenopus laevis

Makoto Asashima[1, 2]

Department of Life Sciences (Biology)[1], CREST Project[2], Graduate School of Arts and Sciences, The University of Tokyo, 3-8-1 Komaba, Meguro-ku, Tokyo 153-8902, Japan

In the process of early vertebrate development, formation of an embryonic body pattern is established through cell division, gene expression, morphogenesis and cell differentiation. The mechanism of body patterning is complex and includes multiple induction events. In the induction events occurring between two cells or tissues, factors secreted by the inducing cells may cause the directive differentiation of the reacting cells. In mesoderm induction the expected factors from vegetal cells are referred to as mesodermal inducing factors (MIFs).

Activin, a member of the TGF-β-super family, can induce several kinds of mesodermal and endodermal tissues in Xenopus and newt animal caps. The effect of activins on animal caps is distinctly dose-dependent, with induction of more dorsal tissues such as muscle and notochord and endodermal tissues as the concentration increases.

In a recent study of the role of activin in organ formation, we succeeded in raising a beating heart by treating animal caps with a high concentration of activin A. Renal tubules were induced in Xenopus animal caps treated with a combination of activin A and retinoic acid (RA) at a high frequency (100%) accompanying several genes such as Xlim-1, Pax 8, XCIRB, Xlcaax, XCIRP, Sal 3, Na^+-K^+ ATPase α-subunit and so on. The renal tubule explants induced by activin and RA in vitro could also function in vivo when the explant was transplanted into the removed presumptive kidney region. Some kinds of blood cells such as leukocytes and erythrocytes were also induced in the animal cap with the combination of activinA and other growth factors.

When an activin-treated animal cap was sandwiched between two non-treated animal caps, the treated animal cap obviously behaved as Spemann's organizer. They induced embryo-like explants with multiple endodermal and mesodermal tissues and a central nervous system. Activin-treated animal caps become artificial organizers which act as "trunk-and-tail organizer" or "head organizer", depending on the preculture time after the treatment of activin on animal cap. We have cloned and analyzed several neural genes such as XILRRP, Xran, XFed, which are closely related neurogenesis.

Using the some kind of Xenopus cell lines such as A8, A6 and XTY, we examined the morphogenesis and gene expression. Depend on the cell line, the morphogenetic movement and expressed genes are changed.

To examine the incorporation of activins and follistatin in Xenopus oocyte, we have studied the uptake of these proteins in developing Xenopus oocyte in vitro. Using ^{125}I- or colloidal gold particle-labeled activins and follistatin, signals were detected in the cytoplasm of the oocyte. Xenopus oocytes has the capacity to incorporate maternal activins and follistatin during oogenesis. And these maternal activins seem to be used as the first molecular signal during early development. Activins or related proteins seem to be the one of the first important induction signals responsible for establishing the fundamental embryo body plan.