CDB SEMINAR

Ryan Range

National Institute of Dental and Craniofacial Research,
National Institutes of Health

Thursday, January 24, 2013

16:00~17:00 A7F Seminar Room

Wnt Signaling Interactions and Anterior-Posterior Neuroectoderm Patterning in Deuterostome Embryos

Summary

Patterning the neuroectoderm along the anterior–posterior (AP) axis is a critical event in the early development of deuterostome embryos. However, the mechanisms that regulate this process are incompletely understood. Remarkably, the anterior neuroectoderm (ANE) of the invertebrate deuterostome sea urchin embryo expresses many of the same transcription factors and secreted regulators of Wnt signaling, as does the early vertebrate ANE (forebrain/eye field). Moreover, as is the case in vertebrate embryos, confining the ANE to the anterior end of the embryo requires a Wnt/β-catenin-dependent signaling mechanism. Unexpectedly, we discovered that in the sea urchin embryo this mechanism integrates information not only from Wnt/β-catenin signaling, but also from at least two alternative Wnt signaling pathways, Wnt/Fzl5/8-JNK and Fzl1/2/7-PKC, to provide precise spatiotemporal control of neuroectoderm patterning along its AP axis. Using morpholino- or dominant negative-mediated interference, we show that Wnt/β-catenin down regulates the maternally specified, ubiquitous ANE regulatory state and up regulates production of two Wnt ligands, Wnt1 and Wnt8, in posterior blastomeres before 5th cleavage stage. These ligands then activate Wnt/Fzl5/8-JNK signaling in more anterior blastomeres starting around 6th cleavage. This signaling pathway causes the progressive restriction of the ANE regulatory state to the anterior-most blastomeres by the mesenchyme blastula stage right before the beginning of gastrulation. These anterior cells maintain the ANE regulatory state because the Wnt receptor antagonist, Dkk1, produced by Wnt-Fzl5/8 signaling in a negative feedback mechanism during late blastula stages, protects them there. Importantly, the balance in the rates of ANE restriction and Dkk1 appearance must be tightly controlled and this relies on the activity of a third Wnt pathway, Wnt/PKC. Because these different Wnt pathways converge on the same cell fate specification process, they likely function as integrated components of an interactive Wnt signaling network.

Once the ANE is restricted to the anterior end of the late blastula-stage embryo, it separates into inner and outer regulatory domains expressing the cardinal ANE transcriptional regulators, FoxQ2 and Six3, respectively. This process is driven by FoxQ2, which is required to eliminate expression of *six3* from the inner domain. FoxQ2 also activates the expression of two secreted Wnt regulators, sFrp1/5 and Dkk3, the activities of which define the correct sizes of the inner and outer ANE territories. Furthermore, the levels of sFrp1/5 and Dkk3 are rigidly maintained via auto-repressive and cross-repressive interactions with Wnt signaling components and ANE transcription factors. Our data support a model in which Six3 and FoxQ2 establish an anterior patterning center that ensures correct ANE patterning and border positions. Our findings, when compared to functional and expression studies in other deuterostome embryos, show striking similarities in deuterostome ANE regulatory states and the molecular mechanisms that position and define its borders, providing strong support for the idea that the sea urchin embryo uses an ancient regulatory patterning system that was present in the common echinoderm/vertebrate ancestor.

Host:
Shigeo Hayashi
Morphogenetic Signaling, CDB
shayashi@cdb.riken.jp
Tel:078-306-3185 (ext:1523)