CDB SEMINAR

Yoshikazu Hirate

Dept. of Cell Fate Control, Institute of Molecular Embryology and Genetics (IMEG), Kumamoto Univ.

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16:00~17:00 Seminar Room A7F

Polarity-dependent distribution of Angiomotin localizes Hippo signaling in preimplantation embryos

Summary

The first cell fate specification in mammalian development creates two cell lineages in the blastocyst embryo, the inner cell mass and trophectoderm. The fate is specified whether the cell is located inside or outside of the embryo. The cell position-dependent specification is regulated by the Hippo pathway. Hippo signaling is turned on and off in the inner and outer cells, respectively. The difference leads to the cell position-dependent fate specification. However, the mechanisms that create the positional difference in Hippo signaling remain unknown. In this talk, I show that a combination of cell–cell adhesion and cell polarity establishes the differential Hippo signaling. Cell-cell adhesion activates the Hippo pathway in the inner cells. The junction-associated proteins Angiomotin (Amot) and Amotl2 are localized to the adherens junctions (AJs) and are essential for Hippo signaling in the inner cells. Amot interacts with E-cadherin-catenin complex via a Hippo pathway component Merlin and also interacts with a Hippo pathway kinase Lats2. Through these interactions, Amot is localized to the AJs and cell–cell adhesion activates the Hippo pathway. We further found that Amot is phosphorylated by Lats2 and this phosphorylation plays a key role for activation of the Hippo pathway. In contrast to the inner cells, the outer cells have no Amot at the AJs. Cell polarity of the outer cells sequesters Amot from the AJs to apical domains, thereby disconnects the Hippo pathway from cell-cell adhesion. The proposed mechanisms convert positional information into differential Hippo signaling, leading to the establishment of the distinct cell fates.

Host:
Yasuhide Furuta
Animal Resources and Genetic Engineering, CDB
frty@cdb.riken.jp
Tel:078-306-0106 (ext:4331)