CDB SEMINAR

Robert Stephenson

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Wednesday, March 7, 2012

16:00~17:00 A7F Seminar Room

Dissecting the role of morphogenesis in the origins of the first two cell lineages in the mouse embryo

Summary

Although the mechanisms underlying the divergence of the first cell types in the mouse, the trophectoderm (TE) and the inner cell mass (ICM) have received considerable attention, the upstream signals stimulating their divergence are still not well understood. We sought to examine the roles that morphogenetic factors such as cell adhesion and polarization play in the development of these cell types. We confirmed that in embryos completely lacking both maternal and zygotic E-cadherin, the normal epithelial morphology of outer cells is disrupted but individual cells still initiate TE and ICM-like fates. However, a larger proportion of cells than normal express TE markers like Cdx2, suggesting that formation of an organized epithelium is not necessary for TE-specific gene expression. Individual cells in such embryos still generate an apical-like domain that correlates with elevated Cdx2 expression. We also demonstrate a role for the Rho-associated kinase ROCK in apical-basal polarization of preimplantation blastomeres. Loss of apical-basal polarization leads to a reduction of Cdx2 expression in outer blastomeres due to activation of Lats1/2 kinase and reduced nuclear Yap1. The influence of polarization upon Yap1 localization is stage-dependent however, as apolar 8-cell blastomeres retain nuclear Yap1. Finally, we demonstrate that cell position serves as an additional cue for nuclear localization of Yap and Cdx2 expression prior to E3.5. The results of this work demonstrate important links between morphogenesis, cell fate and patterning in the preimplantation embryo. Both cell polarization and cell position act as critical cues to determine gene expression and to pattern this expression within the embryo.

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