CDB SEMINAR

Yuichiro Nakajima

Stowers Institute for Medical Research

Wednesday, June 26, 2013

16:00~17:00 A7F Seminar Room

Planar spindle orientation maintains epithelial architecture and prevents tumorigenesis

Summary

Epithelial cell sheets are the fundamental building blocks of animal bodies and also the major source of human cancers. In the development of epithelia, most cell division occurs symmetrically and parallel to the plane of the epithelium. Planar orientation of the mitotic spindle thus ensures a tight coordination between tissue growth and morphogenesis. While the disruption of planar spindle orientation is hypothesized to cause epithelial dysplasia and cancer development, the *in vivo* mechanisms regulating mitotic spindle orientation remain elusive, as do the precise consequences of spindle misalignment. Here we show that Mud (the *Drosophila* NuMA ortholog), the Actomyosin cortex and junction-localized neoplastic tumor suppressors Scribble (Scrib) and Discs Large (Dlg) play essential roles in planar spindle alignment and thus the control of epithelial integrity in *Drosophila* wing imaginal discs. Disruption of either intrinsic or extrinsic cues of spindle positioning leads to abnormal spindle orientations. Moreover, knockdown of Scrib/Dlg does not cause loss of epithelial polarity as an initial phenotype, suggesting a novel role in mitotic spindle control apart from their proposed role as polarity determinants. We further demonstrate that defective alignment of the mitotic spindle correlates with cell delamination and apoptotic death. Remarkably, under conditions where the basally delaminated cells survived, tissue disorganization and EMT-like effects became evident. These findings demonstrate a key role for junction-mediated spindle alignment in the maintenance of epithelial integrity and also reveal a novel cell death-mediated tumor suppressor function inherent in the polarized architecture of epithelia.

Host:
Erina Kuranaga
Histogenetic Dynamics, CDB
kuranaga@cdb.riken.jp
Tel:078-306-3135 (ext:1402)