CDB SEMINAR

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Friday, July 13, 2012

15:00~16:00 A7F Seminar Room

Chromosome and spindle pole-derived signals generate an intrinsic code for spindle position and orientation

Summary

Mitotic spindle positioning by cortical pulling forces defines the cell division axis and location, which is critical for proper cell division and development. Although recent work has identified developmental and extrinsic cues that regulate spindle orientation, the contribution of intrinsic signals to spindle positioning and orientation remains unclear. Here, we demonstrate that cortical force generation in symmetrically dividing human cells is controlled by distinct spindle pole and chromosome-derived signals that regulate cytoplasmic dynein localization at the cell cortex. First, dynein displays a dynamic asymmetric cortical localization that is negatively regulated by spindle pole proximity resulting in spindle oscillations to center the spindle within the cell. We find that this signal is comprised of the spindle pole localized Polo-like kinase (Plk1), which regulates dynein localization by controlling the interaction between dynein/dynactin and its upstream cortical targeting factors NuMA and LGN. Second, a chromosome-derived Ran-GTP gradient restricts the localization of NuMA/LGN to the lateral cell cortex to define and maintain the spindle orientation axis. Ran-GTP acts in part through NuMA's nuclear localization sequence to locally alter the ability of NuMA/LGN to associate with the cell cortex in the vicinity of chromosomes. We propose that these chromosome and spindle pole-derived gradients generate an intrinsic code to control spindle position and orientation in symmetrically dividing human cells. I would be happy to discuss how these intrinsic signals could be regulated in the asymmetric cell division or in different-sized cells during development.

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