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Molecular Crosstalk between Fate Determination and Orientation in Epithelial Cell Divisions

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In multicellular organisms, oriented cell divisions are fundamental for morphogenesis and homeostasis [1]. Division orientation is orchestrated by the microtubule-based motor dynein, which sustains all mitotic spindle functions. During cell division, cortical force generators connect epithelial polarity sites with astral microtubules, allowing dynein movements to orient the mitotic spindle meanwhile astral microtubules depolymerize. Complexes of the LGN and NuMA proteins, that are fundamental components of force generators, are recruited to the cortex by Gαi-subunits of heterotrimeric G-proteins. They associate with dynein/dynactin and activate the motor activity pulling on astral microtubules. I will present the structure of NuMA:LGN hetero-hexamers, and discuss their role in promoting by multivalent interactions the assembly of active cortical dynein/dynactin motors required to oriented divisions in polarized cells. I will also describe the bipartite interaction interface between NuMA and the light intermediate chain (LIC) of eukaryotic dynein, supporting the notion that NuMA acts as a dynein-activating adaptor in the mitotic processes of spindle organization and positioning. Collectively this work elucidates the basis for the structural organization of essential spindle orientation motors.

Key words: cell division, self-renewal, molecular motors, multivalent interactions

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