Nature Reviews Molecular Cell Biology | AOP, published online 5 September 2012; doi:10.1038/nrm3436

CELL CYCLE

Clathrin helps centrosomes come of age

Clathrin has a role in mitotic progression and cytokinesis, mediating spindle stabilization and endosomal traffic, which are needed for cell expansion and abscission. Clathrin-associated proteins have also been suggested to play a part in centrosome formation. Here, Brodsky and colleagues report that clathrin heavy chain 17 (CHC17) promotes centrosome maturation at the onset of mitosis.

Clathrin assembles as a trimer of CHCs, of which there are two isoforms in vertebrates (CHC17 and CHC22);

> “CHC17 is required for centrosome integrity at the onset of mitosis.”

MACMILLAN MEXICO

only the CHC17 isoform associates with clathrin light chains (CLCs). To study the role of clathrin during the cell cycle in more detail, the authors developed a method that allows acute inactivation of CHC17 at specific time points. This involved fusing a CLC isoform (LCa) to a protein tag (SNAP tag). The tagged proteins become crosslinked when cells are treated with a bivalent derivative of glutaric acid, and this specifically inactivates CHC17.

By studying synchronized HeLa cells, the authors found that inactivation of CHC17 during S phase resulted in the appearance of multipolar spindles, fragmented centrosomes and the dispersion of centrosomal γ-tubulin in early mitosis. This indicates that CHC17 is required for centrosome integrity at the onset of mitosis.

CHC17 forms a complex with two non-motor proteins, TACC3 and ch-TOG, which bind to the minus and plus ends of microtubules and function in centrosome organization and in stabilizing mitotic spindles. Thus, the authors hypothesized that the effect observed after CHC17 inactivation could be due to the absence of a functional CHC17–TACC3–ch-TOG complex at the centrosome. Indeed, although both proteins are known to accumulate at the onset of mitosis, Brodsky and colleagues found that inactivation of CHC17 in S phase prevented the accumulation of ch-TOG, whereas it had no effect on TACC3. Importantly, this resulted in reduced levels of ch-TOG at the centrosome at the onset of mitosis, which coincided with the timing of centrosome fragmentation.

Together, these results suggest that CHC17 promotes centrosome maturation in early mitosis by recruiting and stabilizing ch-TOG, and thus allowing the formation of a functional CHC17–TACC3–ch-TOG complex.

Kim Baumann

ORIGINAL RESEARCH PAPER Foraker, A. B. *et al.* Clathrin promotes centrosome integrity in early mitosis through stabilization of centrosomal ch-TOG. *J. Cell Biol.* **198**, 591–605 (2012)