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I E C B

How cells break up at the end of mitosis: a tale of two kinases.

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Animal growth, development and reproduction depend on the accurate process of cell division, which faithfully partitions the genomic information between the two daughter cells. Errors in this process can cause genetic diseases such as chromosomal syndromes, sterility and cancer. For example, failure in the last phase of cell division, cytokinesis, is associated with many human diseases, including cancers, blood disorders, female infertility, Lowe syndrome, and age-related macular degeneration[1]. Research in my lab aims to dissect the functions of serine/threonine kinases during cytokinesis and I will discuss our recent findings about the cytokinetic functions of two kinases: Citron kinase (CIT-K) and Aurora B, the enzymatic component of the Chromosomal Passenger Complex (CPC).

CIT-K was originally identified as a RhoA effector that could regulate myosin contractility by phosphorylating the myosin regulatory light chain (MRLC) during cytokinesis, but we and other labs have recently shown that CIT-K is not required for cleavage furrow ingression or MRLC phosphorylation and that this kinase behaves more like a RhoA regulator than an effector[2,3]. Moreover we found that CIT-K control the formation of the midbody, an organelle essential for completion of cytokinesis, through its interaction and regulation of 3 microtubule-associated proteins. These results, together with previous evidence that CIT-K associates with and controls the distribution of various contractile ring components[2-4], clearly establish for the first time that CIT-K links contractile ring and central spindle components and that this role is important for midbody formation in late cytokinesis.

Recent studies indicate that final separation of the two daughter cells – abscission – is mediated by components of the Endosomal Sorting Complex Required for Transport-III (ESCRT-III). We found that the CPC subunit Borealin interacts with ESCRT-III Snf7 components in both *Drosophila* and human cells and Aurora B kinase phosphorylates one of the three human Snf7 paralogues, CHMP4C, to regulate its function during abscission[5]. We propose that CPC controls abscission

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timing through inhibition of ESCRT-III Snf7 polymerization and membrane association using two concurrent mechanisms: interaction of its Borealin component with Snf7 proteins and phosphorylation of CHMP4C by Aurora B. This model would explain how CPC controls abscission to prevent cell separation in the presence of DNA at the cleavage site and consequent formation of aneuploid/polyploid cells.

References

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