Polo like kinase 1: a master regulator of centriole separation and reduplication

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A centriole of a vertebrate cell is comprised of nine stabilized microtubule triplets organized in a 200 nm wide and 400-500 nm long cylinder. The centriole acts as a scaffold for the assembly of several proteins into a highly structured pericentriolar material, which together with a single or duplicated centriole constitutes a centrosome. Centrosomes are major microtubule organizing centers of the cell. They organize two poles of mitotic spindle during mitosis, and convert into basal bodies during ciliogenesis. Abnormal centrosome number leads to aneuploidy, tumorigenesis and ciliopathies, thus it is critically important that a cell precisely controls the centrosome number, which must be two during the cell cycle. A new (daughter) centriole forms by duplication at the beginning of S phase in orthogonal configuration to resident (mother) centriole. This peculiar orthogonal configuration between mother and daughter centriole has been proposed to block a mother centriole from reduplicating within the same cell cycle, defined as 'block to centriole reduplication'. The role of a mitotic kinase, Polo like kinase 1 (Plk1), has been suggested in regulating the process of centriole separation and reduplication. However, it is still mechanistically unclear how Plk1 does it.

My postdoctoral work aims to understand the role of Plk1 in regulation of block to centriole reduplication in order to maintain the accurate centrosome number. To answer this, we combined high-resolution light microscopy, correlative live-cell and electron microscopy, molecular and biochemical methods.

Our data revealed that centriole block to reduplication relies on a close spatial association between mother and daughter centriole, but not on their orthogonal orientation. We found that new centrioles form at the distance of ~40 nm from the wall of the mother centrioles. This distance increases during cell cycle (centriole distancing), reaching ~80-90 nm in prophase which is sufficient to remove the block to reduplication. We also found that centriole distancing is dependent upon the daughter centriole maturation via Plk1. In addition, the removal of centriole block to reduplication in prophase is coordinated with the APC/C^{Cdh1} mediated degradation of centrosomal proteins such as Sas6 and STIL during mitosis in Plk1 dependent manner. This co-ordination assures that mother centrioles relieved from duplication block do not duplicate prematurely before the beginning of next S phase. The results from this study further emphasize a multifaceted role of Plk1 in synchronization of the centriole cycle with the cell cycle, providing necessary robustness in the maintenance of accurate centrosome number in cycling cells to prevent aneuploidy and tumorigenesis.