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**Emerging roles and functional mechanisms of dynein light chain
DYNLRB1 and DYNLRB2**

Shuwen He

Institutionen för kemi och molekylärbiologi
Naturvetenskapliga fakulteten

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ABSTRACT

Dyneins are a class of molecular ATPase motors that generate force and movement on microtubules in a wealth of biological processes, including organelle distribution, cell division, ciliary beating, and flagella motility, and intracellular transport. DYNLRB1 and DYNLRB2 are the light chain subunits identified both in cytoplasmic dynein and axonemal dynein, but how these two light chains contribute to dynein function remains poorly understood. In our research, DYNLRB2 was found to be specifically upregulated in mouse testis and DYNLRB2 depletion in meiotic spermatogenesis resulted in frequent metaphase arrest with the defects in bipolar spindle formation, spindle assembly checkpoint regulation, chromosome alignment, spindle organization and orientation. DYNLRB2 maintains male meiotic spindle bipolarity by preventing pericentriolar material (PCM) fragmentation through targeting nuclear mitotic apparatus protein (NUMA) to the spindle poles and suppressing premature centriole disengagement. Emerging roles of DYNLRB2 were characterized from ciliogenesis to fertility. DYNLRB2 deficiency caused a series of ciliopathies both in female and male, as well as dysfunctional spermiogenesis with abnormal manchette removal, thereby contributing to male infertility, while DYNLRB2 KO female mice were fertile with normal follicle development and ovulation. In contrast, the mitotic DYNLRB1 regulated bipolar spindle formation by targeting NUMA and suppressing centriole overduplication in mitotic cells. DYNLRB1 KD phenotypes are rectified by ectopic overexpression of DYNLRB2, supporting the notion that DYNLRB1 and DYNLRB2 have interchangeable roles in mitosis.

Correspondingly, downregulation of DYNLRB1 during mouse oocyte meiosis by siRNA injection resulted in several defects on decrease of germinal vesicle breakdown rate, spindle organization, formation of actin cap and cortical granule-free domain (CGFD) and reduced polar body extrusion rate with abnormal cytokinesis. In summary, the results defined the distinct roles and functional mechanisms of DYNLRB1 and DYNLRB2.

Keywords: dynein light chain, DYNLRB1, DYNLRB2, spindle, centrosome, PCM, NUMA, meiosis, mitosis, ciliogenesis, fertility, spermatogenesis