Online Proceedings

POSTER SESSION 2

MGH 206, Easel 171

1:00 PM to 2:30 PM

The Role of Kinesins in Asymmetric Cell Division

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Asymmetric cell division (ACD), a process that generates daughter cells with different cell fates and sizes, is a fundamental mechanism for generating cellular diversity during development. We use *Drosophila* melanogaster neural stem cells, or neuroblasts, to study ACD. Neuroblasts provide an ideal model for ACD since they are intrinsically polarized and divide with physical as well as molecular asymmetry, resulting in a self-renewed stem cell and a smaller ganglion mother cell (GMC). Kinesins, plus-end-directed motor proteins, have previously been implicated in asymmetric cell division and spindle dynamics. However, the specific kinesins that influence ACD and the mechanism by which they do so remains unknown. Elucidating the function of kinesins in cell division will help establish a more holistic view of cell development. To learn the role that kinesins play in asymmetric cell division, we performed an RNAi knockdown-based live-cell imaging screen of most kinesins in *Drosophila*. We found that knocking down the *Drosophila* kinesin genes Klp3A, Klp10A, Klp59C, Klp67A, Klp68D, CG14535, cos, or ncd causes the mitotic spindle to bend during metaphase and anaphase. We hypothesize that this phenotype is due to the spindle being so large that it buckles under the pressure of the cell as it divides. We are currently investigating this hypothesis by imaging knockout mutants to confirm this phenotype and tagging each kinesin with GFP to study how these proteins are localized during typical ACD.

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Impact of Na+/H+ Antiporter on Asymmetric Cell Division in *Drosophila* Neural Stem Cells

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Asymmetric cell division (ACD) is an integral process that multicellular organisms use to create cellular diversity. For instance, stem cells use ACD to form differentiating sibling cells while recreating the stem cell in order to maintain the stem cell pool. Defects in ACD can result in a variety of diseases ranging from neurodevelopmental disorders to cancer. Using *Drosophila melanogaster* neural stem cells (neuroblasts) as a model to study cellular asymmetries, we recently found that hydrostatic pressure is an important factor contributing to ACD. However, the mechanisms and proteins that regulate hydrostatic pressure are unknown. Based on our previous results, I hypothesized that Na+/H+ antiporters are involved in establishing hydrostatic pressure. To examine this hypothesis, I tested the function of four Na+/H+ channels in *Drosophila* using RNAi knock-down experiments and subsequent live cell imaging. This imaging allowed visualization of fluorescently tagged myosin and microtubules–two critical components of the cell division process. I found that knocking down each of the four antiporters results in a bent mitotic spindle, delayed division times, and centrosome abnormalities. I conclude that the four antiporters play a role during ACD in fly neural stem cells. To validate these results, I will use CRISPR/Cas9 gene editing to develop deletion mutants and EGFP-tagged versions of the four antiporters—two crucial steps in studying the regulation of Na+/H+ channels. Further in the future, I will use CRISPR/Cas9 to create optogenetically controllable Na+/H+ antiporters, such that I can use light to control hydrostatic pressure in *Drosophila* neuroblasts. I also plan on measuring the intracellular pH using genetically edited *Drosophila*, as disruptions in pH could cause the described phenotypes. These studies will provide mechanistic and functional insight into how hydrostatic pressure contributes to successful ACD.