Lucas V. Cairo

Department of Cell Biology

Ph.D. Candidacy Examination

Topic Proposals

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Primary Proposal:

***Investigating how phosphorylation status of Mad1p affects its dynamic SAC signaling function.***

The spindle assembly checkpoint (SAC) is an evolutionarily conserved surveillance mechanism that monitors chromosomal segregation and halts mitotic progression when kinetochore-microtubule attachments are aberrant. Initiation and maintenance of mitotic checkpoint signaling requires phosphorylation of several key SAC signaling components, including Mad1p, upon which it targets onto and off of kinetochores lacking attachment to spindle microtubules. What remains ill defined is the extent to which phosphorylation, and potentially dephosphorylation, controls the activity and localization of this dynamic signaling protein. Using budding yeast as a model, this proposal will aim to explore how disrupting Mad1p’s phosphorylation status affects its ability to target and turnover at kinetochores and ultimately how this impacts SAC signaling dynamics.

Alternate proposal:

***Spindle assembly checkpoint activation in anaphase: Investigating the sensing and signaling mechanisms required for SAC activation following sister chromatid separation.***

Recent work demonstrates that spindle assembly checkpoint (SAC) signaling can be re-engaged in response to lack of tension across sister kinetochores upon anaphase onset. However, what remains to be addressed is whether anaphase cells lacking kinetochore-microtubule attachments can effectively re-activate mitotic checkpoint signaling.

In yeast *Saccharomyces cerevisiae*, the essential SAC signaling kinase Mps1p is degraded with relatively slow kinetics following the metaphase to anaphase transition. Therefore, a significant time frame exists, immediately following anaphase onset, where it is feasible for the SAC machinery to detect unattached kinetochores and elicit the proper signaling events required for APC inhibition. This proposal will therefore aim to explore whether destabilization of kinetochore-microtubule interactions in early anaphase is sufficient to elicit hallmark “metaphase-like” SAC signaling events.

Topics submitted to:

Dr. Rick Wozniak

Dr. Rick Rachubinski

Dr. Gordon Chan