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RESEARCH ABSTRACT FORM

TITLE: Identification of functional determinants within the degradation signal of the Mps1 protein kinase

AUTHOR: Kate Ehrensberger

MENTOR(S): Dr. Harold Fisk

INSTITUTION: The Ohio State University

ABSTRACT:

Centrosomes are the main microtubule organizing centers (MTOCs) of the eukaryotic cell. They consist of a pair of centrioles surrounded by a mass of pericentriolar material (PCM). Centrosomes serve several purposes in the cell; controlling a cell's entry into the cell cycle, mitotic spindle assembly, and cytokinesis. Much like DNA replication, centrosomes go through one round of duplication during S-phase of the cell cycle; however in mutated cells, the may be duplicated several times or re-duplicated causing an aberrant centrosome number. Previous research has shown that the Mps1 protein kinase is required for centrosome duplication which occurs near the G1/S transition. Levels of Mps1 are regulated by Cdk2 phosphorylation and the degradation by the proteasome. While phosphorylated, Mps1 is not degraded. However, when Cdk2 is absent, Mps1 can no longer be phosphorylated and thus is degraded by the proteasome. If Mps1 is not degraded at centrosomes, it can cause centrosome re-duplication to occur. We have found that by mutating bases within the degradation signal to mimic phosphorylation/ ubiquitination, we can directly cause centrosome re-duplication.