Susan G. Komen for the Cure
Research Grants – Fiscal Year 2011

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The Role of Separase in Centrosome Duplication and Genome Stability

Investigator(s): Tim Stearns, PhD
Stanford University, CA
Grant Mechanism: Post Doctoral Fellowship - Basic Research

Fellow: Erkang Ai, PhD
Awarded: $178,225.00
Research Focus: Biology

Public Abstract:
A hallmark of breast cancer cells is that they often have extra centrosomes. Centrosomes organize a network of protein filaments, called the microtubule cytoskeleton, in animal cells. Centrosomes assist in arranging microtubules to form the mitotic apparatus that separates chromosomes during cell division. Like chromosomes, centrosomes duplicate once and only once in each cycle of cell division. This duplication is initiated by "disengagement" of the pair of centrioles that are the core of the centrosome at the end of mitosis, allowing the centrioles to be duplicated in the next cycle. Errors in this process can lead to abnormal centrosome number, resulting in genome instability and aneuploidy (abnormal number of chromosomes), important genetic factors in cancer. Previous work in our lab showed that a protein called Separase is required for centriole disengagement, and thus for centriole duplication. Separase is an enzyme that cleaves other proteins (a protease) that is most well-known for its role in chromosome separation at mitosis, in which it cleaves the link holding the chromosomes together before separating. Importantly, Separase is misregulated in breast tumors. In the research that I have proposed, I will seek to identify the protein that is cleaved by Separase in centrosome duplication, and to understand the mechanisms by which misregulated Separase leads to genome instability. This research will provide insight into how centrosome number is controlled, with important implications for the basic biology behind genome stability and breast cancer.

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