Field: ***Chemistry/Biochemistry***

Session Topic:

Chemical biology- New approaches for drug discovery

Speaker:

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Title: Small molecules as a versatile tool to study cell division

A major challenge in modern cell biology is the study of the function of proteins whose activities vary according to time and position within the cell. This is especially true for many components of the cytoskeleton that have localization- and context-dependent functions that can change dramatically over the course of minutes. Examples of these include components of the mitotic spindle, mediators of actin/microtubule interactions during cytokinesis or in the leading edge of migrating cells. Small molecule inhibitors of proteins can be used to effect perturbations on a very rapid timescale and with precise spatial control, and the use of these tools can thus complement traditional genetic approaches in the study of such dynamic processes.

Following a phenotype-based screening approach we identified monastrol, a specific inhibitor of the mitotic motor protein Eg5. The activity of Eg5 is essential to separate the two spindle poles as cells enter mitosis and, thus, inhibition of Eg5 results in the collapse of the bipolar spindle and the formation of a star-like ("monoastral") spindle. Given its fast and reversible mode of action monastrol was key for novel insight into the mechanism of spindle formation in higher eukaryotes. Currently, we are searching for novel inhibitors of proteins involved in mitosis. By combining these molecules with fluorescent live-cell microscopy we expect to deepen our understanding of the process of chromosome segregation and the formation of daughter cells in mammals.

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