**Goal**

To study spindle positioning in asymmetric cell divisions using yeast as a model system.

**Background**

Polarized cells have two options when they divide: they can either divide symmetrically, or asymmetrically, in which case they partition cellular factors like proteins or mRNAs unequally between progeny. Asymmetric divisions are encountered whenever the goal is the generation of cellular diversity, for example during embryonic divisions or the divisions of stem cells. In many of these cases, factors that determine cell fate are segregated in one of the two daughters, that consequently differentiates. Asymmetric divisions require a high degree of spatial and temporal coordination of the actin and the microtubule cytoskeleton. Alignment of the mitotic spindle with the axis of cell polarity is essential to ensure asymmetric segregation of polarized factors between daughters after cytokinesis. The positioning of the spindle depends universally on interactions of astral microtubules (cMTs) with cortical cues. A complex network of proteins involving non-motor microtubule associated proteins (+TIPs), kinesins, dynein and actin-interacting proteins mediate these interactions. Our lab studies the mechanisms and regulation of spindle positioning using one of the simplest asymmetrically dividing organisms, the yeast *S. cerevisiae*.

**Research Highlights**

In budding yeast the spindle aligns along the mother bud axis prior to anaphase. Spindle positioning depends on two pathways, comprising complexes of the microtubule-dependent motor dynein (DHC1, dynein pathway) and the protein Kar9 (Kar9 pathway). The latter protein is the yeast functional equivalent of the Adenomatous Polyposis Coli (APC) tumor suppressor, a protein with a central role in spindle positioning from *Drosophila* to mammals.

One research highlight is the discovery of spindle polarity. We have shown that the spindle possesses an intrinsic polarity, which is required for spindle orientation in the polarized yeast cell, much like the polarity of a compass needle is required to orient it in a polarized magnetic field. Spindle polarity is manifested in the asymmetric localization of proteins required for spindle positioning, like Kar9 and dynein, on the astral microtubules of only one of the two spindle poles. Another feature is that the one spindle pole nucleates astral microtubules that are more stable than the ones originating at the second spindle pole. The result of these asymmetries is that only one spindle
pole is pulled towards the bud and the spindle acquires a specific orientation. We are currently investigating the biochemical mechanisms that lead to the generation of spindle polarity and involve the regulation of the dynein and Kar9 complexes through posttranslational modifications, as well as the phosphorylation of astral microtubule-associated factors by the Cdk1 kinase.

Spindle asymmetry has been lately encountered in numerous organisms. Our goal is to reveal the biochemical basis of this common biological phenomenon.

**Selected Publications**


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