CDB SEMINAR

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16:00~17:00 A7F Seminar Room

Molecular Mechanisms of the Initial Kinetochore-Microtubule Interaction in Early Mitosis

Summary

Cell reproduction is a highly regulated series of events that ensure the accurate passing of genetic information to daughter cells, and it is fundamental to the development and function of all life. Establishing correct kinetochore–microtubule interaction efficiently is crucial for proper chromosome segregation in mitosis.

To ensure kinetochore capture and alignment on the mitotic spindle, microtubules extending from spindle poles must efficiently locate and interact with kinetochores. How do kinetochores efficiently interact with microtubules? In the first project, we found evidence that kinetochores generate microtubules in early mitosis. Once generated, kinetochore–derived microtubules often interact with spindle pole microtubules along their length, which may facilitate kinetochore loading onto the lateral surface of spindle pole microtubules. Intriguingly, kinetochore-derived microtubules are generated more often when kinetochore interactions with spindle pole microtubules is delayed, and thus the appearance of microtubules at kinetochores has a greater effect in facilitating kinetochore interaction with spindle pole microtubules.

Kinetochores initially interact with the lateral surface of single microtubules extending from a spindle pole, and are transported along microtubules towards spindle poles in two distinct modes: lateral transport (sliding) and end-on pulling (tethering at distal end of microtubule) (Tanaka et al, 2005). However the lateral attachment is relatively weak and must be subsequently converted to more robust end-on attachment (i.e. kinetochores being tethered at the distal end of spindle pole microtubules). The conversion from lateral to end-on attachment is crucial to sustain kinetochore-microtubule attachment upon establishment of bi-orientation. The Ndc80 complex is an outer kinetochore component that is essential for the kinetochore-microtubule interface; however, the mechanism for the conversion is still unknown. In the second project, we studied the role of the Ndc80 loop region, a distinct motif looping out from the coiled-coil shaft of the complex. We found that the Ndc80 loop region mediates the interaction with the Dam1 complex to ensure proper kinetochore-microtubule attachment. In Ndc80 loop-region mutants, the lateral attachment occurred normally, however subsequent conversion to end-on attachment was defective, leading to a failure in sister kinetochore bi-orientation. Our study revealed that the Ndc80 loop region has an important role in conversion from lateral to end-on attachment, a crucial maturation step in kinetochore-microtubule interaction.

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