

BDR SEMINAR in Kobe

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16:00-17:00, 1F Auditorium, DB Building C

Timely assembly of the mitotic spindle for accurate chromosome segregation

Summary

The accuracy of chromosome segregation by the mitotic spindle is crucial to maintain genomic stability. One of the first steps of mitotic spindle assembly is the dissolution of the centrosome linker connecting the two centrosomes of interphase cells. Loss of centrosome disjunction allows centrosome separation that is driven by the Eg5 plus-end directed tetrameric kinesin-5 for the assembly of a bipolar spindle. Although premature or delayed centrosome separation causes chromosome mis-segregation, the mechanism controlling the timely separation of the two centrosomes is poorly understood. Recently, we reported that, even in the absence of the centrosome linker, the two centrosomes are kept together by an ill-defined microtubule-dependent mechanism. Here we show that KIFC3, a minus-end directed kinesin-14, provides microtubule-based centrosome cohesion. KIFC3 forms a tetramer that pulls the two centrosomes close together via a specific microtubule network. At mitotic onset, KIFC3 activity becomes the main driving force of centrosome cohesion to prevent premature spindle formation after the linker dissolution as it counteracts the increasing Eg5-driven pushing forces. Interference with the counterbalance between these tetrameric kinesins results in chromosome mis-segregation. Our findings reveal an unanticipated aspect of early mitotic spindle assembly that ensures genomic stability in humans.



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