

Centrosome Disruption Suppresses Multipolar Spindle Formation after Cytokinesis Failure

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Multipolar spindles (MS) are frequently observed in cancer cells, and may play a role in genomic instability. Although polyploid cells induced by cytokinesis failure seem to increase MS frequency in various cell types, the underlying mechanism is unclear, since centrosome number, chromosome/kinetochore number, total protein amount and cell size all increase after cytokinesis failure. In this study using the *Drosophila* S2 cell line as a test system we employed RNAi screening and automated microscopy to investigate which factors/genes are important for MS formation. First, we confirmed that cytokinesis failure induced by Pavarotti(Kinesin-6) RNAi significantly increased MS formation in S2 cells (from 15% to ~35). The multiple poles often contain mature centrosomes, but acentrosomal poles (non γ -tubulin containing) were also observed. We then used double RNAi treatment (Pavarotti + gene X) to identify genes that suppress or enhance MS formation. Of the 19 genes selected in this double RNAi screen, two genes (CNN, SAK) were identified that rescued Pavarotti-induced MS formation. Both of these genes affect centrosome function, CNN by inhibiting γ -tubulin recruitment to centrosomes and SAK by blocking centriole duplication. The rescue by CNN RNAi was particularly striking, resulting in almost all spindles showing bipolar shapes (spindles formed by chromosome-mediated nucleation). These results indicate that increased numbers of centrosomes is the critical factor in MS formation.