In vivo FRET imaging revealed a regulatory role of RanGTP in kinetochore-microtubule attachments via Aurora B kinase.

Abstract

The multi-faceted RanGTPase has been implicated to be critically involved in nucleocytoplasmic transportation and cell cycle progression. However, the role of mitotic RanGTP in kinetochore-microtubule attachments at metaphase has yet to be described. Here, we report a molecular link between the mitotic RanGTP and Aurora B kinase in maintaining stable kinetochore-microtubule attachments after proper chromosome congression. With the application of in vivo FRET imaging and the Rango biosensor, we show that the real-time decay in RanGTP levels at metaphase is coupled with a progressive displacement of pre-aligned chromosomes from the cell equator. Based on live-cell time lapse imaging and immunofluorescence analysis, our results indicate that an enrichment of mitotic RanGTP is necessary for recruitment of Mst1 to restrict Aurora B kinase’s influence in promoting reorientation of kinetochore-microtubule attachments at the kinetochores. By ensuring precision of metaphase chromosome alignment prior to chromosome segregation, this additional role of the RanGTP underscores its significance in protecting genomic integrity and preserving the fidelity of mitotic progression.