CHROMOSOMAL SEGREGATION FIDELITY

The spindle assembly checkpoint (SAC) is a signaling pathway that prevents cells from exiting mitosis until all chromosomes are correctly attached to spindle microtubules. This ensures that daughter nuclei receive one copy of each chromosome, thus maintaining the appropriate karyotype. The SAC relies on the localization of the Mad1-C-Mad2 complex at unattached kinetochores but also on its binding to Megator/Tpr at nuclear pores (NPs) during interphase. However, the molecular mechanism controlling the spatiotemporal redistribution of Mad1-C-Mad2 as cells progress into mitosis remain elusive. A very recent paper in the Journal of Cell Biology (https://rupress.org/jcb/article-abstract/doi/10.1083/jcb.201906039/133569/Mps1-mediated-release-of-Mad1-from-nuclear-pores) shows that activation and nuclear import of Mps1 kinase during prophase triggers Mad1-C-Mad2 release from NPs and that this is required for kinetochore recruitment of Mad1-C-Mad2 and robust SAC signaling. The authors provide evidence that Mps1 phosphorylates Megator/Tpr to reduce its interaction with Mad1 in vitro and in cells. Furthermore, artificially preventing Mad1 from binding to Megator/Tpr was sufficient to restore Mad1 accumulation at unattached kinetochores, the fidelity of chromosome segregation, and genome stability in *mps1*-null mutant cells. These findings demonstrate that the subcellular localization of Mad1 is tightly coordinated with cell cycle progression by kinetochore extrinsic activity of Mps1. This strategy ensures that both NPs in interphase and kinetochores in mitosis contribute to generate an efficient SAC response to preserve genomic stability.