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On the robustness of SAC silencing in closed mitosis[1] DONOVAN RUTH, JIAN LIU, Natl Inst of Health - NIH — Mitosis equally partitions sister chromatids to two daughter cells. This is achieved by properly attaching these chromatids via their kinetochores to microtubules that emanate from the spindle poles. Once the last kinetochore is properly attached, the spindle microtubules pull the sister chromatids apart. Due to the dynamic nature of microtubules, however, kinetochore-microtubule attachment often goes wrong. When this erroneous attachment occurs, it locally activates an ensemble of proteins, called the spindle assembly checkpoint proteins (SAC), which halts the mitotic progression until all the kinetochores are properly attached by spindle microtubules. The timing of SAC silencing thus determines the fidelity of chromosome segregation. We previously established a spatiotemporal model that addresses the robustness of SAC silencing in open mitosis for the first time. Here, we focus on closed mitosis by examining yeast mitosis as a model system. Though much experimental work has been done to study the SAC in cells undergoing closed mitosis, the processes responsible are not well understood. We leverage and extend our previous model to study SAC silencing mechanism in closed mitosis. We show that a robust signal of the SAC protein accumulation at the spindle pole body can be achieved. This signal is a nonlinear increasing function of number of kinetochore-microtubule attachments, and can thus serve as a robust trigger to time the SAC silencing. Together, our mechanism provides a unified framework across species that ensures robust SAC silencing and fidelity of chromosome segregation in mitosis.

[1]intramural research program in NHLBI at NIH

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