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Microtubule Depolymerization as a Driver for Chromosome Motion[1]

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Microtubules (MTs) are rigid polymers of the protein, tubulin, which function as intracellular struts. They are also tracks along which motor enzymes can run, carrying cargo to specific cellular locations. Most MTs are dynamic; they assemble and disassemble rapidly, particularly during cell division when the cell forms the "mitotic spindle," a machine that organizes the duplicated chromosomes into a planar disk, then pulls the duplicate copies apart, moving them to opposite ends of the cell. This process is necessary for the daughter cells to have a full complement of DNA. The mitotic spindle is a labile framework that exerts several kinds of forces on the chromosomes to move them in well organized ways. It contains many motor enzymes that contribute to spindle formation, but genetic evidence shows that the motors that attach to chromosomes and might contribute to chromosome motion are dispensable for normal mitosis. Apparently MT dynamics can also serve as a motor and is an important source of force for chromosome motion. We have studied this process and find that MTs can be coupled to a load by specific spindle proteins so that MT depolymerization can exert substantial force. With the yeast protein, Dam1, a single MT can generate 30 pN, about 5-fold more than is generated by a motor enzyme like kinesin or myosin. The resulting motions are processive, so a depolymerizing MT can carry its load for many micrometers. However, Dam1 is found only in fungi. We have therefore sought other proteins that can serve as analogous couplers. Several MT-dependent motor enzymes can do the job in ways that do not require ATP, their normal source of energy. Some non-motor MT-associated proteins will also work, e.g., the kinetochore proteins NDC80 and CENP-F. Data will be presented that show the strengths and weaknesses of each coupler, allowing some generalization about how the mitotic machinery works.

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