

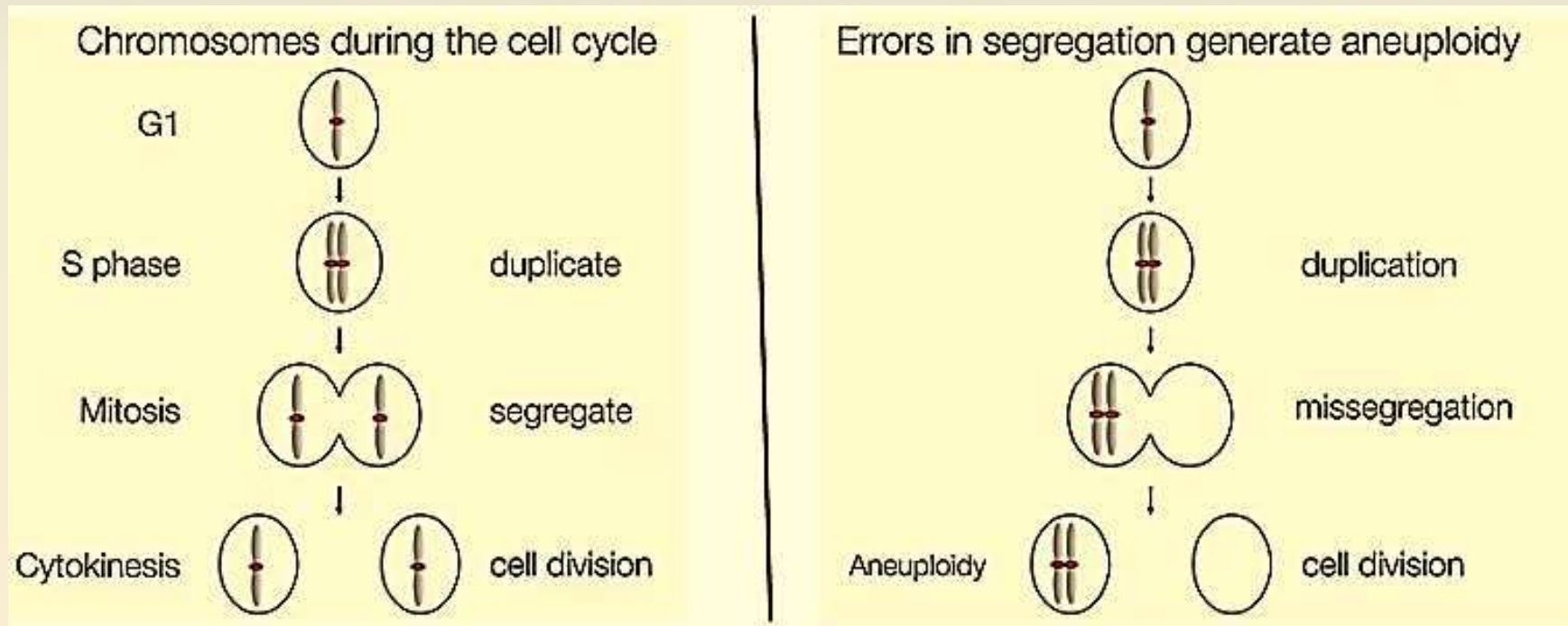
Organization and maintenance of kinetochore

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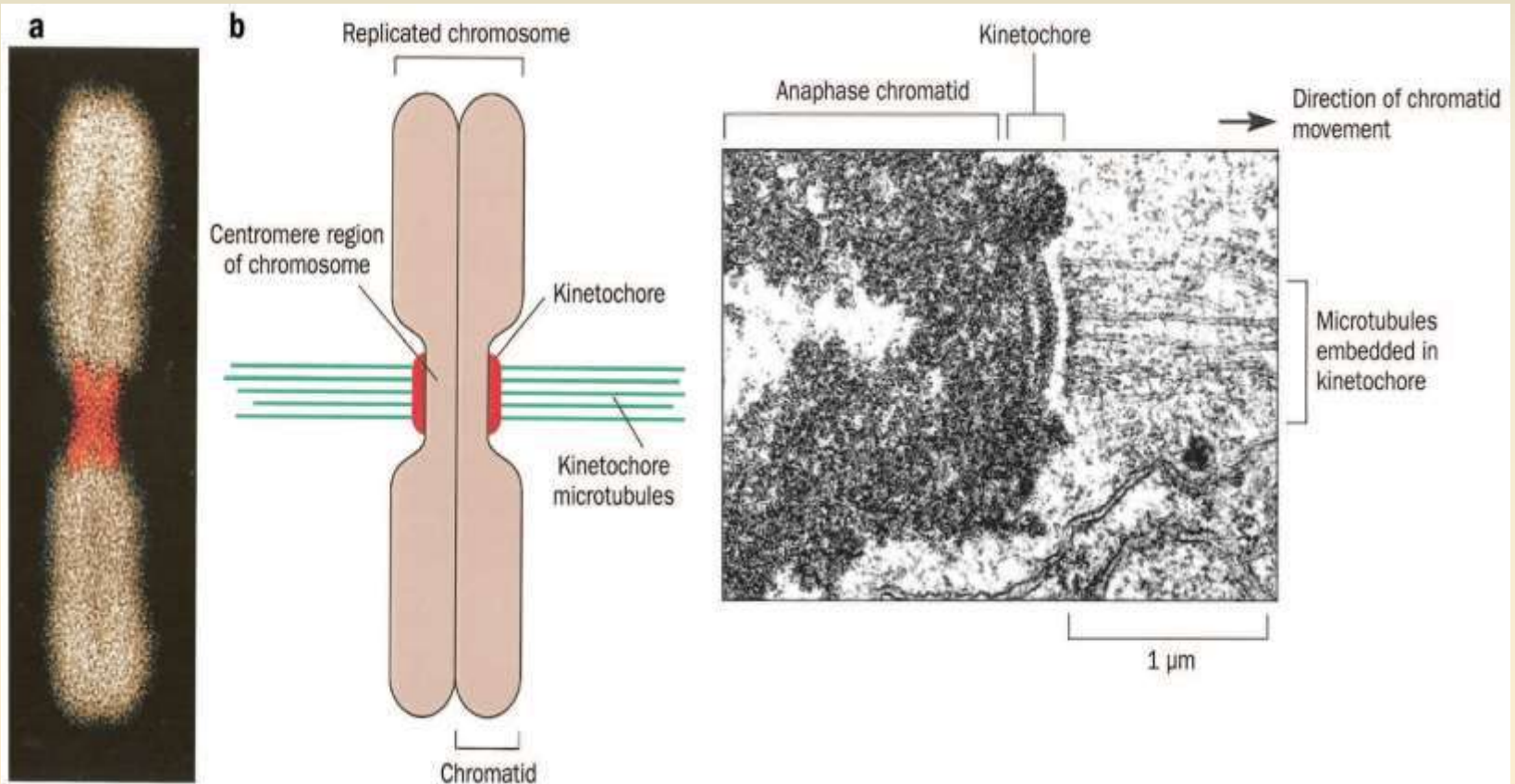
Introduction

- ❑ It is a two large disc-shaped large proteinaceous structure at the centromeric region of the chromosome located on opposite sides of the chromosomes.
- ❑ The kinetochore is made of more than 80 identified kinetochore proteins.
- ❑ It mediates interactions between chromosomal DNA and spindle-microtubule polymers.
- ❑ Its protein components assemble on the centromere and links the chromosome to microtubule polymers from the mitotic spindle during cell division.
- ❑ It is the important element of a cell cycle checkpoint. Failure of kinetochore to bind the microtubule or incorrect association results in cell cycle delay (mitotic delay) or cell cycle arrest (mitotic arrest).
- ❑ Since it is the attachment site of spindle fibers, its ultimate goal is to move chromosomes during cell division.
- ❑ It is the fundamental component of chromosome that is essentially required for maintaining accurate genome segregation and stability.
- ❑ The microtubules that attach to the chromosomes actually attach to the kinetochores (which are why those microtubules are called kinetochore microtubules).

Why kinetochore is important?

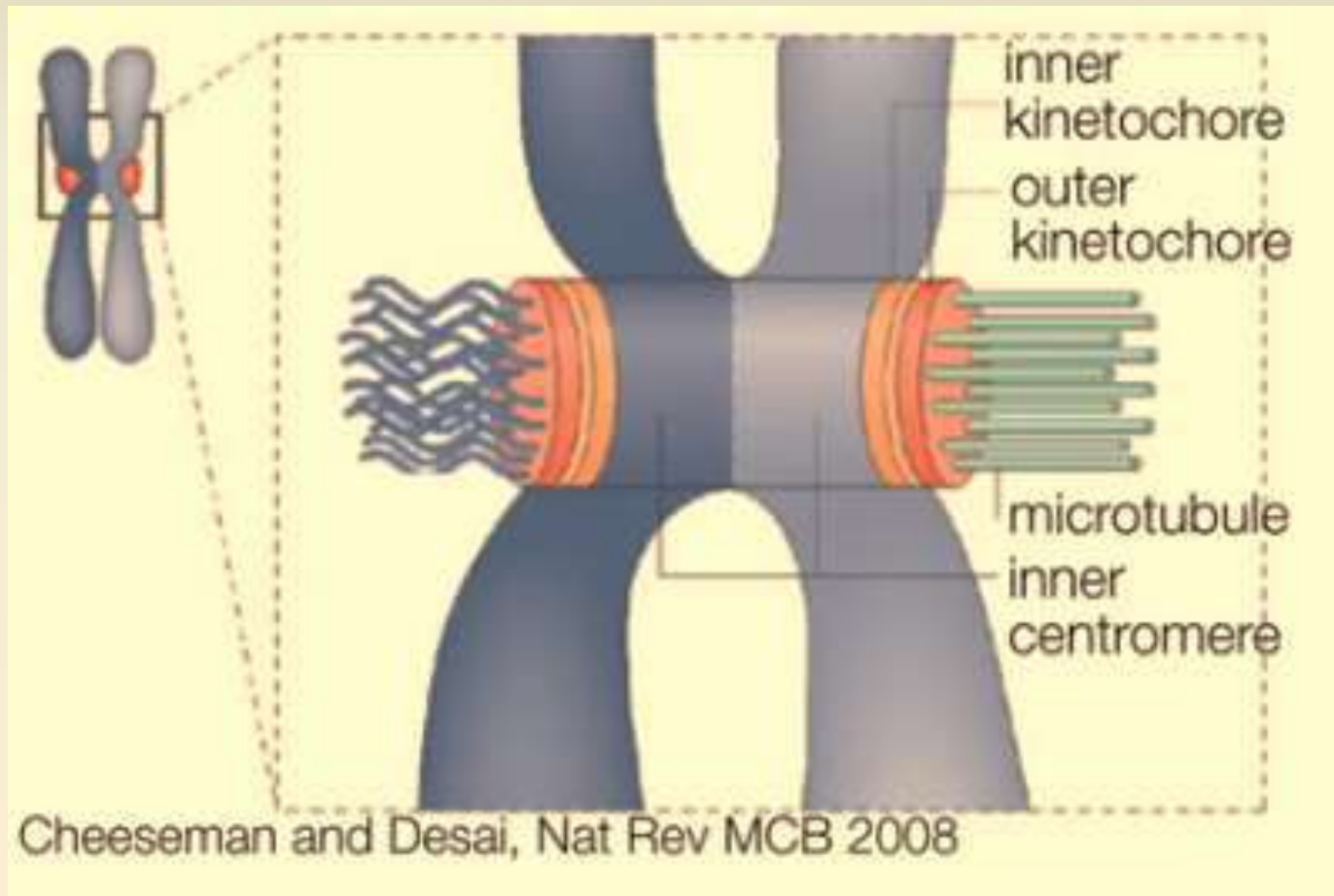


Kinetochores organization

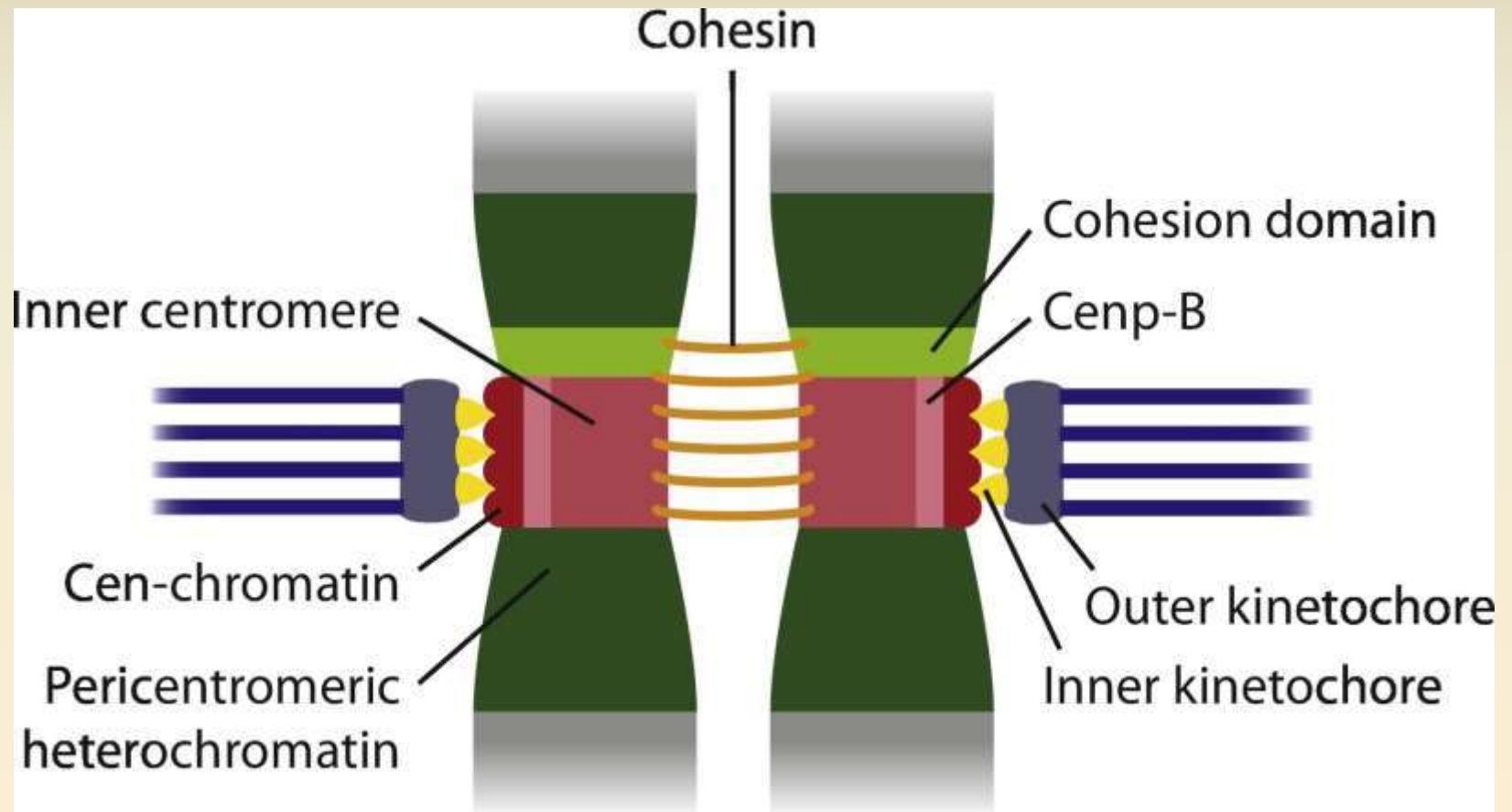


Johnson M. K.. & Wise D. A. BioScience 2009; 59(11): 933–943,.

Kinetochores direct segregation

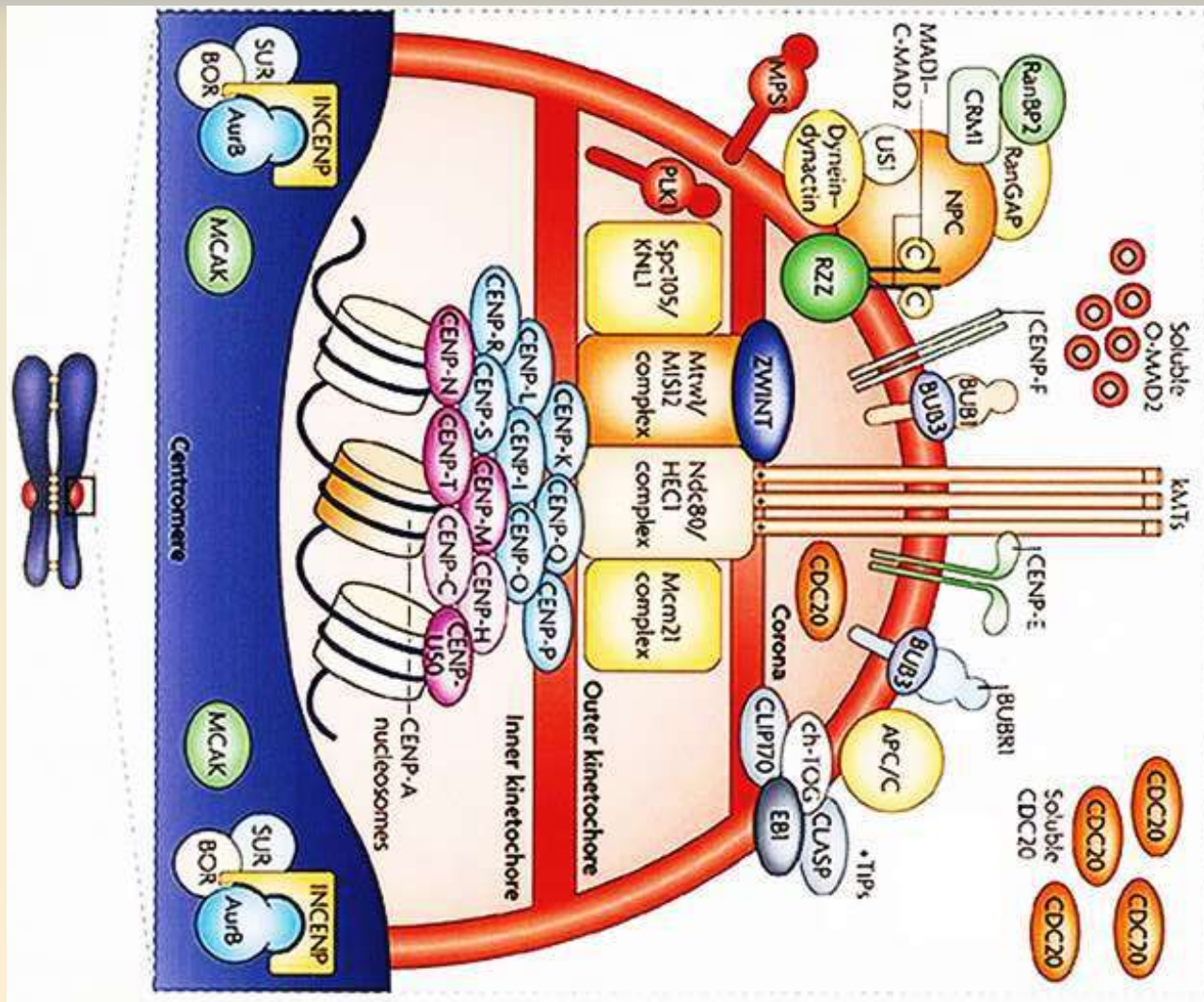


Structural organization with respect to centromere



Chromatin domain organization of eukaryotic centromeres.
Journal of Molecular Biology 2020; 432(15): 4257-4269 .

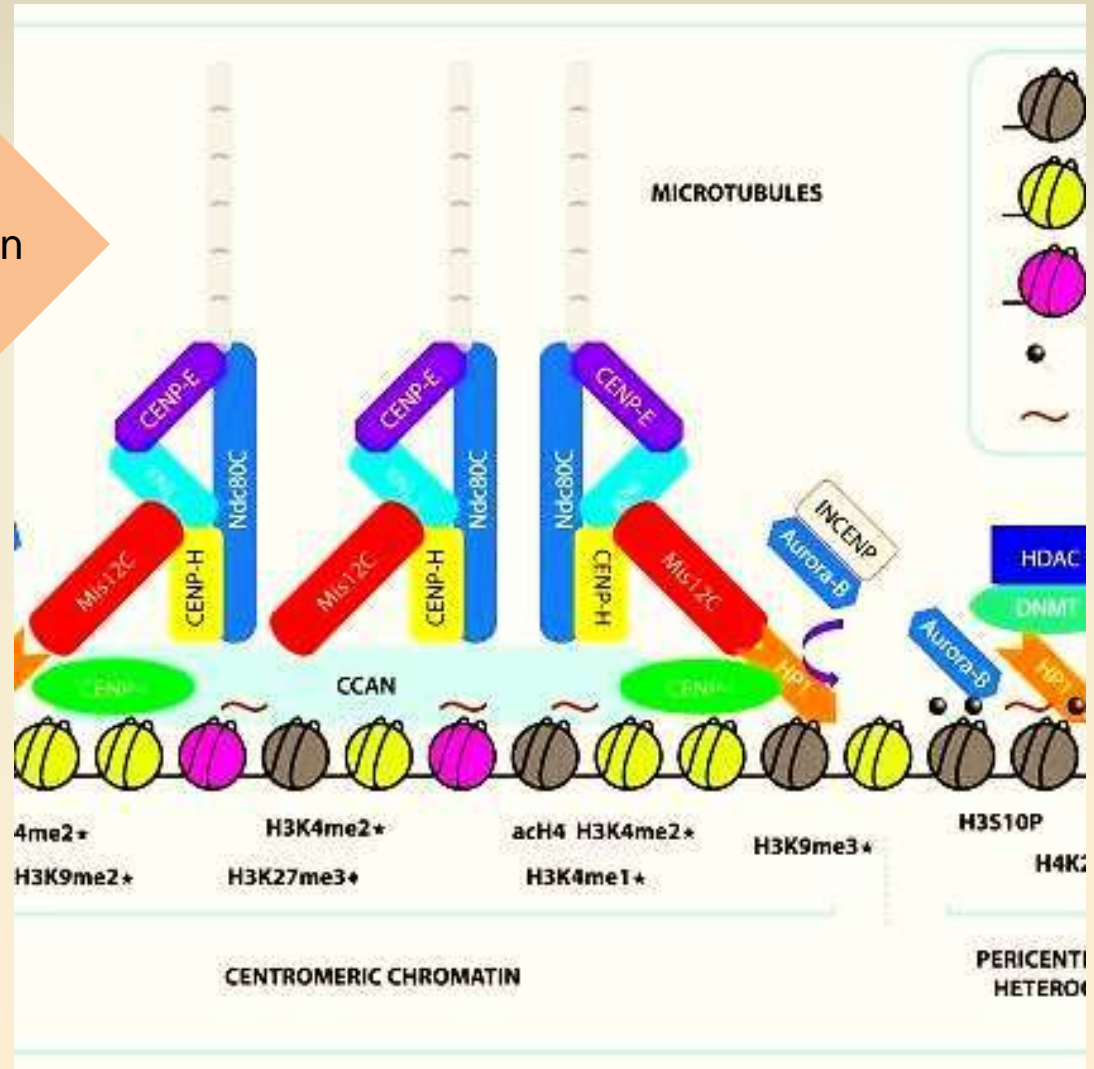
Molecular organization of kinetochore



<http://dx.doi.org/10.1038/nrm2163>

Kinetochores assembly with the centromere

Schematic representation of centromeric and pericentromeric chromatin and the formation of an epigenetic complex that further shapes the kinetochore.



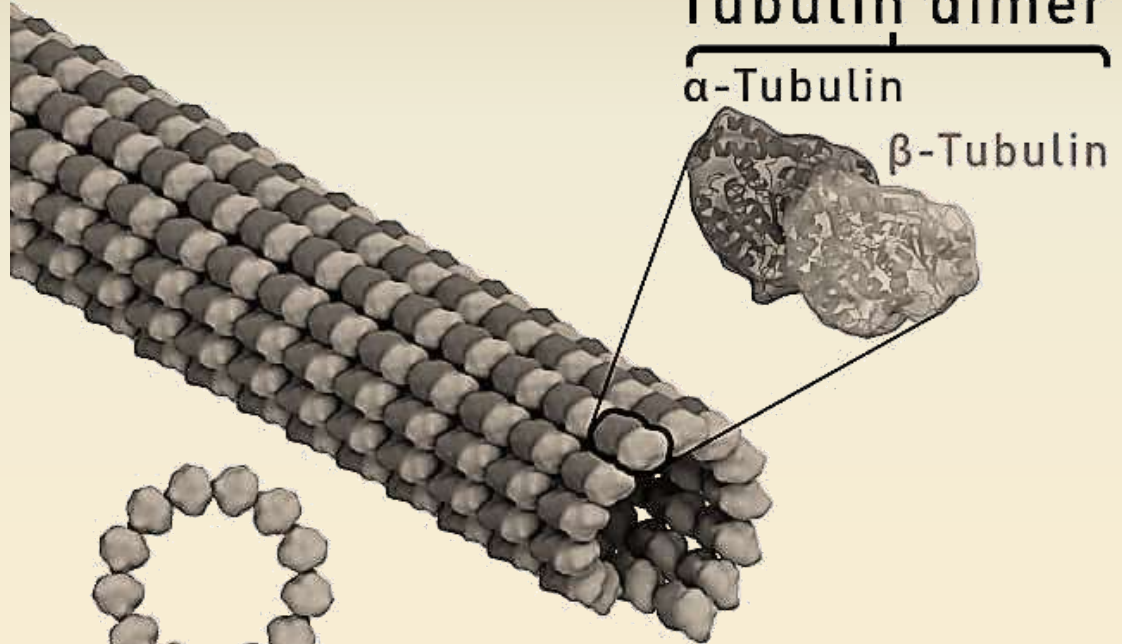
Epigenetics : Official journal of the DNA Methylation Society. 2012, 7. 3-13. DOI: 10.4161/epi.7.1.18504.

Microtubules



Centriole

Microtubular filaments originate from centriole and attach to the chromosome after finding them in the cytosol



Cross section

Microtubule

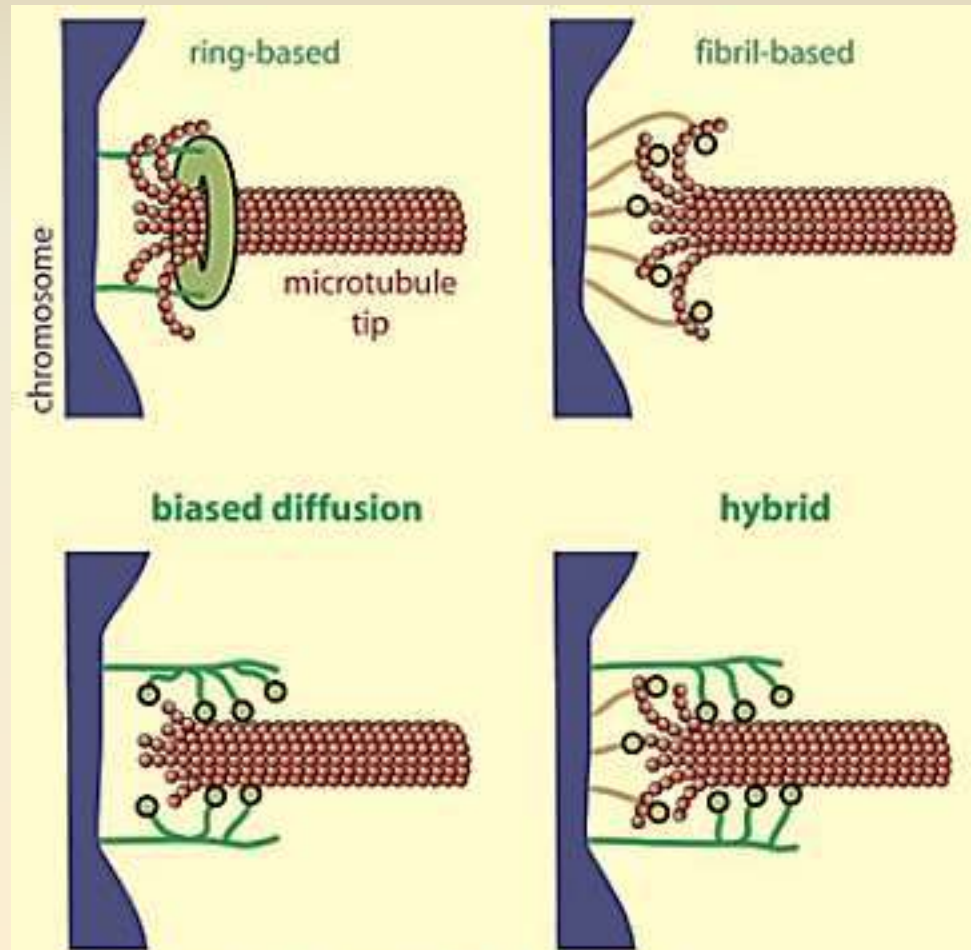
Nup133 with CENP-F & NudE/EL



NE

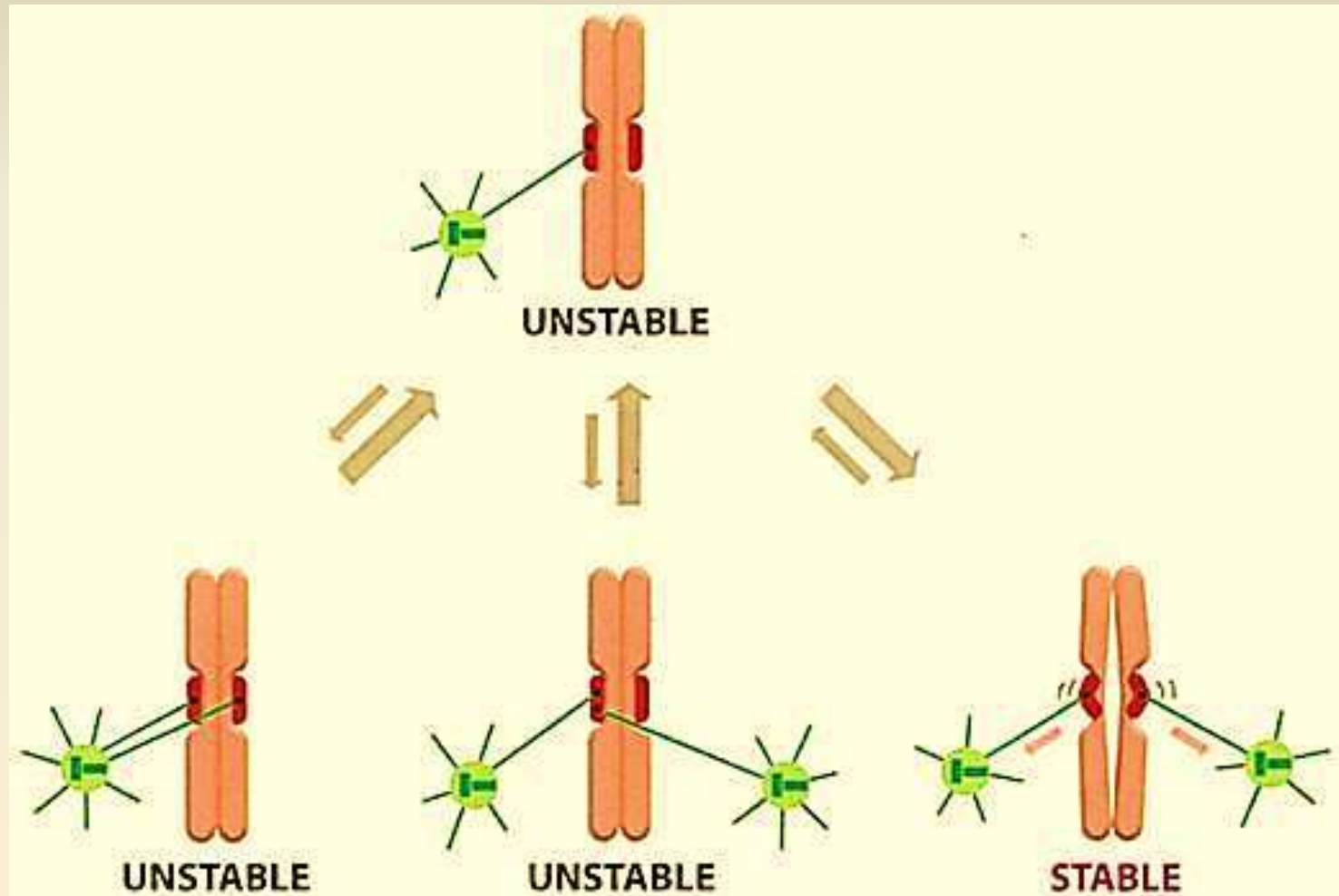
CENP-F, NudE, NudEL, dynein, dynactin

Coupling of kinetochore to microtubule



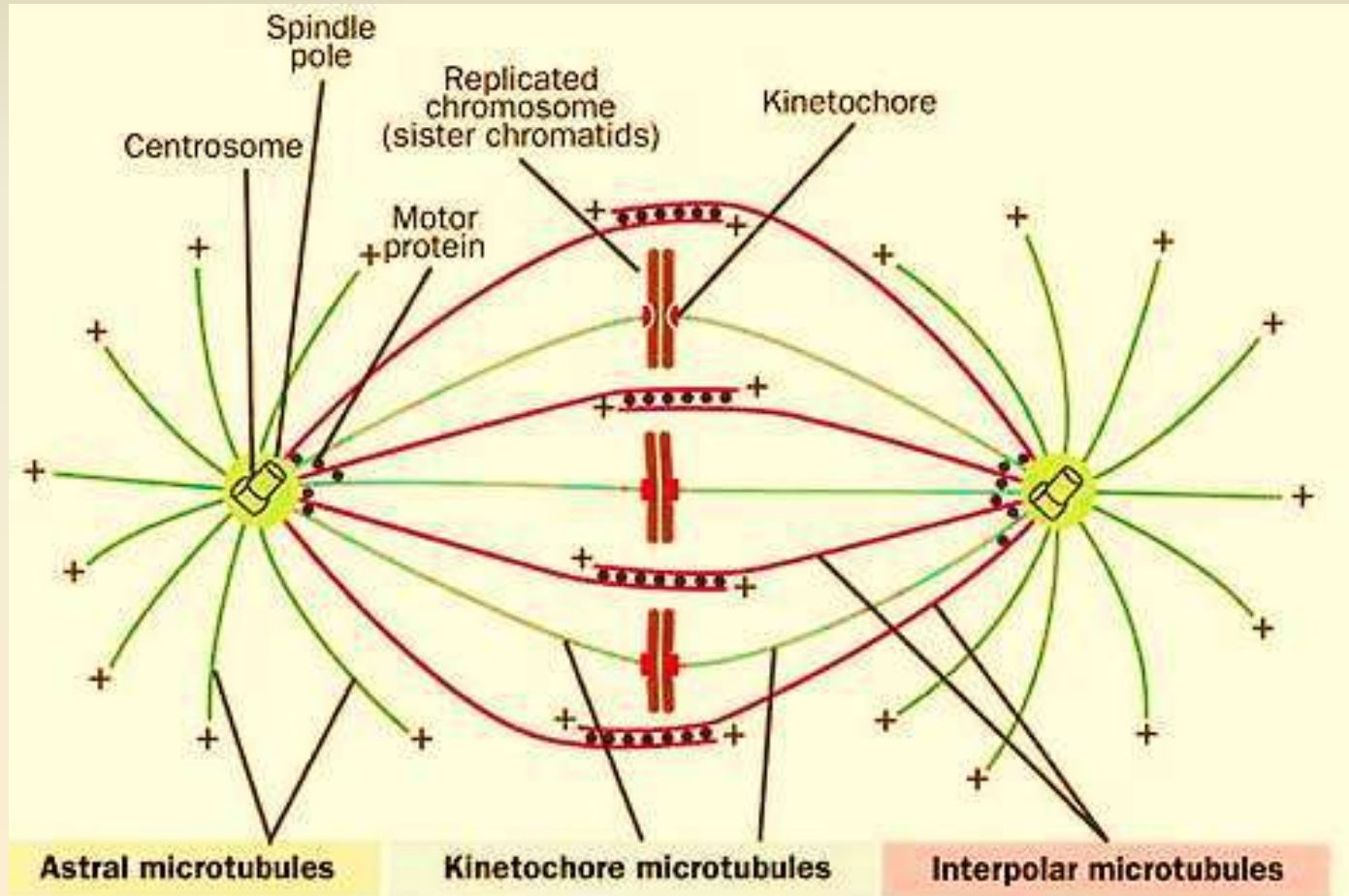
Asbury et. al., Trends Cell Biol 2010

Orientation of kinetochore



<https://academic.oup.com/bioscience/article/59/11/933/251088>

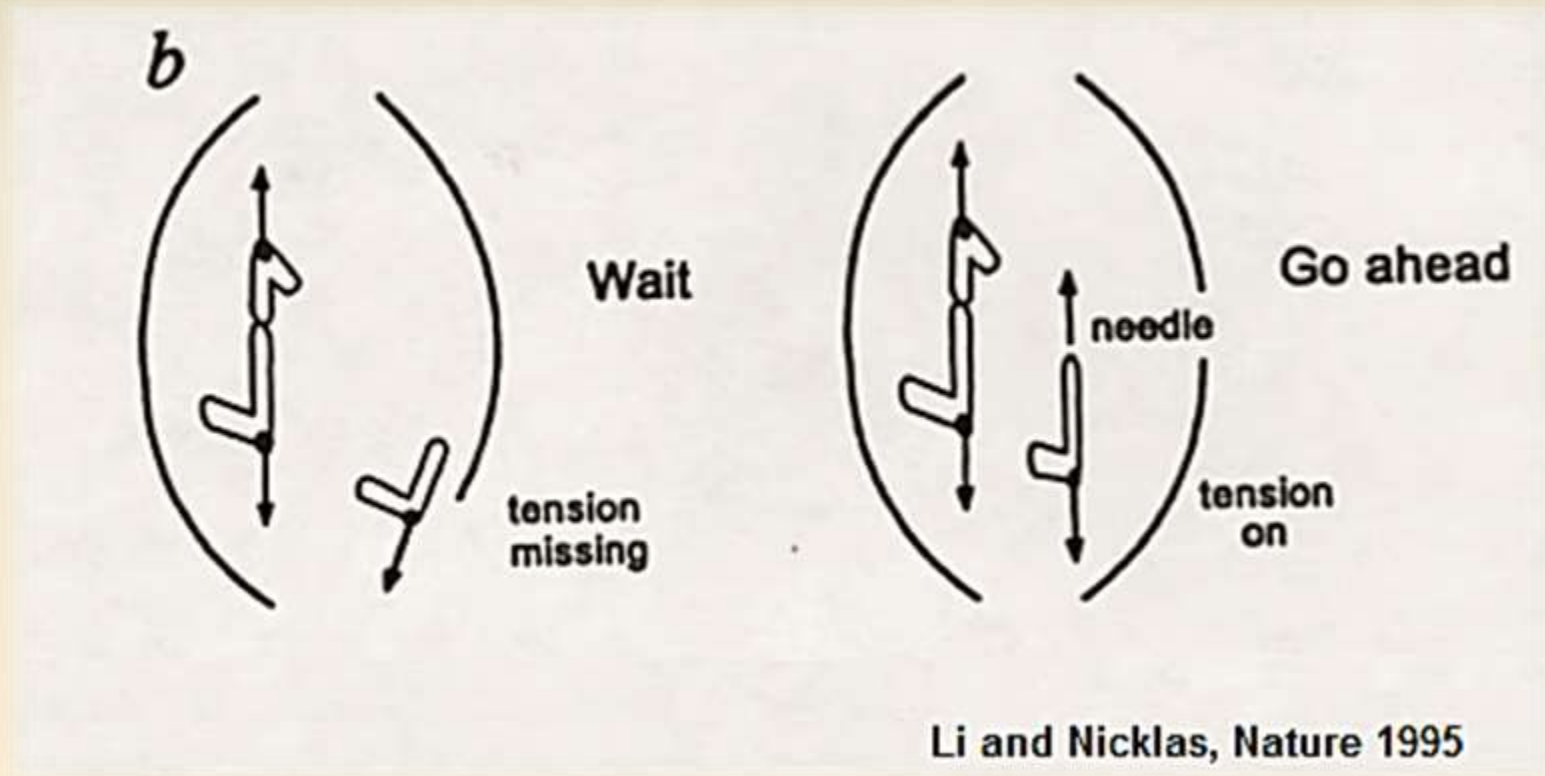
Kinetochores during mitosis



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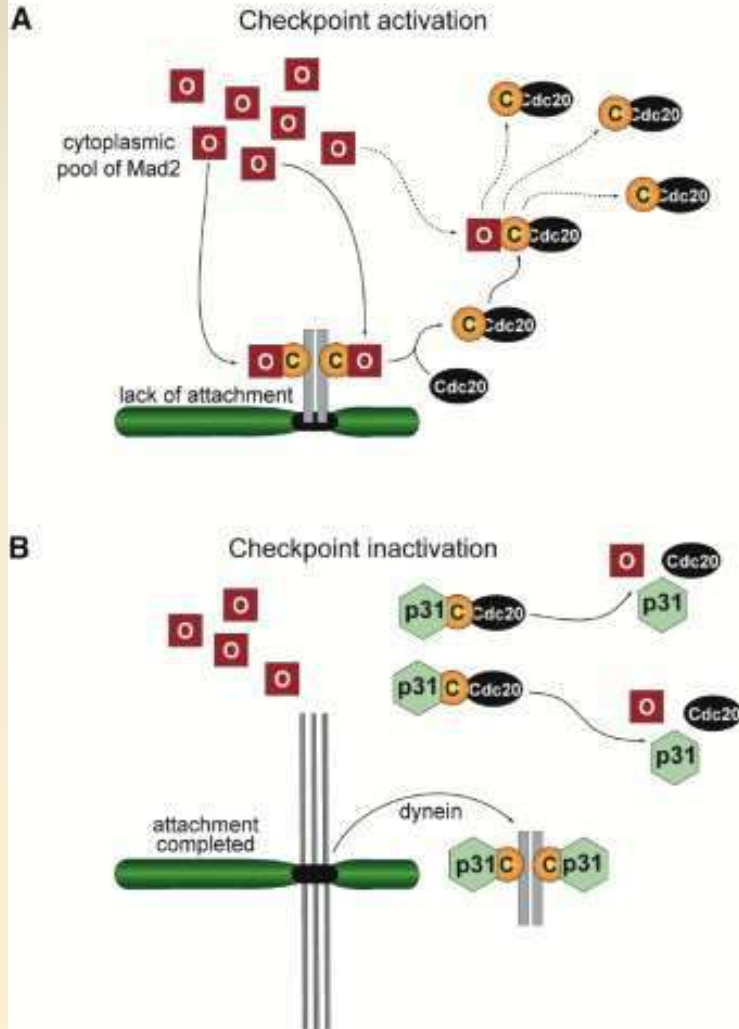
Kinetochores tension – key to segregation



- These tension comes from assembly and disassembly of spindle tubule polymer in spindle microtubule fiber??
- CENP-E is a member of kinesin family acting as motor protein.

A New Model for the Spindle Checkpoint

The "Mad2 template" model



- Anaphase promoting complex (APC) is involved in ubiquitination and degradation of cyclin B1 (Holloway et al. 1993) and anaphase inhibitory proteins, such as Pds1/Cut2 (King et al. 1996).
- Its activation during mitosis requires an interaction with Cdc20 (Hwang et al. 1998).
- Cdc20 localizes to kinetochores from late prophase to telophase, and partially to spindle microtubules and spindle poles (Kallio et al. 1998).
- Mutations in Cdc20 that block the binding of Mad2 destroy the checkpoint, and a tetrameric form of Mad2 binds Cdc20 and interferes with its ability to activate the APC

Further reading

- Karp G., Iwasa J., Marshall W. Karp's Cell and Molecular Biology, 9th Edition. John Wiley & Sons, New Jersey, USA.
- Watson J.D., Baker T.A., Bell S.P., Gann A., Levine M., Losick R. 2013. Molecular Biology of the Gene, 7th Edition. Pearson education, London, UK.
- Alberts B., Johnson A., Lewis J., Raff M., Roberts K., Walter P. 2002. Molecular Biology of the Cells. Garland Science, New York, USA.
- Lodish H., Berk A., Lawrence Zipursky S., Matsudaira P., Baltimore D., Darnell J.E.. 2000. Molecular Cell Biology. W. H. Freeman and Com pany, New York, USA.
- Krebs J.E., Goldstein E.S., Kilpatrick S.T. 2017. Lewin's Genes XII. Jones and Bartlett Publishers, Inc., Burlington, MA, USA.
- <https://www.hubrecht.eu/research/kops-molecular-mechanisms-and-evolution-of-cell-division/>