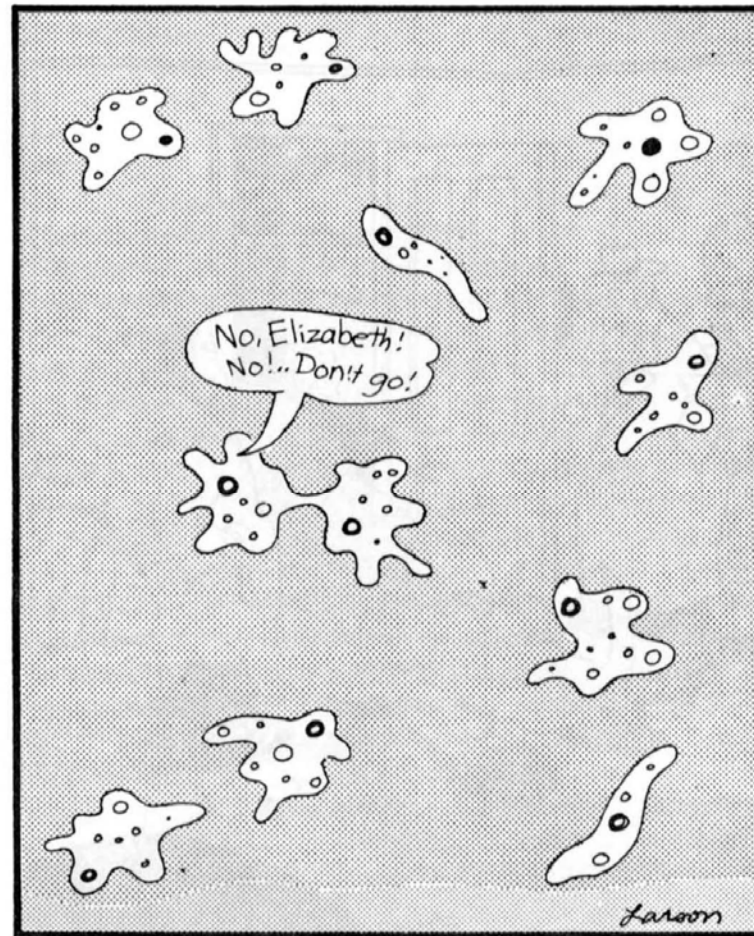


Cell Division & the Cell Cycle



Life in the petri dish (Paul A. S. 1971)

1 x 10¹⁴

684,931

1

Cell divisions in your body

-every cell from a cell-

- Bone marrow stem cells >1,000,000 divisions per minute
- Skin stem cells
- Intestinal stem cells
- Muscle satellite cells
- Liver cells

Cancer = excess cell division

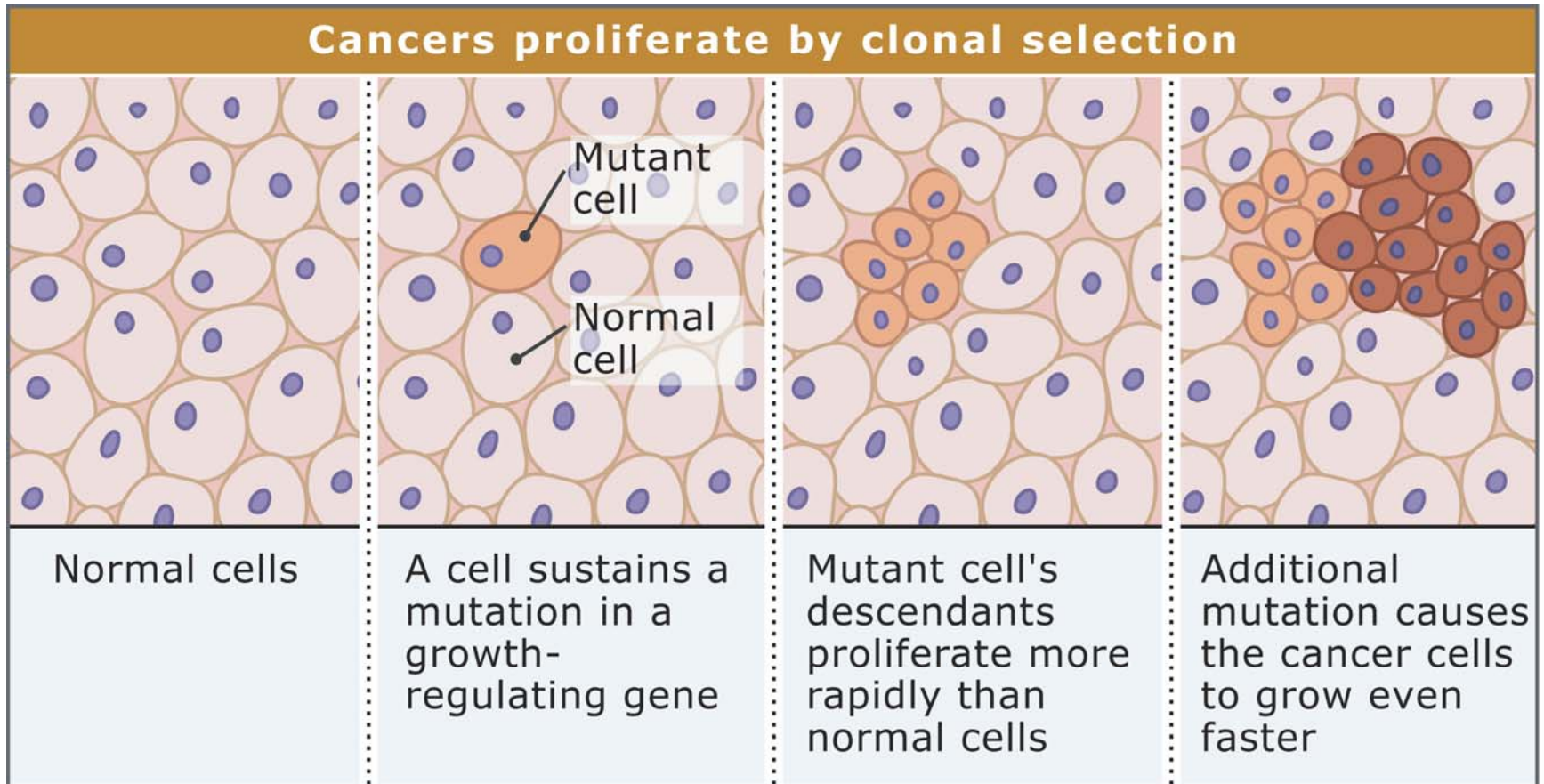


Figure 13.17. Cells. Jones and Bartlett Publishers.

Cell Division Cycle

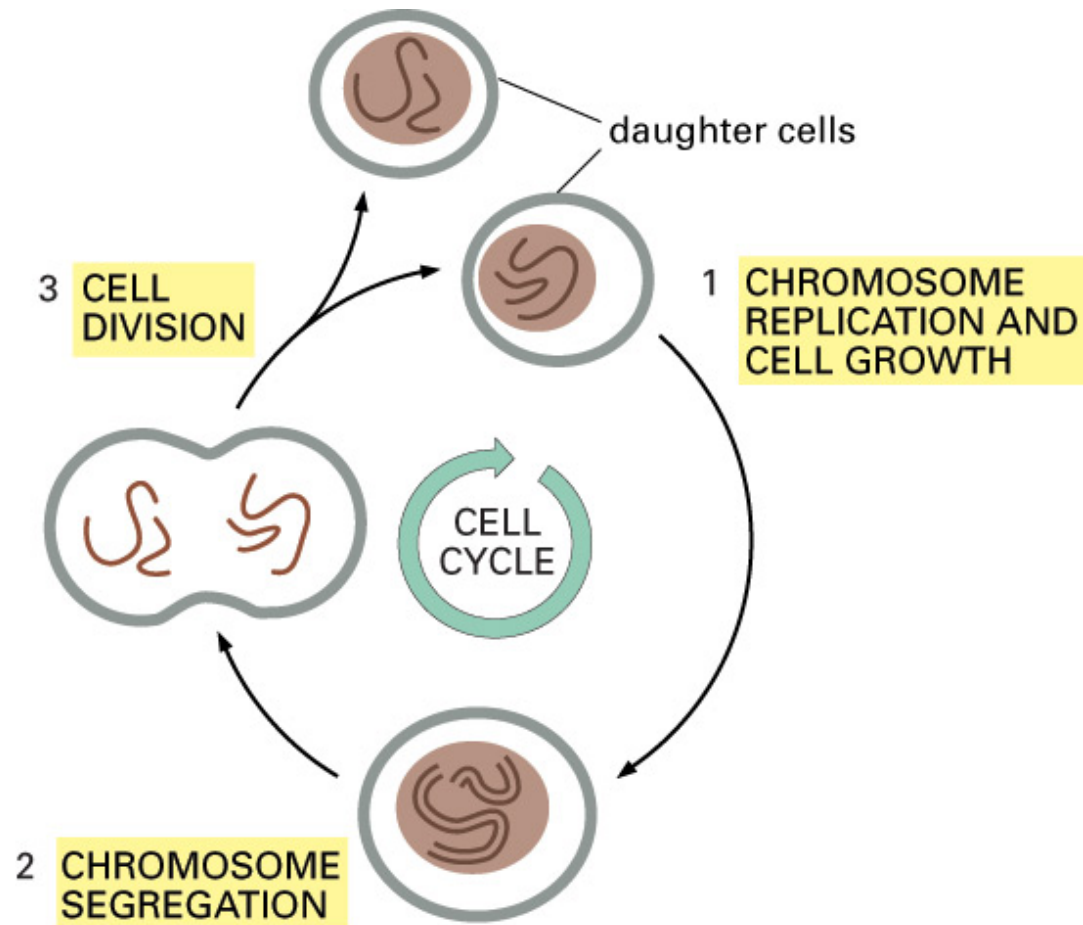
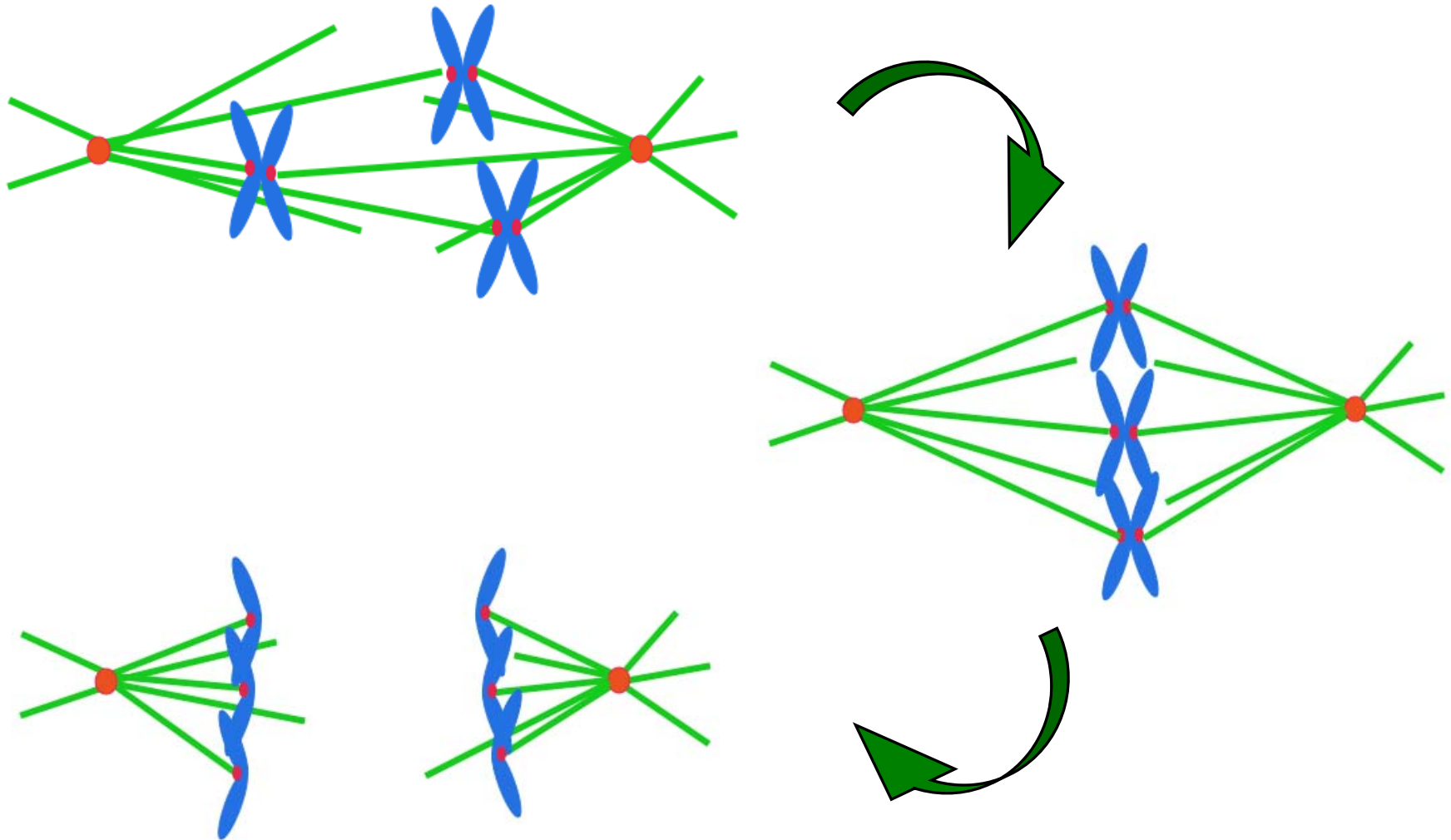


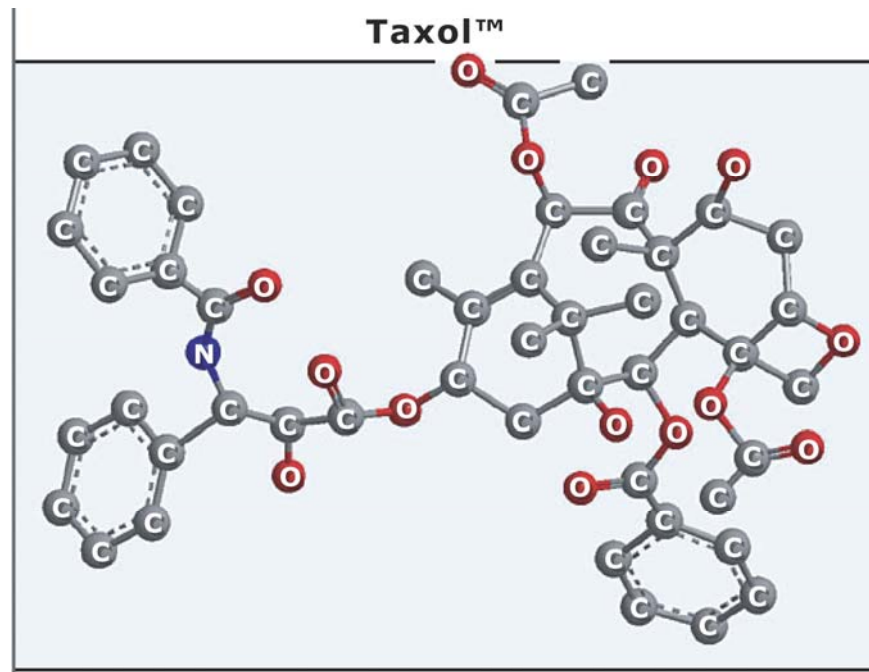
Figure 17-1. Molecular Biology of the Cell, 4th Edition.

Mitosis Overview

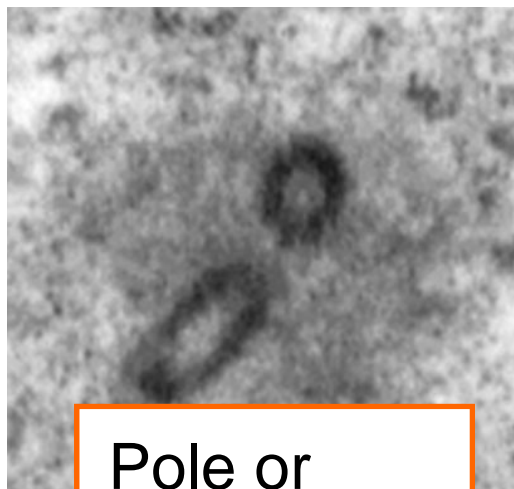
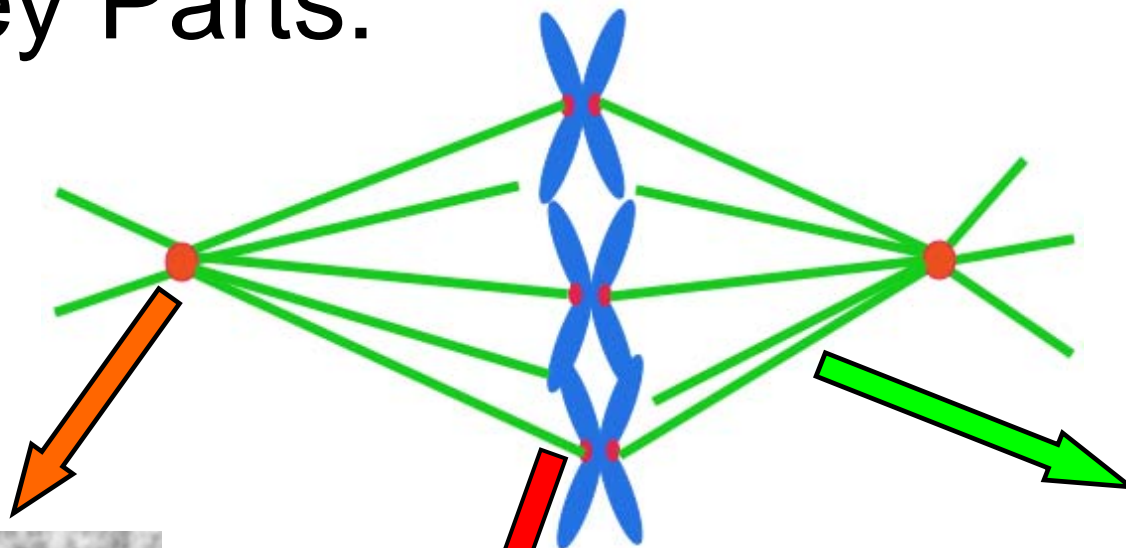


(a movie of mitosis was shown here)

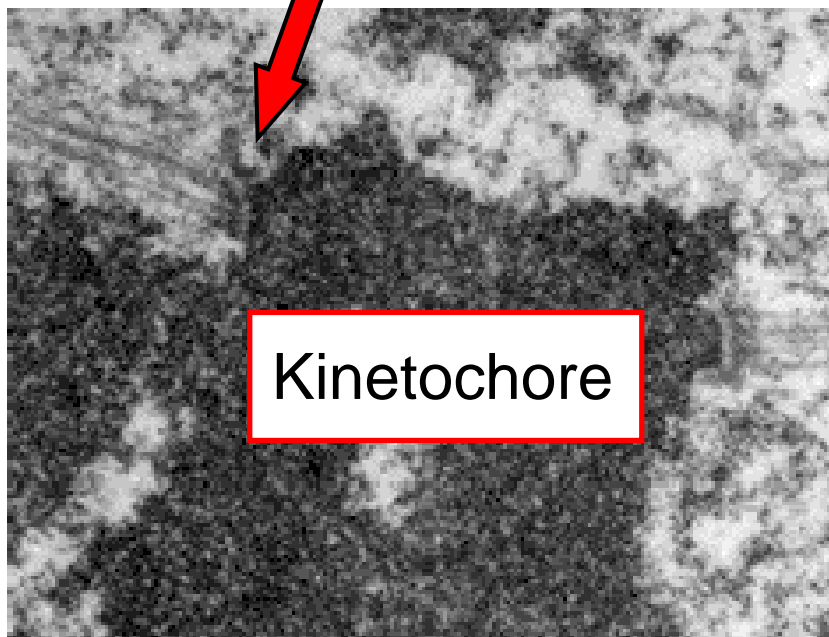
Mitosis-blocking drugs are used to treat cancers



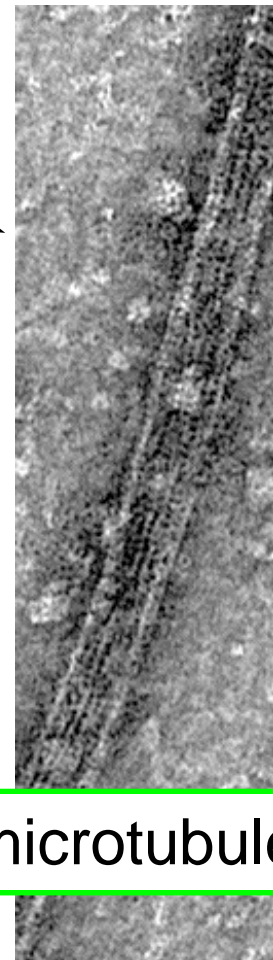
The Key Parts:



Pole or
centrosome

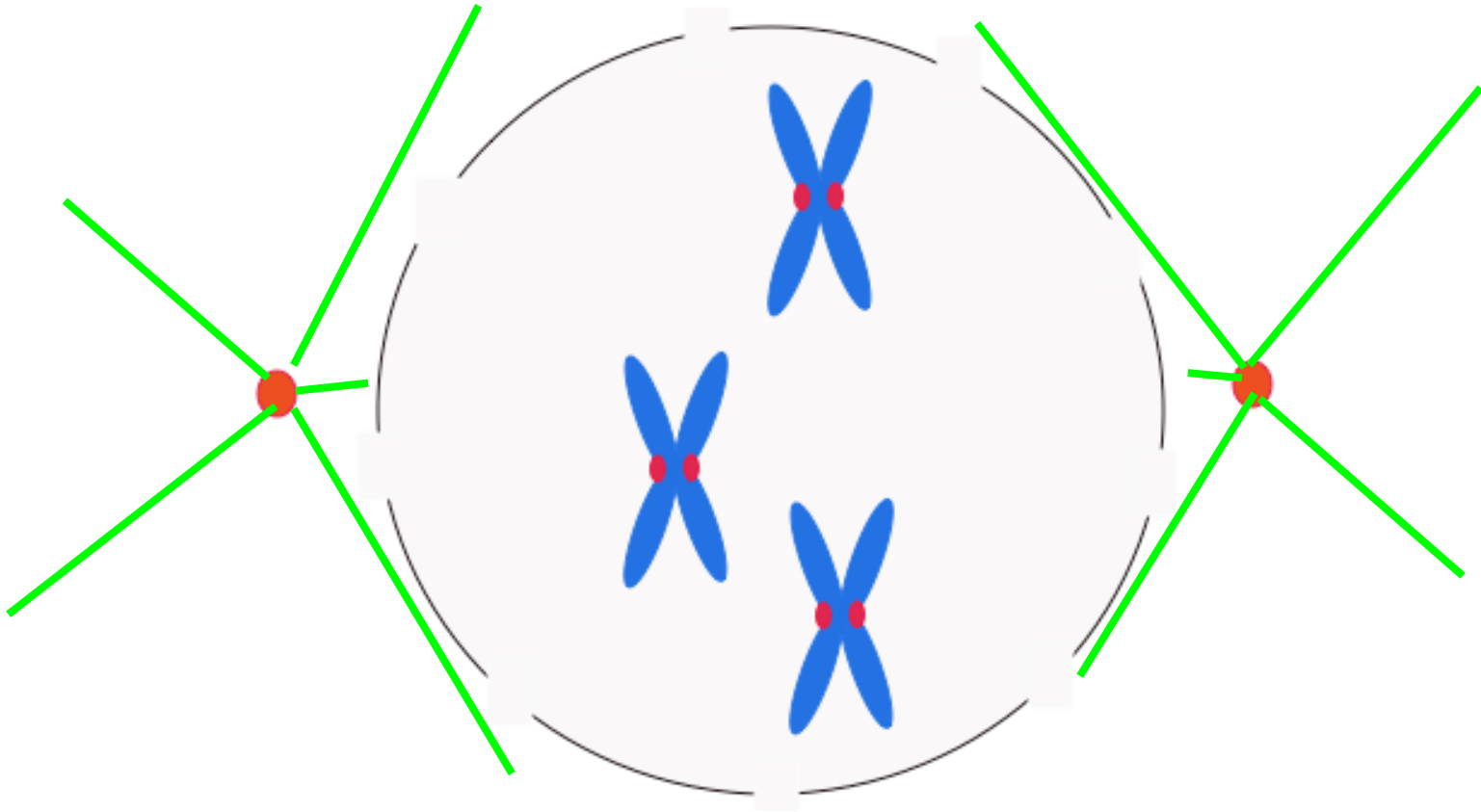


Kinetochore

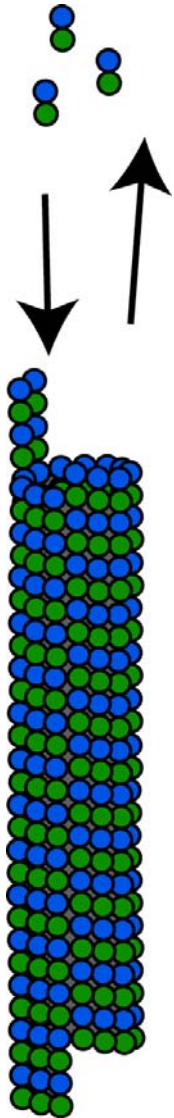


microtubule

How do chromosomes make correct attachments when mitosis begins?

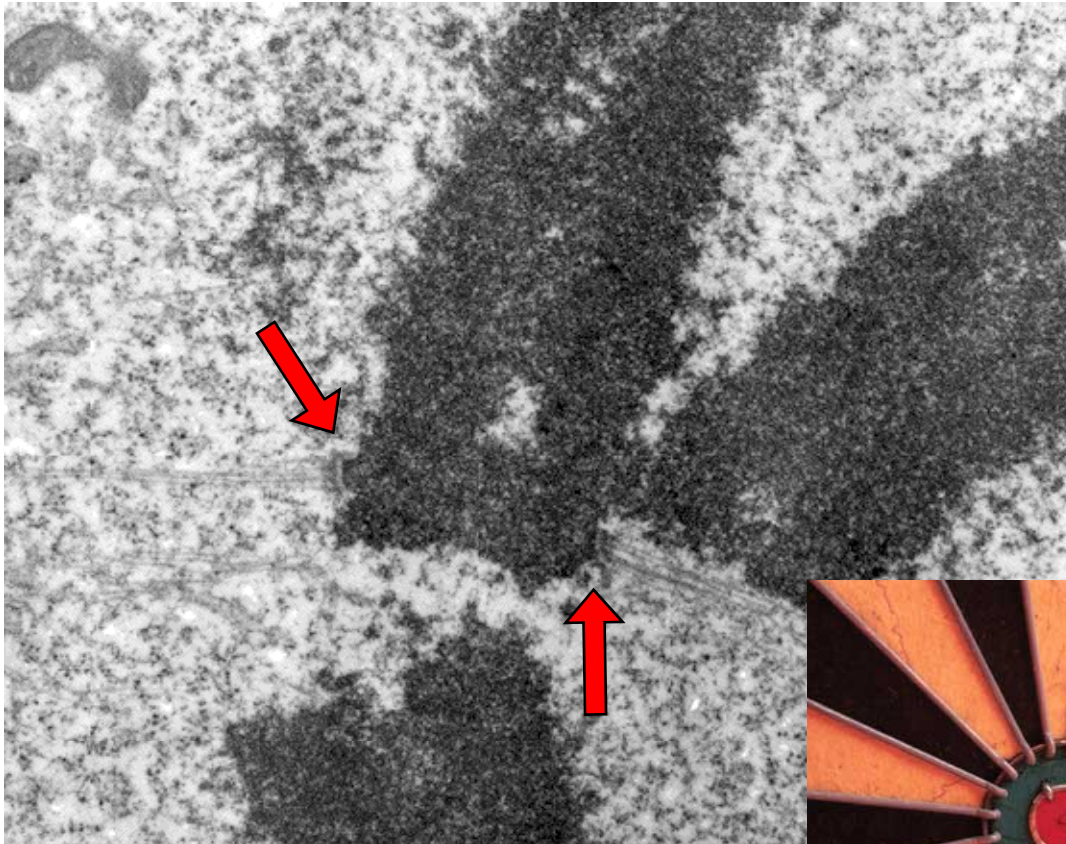


Microtubules find things

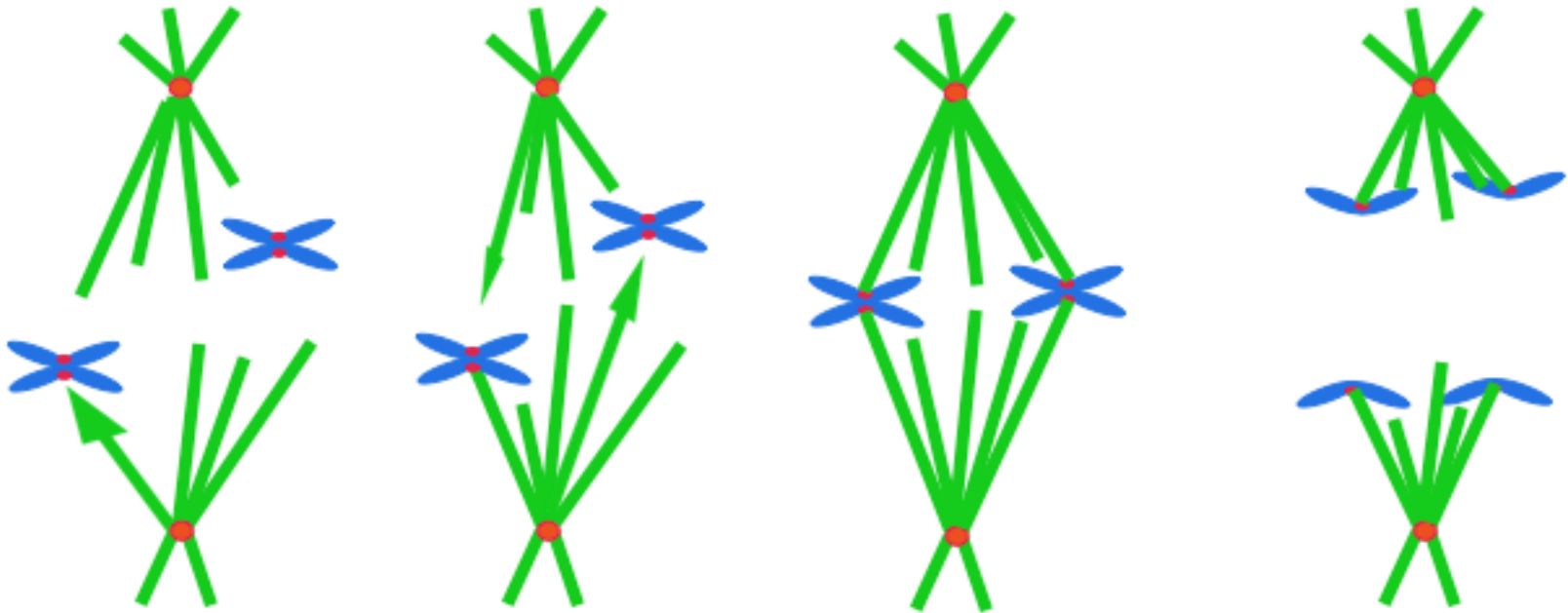


(a movie of microtubule assembly & disassembly was shown here)

Search & Capture



The right connections



Form attachments

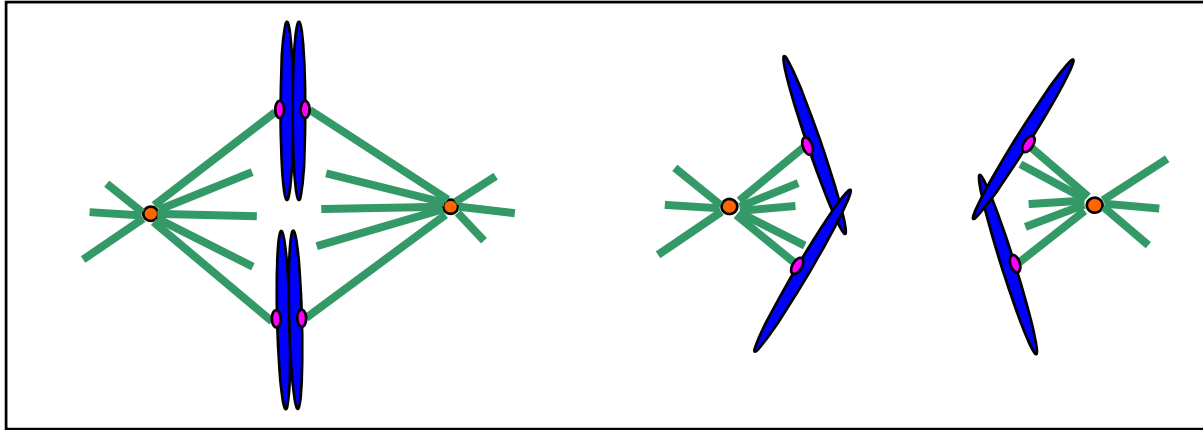


Check
attachments



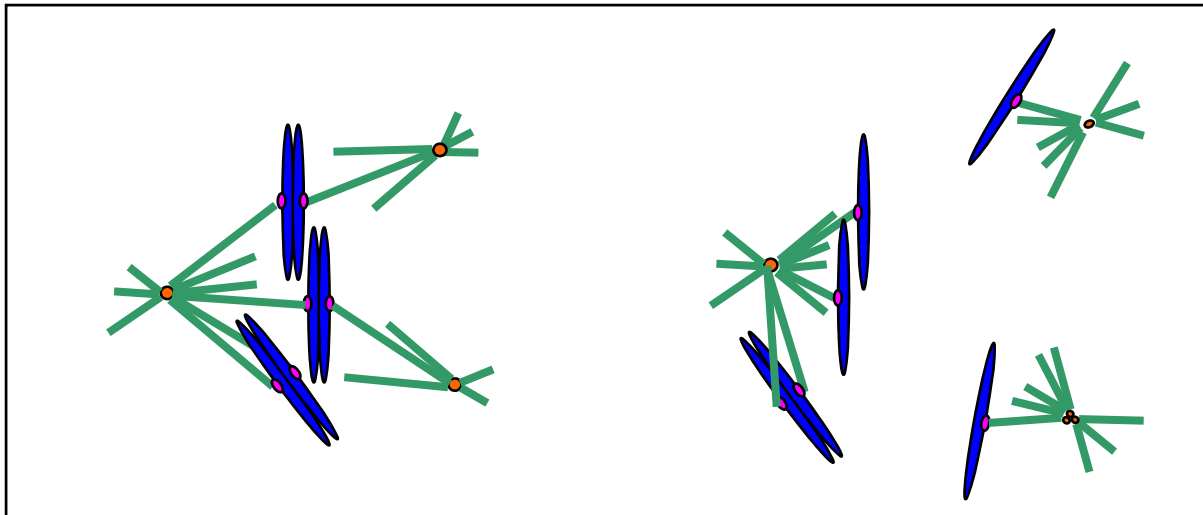
Divide

Mitotic Errors are Deadly



Normal mitosis

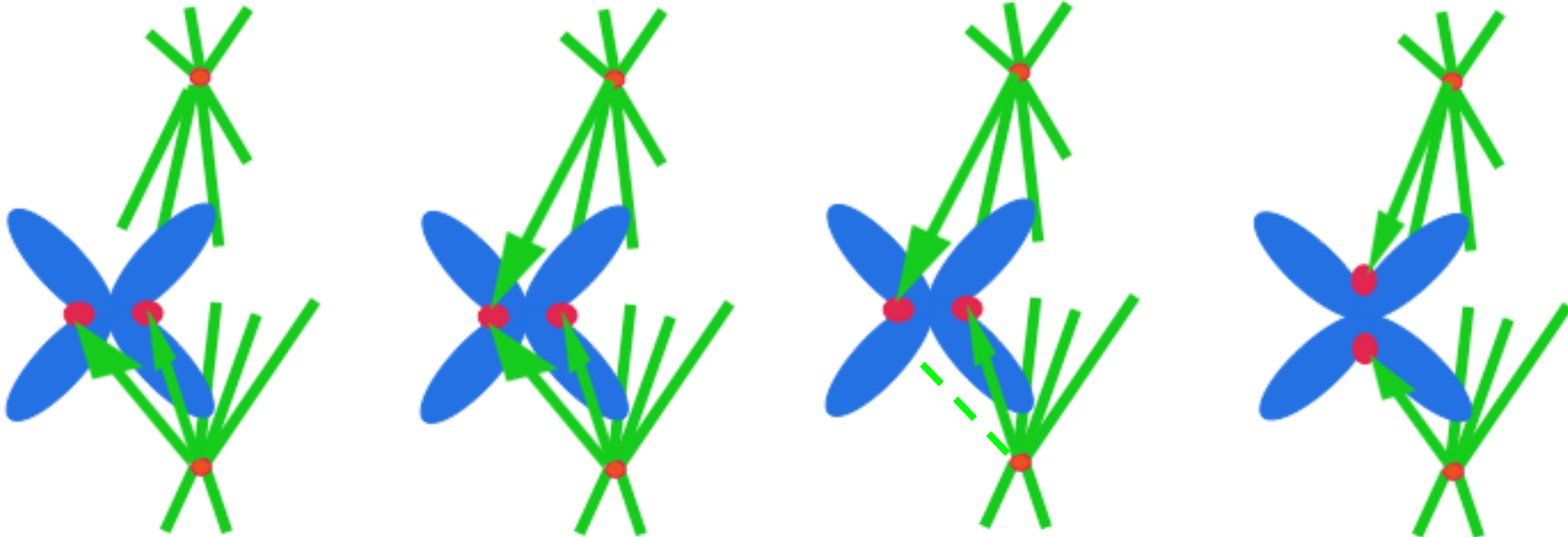
Equal genome
division



Abnormal mitosis

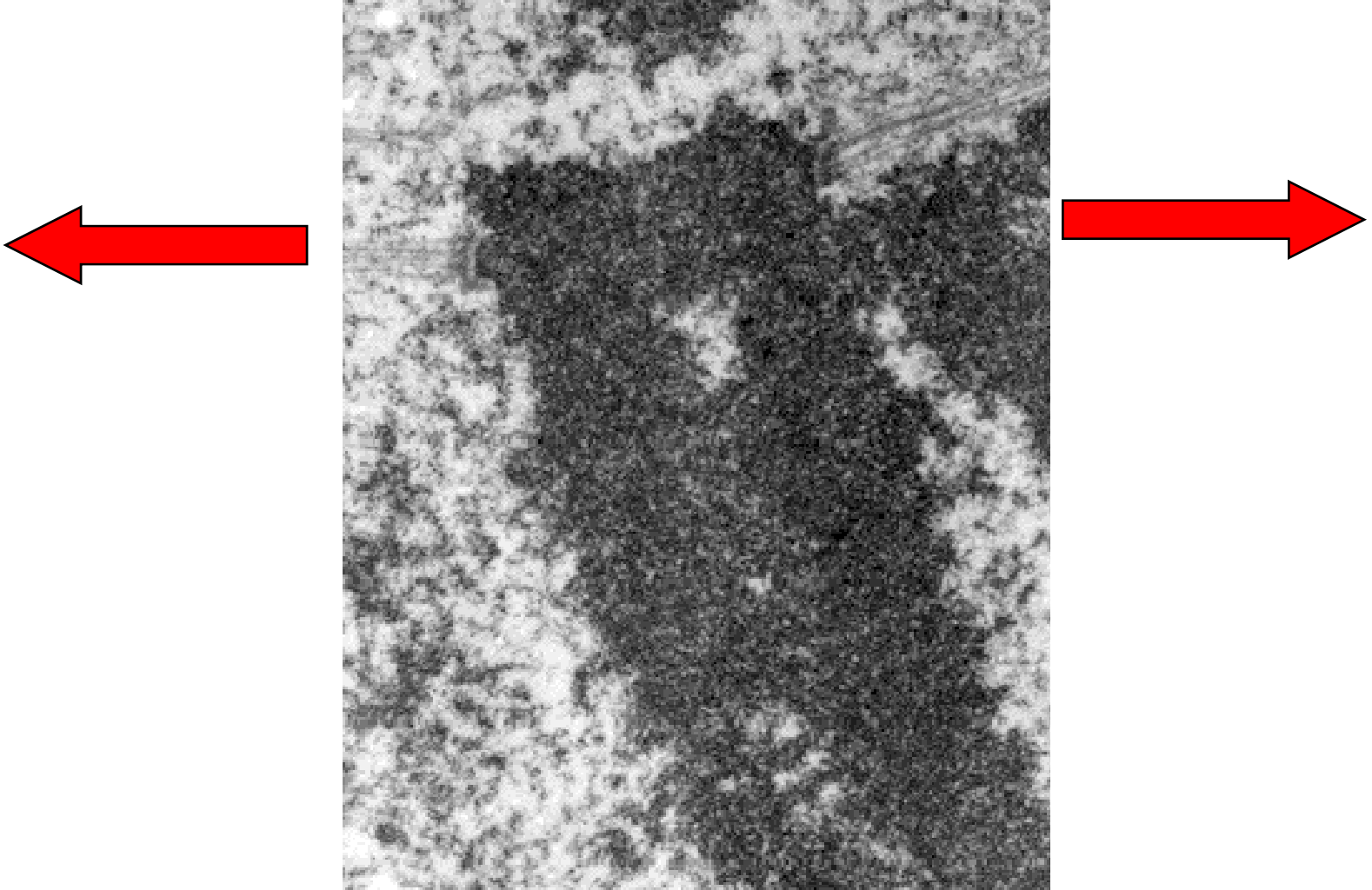
Unequal genome
division

Error Correction

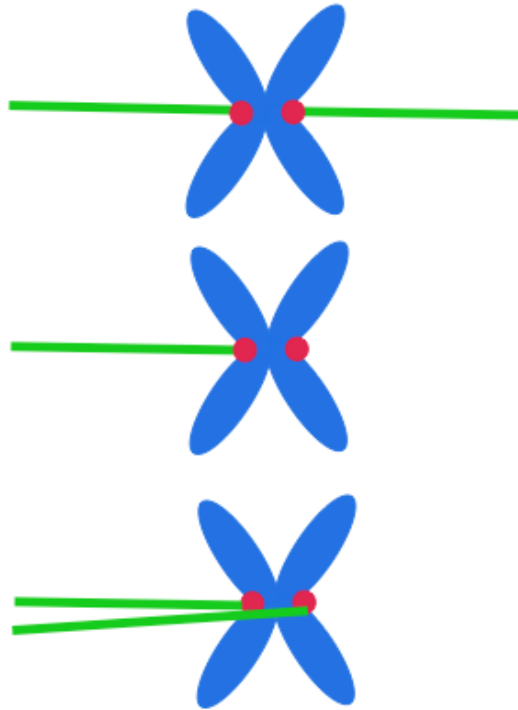


error → new capture → Release → wrong attachment → Tension = correct

Kinetochores sense tension



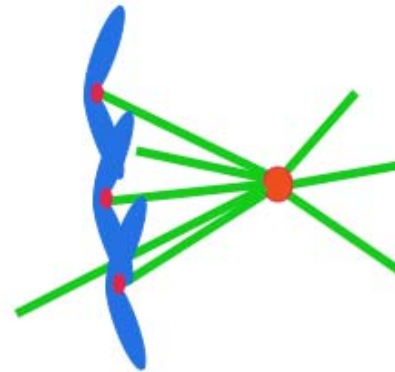
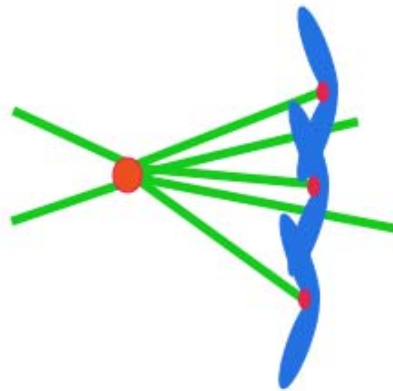
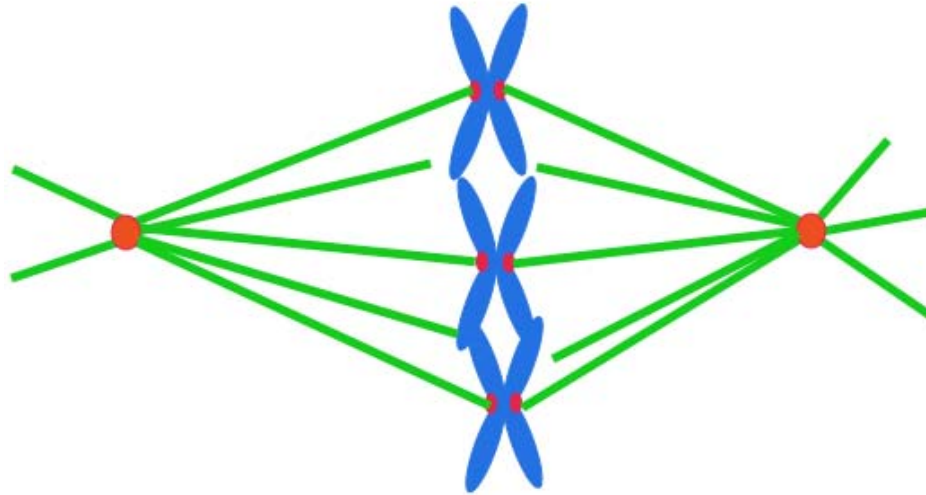
Errors are detected & fixed



Correct attachments

Activate
checkpoint,
“WAIT”
& correct

When all goes well.....



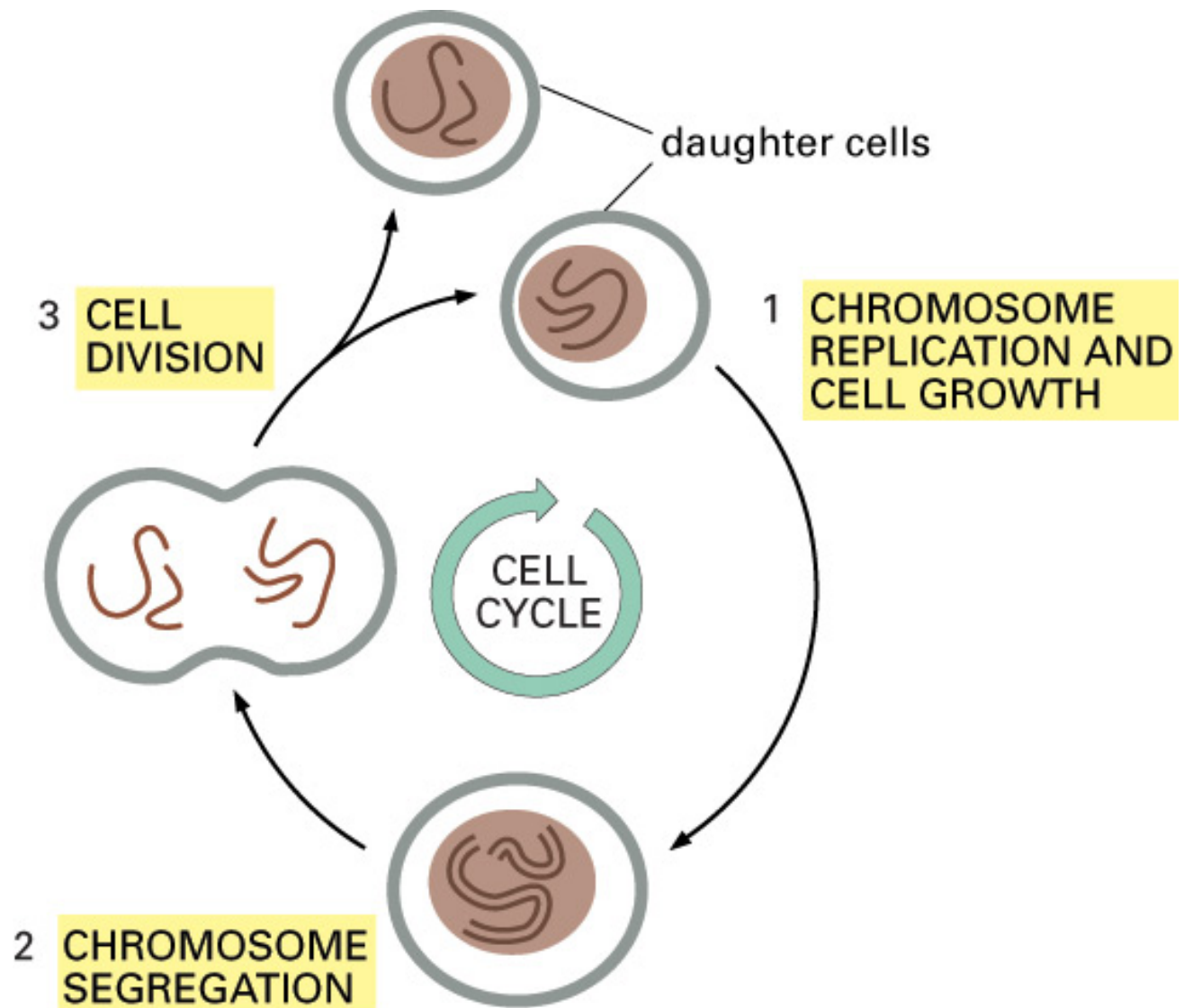


Figure 17-1. Molecular Biology of the Cell, 4th Edition.

Cell cycle overview

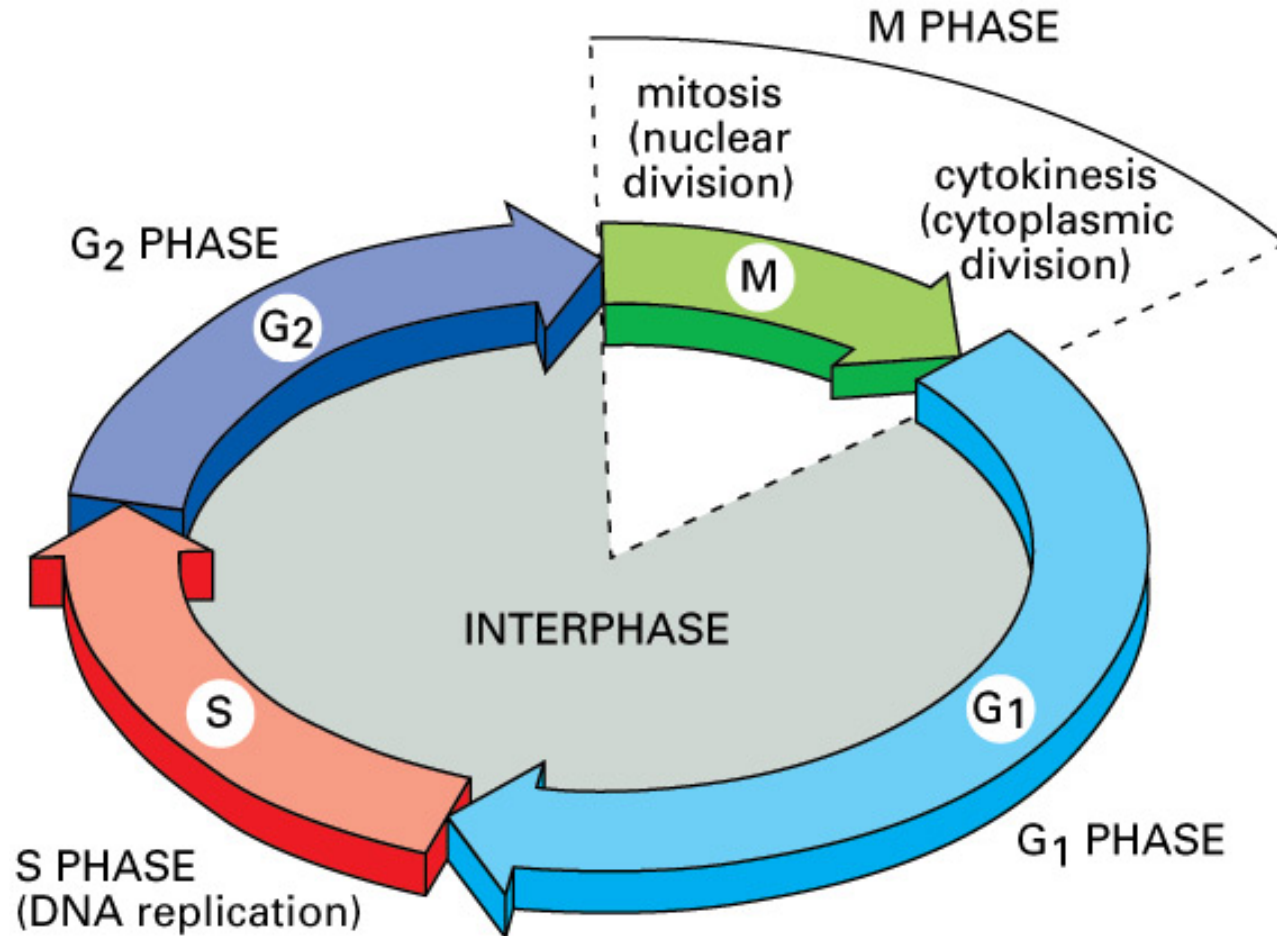


Figure 17-3. Molecular Biology of the Cell, 4th Edition.

Cell cycle checkpoints

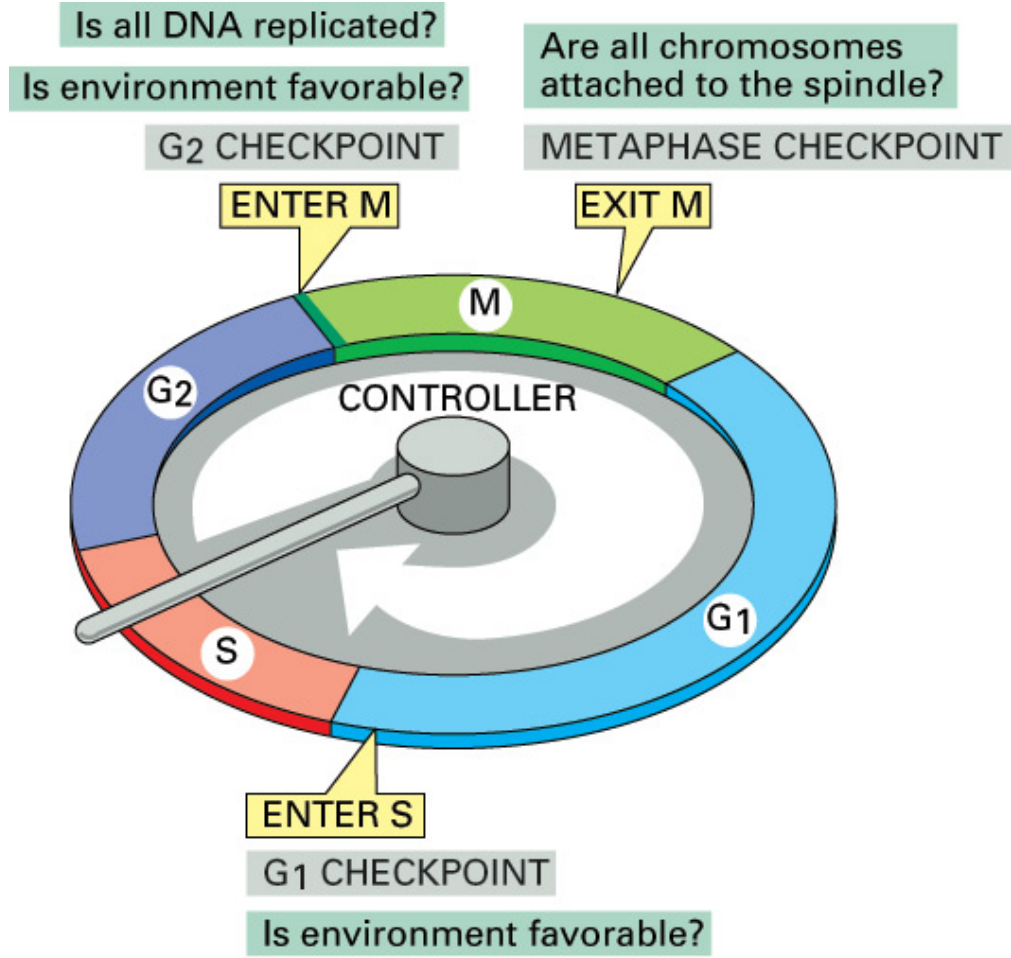


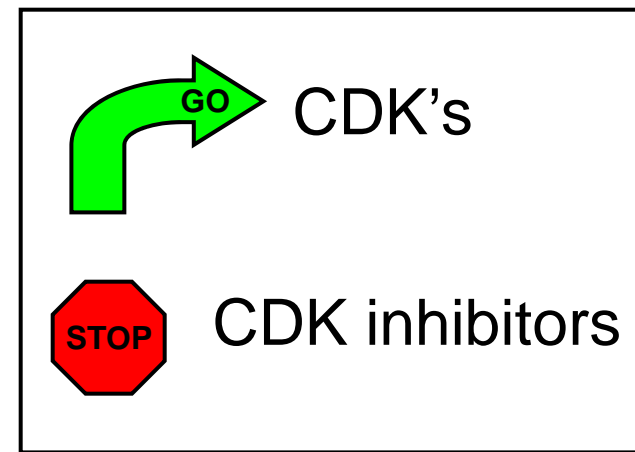
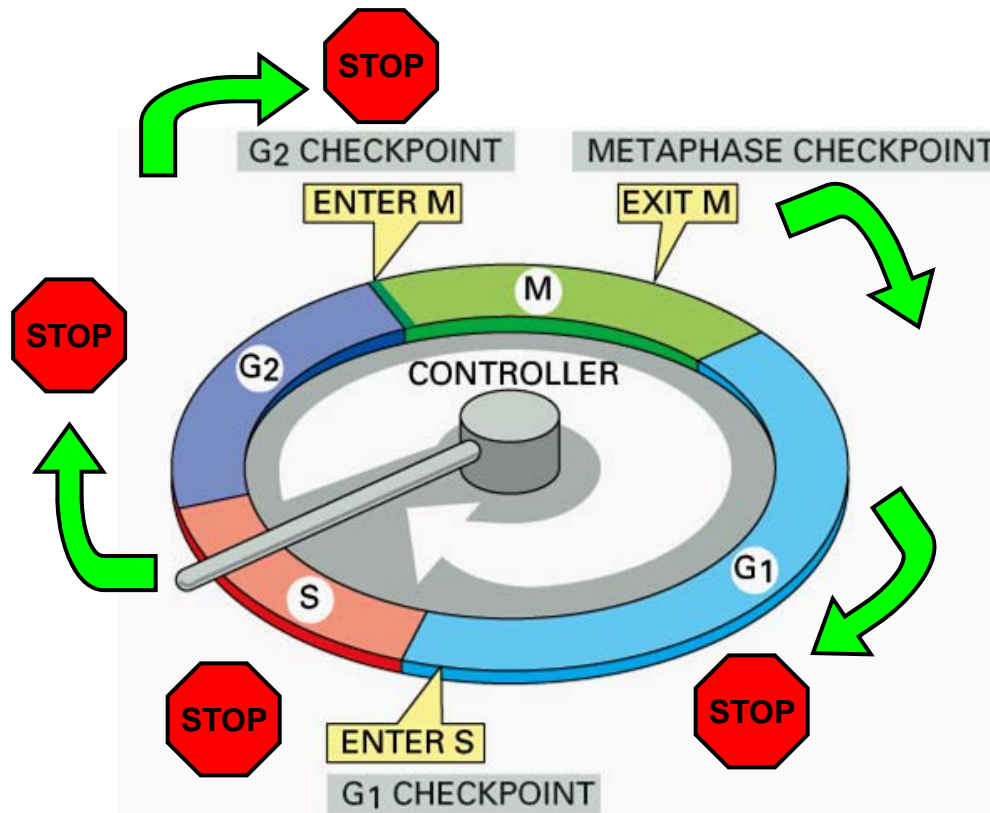
Figure 17-14. Molecular Biology of the Cell, 4th Edition.

Checkpoints are “WAIT” signals

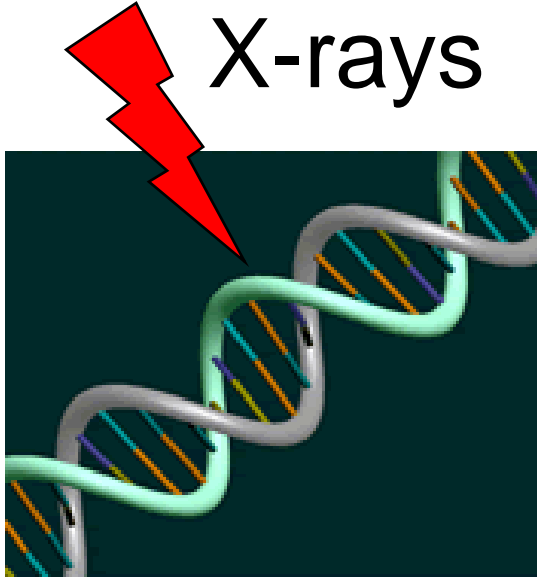


Damage is repaired before cycle continues

General Cell Cycle Controls



One Example:
DNA damage

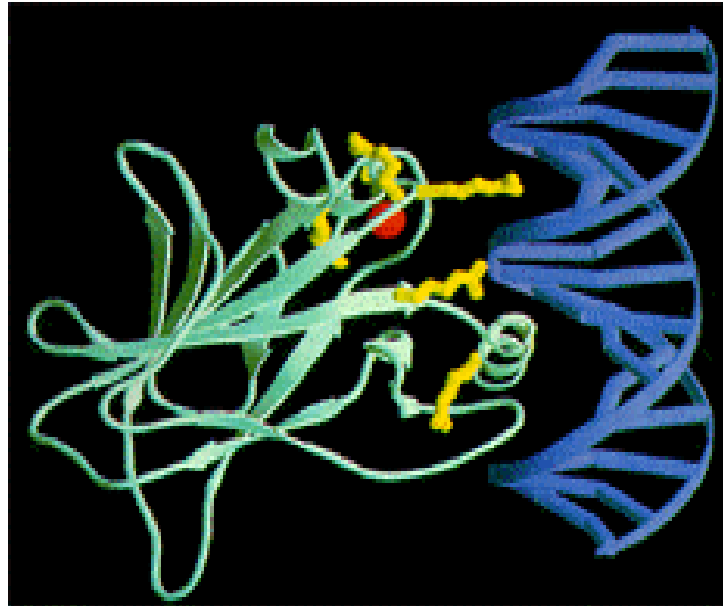


p53



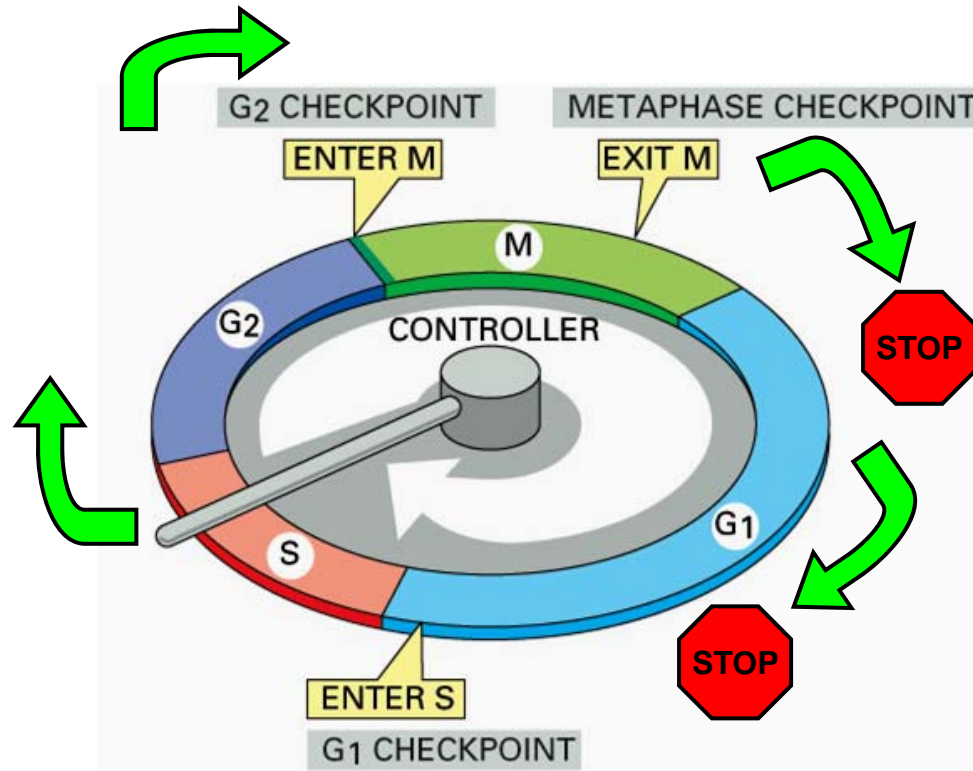
CKI → WAIT

p53 (detector) is often mutated in cancer

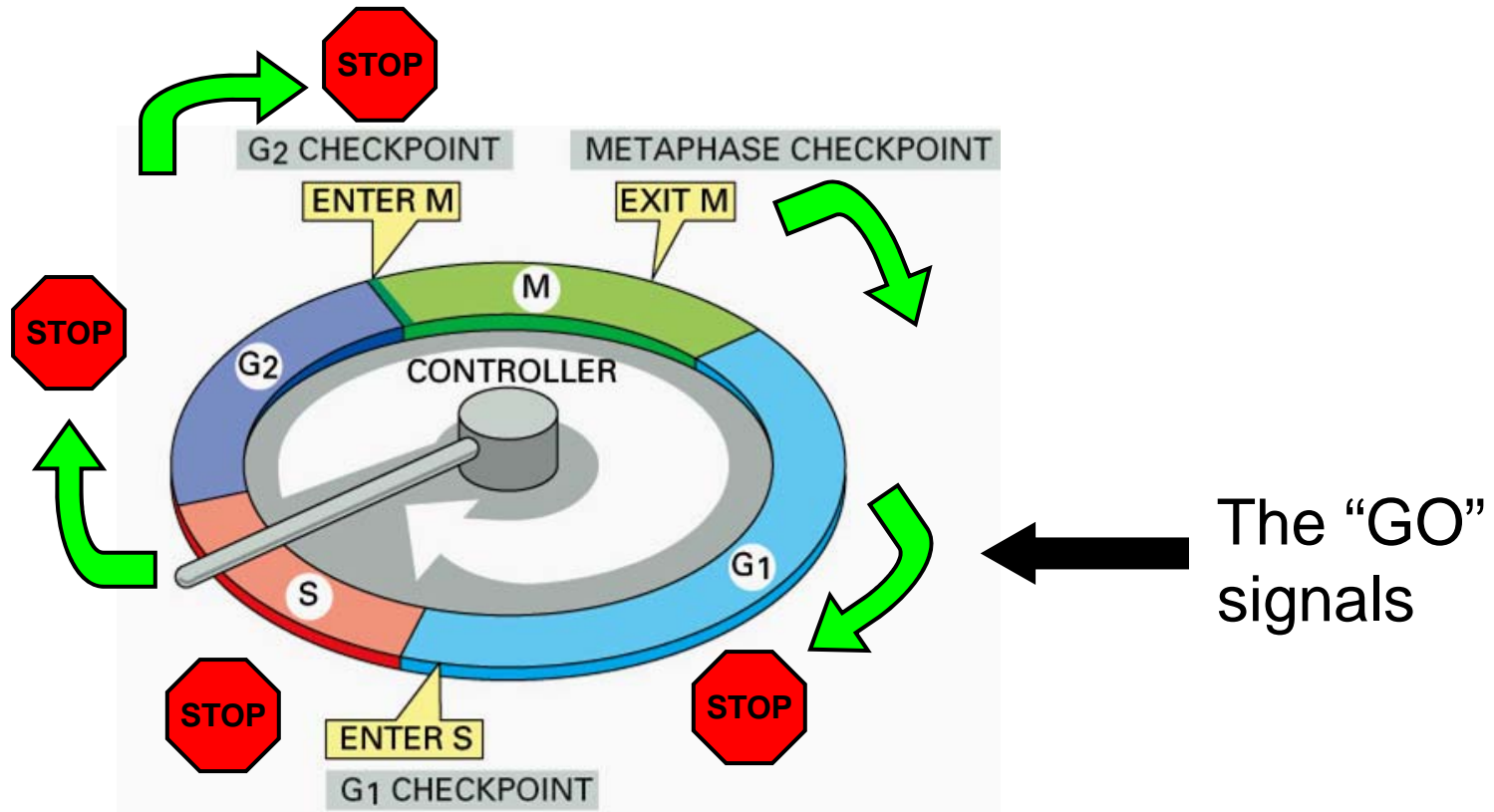


The structure of the core domain of the p53 protein (light blue) bound to DNA (dark blue). The six most frequently mutated amino acids in human cancers are shown in yellow - all are residues important for p53 binding to DNA. Red ball: zinc atom. [Reproduced from Cho, Y., et al. (1994) *Science*, 265, 346-355, with kind permission.]

Without p53, some of the brakes are missing



Commitment to divide in G_1



Cancer results from inappropriate “GO” or not enough “STOP”

General mutations that disrupt normal balance:

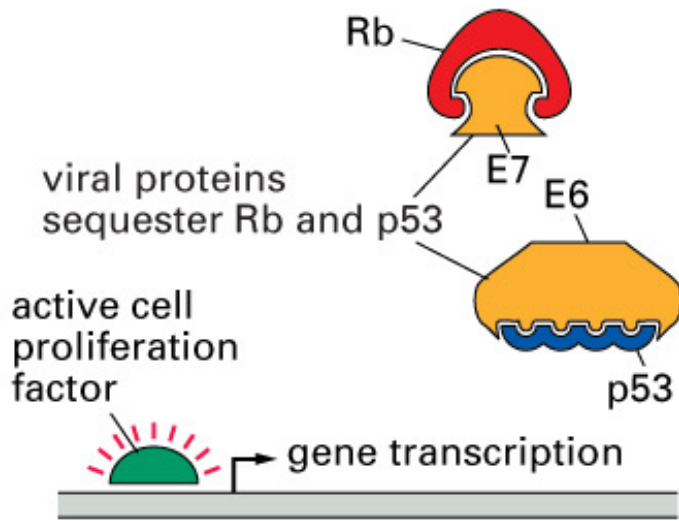
Over-active mutation too much “GO”

Under-active mutation too little “STOP”

Source of mutations: inherited or acquired

Other sources of cell-cycle disruption

Viral proteins



CELL PROLIFERATION
ACTIVATED
BY DNA VIRUS

Gene Rearrangements

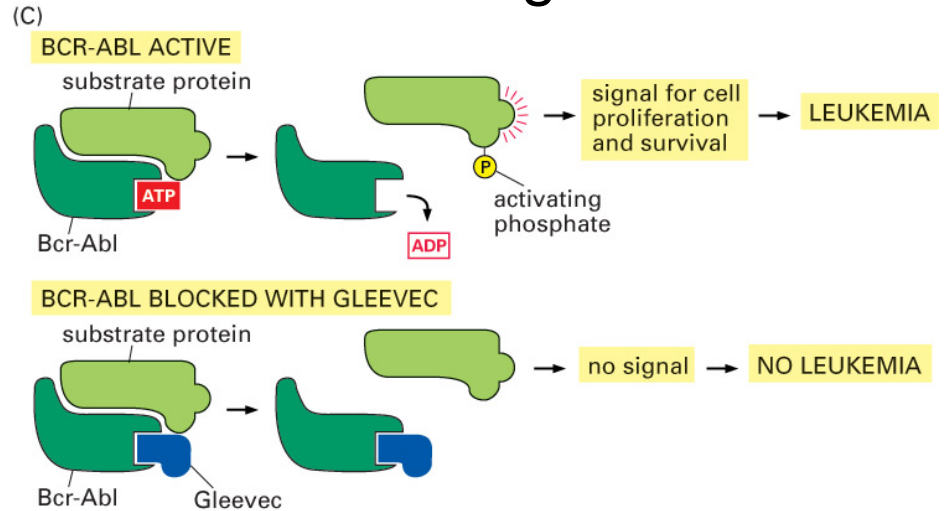


Figure 23-45 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Cancer results from > 1 mutation

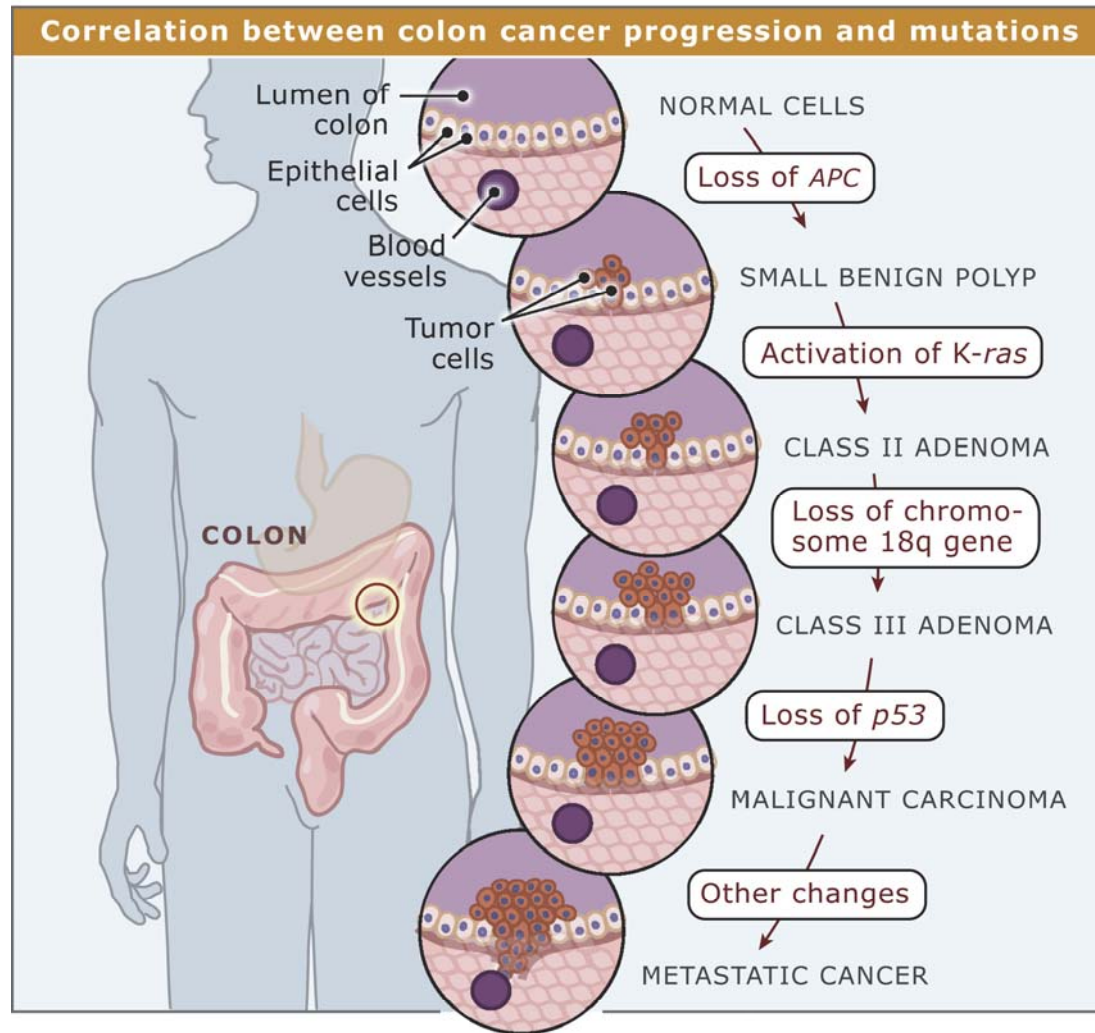


Figure 13.14. Cells. Jones and Bartlett, publishers

Nobel Prize Winners in Cell Cycle Research



Lee Hartwell

Yeast



Tim Hunt

Sea urchins & Frogs



Sir Paul M. Nurse

Yeast