Cell Division & the Cell Cycle
$1 \times 10^{14}$
684,931
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

Cancers proliferate by clonal selection

| Normal cells | A cell sustains a mutation in a growth-regulating gene | Mutant cell's descendants proliferate more rapidly than normal cells | Additional mutation causes the cancer cells to grow even faster |

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
Kinetochore proteins 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.
Figure 17–14. Molecular Biology of the Cell, 4th Edition.
Checkpoints are “WAIT” signals

Damage is repaired before cycle continues
General Cell Cycle Controls

CDK’s
CDK inhibitors
One Example: DNA damage

X-rays

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**

- Viral proteins sequester Rb and p53
- Active cell proliferation factor

**Gene Rearrangements**

- BCR-ABL ACTIVE substrate protein
- Signal for cell proliferation and survival → LEUKEMIA
- BCR-ABL BLOCKED WITH GLEEVEC substrate protein
- No signal → NO LEUKEMIA


CELL PROLIFERATION ACTIVATED BY DNA VIRUS
Cancer results from > 1 mutation

Figure 13.14. Cells. Jones and Bartlett, publishers
Nobel Prize Winners in Cell Cycle Research

Lee Hartwell  Tim Hunt  Sir Paul M. Nurse

Yeast  Sea urchins & Frogs  Yeast