Cell Division & the Cell Cycle
1 \times 10^{14}
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

1. CHROMOSOME REPLICATION AND CELL GROWTH
2. CHROMOSOME SEGREGATION
3. CELL DIVISION

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:

- Kinetochore
- Microtubule
- Pole or centrosome
- 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......
Cell cycle overview

Figure 17–3. Molecular Biology of the Cell, 4th Edition.
Cell cycle checkpoints

Is all DNA replicated?
Is environment favorable?
G2 CHECKPOINT

Are all chromosomes attached to the spindle?
METAPHASE CHECKPOINT

ENTER M
EXIT M

ENTER S
G1 CHECKPOINT
Is environment favorable?

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 inhibitors

CDK’s

GO
One Example:
DNA damage

X-rays

p53

CKI \rightarrow\text{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 $G_1$

The "GO" signals
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

Gene Rearrangements

CELL PROLIFERATION ACTIVATED BY DNA VIRUS

Cancer results from > 1 mutation
Nobel Prize Winners in Cell Cycle Research

Lee Hartwell  Tim Hunt  Sir Paul M. Nurse

Yeast  Sea urchins & Frogs  Yeast