Fig. E.15

HOX genes: Comprehensive example

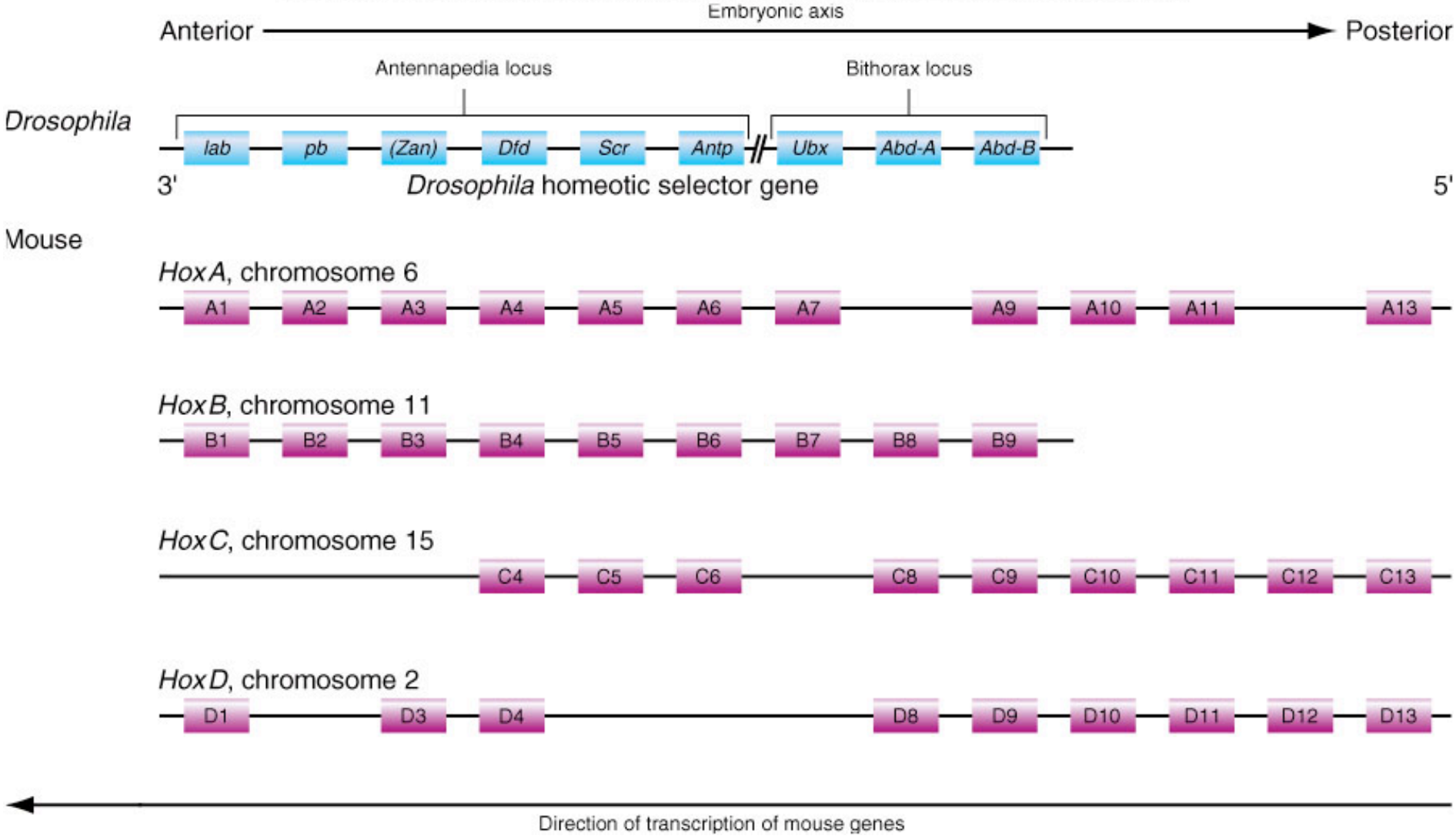
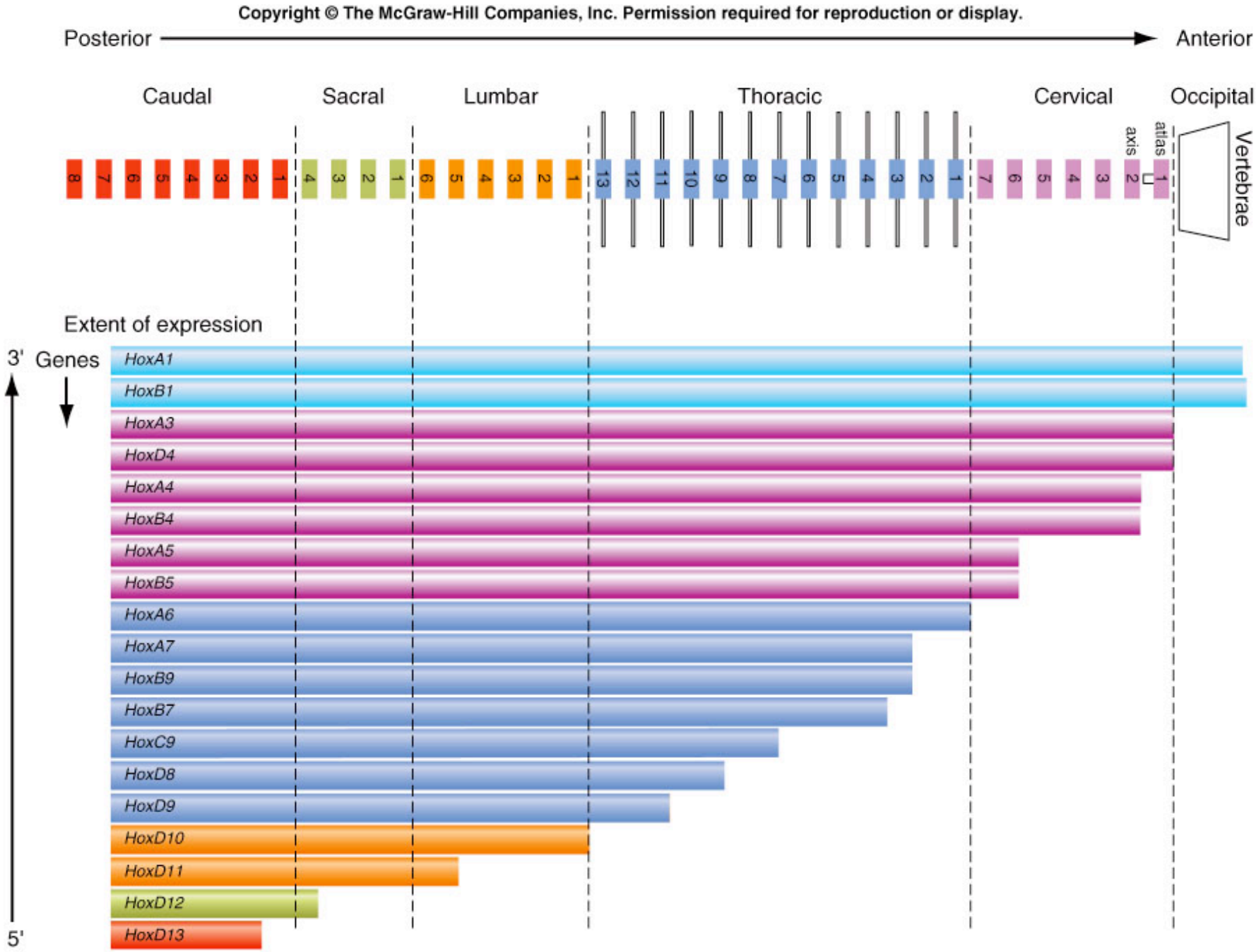


Fig. E.16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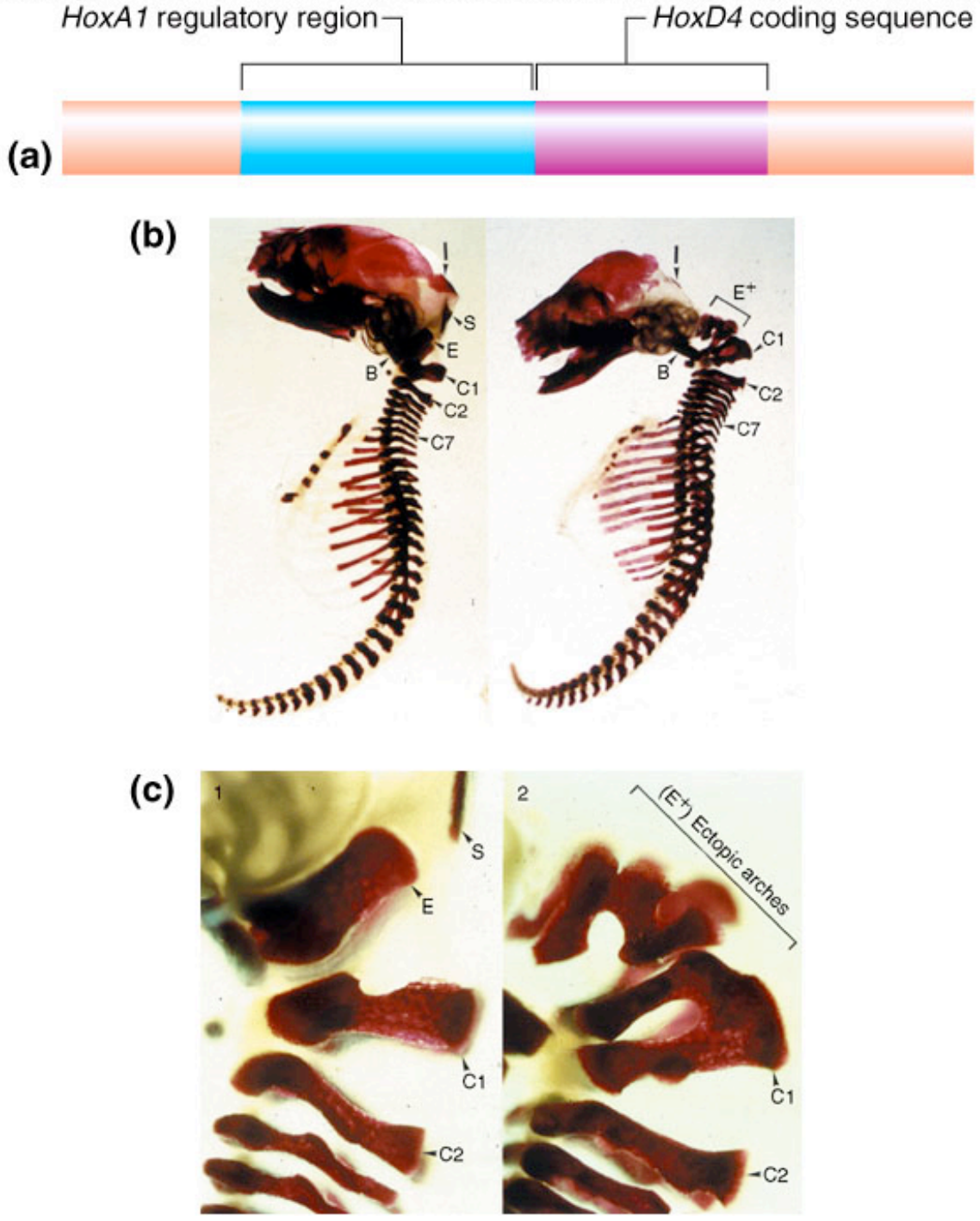
Posterior
Anterior
Caudal
Sacral
Lumbar
Thoracic
Cervical
Occipital
atlas
axis
Vertebrae
Extent of expression
3'
Genes
5'
HoxA1
HoxB1
HoxA3
HoxD4
HoxA4
HoxB4
HoxA5
HoxB5
HoxA6
HoxA7
HoxB9
HoxB7
HoxC9
HoxD8
HoxD9
HoxD10
HoxD11
HoxD12
HoxD13

Fig. E.17

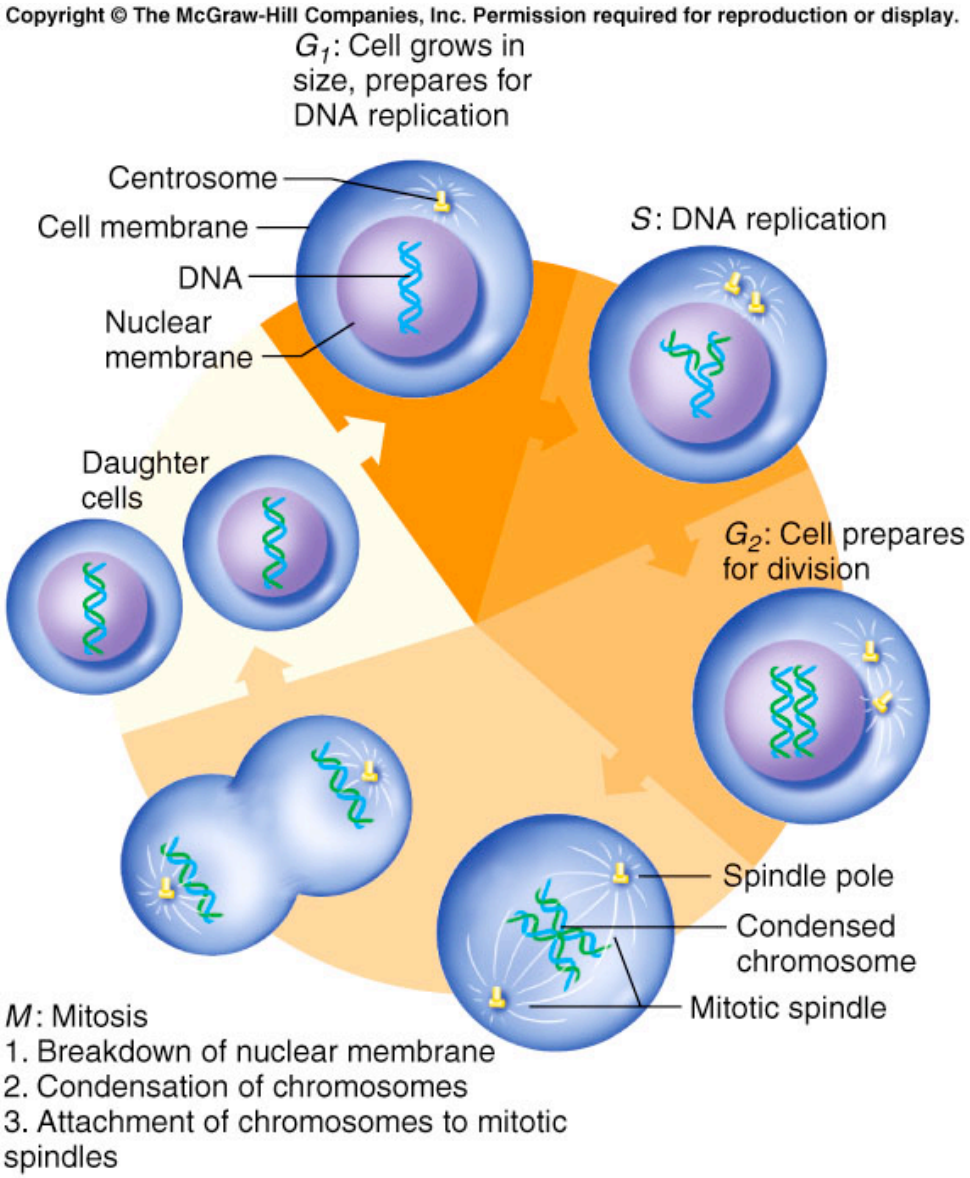


Lecture 22: Cell-Cycle Regulation and the Genetics of Cancer I

Read 617-626

Fig. 18.2-18.13

The normal cell division

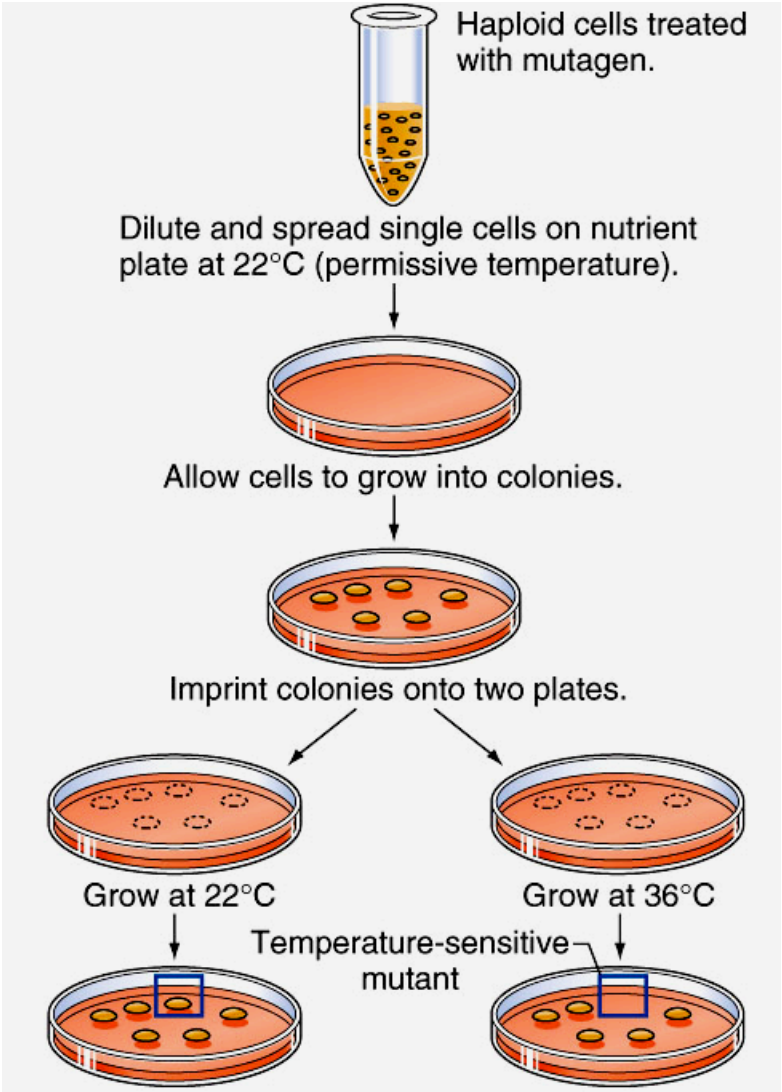


The cell cycle has four phases:

G_1, S G_2, and M

Fig. 18.2

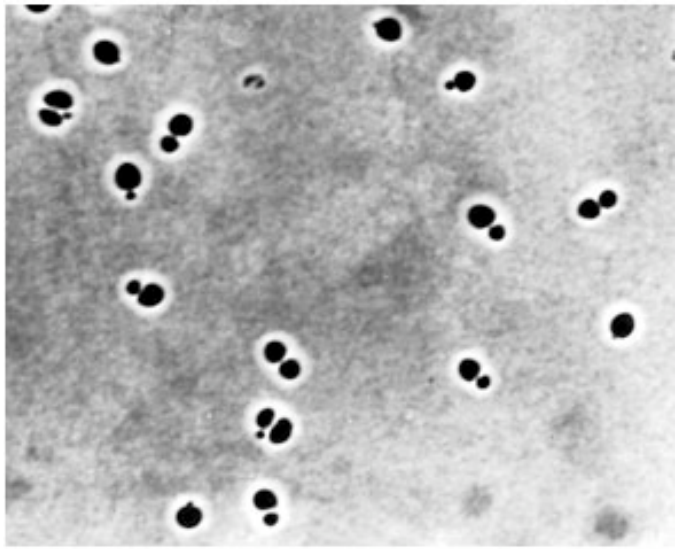
Isolation of temperature-sensitive mutants in yeast



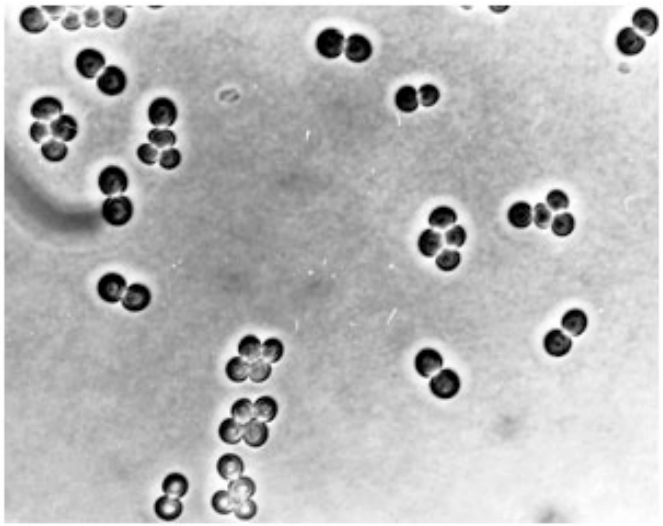
- Mutants grow normally at permissive temperature
- Mutants loses gene function at restrictive temperature
- Thousands of cell cycle mutants have been identified

Fig. 18.3

A cell-cycle mutant in yeast



(a)



(b)

- (a) growth at permissive temperature displays buds of all sizes
- (b) growth at restrictive temperature shows cells have finished first cell cycle and arrested in the second

Fig. 18.4

70 cell-cycle genes identified through temperature-sensitive mutation screens

TABLE 18.1 Some of the Cell-Cycle Genes in Which Mutations Contribute to Cancer

Genes	Gene Products and Their Function
CDKs	Enzymes known as cyclin-dependent protein kinases that control the activity of other proteins by phosphorylating them
CDC28	A CDK discovered in the yeast *Saccharomyces cerevisiae* that controls several steps in the *S. cerevisiae* cell cycle
CDC2	A CDK discovered in the yeast *Schizosaccharomyces pombe* that controls several steps in the *S. pombe* cell cycle; also the designation for a particular CDK in mammalian cells
CDK4	A CDK of mammalian cells important for the G_1-to-S transition
CDK2	A CDK of mammalian cells important for the G_1-to-S transition
cyclins	Proteins that are necessary for and influence the activity of CDKs
cyclinD	A cyclin of mammalian cells important for the G_1-to-S transition
cyclinE	A cyclin of mammalian cells important for the G_1-to-S transition
cyclinA	A cyclin of mammalian cells important for S phase
cyclinB	A cyclin of mammalian cells important for the G_2-to-M transition
E2F	A transcription factor of mammalian cells important for the G_1-to-S transition
RB	A mammalian protein that inhibits E2F
p21	A protein of mammalian cells that inhibits CDK activity
p16	A protein of mammalian cells that inhibits CDK activity
p53	A transcription factor of mammalian cells that activates transcription of DNA repair genes as well as transcription of *p21*
RAD9	A protein that inhibits the G_2-to-M transition of *S. cerevisiae* in response to DNA damage
E6	A protein of the HPV virus that inhibits p53
E7	A protein of the HPV virus that inhibits Rb

Normal gene product must be produced at a particular stage in cell cycle

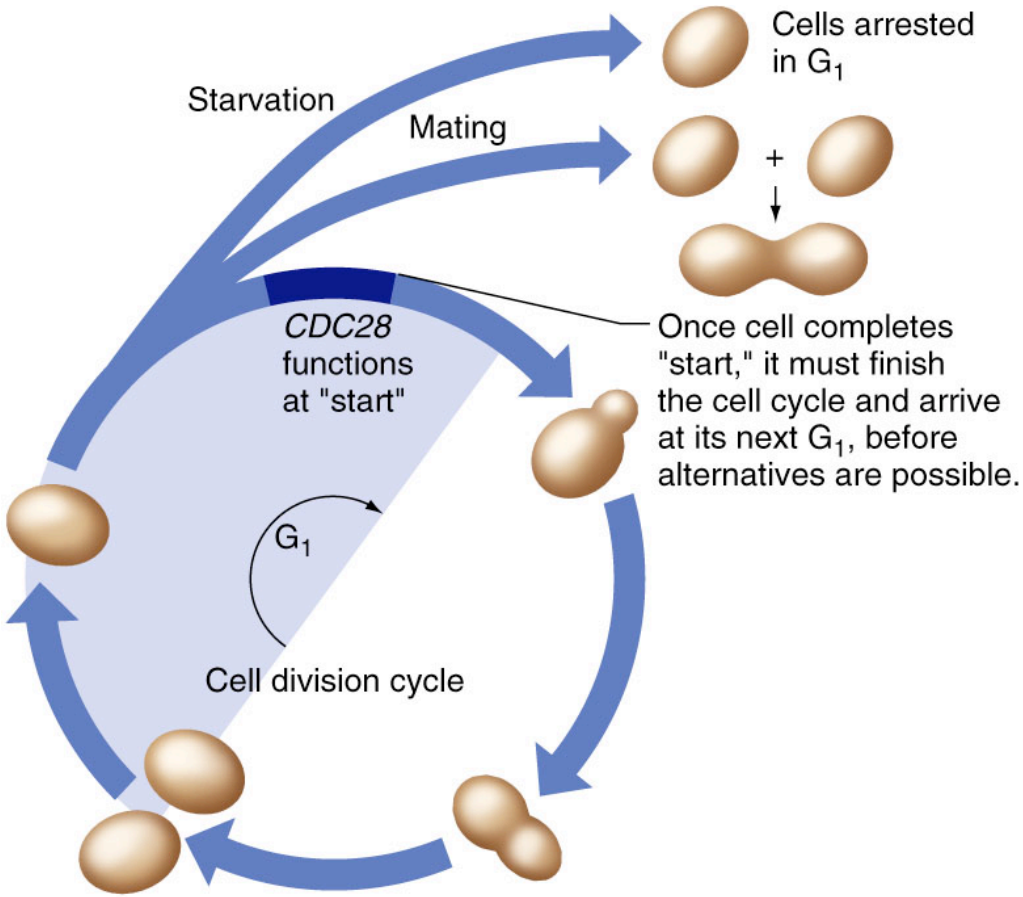


Fig. 18.6

A double mutant reveals which mutation is epistatic to which

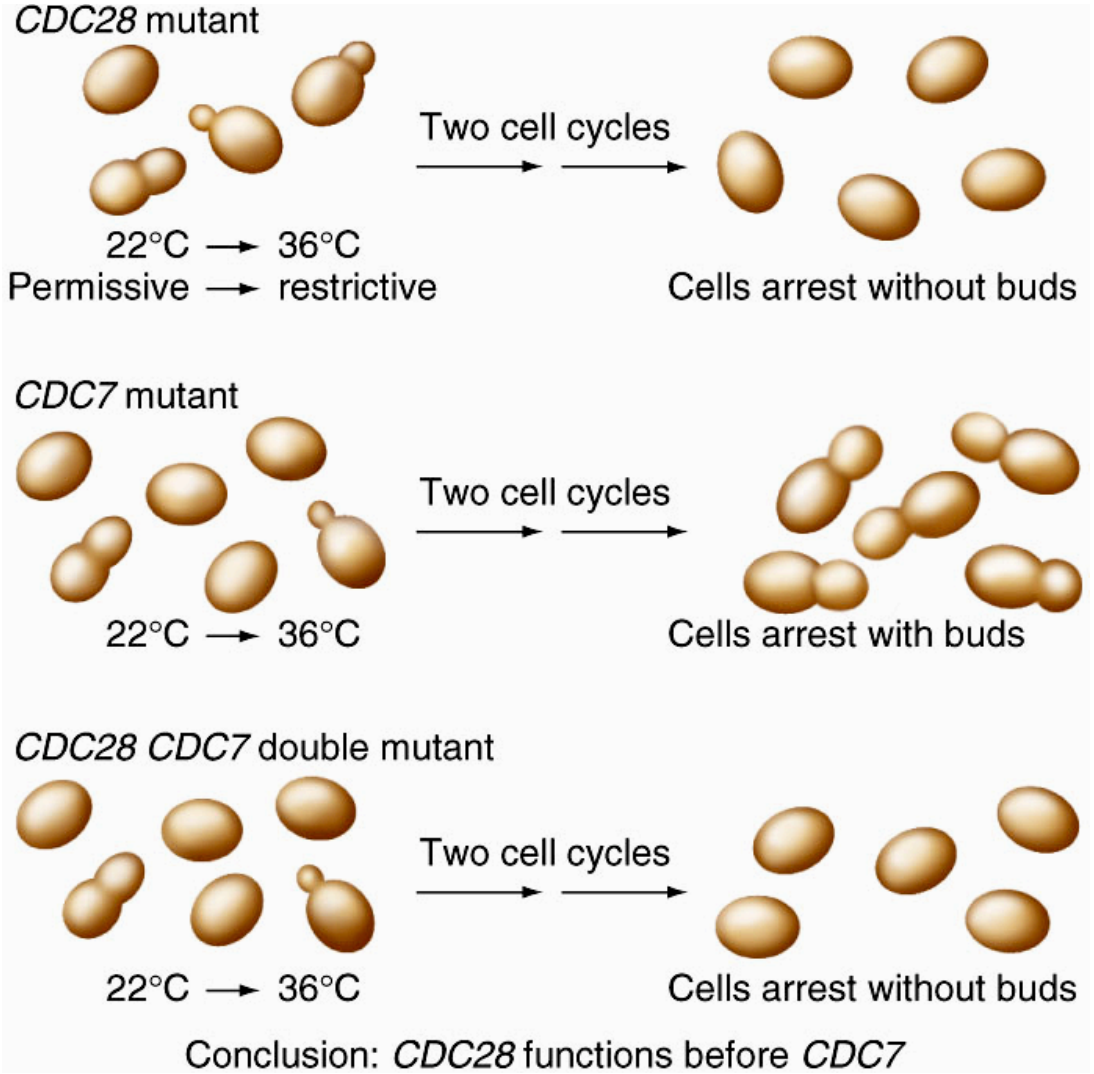


Fig. 18.5

Cyclin-dependent kinases (CDK) control the cell cycle by phosphorylating other proteins

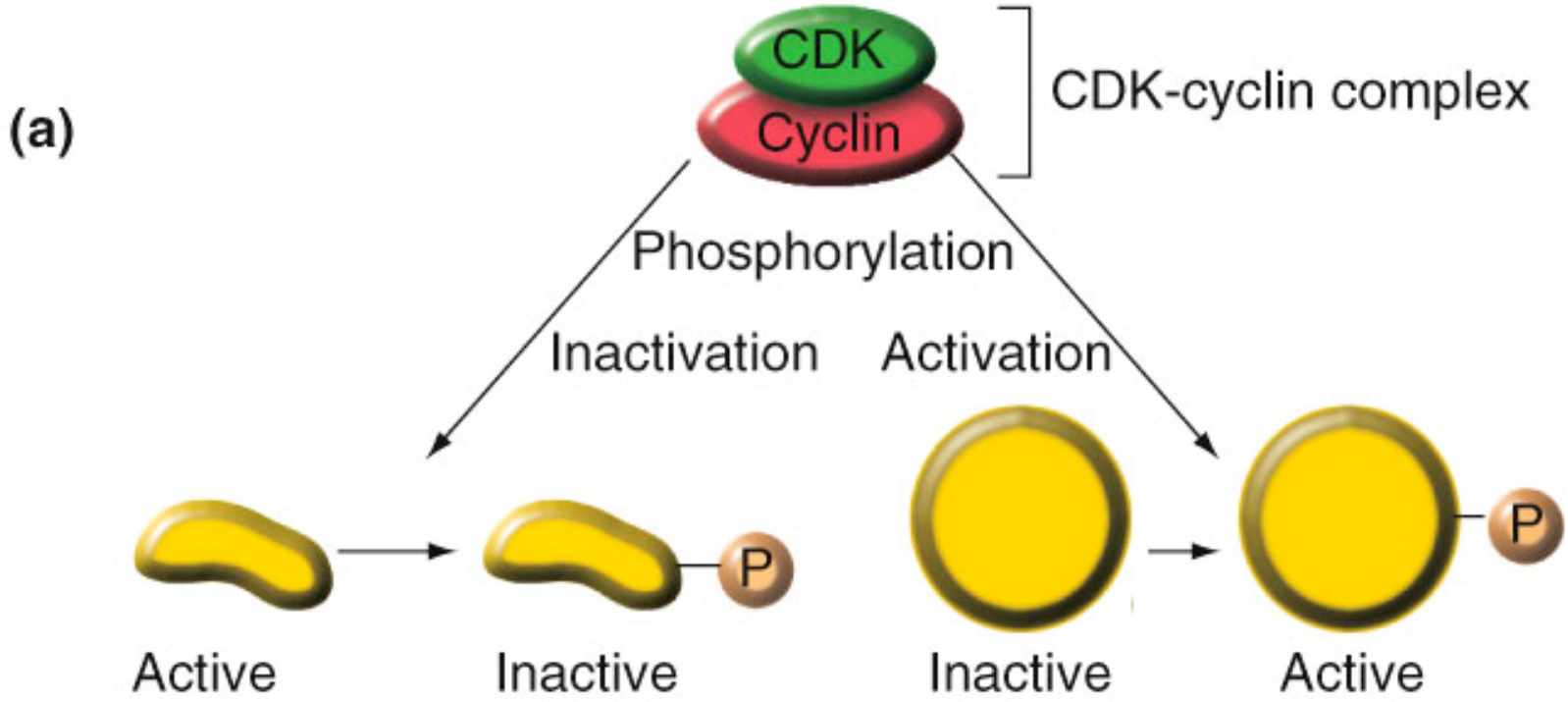


Fig. 18.7a

Nuclear lamins are one of the substrates of CDK

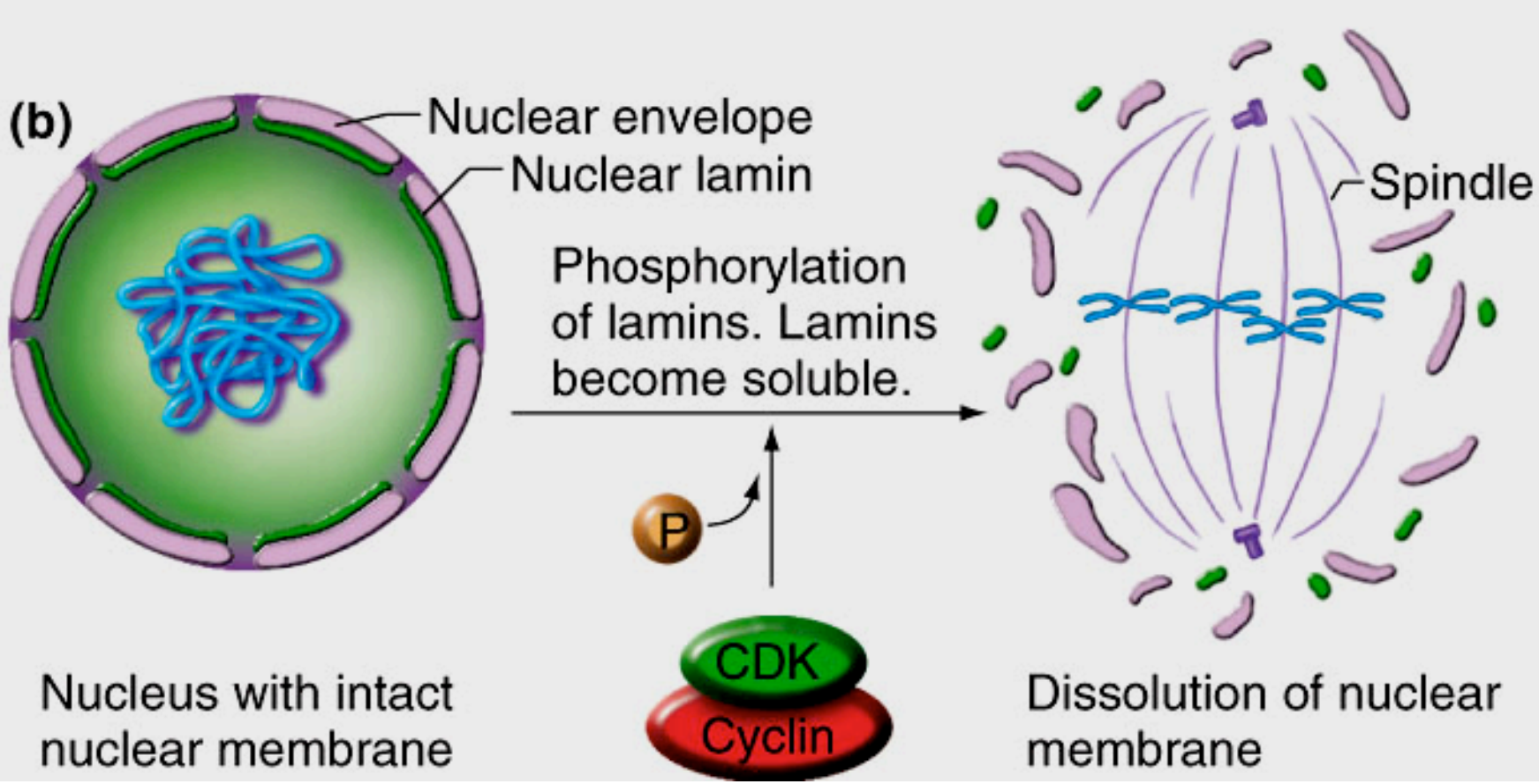


Fig. 18.7b

Human CDKs and cyclins can function in yeast in place of native proteins

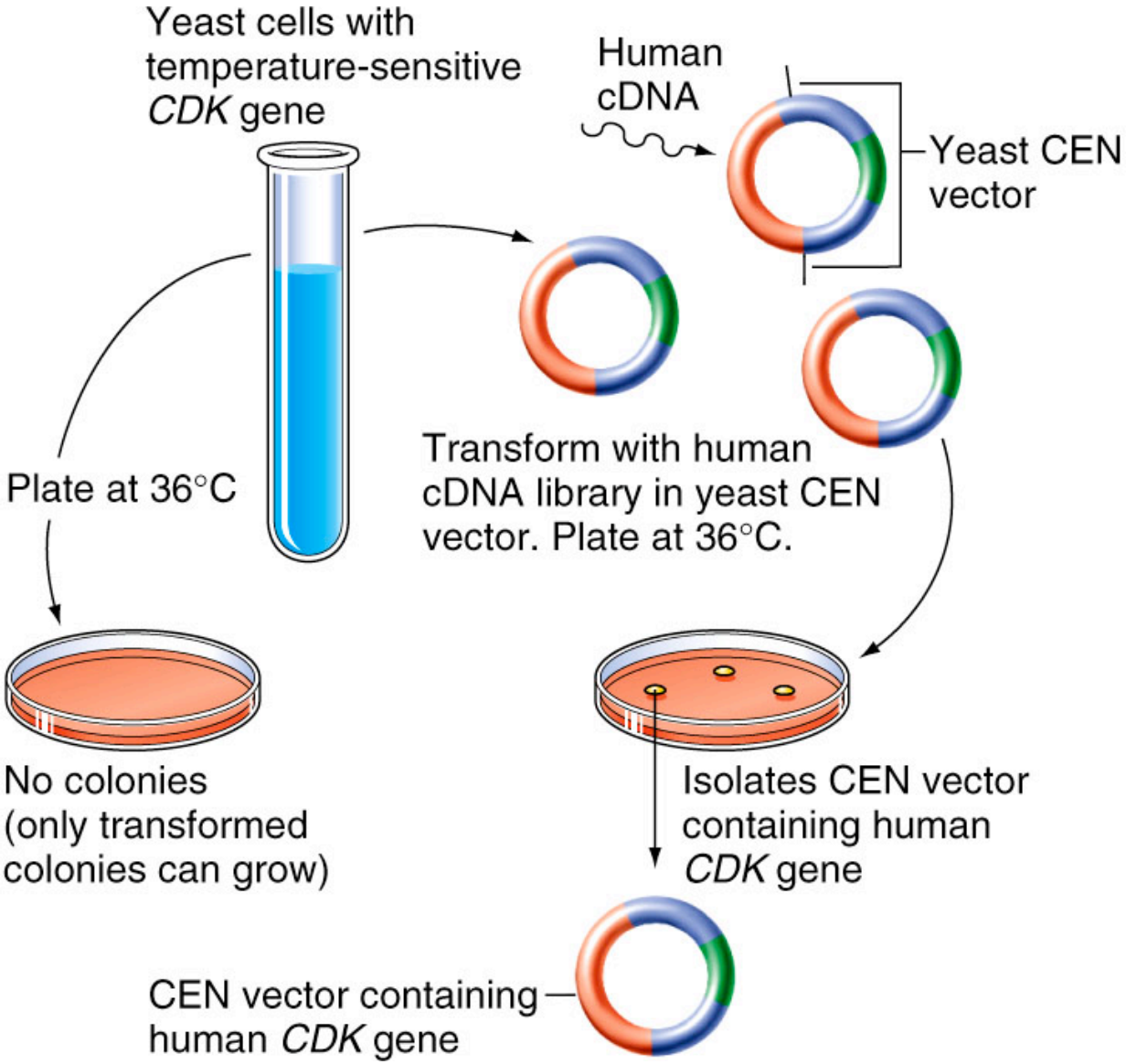


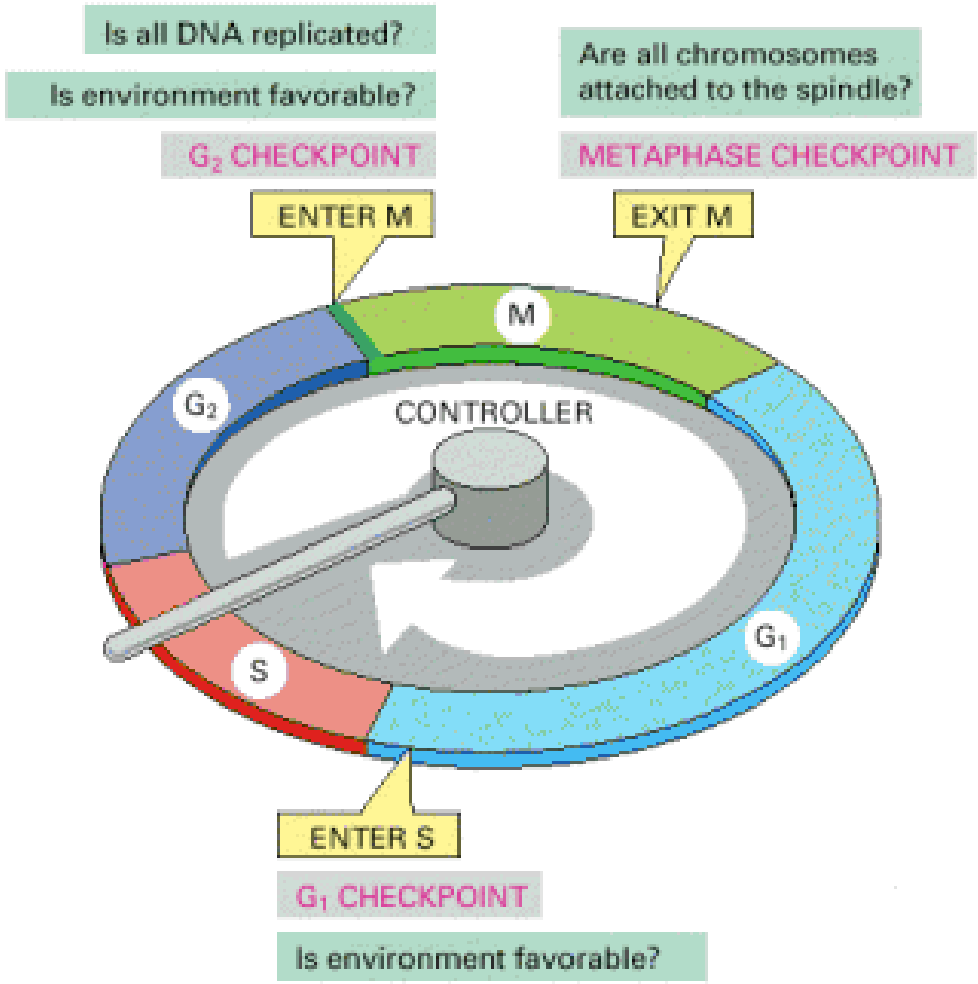
Fig. 18.8

Three cell cycle check points ensure genomic stability

G1 to S (start) check points

G2 to M check points

Metaphase-anaphase check points



CDKs mediate the transition from the G_1-to-S phase in human cells

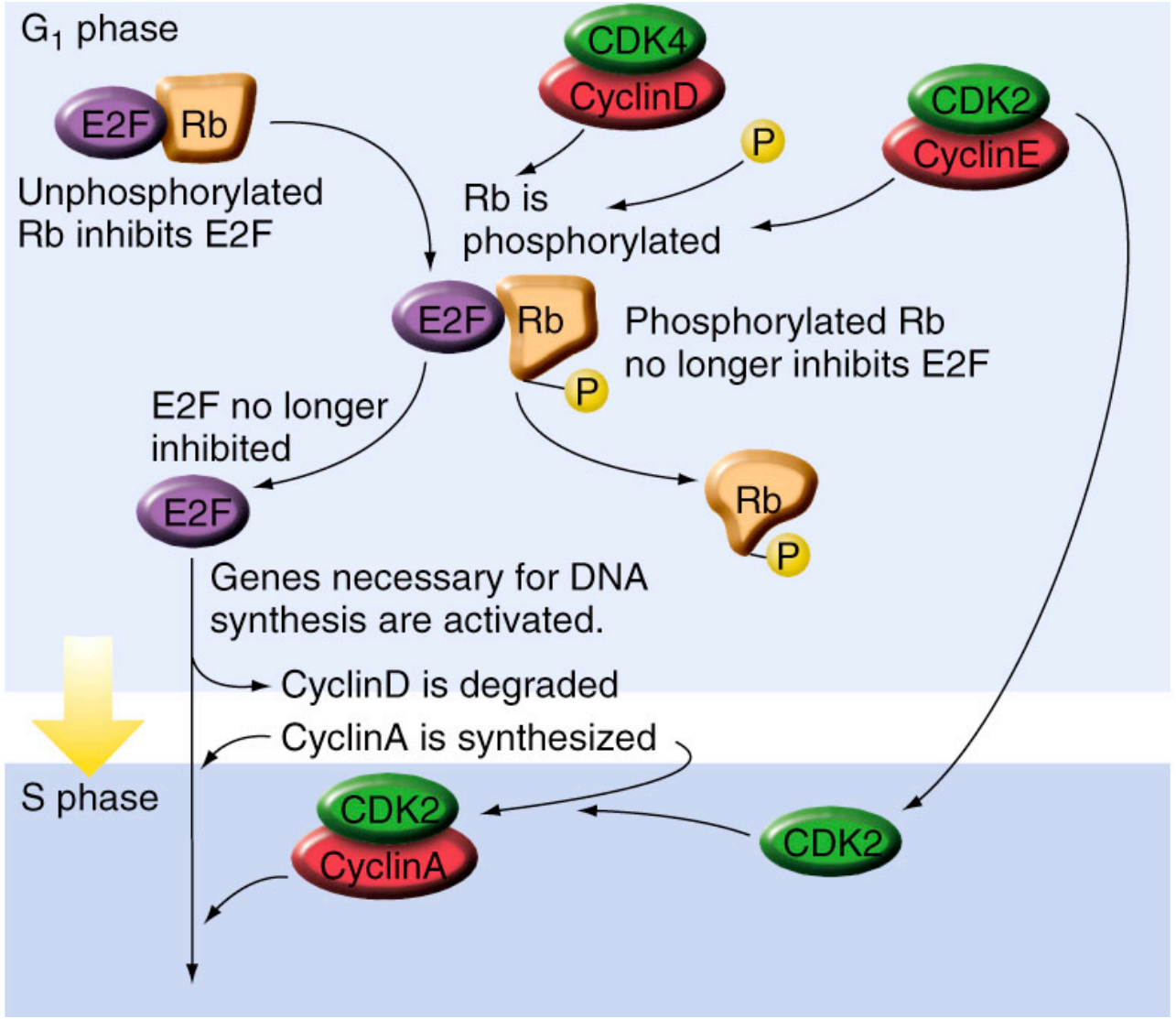
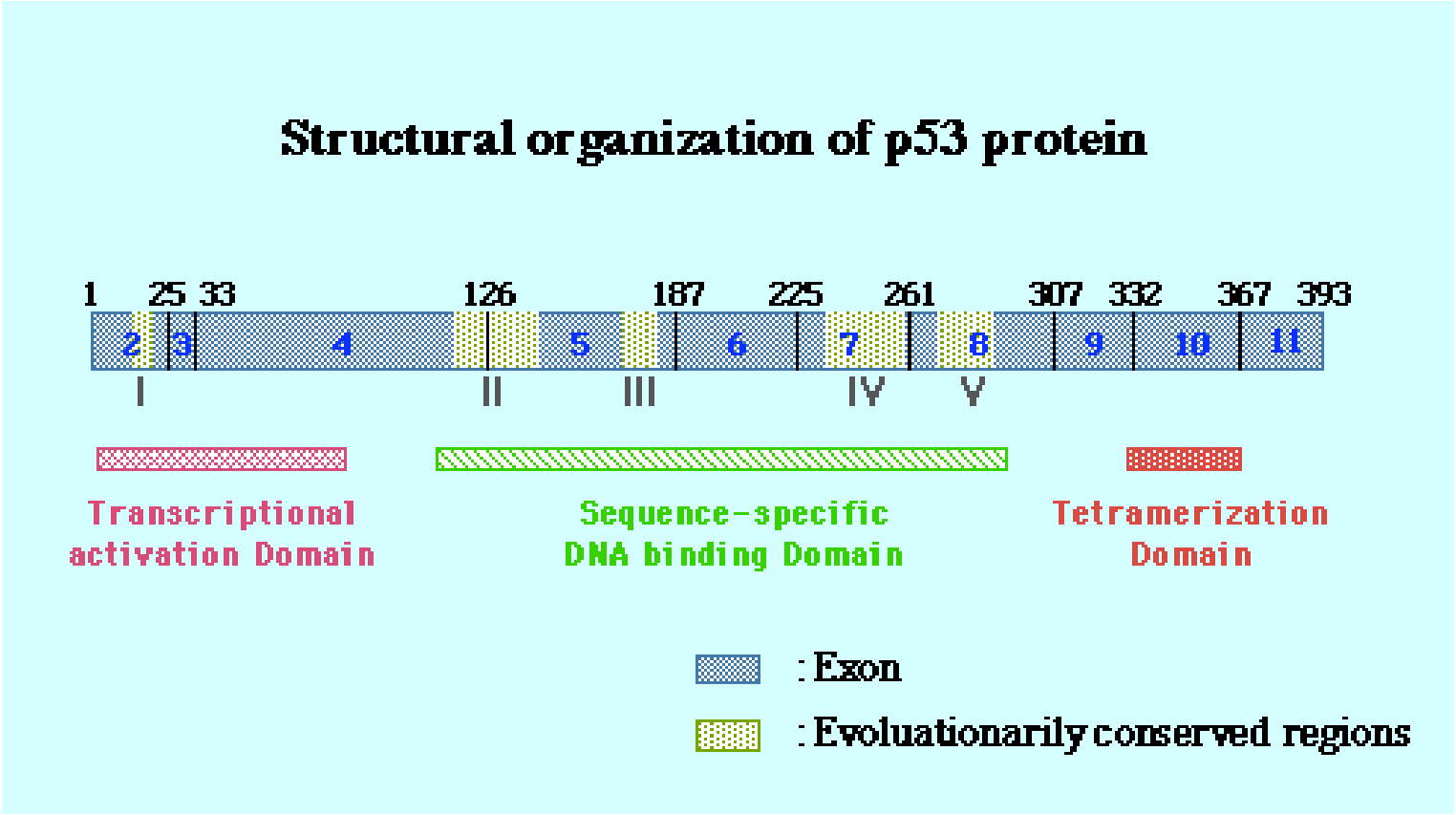


Fig. 18.9

p53: an anti-oncogenic protein



-members of Li-Fraumeni cancer-prone families were shown to carry germ-line p53 mutations.
-mice that are homozygous null for p53 are highly predisposed to tumors.

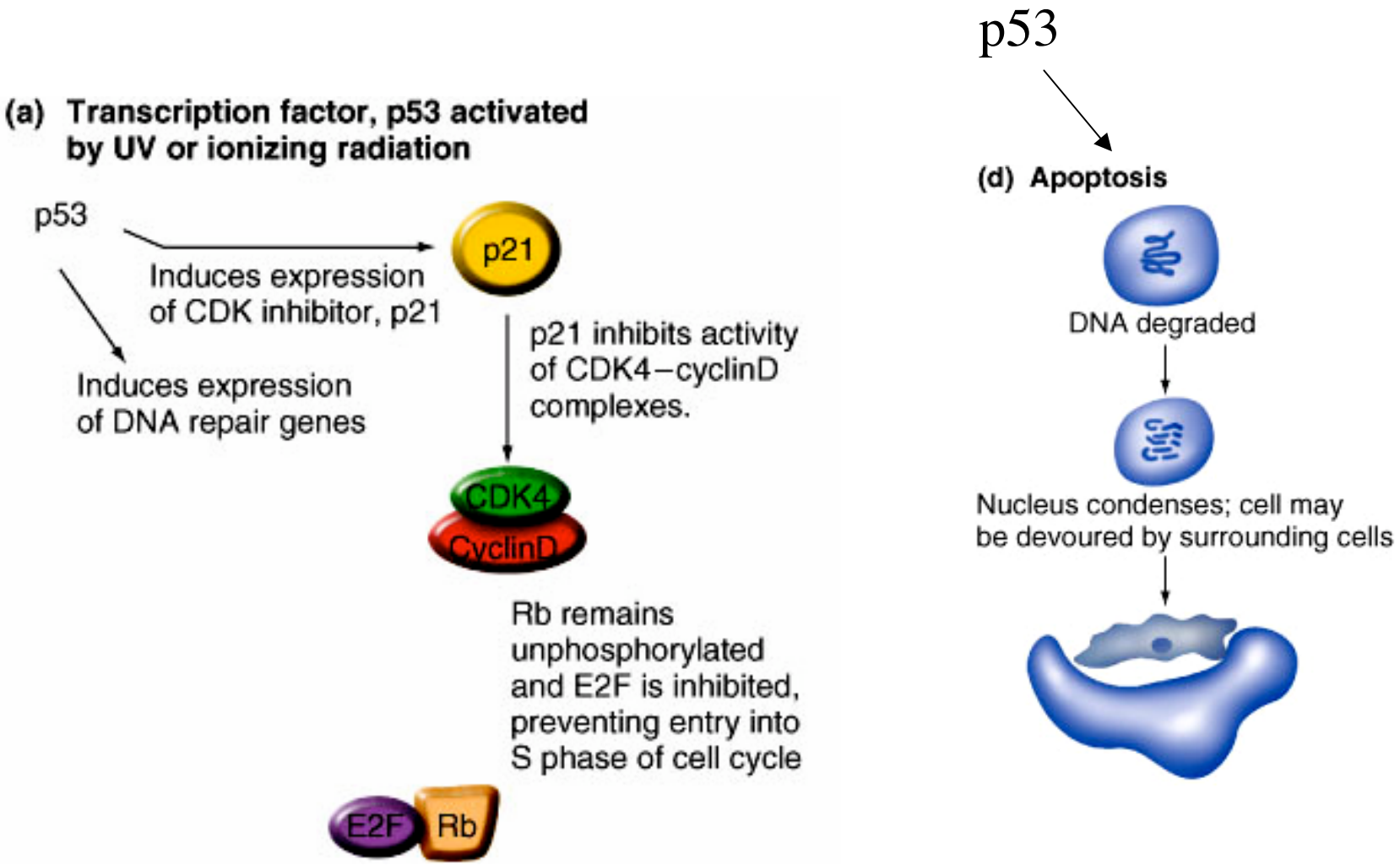

(a) Transcription factor, p53 activated by UV or ionizing radiation
p53
Induces expression of CDK inhibitor, p21
p21
Induces expression of DNA repair genes
p21 inhibits activity of CDK4–cyclinD complexes.
CDK4
CyclinD
Rb remains unphosphorylated and E2F is inhibited, preventing entry into S phase of cell cycle
E2F
Rb
p53
(d) Apoptosis
DNA degraded
Nucleus condenses; cell may be devoured by surrounding cells

Fig. 18.11 a

Over 50% cancer cells contain mutations in p53

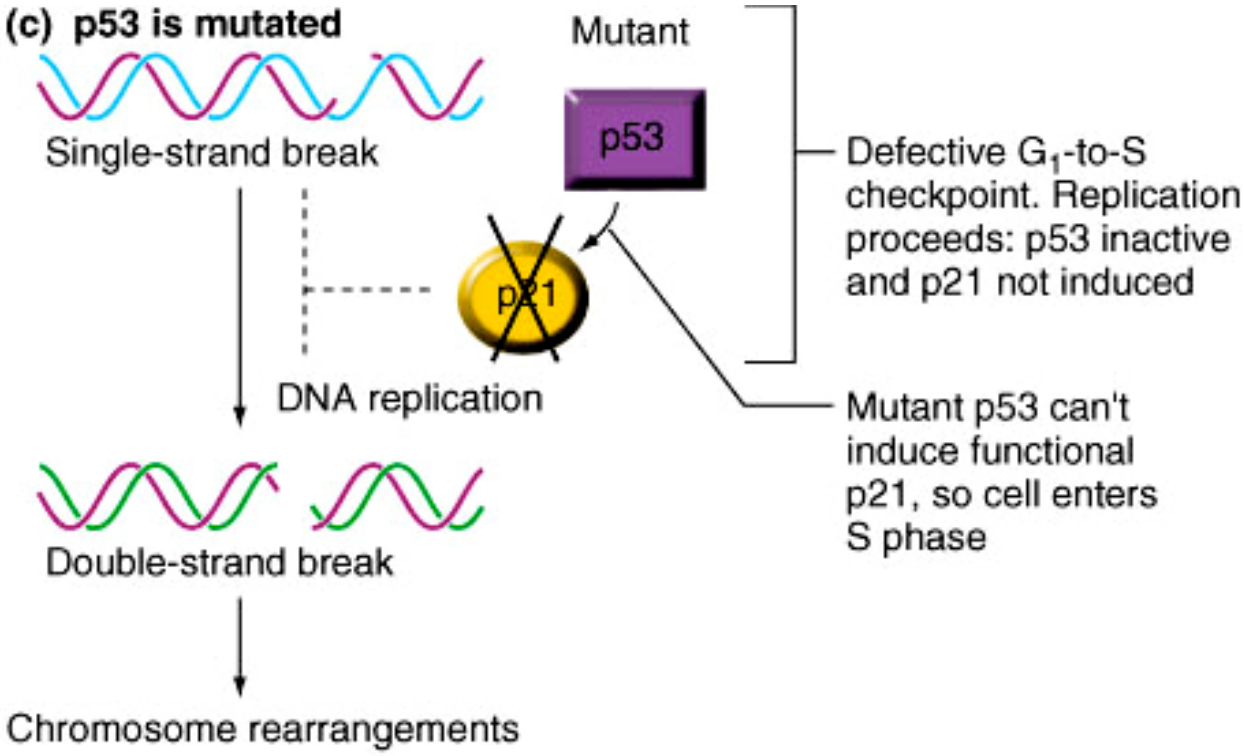


Fig. 18.11 c,d

G2-to-M check points

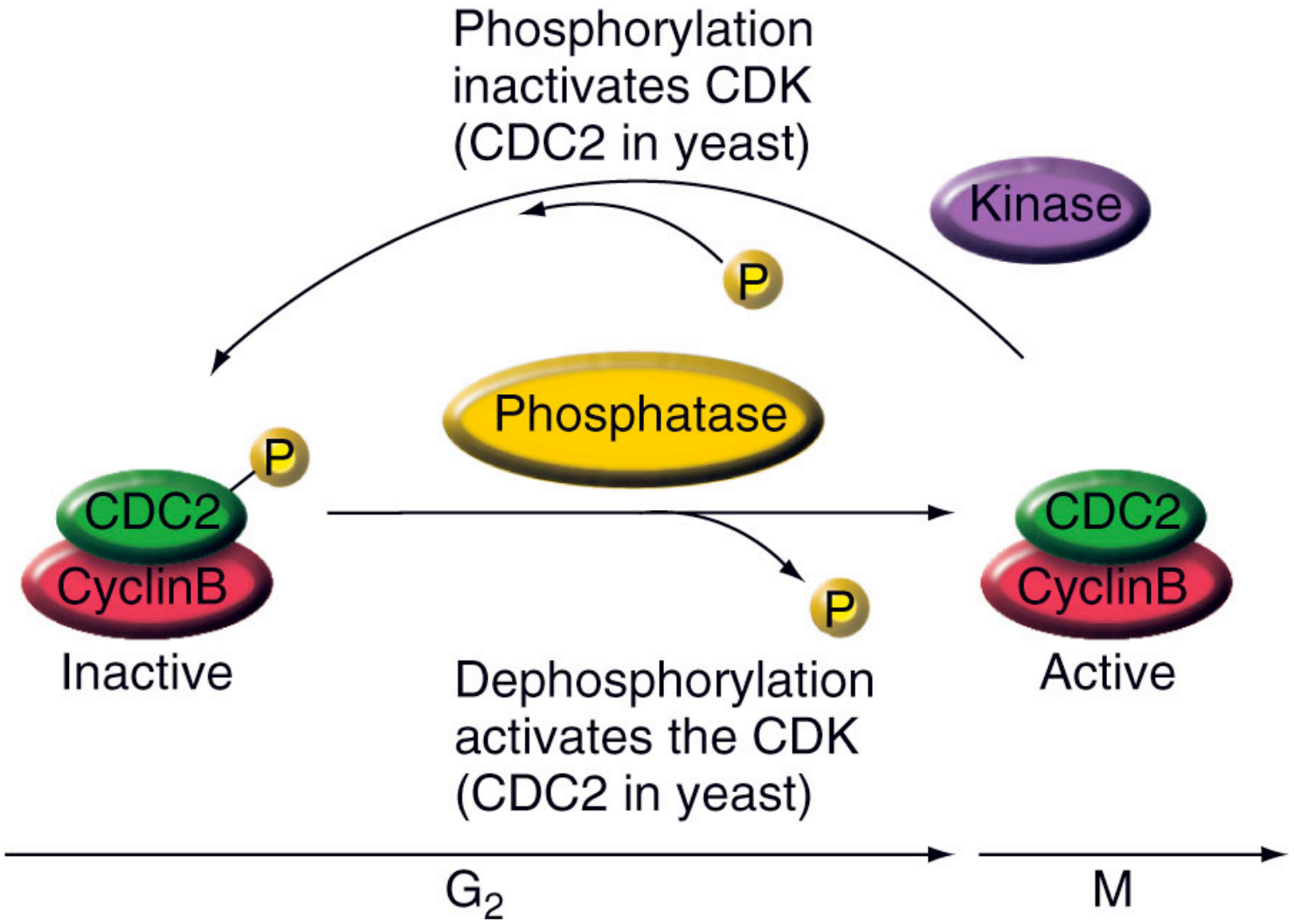


Fig. 18.10

G_2-to-M check points

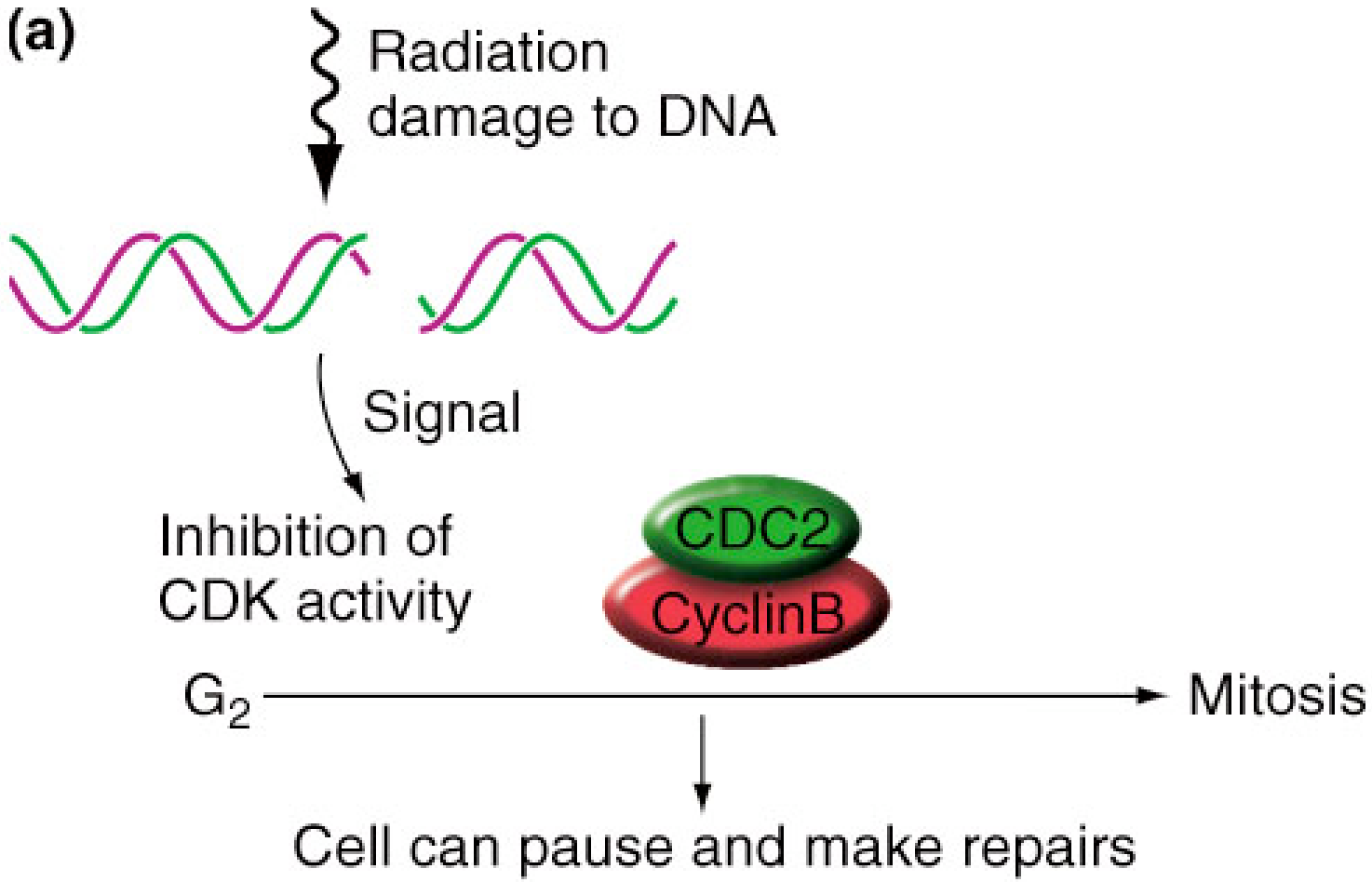


Fig. 18.12a

Metaphase to anaphase checkpoint

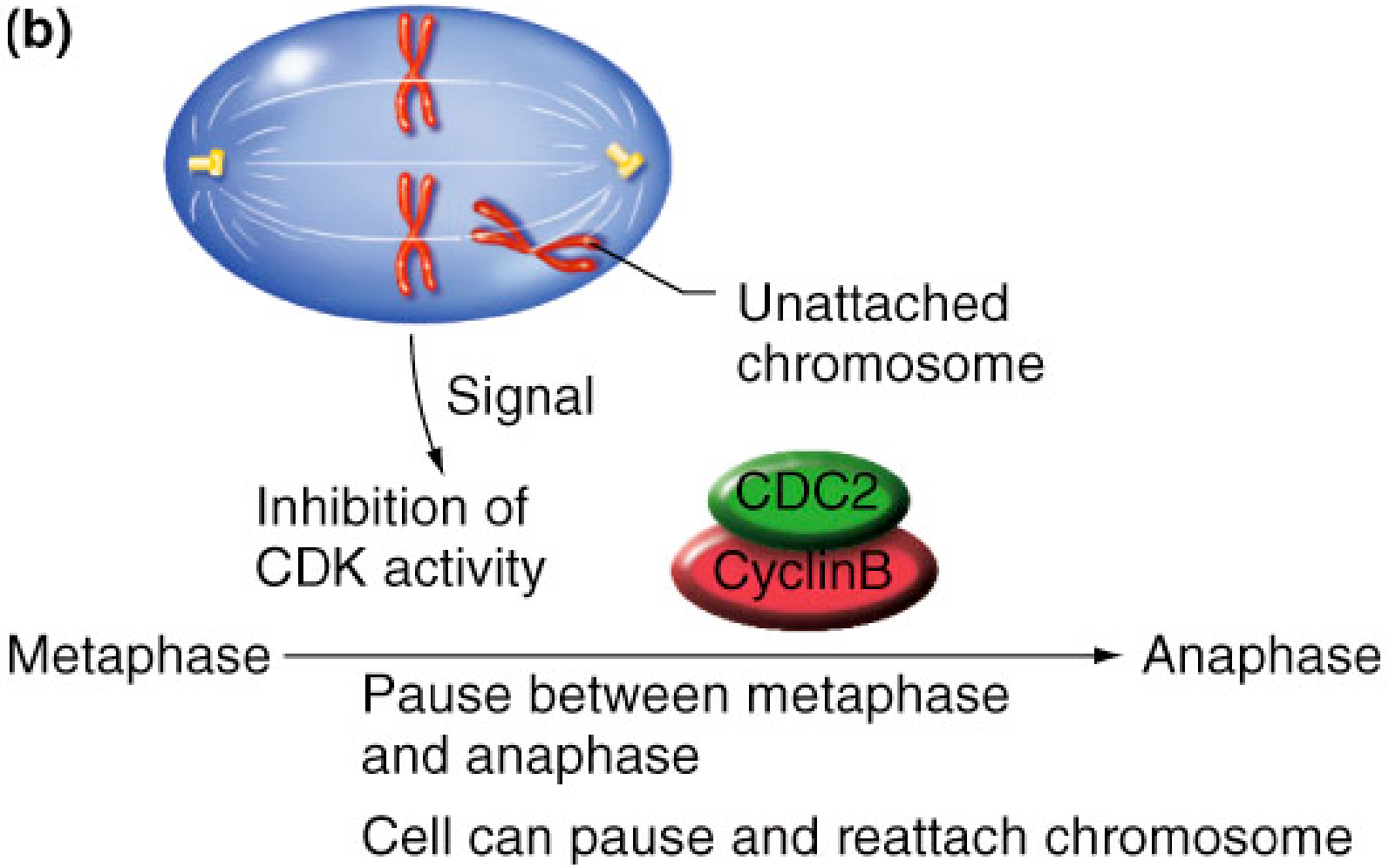


Fig. 18.12b