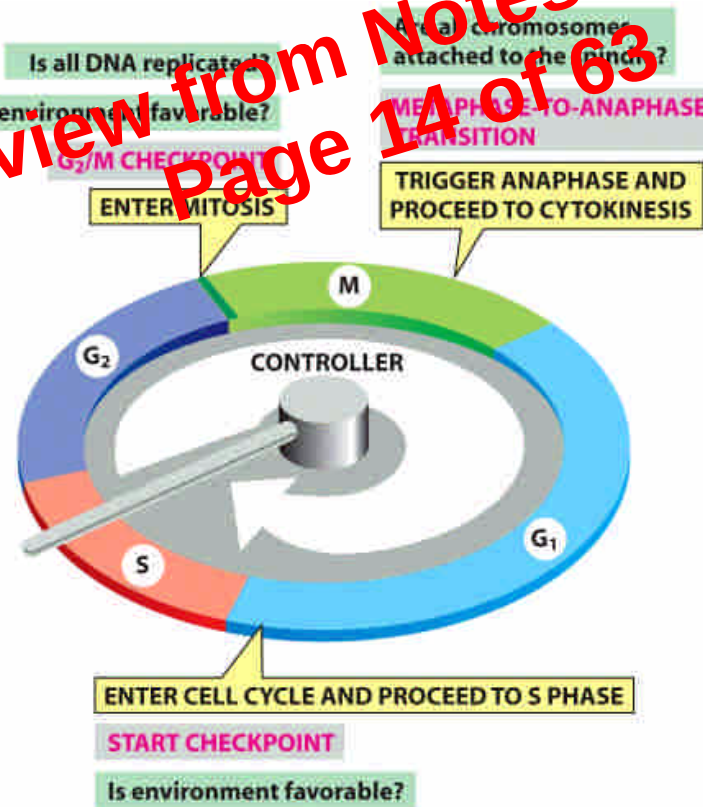


The control of cell cycle

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Operates like a timer that triggers the events in a set sequence

The system of switches is binary (ON/OFF) and launches events in a complete, irreversible fashion

The control system is independent of the events it controls

The system is highly adaptable and can be modified to suit specific cell types

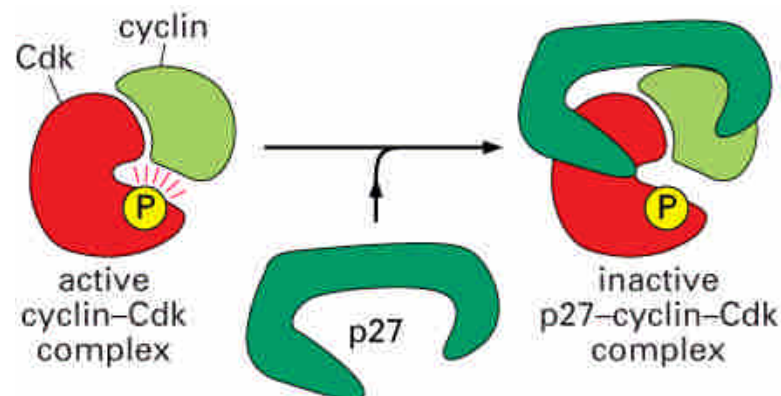
The inhibition of a cyclin-Cdk complex by Cdk inhibitor proteins (CKI)

CKI (Cdk inhibitor proteins):

(during G1) The INK family, p15, p16, p18, and p19 target to CDK4, 6

(during all phases) The CIP/KIP family, p21, p27, and p57 target to most CDKs

Binding of CKI renders Cdk inactive by conformation change and rearranged structure of active site



Initiation of S phase in animal cells

In G₁, cells are in a state of Hct-1 activation, accumulation of a CKI, and inhibition of cyclin gene expression (M-cyclin)

In late G₁, activation of G₁S-Cdk reverses the inhibitory state of G₁

G₁S-Cdk and G₁/S-Cdk phosphorylate Rb, an inhibitor of cell cycle progression, and results in release of E2F

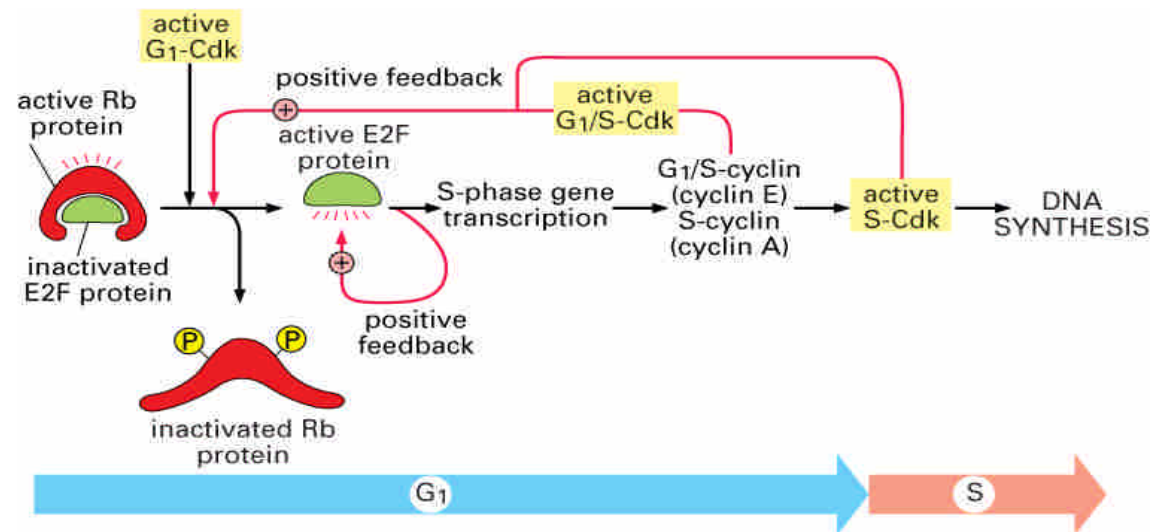
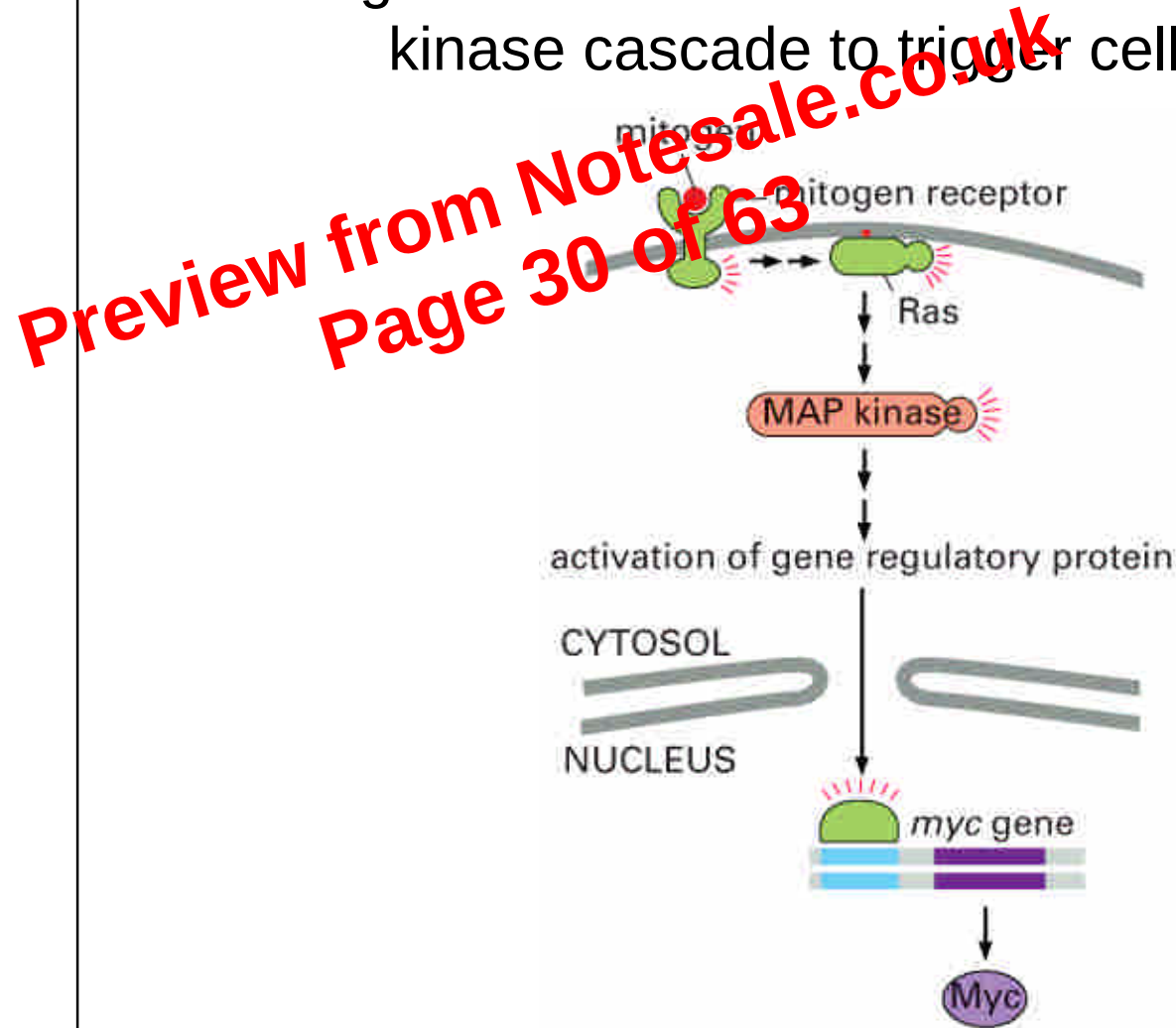


Figure 17-30. Molecular Biology of the Cell, 4th Edition.

Mitogens stimulate activation of Ras and a MAP kinase cascade to trigger cell division



The spindle-attachment checkpoint

Ensure that all chromosomes are properly attached to the spindle before sister chromatid separation occurs

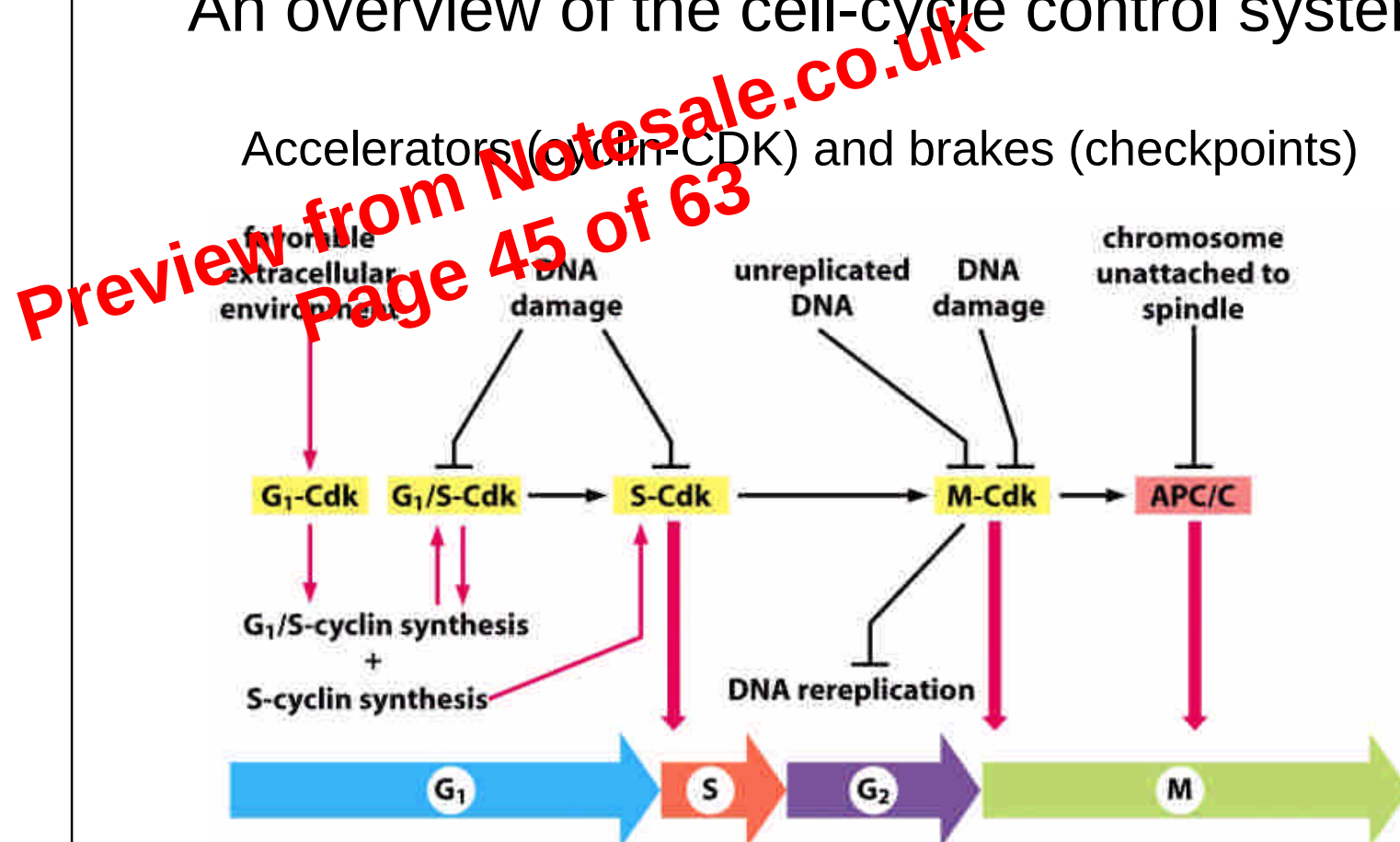
A sensor mechanism monitors the state of the kinetochore, the specialized region of the chromosome that attaches to microtubules of the spindle

Improper attachment of kinetochore to the spindle sends out a negative signal to the cell-cycle control system, blocking Cdc20-APC activation and sister chromatid separation

Several proteins, including Mad2, are recruited to unattached kinetochores. Mad2 binding results in inhibition of Cdc20-APC and blocking securin destruction

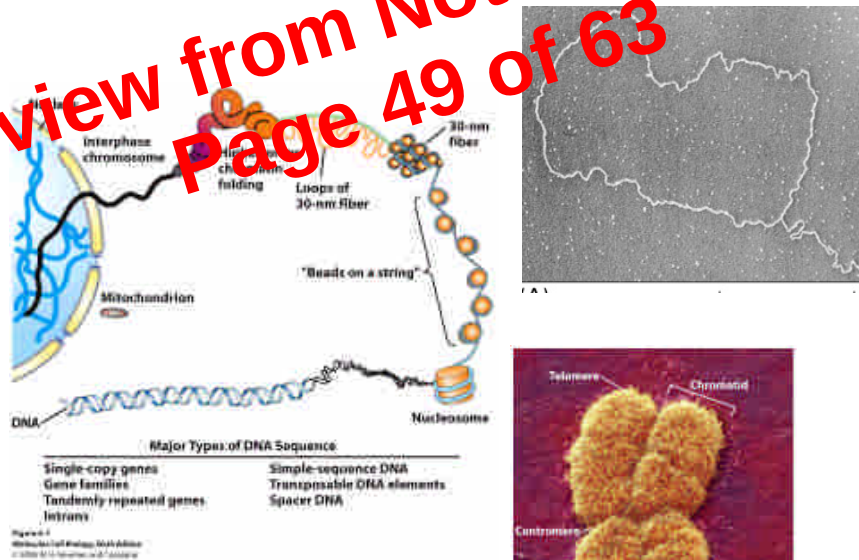
An overview of the cell-cycle control system

Accelerators (cyclin-CDK) and brakes (checkpoints)

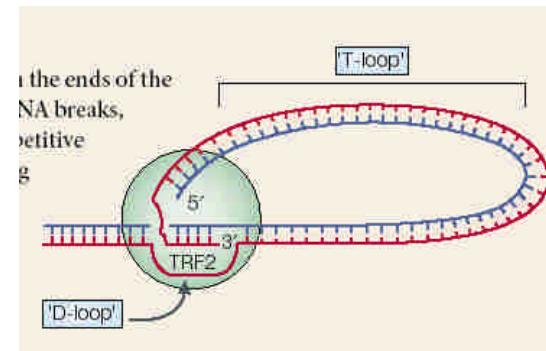


Telomere

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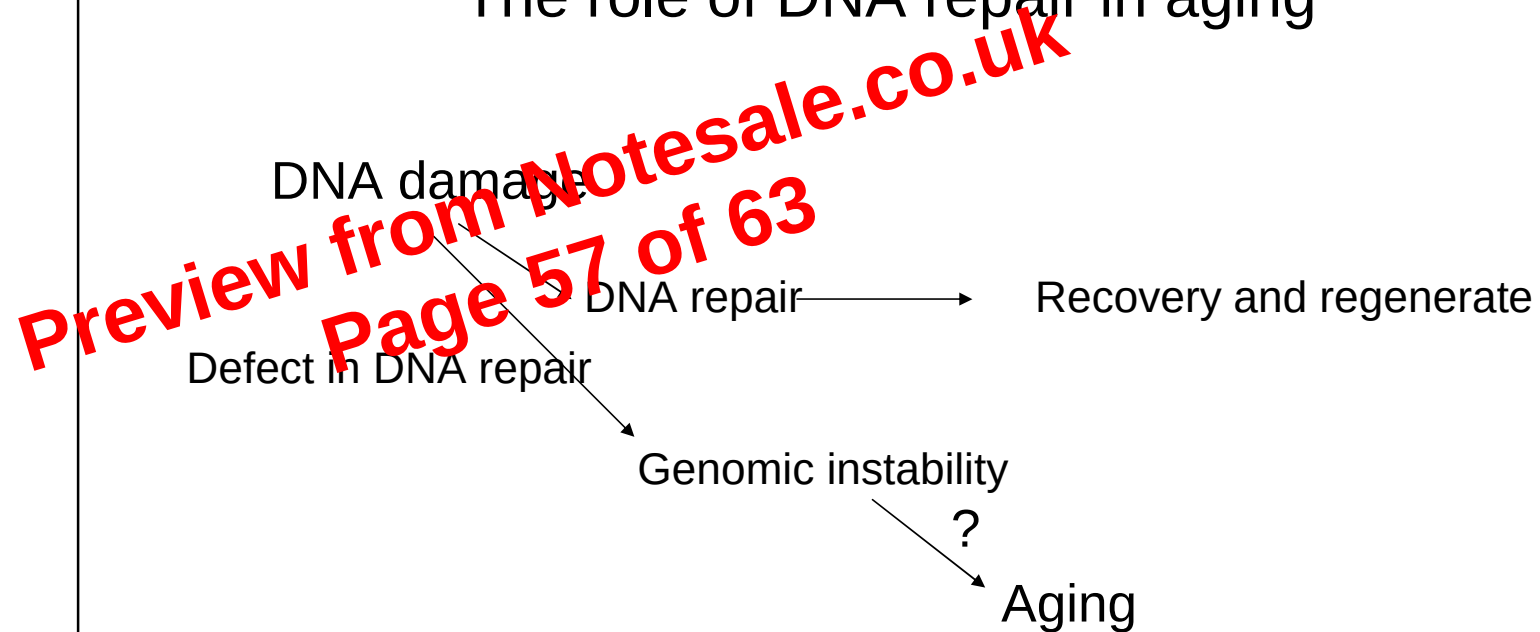
Molecular Cell Biology, 6th edition



Nature Reviews Cancer 1:203, 2001

GGGTTA repeats (near thousands) in human's telomere 49

The role of DNA repair in aging



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Genomic instability increased not only in aging cells but also in most cancer cells

Excessive oncogenic induction can result in cell-cycle arrest or apoptosis

