#### Chapter 14: Cellular Reproduction Review

#### Role of protein kinases

Entry into M-phase initiated by protein kinase "maturation promoting factor" (MPF)

- Kinase activity dependent on cyclin levels (cytoplasmic components)
- Discovered with progesterone stimulation of first meiotic division (germinal vesicle breakdown is maturation)

MPF has two subunits: Catalytic (kinase) and regulatory units (cyclin)

- Catalytic subunit CDC2 required for entry into M-phase phosphorylating lamin proteins
- CDC2 also present in G<sub>s</sub>/S phase which phosphorylates ORC

#### Regulation of Cdks

a) Cyclin concentration

Differential transcription of cyclins at stages of cell cycle

#### b) Controlled proteolysis

Cyclin concentration regulated by controlled synthesis and degradation

- SCF (G<sub>1</sub> cyclin) and APC (Mitotic cyclin) complexes link cyclins to polyubiquitin chain and tags with degradation signal
- c) Cdk phosphorylation state

Kinases CAK (phosphorylates Thr161) and Wee1 (phosphorylates Tyr15)

- Wee1 phosphorylation renders Cdk inactive therefore cannot enter into mitosis
- Cdc25 phosphatase removes Tyr15 phosphate and reactivates CDC2 kinase
- Wee1 mutant enters mitosis prematurely
- Cdc25 mutant causes cell to continue to grow without dividing

#### Cyclins and Cdks

G, Phase Cyclin D + Cdk4 & Cdk6

- Activates pRB which increases transcription of Cyclins E & A
- Cyclins E + Cdk2 initiates G<sub>1</sub> to S-phase

S-Phase Cyclin A + Cdk2

- Cyclin B/A + Cdk1 initiates G<sub>2</sub> to M-phase
- Cdk1 absolutely required for development

Subcellular localization of Cyclin B<sub>1</sub>

Cyclin B<sub>1</sub> accumulates in the nucleus just prior to mitosis

Phosphorylation of nuclear export signal (NES) stops export from nucleus

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**Douglas F. Paulsen** 

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