

• **checkpoints**: cells arrested in G<sub>1</sub>, S, G<sub>2</sub> until DNA is error-free.

- restriction point in late G<sub>1</sub> is regulated by Growth factors.

• Regulation of cell cycle happens by **dimer**.

- Dimer consist of **cyclins + cyclin dependent-kinase (CDK)**

	Proteins activated during synthesis	activated when dimerized with cyclin
DE [	- cyclin D dimerized with	CDK 4/6 to start the cell cycle.
	- cyclin E dimerized with	CDK 2 to transport cell from G <sub>1</sub> to S.
AAB [	- Cyclin A ↗ ↘	CDK 2 to transport cell from S to G <sub>2</sub> .
	- cyclin A ↖ ↙	CDK 1 } → transport it from G <sub>2</sub> to M ]
	- cyclin B ↗ ↘	

• Example of regulation of cell cycle progression.

- 1 cyclin B dimerize with CDK1 in G<sub>2</sub> → CDK1 is phosphorylated <sup>بغير فسفات</sup> CDC 25 dephosphorylate it to become active. <sup>بغير فسفات</sup> <sup>2 @ بنجیل</sup> CDK1 <sup>1 @</sup>
- 2 CDK1 phosphorylate different protein that entry the cell to M phase.

• Stopped of complex working due to degradation of cyclin B

• Dephosphorylation for CDK1 make it Active.

• CDC25 dephosphorylate.  
• when Kinase is active it can phosphorylate proteins

• active CD kinase → cell division occur.  
بالذات يكون اياهم يكون اوليا active → في طين انقسامات و بدنا اني يتكاثر

• **CDK inhibitors** (mutation in these inhibitors causes cancer).

- Ink 4 family: p15, p16, p18, p19 (inhibit cdk 4/6).
- Cip/Kip family: p21, p27, p57 (inhibit Cdk 2).

• Cell signaling and cell cycle.

- Growth factors → restriction point → synthesis of cyclin D → Division occur.  
to start cell cycle.

• Retinoblastom protein comes from tumor suppressor gene

- dephosphorylated RB binds to E2F repressing transcription gene as cyclin E (no cyclin E, no division).

(by CDK 4/6)

- phosphorylated RB keeps E2F free → complete the division.

• Activation of Cdk 2

- its inhibitor P27 (activated CDK2 (kinase) phosphorylate P27 to degrad it).

• ATR and ATM (2 protein kinase).

- Normal DNA → adding P for CDC 25 → dephosphorylate CDK1 make it active → division.

- DNA damage → ATM kinase phosphorylate P53 → activate p21 → arrest cell cycle (allow repair)  
CDK inhibitor