Growth Strategies:

- **Growth coupled Division:** cell division where the daughter cells are the same size as the 'adult' cell.
- **post-mitotic growth:** the cell is not dividing but still continuing to get larger. (ex: neuron)
- **Growth by accretion:** cells ~~absorb~~ secrete matrix that absorbs water and forms protective gel. (ex: cartilage)

What are the most downstream drivers of the cell cycle?
→ Cyclin/CDK's

Nutrition, Hormone, Gradients → Act on cyclin/CDK's to affect growth

Cyclin/CDK in G1 ~~trigger~~ that phosphorylate proteins to trigger entry (into the S phase ~~synthesize~~ DNA)
→ which proteins are downstream targets?
→ things that synthesize nucleotides
→ activator of DNA polymerase
→ markers of origin of DNA that recruits polymerase and helicase:
ORCs
Origin recognition complexes.
→ co-operate with MCMs (mini chromosome maintainence protein)

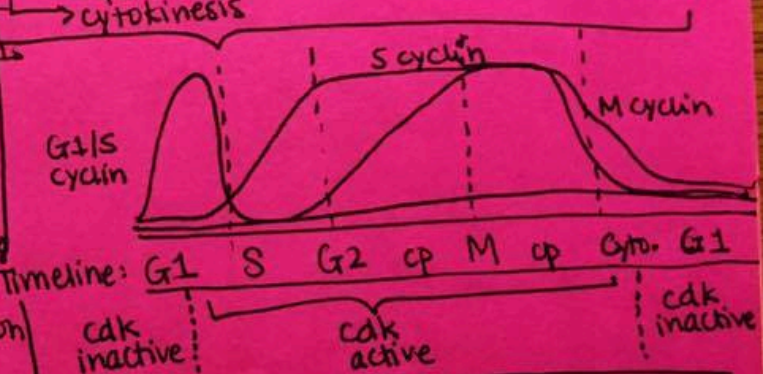
their binding controlled by cyclin CDK → targets of G1/S cyclin/CDK

CYCLIN/CDK KINASE COMPLEXES DRIVE THE CELL CYCLE

→ what are cyclin/CDK's?
→ complexes made of both proteins
→ cyclin
→ CDK → cyclin dependant kinase → phosphorylate proteins.

→ cell cycle phases refresher:
→ G1: Gap phase 1: chromosome from mama & papa
→ S phase: duplicate the chromosomes
→ G2: Gap phase 2:
→ checkpoint: all duplicated properly?
→ M phase: mitosis: micro tubules and spindle formed, separated chromo.
→ checkpoint: separation ok?
→ cytokinesis

cell cycle for xenopus: 20 min
fibroblast: 16 hrs.



→ this happens in oscillations:
An oscillator needs → periodicity, Amplitude

- depending on cell type and organism, periodicity varies.
- we have different cyclins.
  - → G1/S cyclins
  - → S cyclin
  - → M cyclin
  - the CDK cannot phosphorylate without cyclin

cyclins oscillate in protein levels.
→ why? control activity of CDK partner at right place and time.

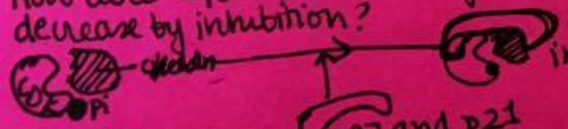
How can we control the cell cycle?

→ control amount of cyclin/CDK → control phosphorylation of downstream proteins → control movement into the next phase of cell cycle.
→ How can we control Amount of Cyclin/CDK?
→ 1. Activation of transcription of CDK/cyclin
→ 2. Binding of activator/repressor for cyclin/CDK
→ 3. Proteolysis
→ 4. Activating phosphorylation
→ 5. Inhibitory phosphorylation.

→ how do they cycle? proteolysis, drop off level. After mitosis: all cyclin levels fall.

What do all oscillators need?
→ Activation
→ Repression
→ Dependancy.

How does cyclin/CDK activity decrease by inhibition?



Active cyclin/CDK complex

p27 and p21 (CDK inhibitor: CKI)
* when conditions aren't right for cell cycle or we need to slow down → then we have ↑ CKI = ↓ CDK/cyclin

p21 is a tumor suppressor. {p57 and p27.

S-phase cyclin: needs to phosphorylate things involved in making ~~histones~~ histones.
→ phosphorylates the HISTONE-LOCUS BODY in the nucleus, which has proteins responsible for making histones.

M-phase cyclins: phosphorylate microtubule motor proteins, nuclear ~~pores~~ (break nuclear membrane)