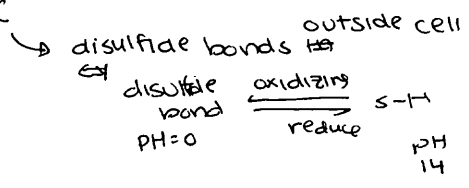
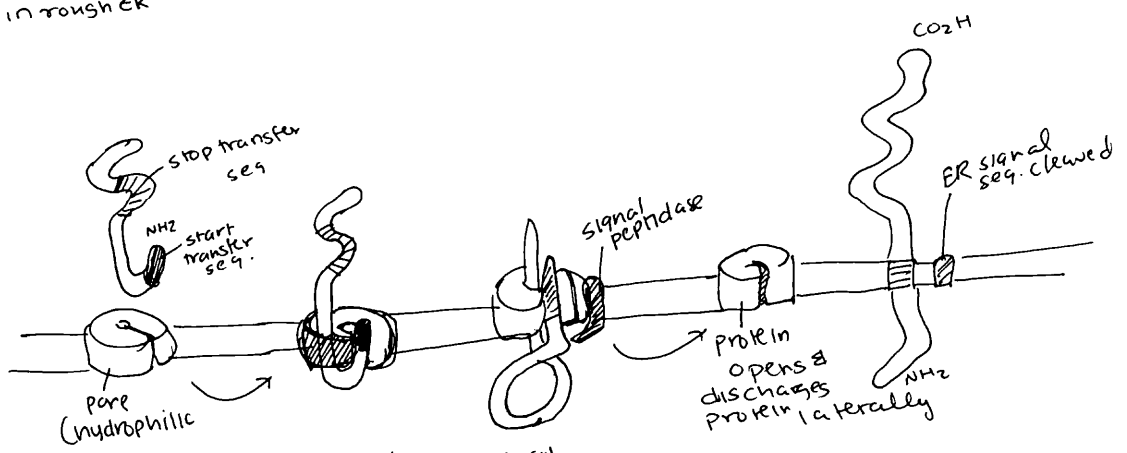
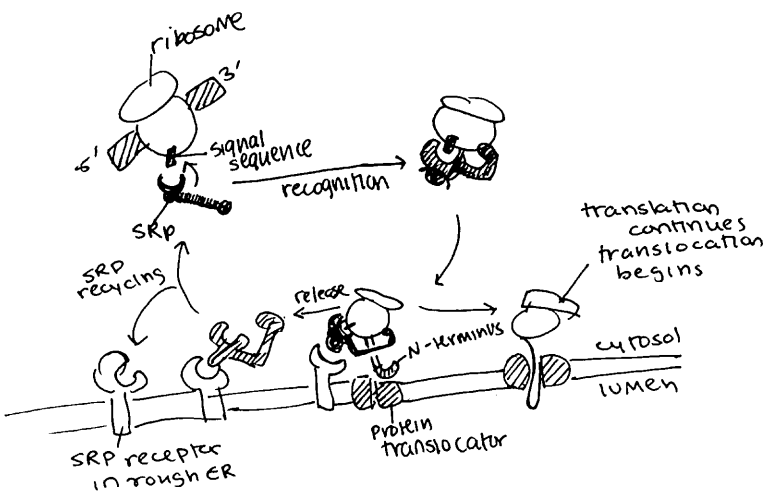


Amino Acids:

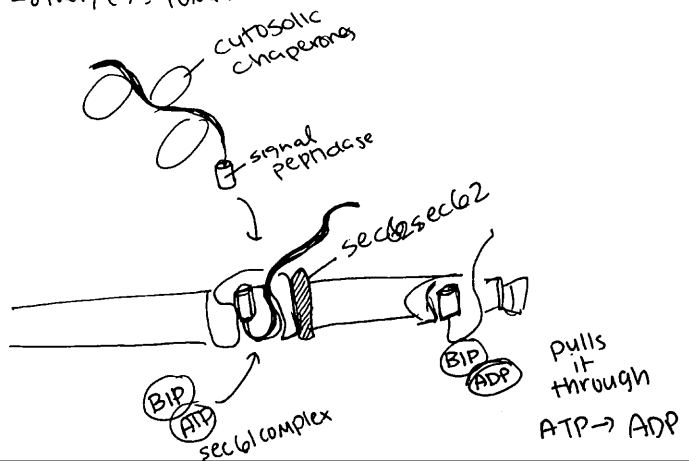
Acid: D, E      Polar : (Amine): N, Q (alcohol): S, Y, T  
Basic: K, R, H      Nonpolar: A, V, L, I, P, F, M, W, G, C



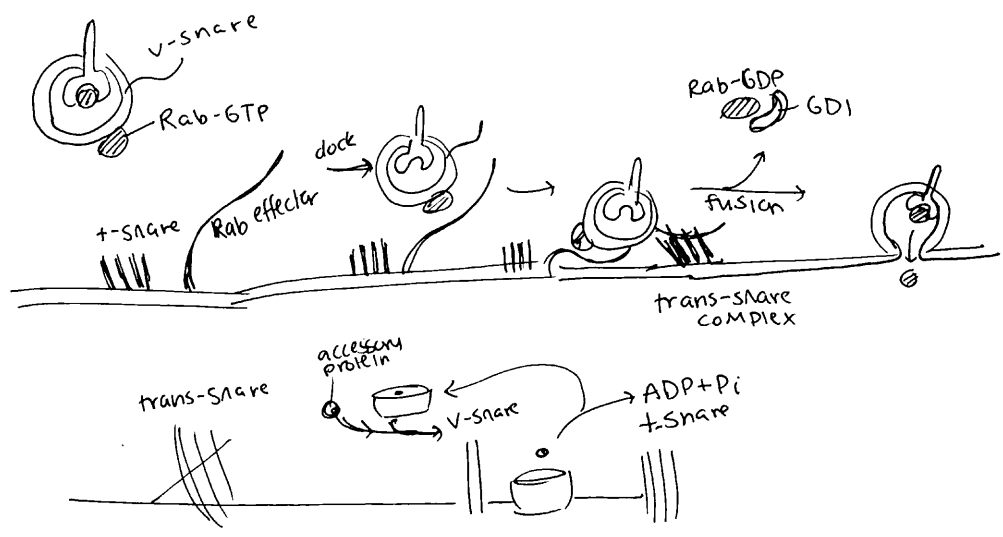
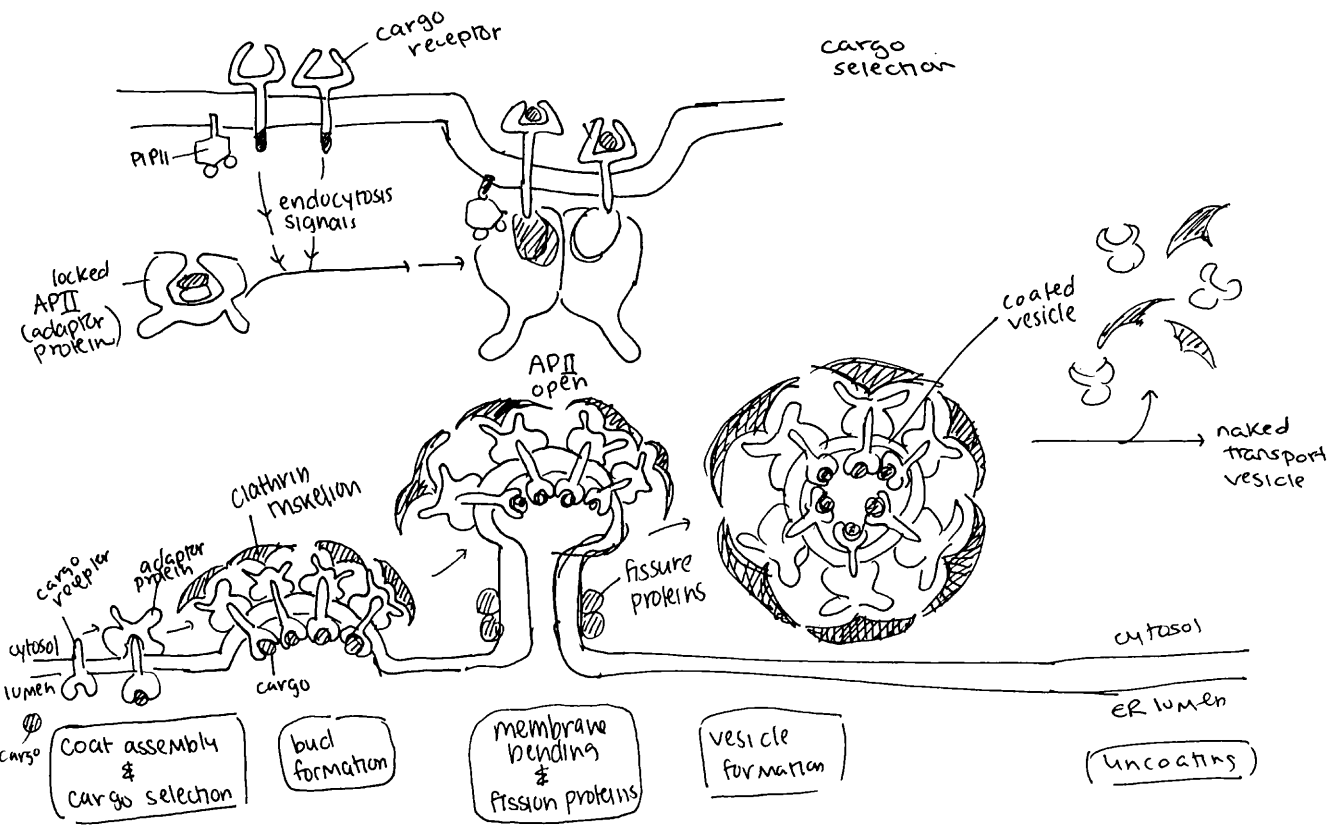
Protein translocation



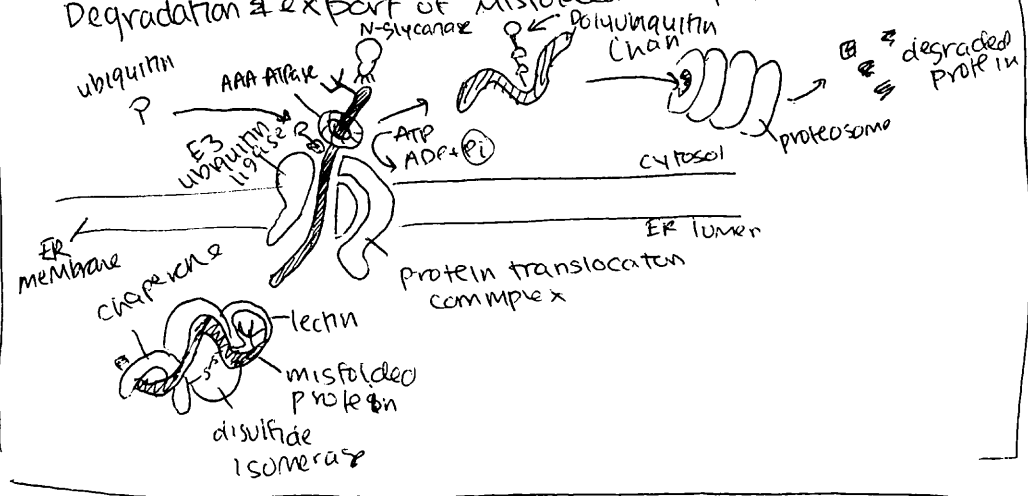
- k-termini w/ (+) flanking start seq = cytosol  
 - other / (-) = lumen



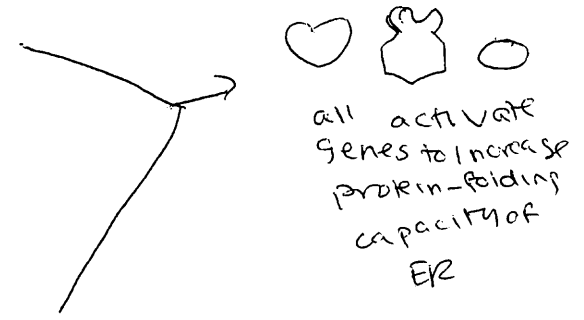
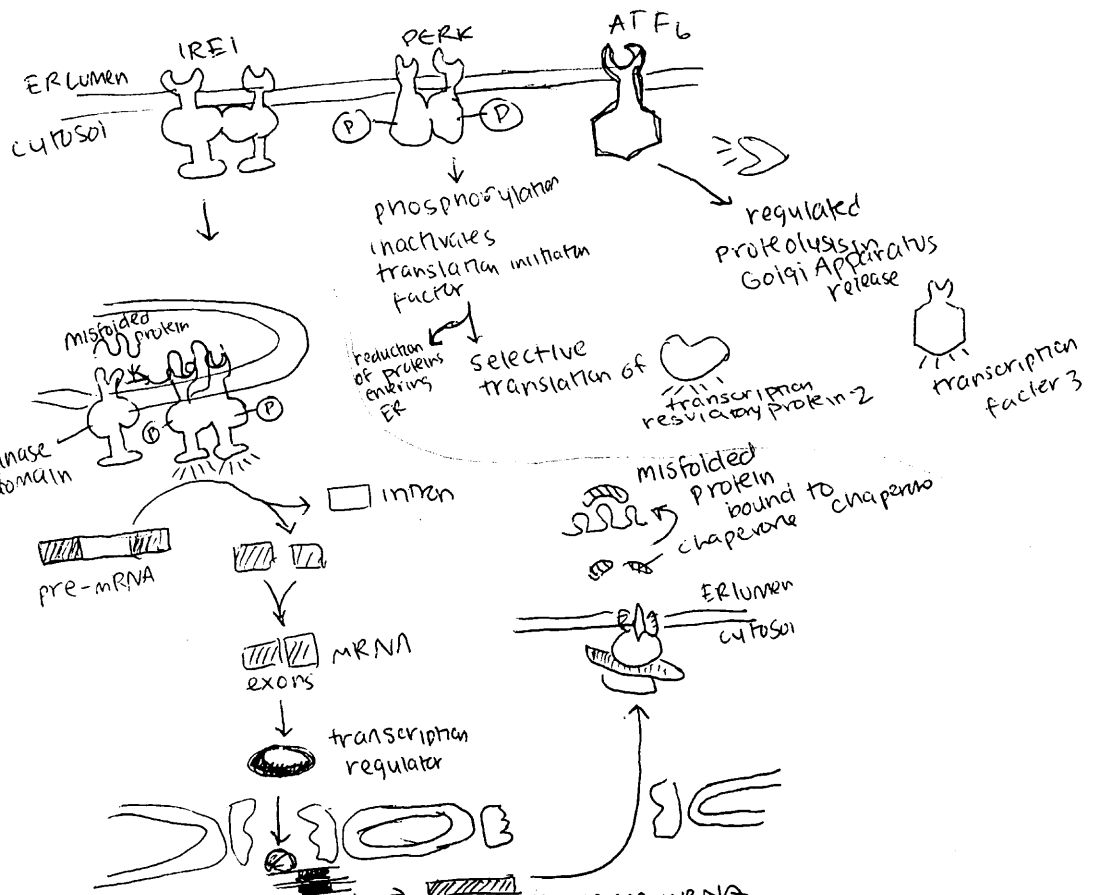
vesicle transport



Degradation & export of misfolded ER proteins

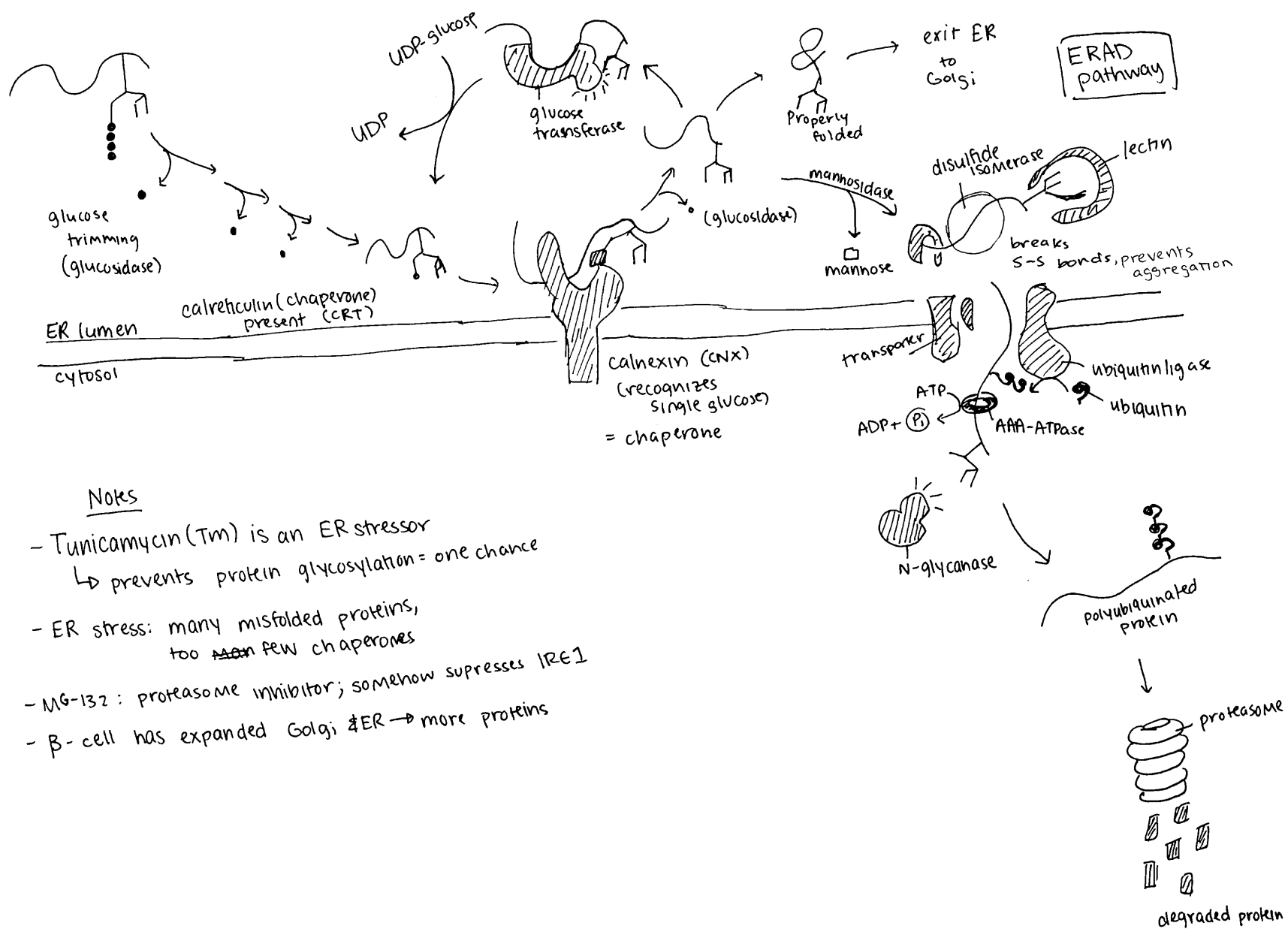


← overall degradation/export



Heatshock = cytosol  
UPR = ER

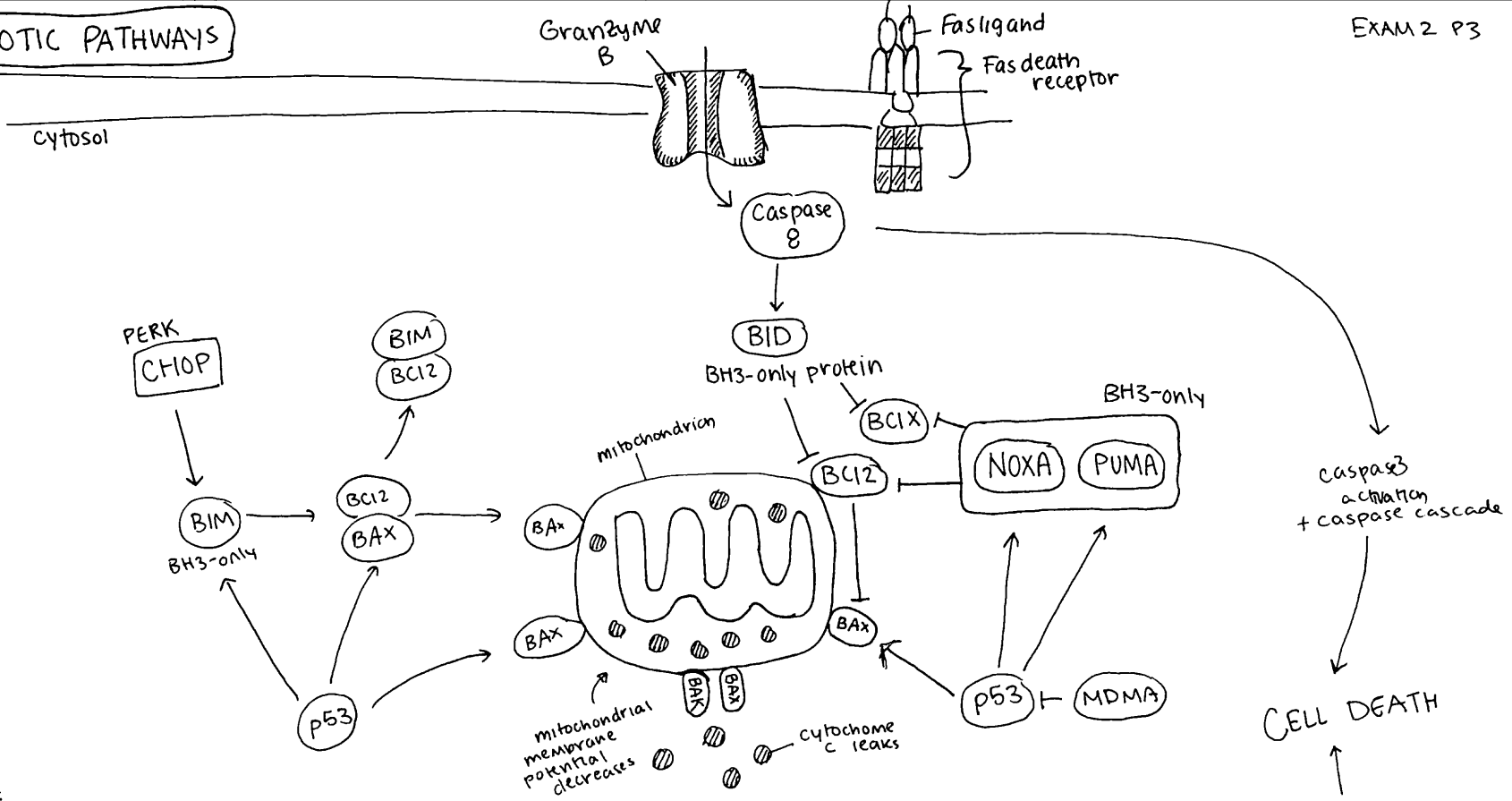
Protein folding



Notes

- Tunicamycin (Tm) is an ER stressor  
↳ prevents protein glycosylation = one chance
- ER stress: many misfolded proteins, too ~~many~~ few chaperones
- MG-132: proteasome inhibitor; somehow suppresses IRE1
- $\beta$ -cell has expanded Golgi & ER  $\rightarrow$  more proteins

# APOPTOTIC PATHWAYS



**Notes:**

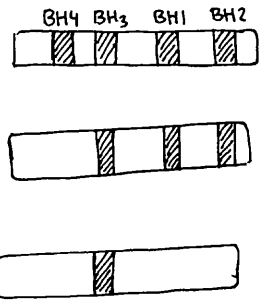
- External: Granzyme B & Fas  
↳ can trigger intrinsic
- Intrinsic: APAF1 → apoptosome

- apoptosis for viral, cancerous, genetic diseases
- phosphatidylserine exposed by "flipase" = "eat me"
- caspase can cause DNA fragmentation

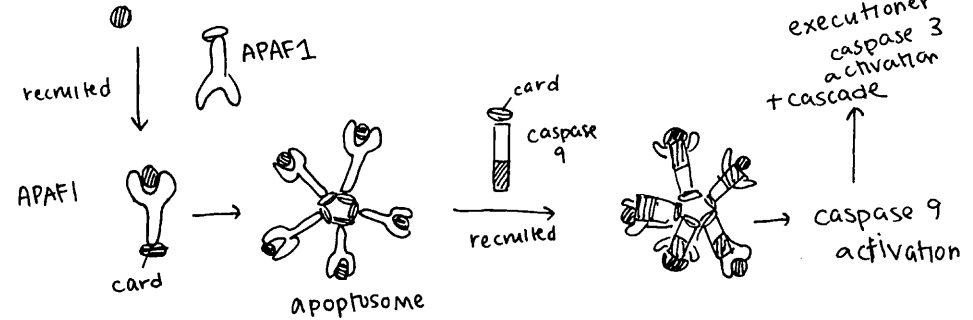
antiapoptotic  
BCL2 family:  
BCL2, BCLX

proapoptotic effector:  
BAX, Bax

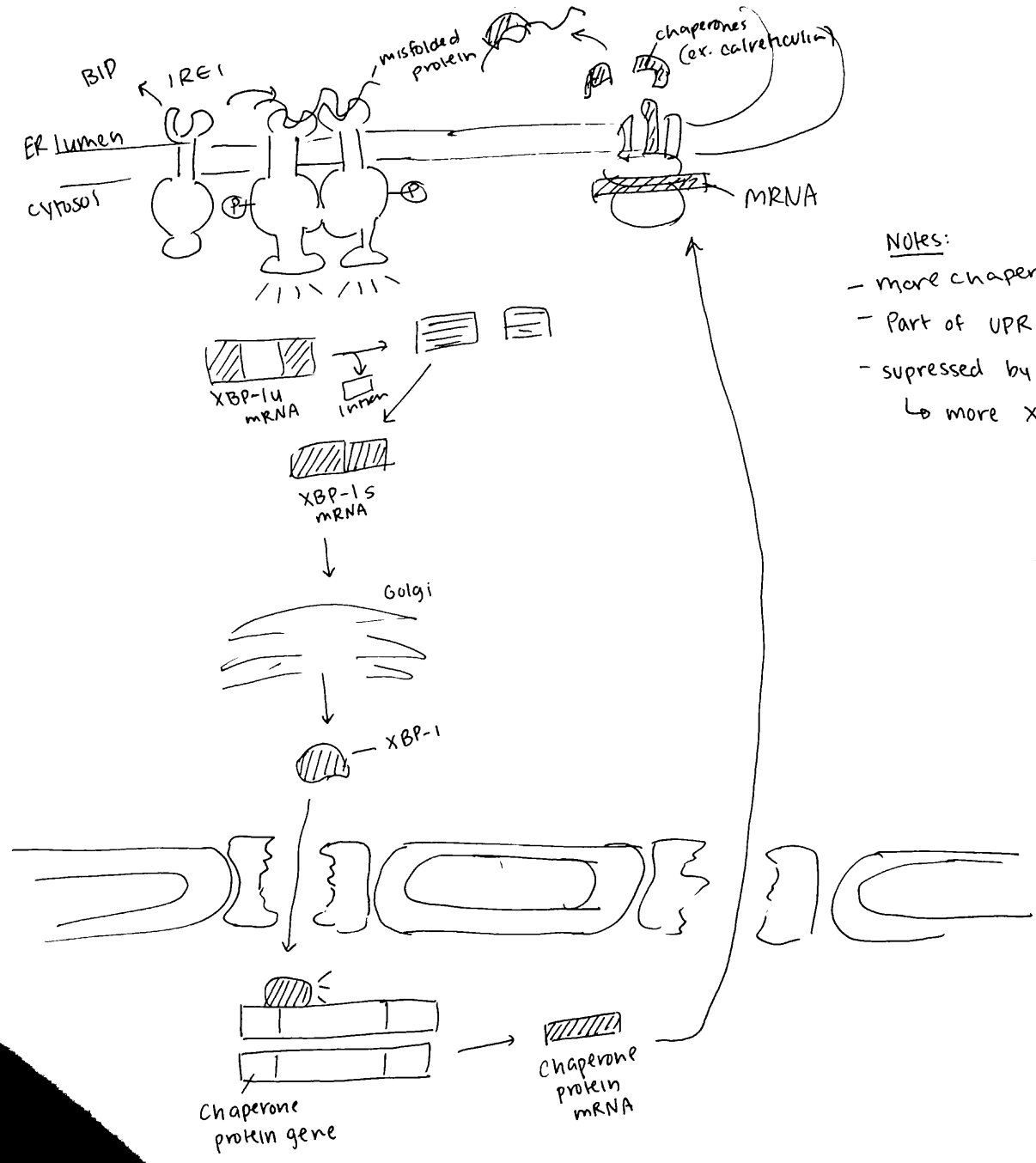
proapoptotic BH3 only  
(Bad, BIM, Bid, Puma, Nox)



- pro large small  
2, 8, 9 = initiator
- large small  
3, 6, 7 = executioner
- caspase cascade = beneficial due to escalation

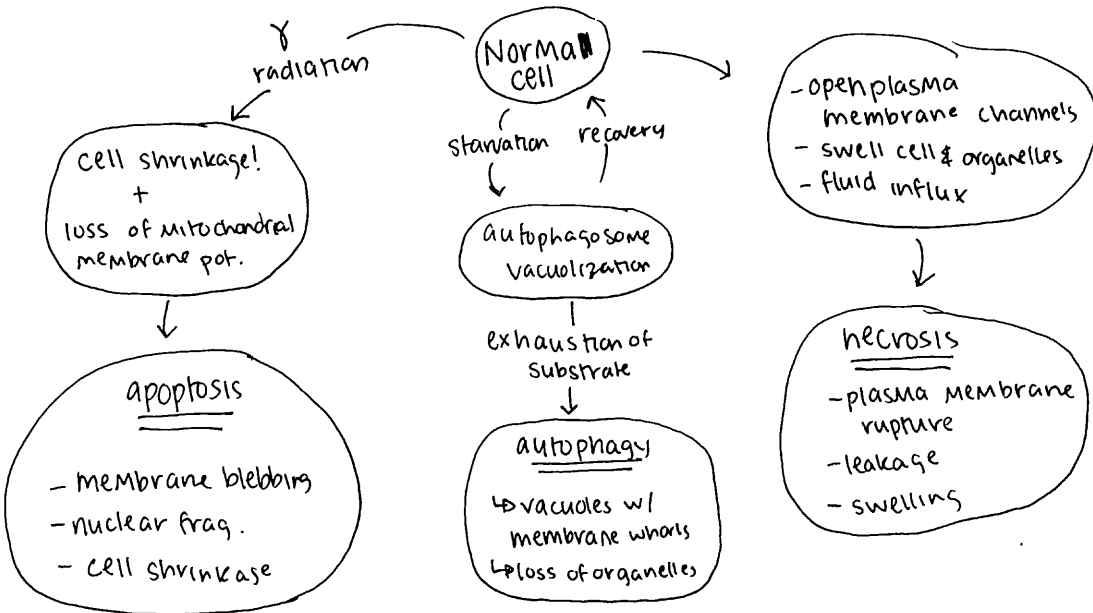


IRE-1 Pathway

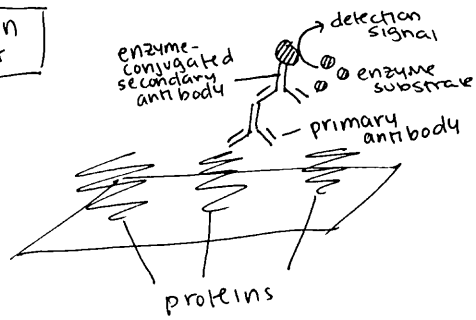


- Notes:
- more chaperones
  - Part of UPR (short term ER stress)
  - suppressed by MG-132
    - ↳ more XBP-1u present

**Cell Death**

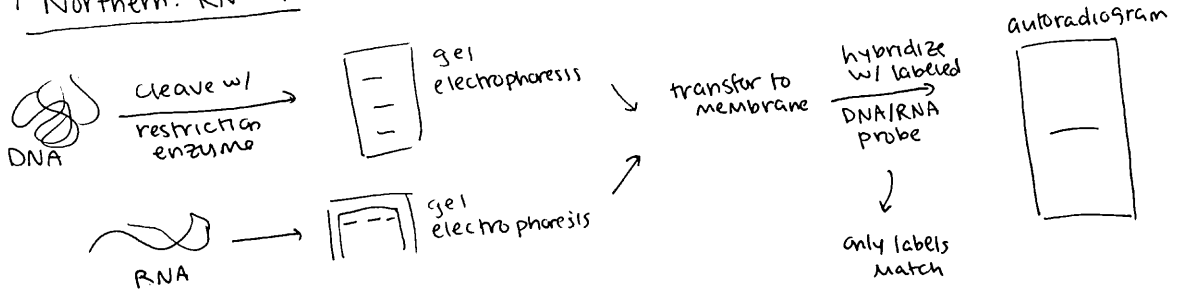


**Western blot**



protein detection & separation by mass

**Southern: DNA  
Northern: RNA**



parameters of apoptosis

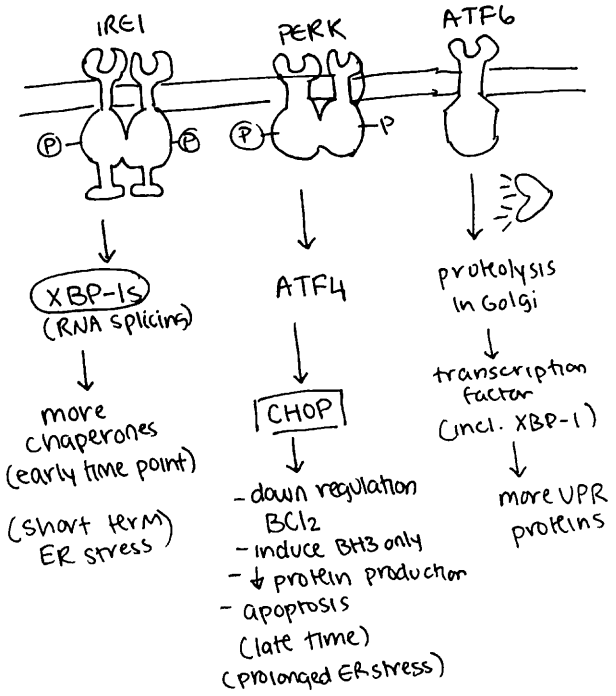
1. asymmetry
  2. proapoptotic protein active (Bcl2)
  3. caspase active
  4. cyt. C release + loss mem. pot
  5. nuclear condensation
  6. DNA frag.
  7. cell mem. blebbing
- ↑  
reversible

# General UPR

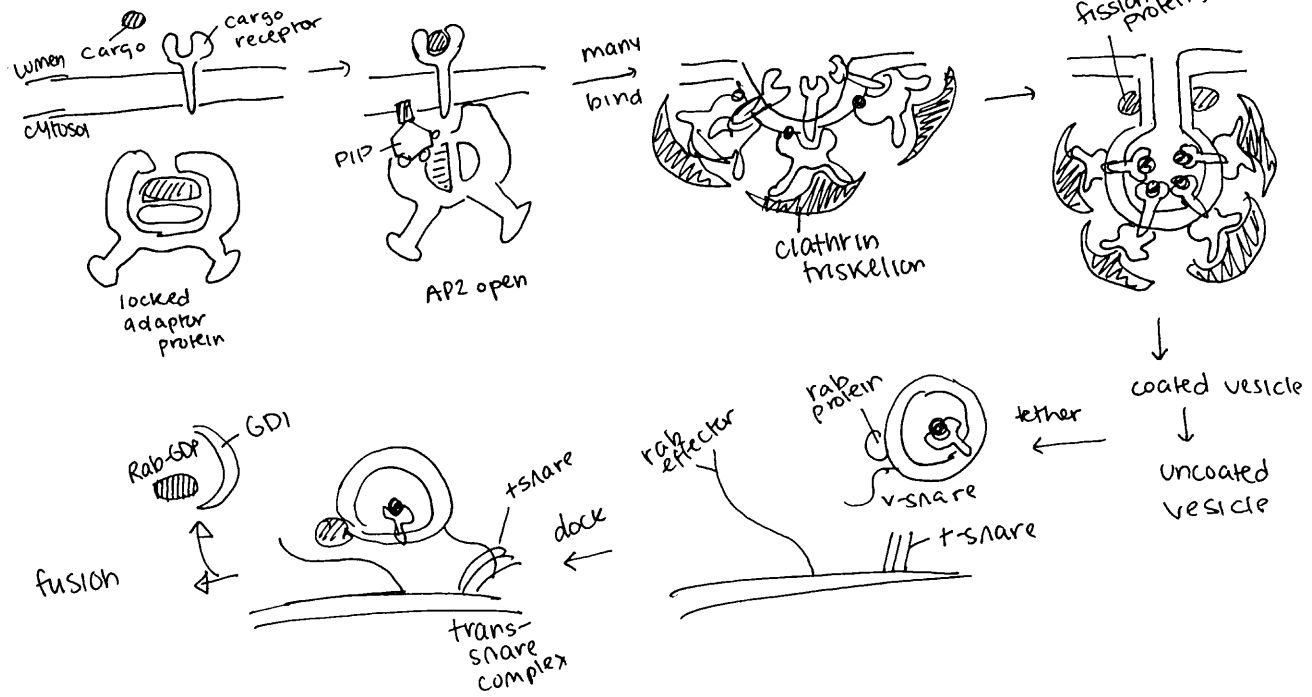
- IRE-1 → more XBP-1s → more chaperones
- PERK → reduction of proteins entering ER & ↓ protein production
- ATF6 → transported to Golgi (vesicle), proteolysis → transcription factor  
↓  
more UPR proteins

- Heatshock → in cytosol
- UPR → ER lumen
- LPS (found on bacterial cells) → body mounts immune defense (β-cell differentiation)  
↳ deactivates PERK

binds hydrophobic parts

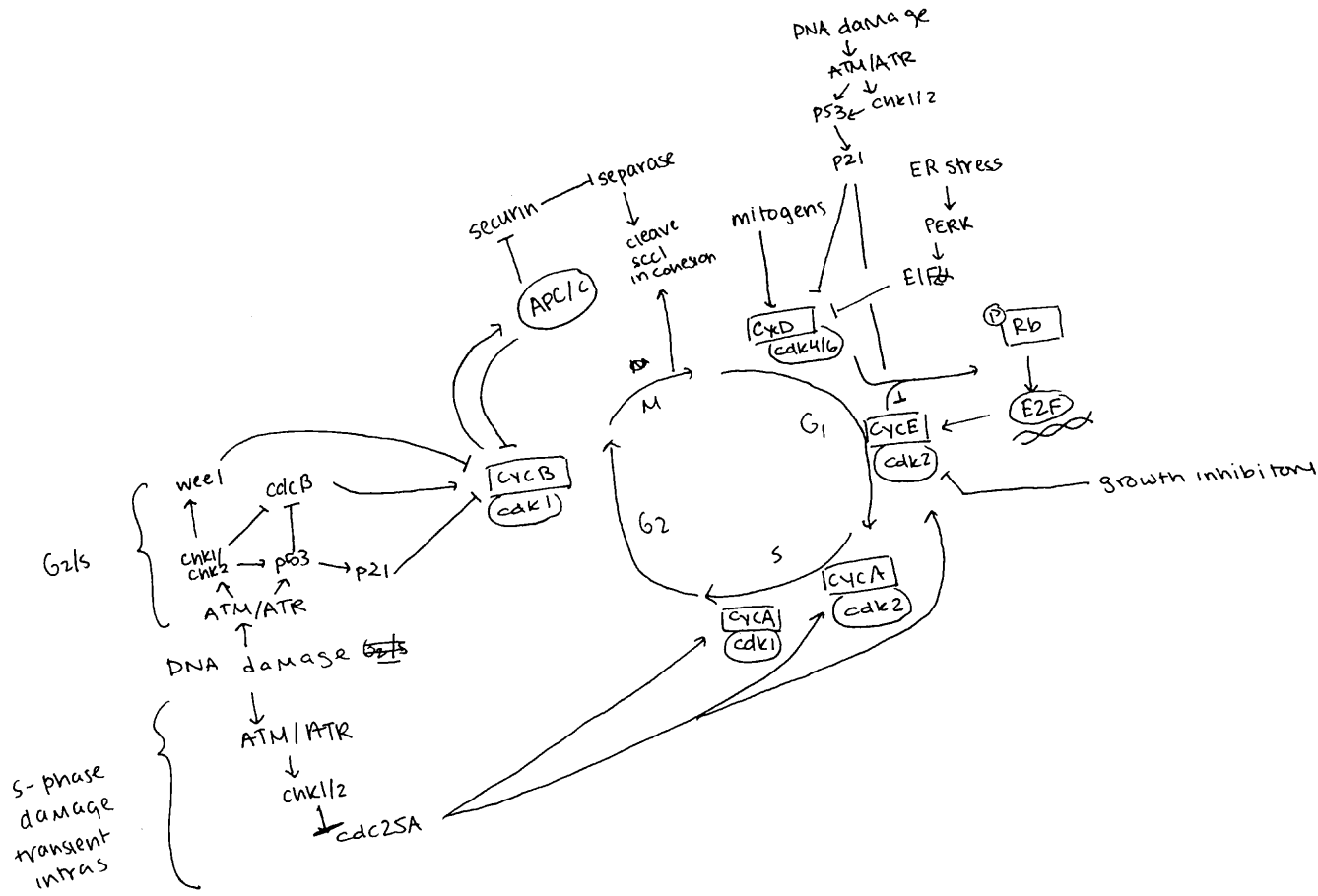
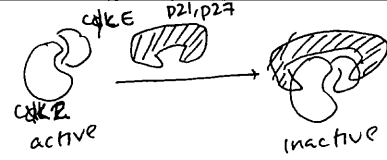


# Vesicular Trafficking

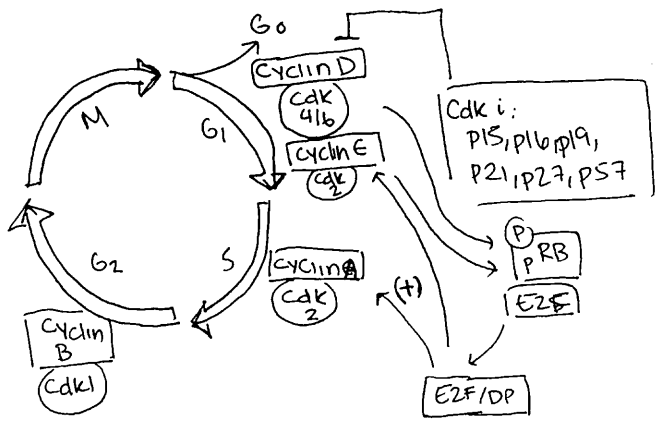
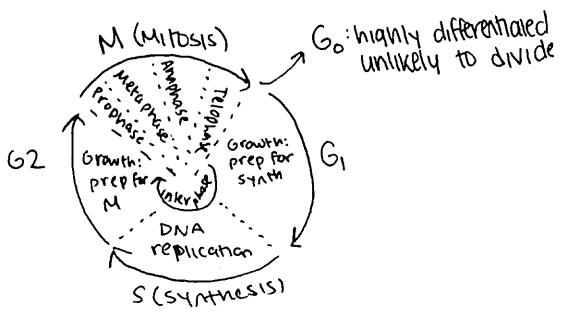




EXAM 3 P1



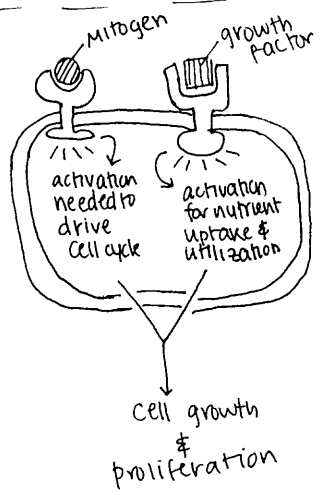
# Many cell cycle components



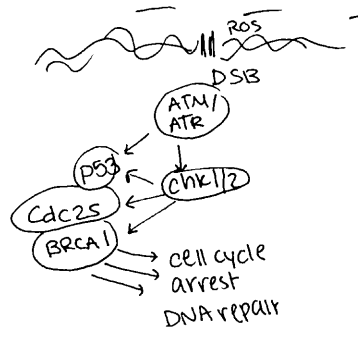
## Notes: EXAM 3 P2

Tm = no N-glycosylation  
 = G0/G1 arrest through CYC D1 regulation  
 cell lines: used to study systems in human cells that won't die  
 Dynamic stability: unbound microtubules quickly degrade & bound w/ R star grow connected to kinetochore  
 activated Cdk prevent apoptosis

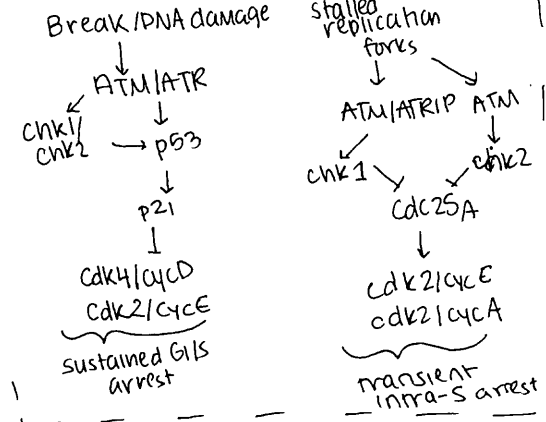
## malignant tumor: metastasizes



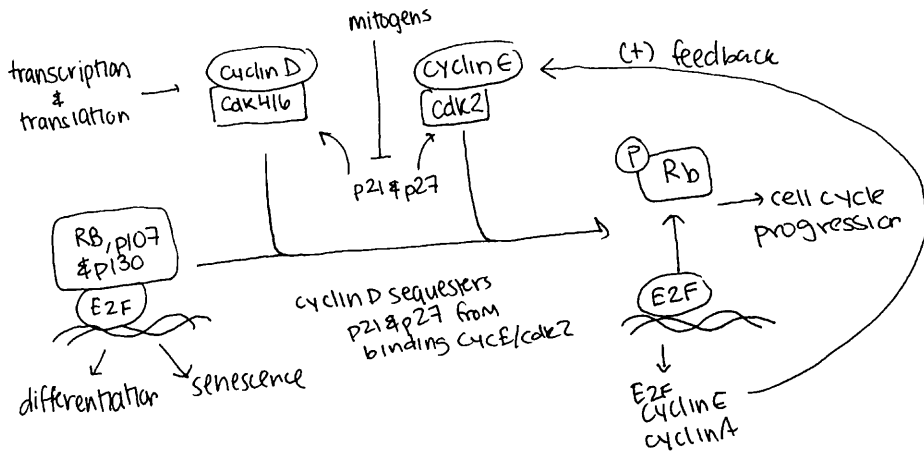
## DNA damage checkpoint



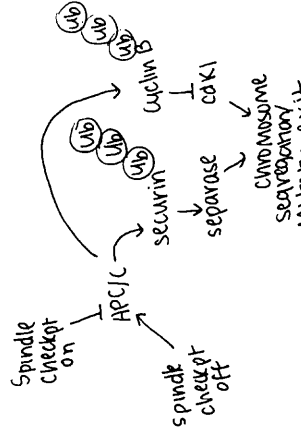
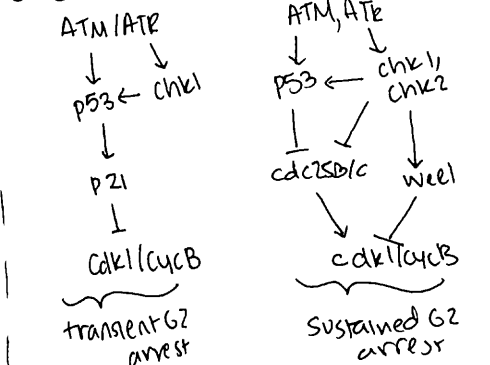
## S-phase Damage



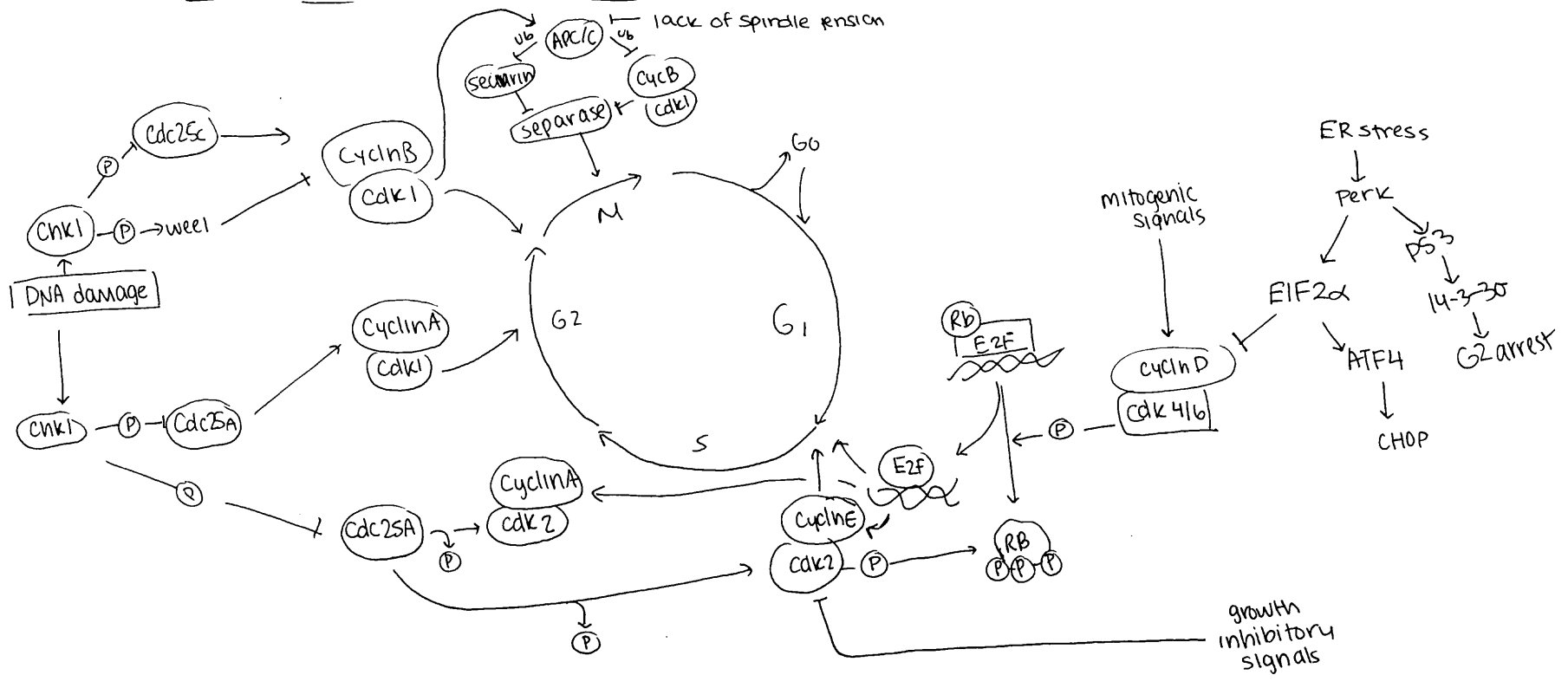
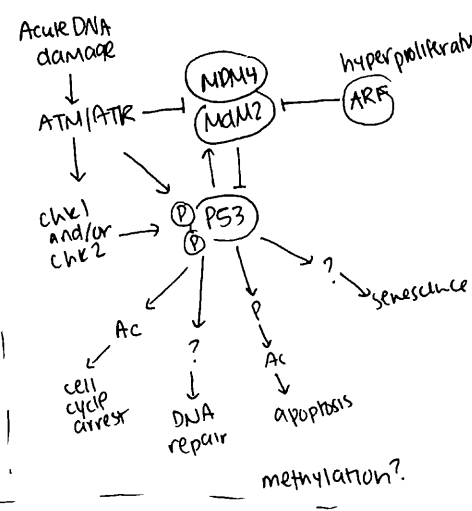
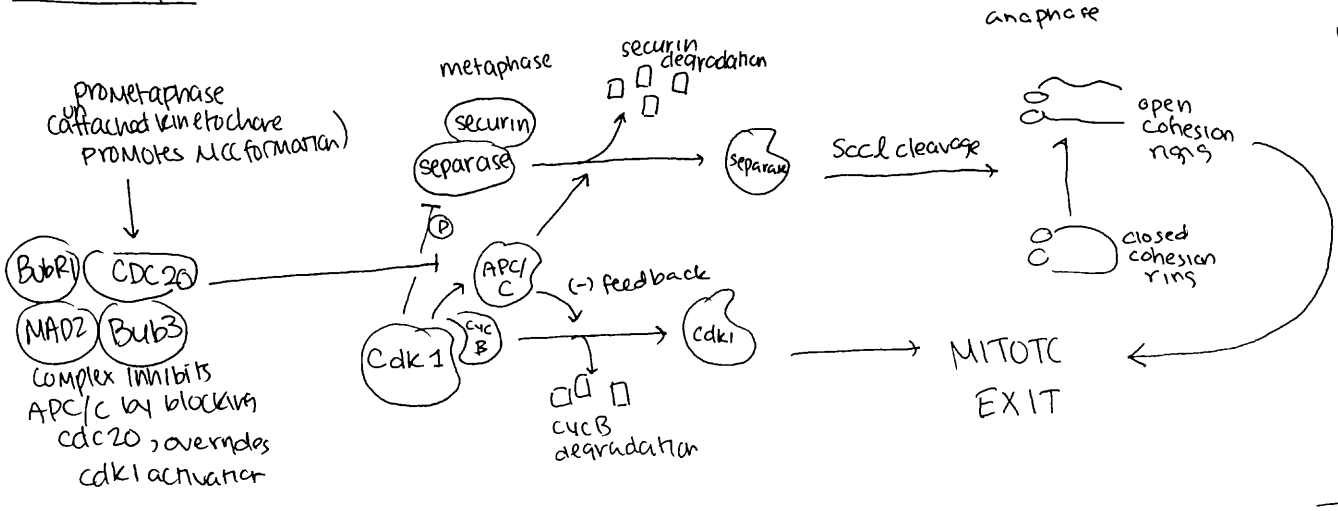
phosphor: unphosphor p53 = ~~cell~~ apoptosis cell cycle arrest  
 acetylated cell cycle arrest  
 unattached spindles bound by MAD/aurora/bud  
 ↳ bind to Ubq.lig-APC/C



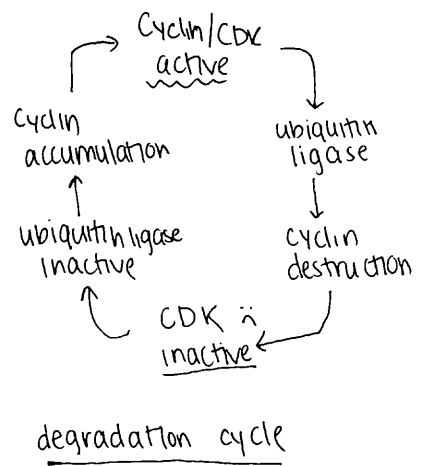
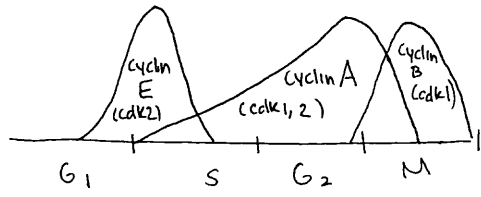
## G2/M phase damage



Spindle checkpoint



**Cyclins**



**G1/S cyclin (Cyc E, Cdk2)**

- nucleotide biosynthesis (ex. Thymidine Kinase)
- components of DNA replication machinery

**S Cyclin (Cyc A, Cdk1, 2)**

- initiators of DNA replication
  - ↳ allows replication complex to form
- recruitment of DNA pol & replication proteins
- helicase activation

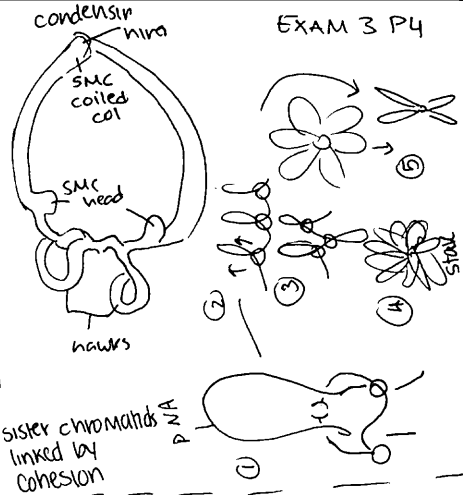
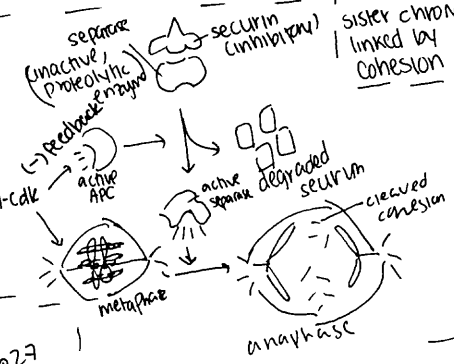
**M-Cyclins (Cyc B, Cdk 1)**

- condensin (condense chromosomes)
- lamin (stabilize nuclear envelope)
- assemble Mitotic spindle (Microtubules)
- interactors of Kinetochore complex (chromosome segregation)

**Cdk2 (G1/S)**

- inhibit cell cycle inhibitors
  - ↳ Rb, p27, APC
- activate cell cycle activators
  - ↳ origin: MCM
  - centrosome duplication - NPM
  - histone gene transcription - NPAT
  - chromatin structure - p300/CBP
- DNA replication (helicase)
- DNA repair
- centrosome duplication
- block MITOTIC entry

activation & phosphorylation



EXAM 3 P4

