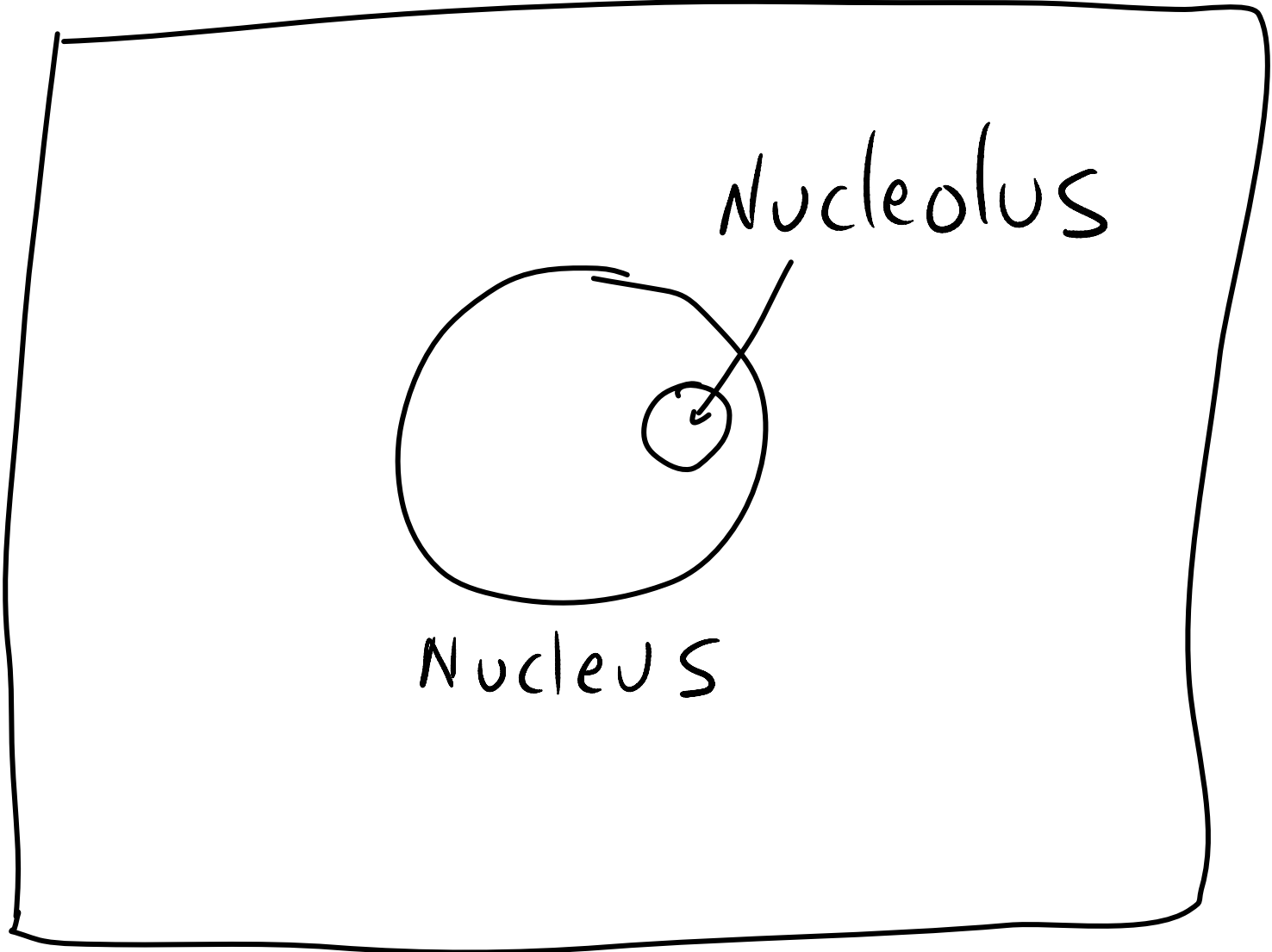


CELLULAR PHYSIOLOGY

- **CELL ORGANELLS**



Nucleolus

Nucleus

IRREVERSIBLE CELLULAR INJURY

● APOPTOSIS

- CELL MEMBRANE DISSOLVES FIRST
- PROGRAMMED CELL DEATH
- NONINFLAMMATORY
- PYKNOSIS
- KARYORHEXXIS
- KARYOLYSIS

● NECROSIS

- NUCLEUS DISSOLVES FIRST
- UNEXPECTED
- INVOLVES INFLAMMATION
- PYKNOSIS
- KARYORHEXXIS
- KARYOLYSIS

NECROSIS

- **ISCHEMIC**(COAGULATIVE)
- **PURULENT**
- **GRANULOMATOUS**
- **FIBRINOUS**
- **CASEOUS**
- **FAT**
- **HEMORRHAGIC**
- **LIQUEFACTIVE**

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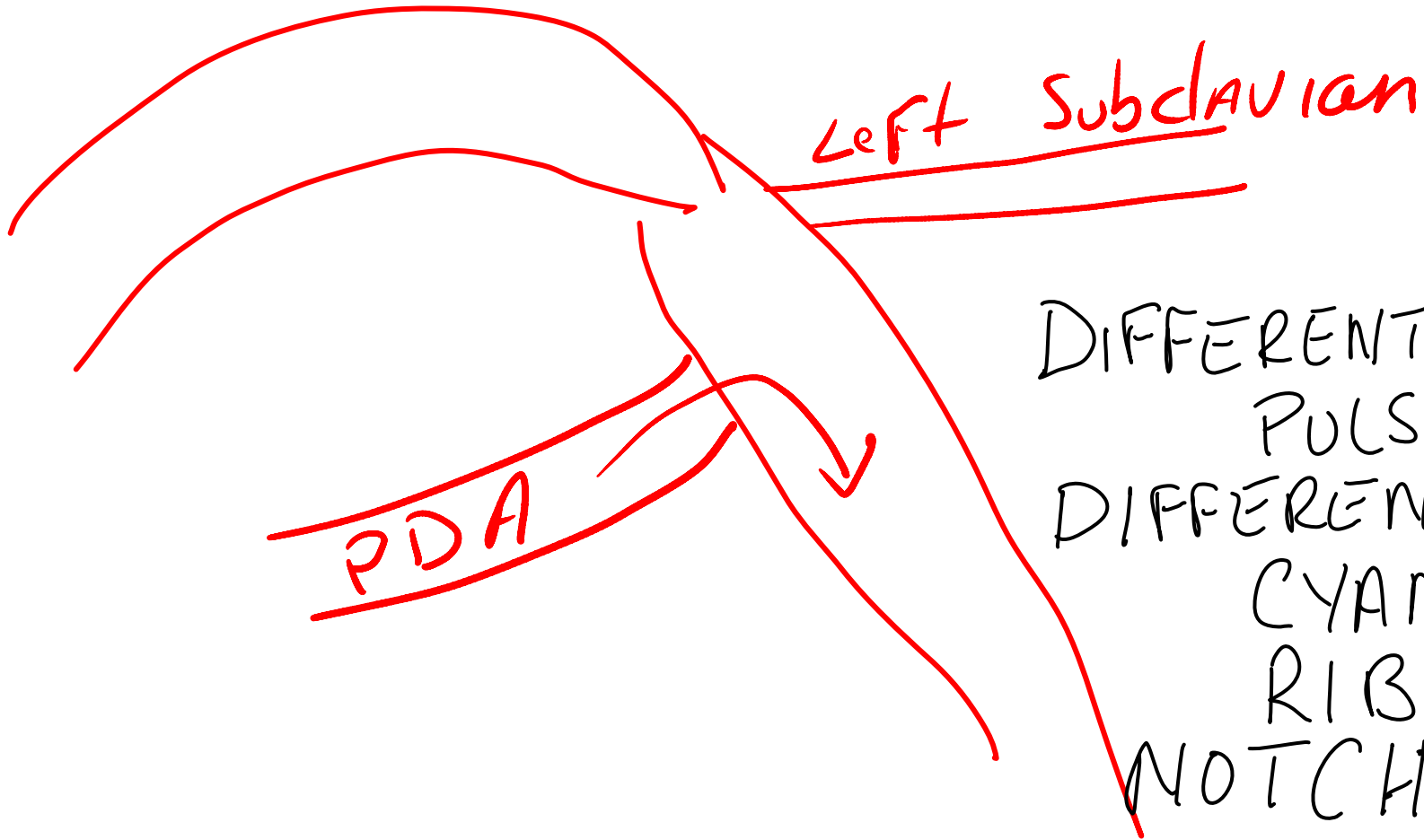
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MESS WITH THE CHROMOSOMES

- **MONOSOMIES: DIE! DIE! DIE!**
 - MCC: NONDISJUNCTION
 - 90% IN DAD, USUALLY IN MEIOSIS 1; BUT SPERM DIE ON A DAILY BASIS
 - FEWER OCCUR IN MOM; BUT MOM KEEPS HER EGGS FOR LIFE AND IS THEREFORE MORE LIKELY TO TRANSMIT HERS
 - IF ONE WERE TO SURVIVE TO BE BORN, IN THE LEAST, **THINGS WILL NOT GROW**

TURNER SYNDROME

- **WEBBED NECK**
- **CYSTIC HYGROMA**
- **GONADAL STREAKS**
- **SHIELD-SHAPED CHEST**
- **COARCTATION OF AORTA**



Left Subclavian

PDA

DIFFERENTIAL
PULSES
DIFFERENTIAL
CYANOSIS
RIB
NOTCHING

TRISOMIES

- DIE! DIE!
- FEW LIVE
- TRISOMIE 13: **PATAU SYNDROME**
 - POLYDACTYLY
 - PALATE IS HIGH-ARCHED
 - PEE-ING SYSTEM ABNORMALITY

TRISOMIES

- TRISOMIE 18: **EDWARDS SYNDROME**
 - ROCKERBOTTOM FEET (IN 95%)

TRISOMIES

- TRISOMIE 21: **DOWN'S SYNDROME**
 - MCC: NONDISJUNCTION
 - ROBERTSONIAN TRANSLOCATION: HIGHEST INCIDENCE (33% OF OFFSPRING)
 - HAS MANY THINGS TO CONSIDER

DOWN'S SYNDROME

- **MENTAL RETARDATION** – 100%
 - IQ: AVERAGE IS 85 TO 100 WITH A STANDARD DEVIATION OF 15
 - SUPERIOR INTELLIGENCE: IQ > 130
 - MILD MR: IQ < 70
 - MODERATE MR: IQ < 55
 - SEVERE MR: IQ < 40
 - PROFOUND MR: IQ < 25 – NEEDS 24HR CARE
 - MILD TO MODERATE MR CAN BE TAUGHT BASIC ADLS

DOWN'S SYNDROME

- EARLY-ONSET **ALZHEIMER DISEASE**
- HIGHER FREQUENCY OF **AML**; BUT **ALL** IS THE MOST COMMON LEUKEMIA
- 20 TO 40% HAVE **congenital heart DISEASE**
- -ENDOCARDIAL CUSHION DEFECTS
 - VSD and ASD
 - VSD
 - ASD

Septum
Primum

Septum
Secundum

ENDO

ventricular
septum

Common
AV
CANAL



ASD
VSD



VSD



ASD

DOWN'S SYNDROME

- **CYANOTIC CONGENITAL HEART DISEASE**
 - TRANSPOSITION OF GREAT ARTERIES
 - TETROLOGY OF FALOT

DOWN'S SYNDROME

- 50% HAVE **HYPOTHYROIDISM**
- WIDELY-PACED CRANIAL SUTURES
- **MACROGLOSSIA**
- **DUODENAL ATRESIA**
- **HIRSCHSPRUNG'S DISEASE**
- CLUES:
 - MONGLIAN SLANT TO EYES
 - WIDELY SPACED FIRST AND SECOND TOES
 - SIMIAN CREASE

TRISOMIES

- **XXX**: Normal female; has two Barr bodies
- **XXY**: **Klinefelter's syndrome**. Tall male with gynecomastia, small penis and testicles
- **X- Fragile X syndrome**
 - Mcc of chromosomal induced MR
 - Short stature; macrochordism
 - Collagen disorder (increased risk of MVP)
 - Isolated using the drug METHOTREXATE

Chemotherapy

CHEMOTHERAPY

- Stops rapidly dividing cells
- Attacks the nucleus in some way
- Causes irreversible cellular death
- WILL kill some patients
- No such thing as safe chemo

ANTIMETABOLITES

- **ARA-A**
- **ARA-C**
- **5-FU**: blocks thymidylate synthetase
- **6-MERCAPTOPURINE**: promotes gout; recognized by xanthine oxidase
- **THIOGUANINE**
- **METHOTREXATE**: inhibits dihydrofolate reductase(as does TRIMETHOPRIM and PYRE METHAMINE)
 - Most commonly used antimetabolite
 - Used to treat molar pregnancies
 - Used to treat STEROID RESISTANT disease(followed by AZOTHIOPRINE and CYCLOSPORINE)

ANTIMETABOLITES

- **METHOTREXATE**

- Causes folate deficiency and megaloblastic anemia
- Give LEUCOVORIN > FOLINIC ACID to prevent the anemia

ANTIMETABOLITES

- **AZOTHIOPRINE**

- Used for steroid resistant diseases
(behind METHOTREXATE and before
CYCLOSPORINE)

ALKYLATING AGENTS

- Bind to double stranded DNA
- Used primarily for slow growing cancers
- Cause the most nausea and vomiting
 - **ONDANSETRON**: serotonin blocker used to treat nausea and vomiting in chemotherapy

ALKYLATING AGENTS

- Bleomycin
- Busulphan
- Adriamycin
- Cisplatin
- Cyclophosphamide
- Isophosphamide
- Mitomycin
- Antimycin
- Acridine dyes
- Hydroxyurea
- Melphalan
- Mechlorethamine
- Procarbazine
- Dacarbazine
- Chlorambucil
- FOR RESCUES
- **Desrozasane**
- **Mesna**

MICROTUBULE INHIBITORS

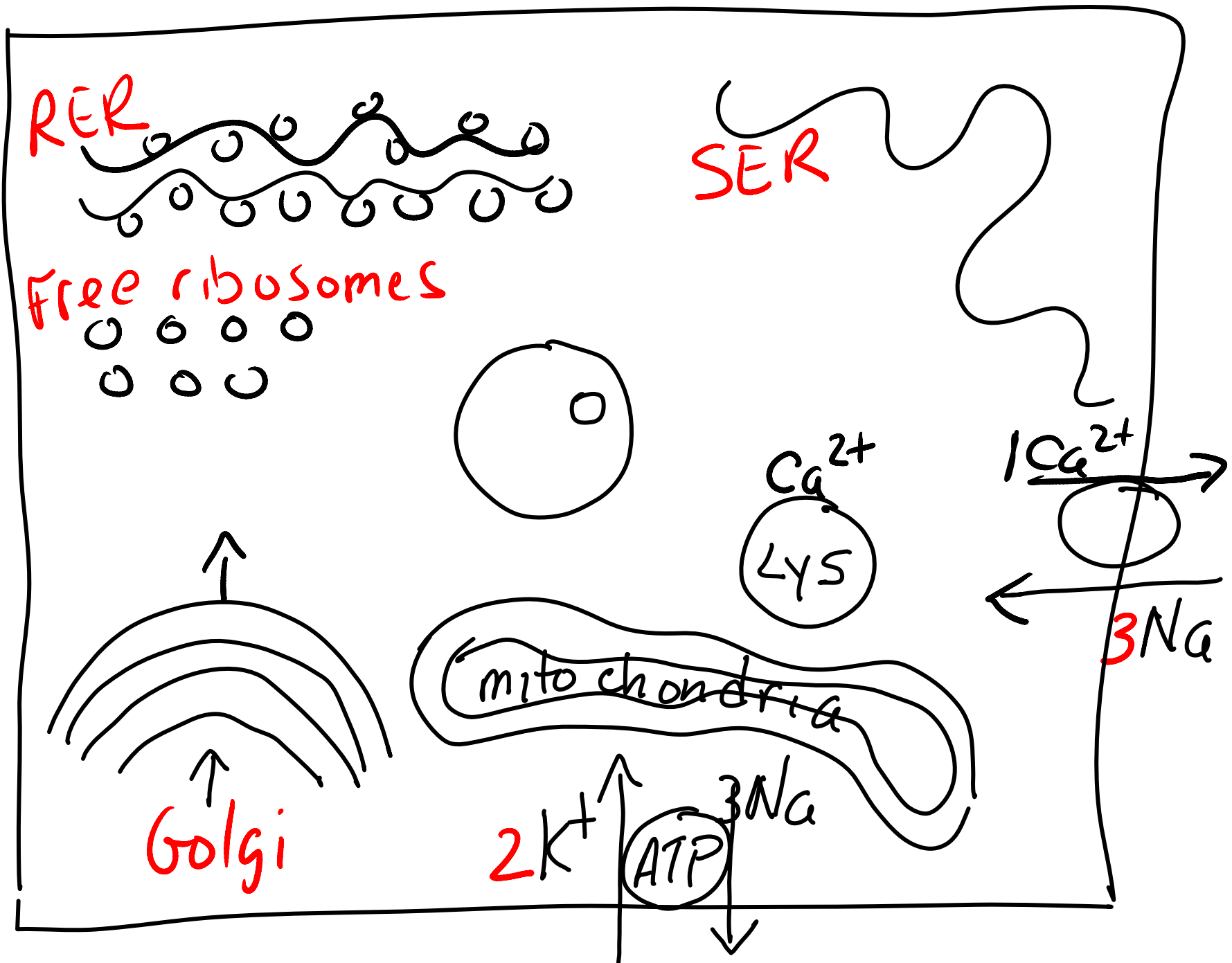
- Vinblastine
- Vincristine
- Paclitaxel

NUTRIENT DEPLETION

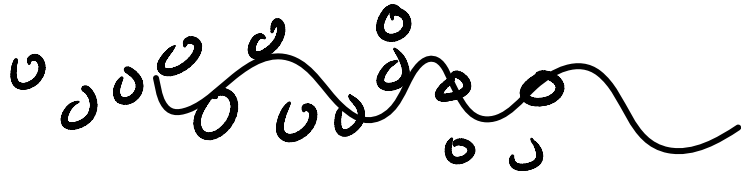
- **L-ASPARAGINASE**

IMMUNEMODULATORS

- **LEVAMISOLE**



PreProProtein

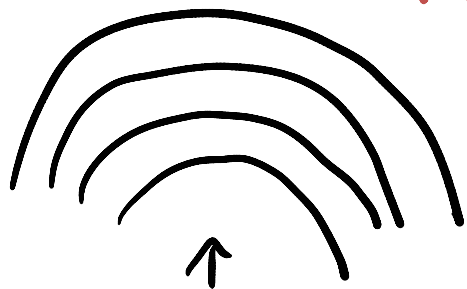


Short N-terminal
sequence

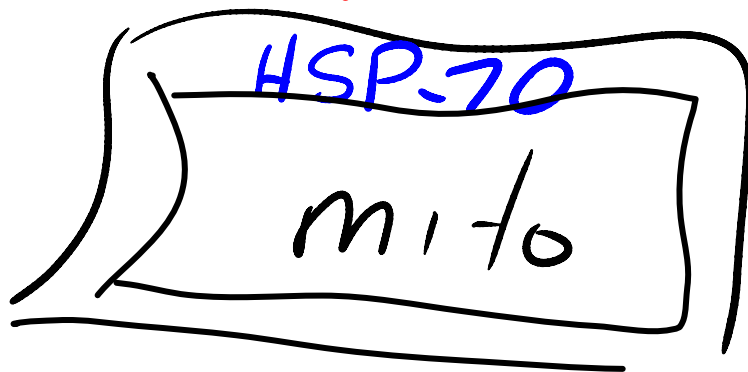
ACID Hydrolases

Lys

Protein-mannose
6
Phosphate



ProProtein



Phosphatidylserine

- Marker for **Apoptosis**
- Activates **Caspases**

Metalloproteinases

- Require zinc to be activated
- Digests connective tissue, allowing cells to migrate
- Very active in cancer cells, allowing metastasis

IRREVERSIBLE CELLULAR DEATH

- NUCLEAR DAMAGE
- LYSOSOMAL DAMAGE
- MITOCHONDRIAL DAMAGE
- OCCURS IN **6 HOURS** in all tissues

IRREVERSIBLE CELLULAR DEATH

- NUCLEAR DAMAGE
- LYSOSOMAL DAMAGE
- MITOCHONDRIAL DAMAGE
- OCCURS IN 6 HOURS in all tissues **except the brain**

IRREVERSIBLE CELLULAR DEATH

- OCCURS IN **20 MINUTES** IN THE BRAIN

The End?

To Be Continued...