Cyto-Diseases

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#DST

Mitochondria

Biochemical

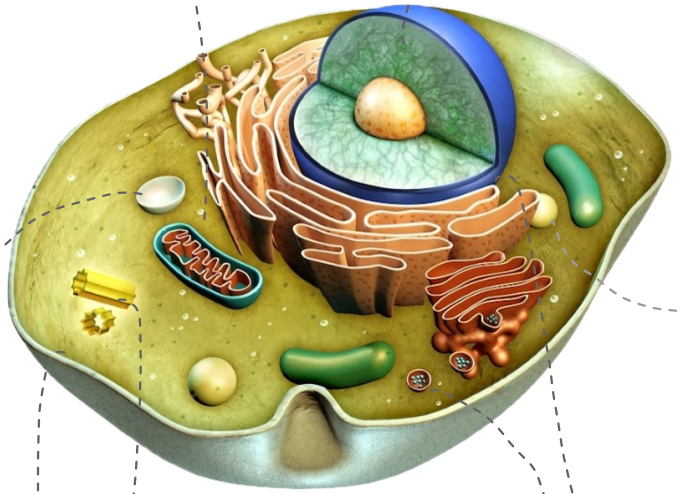
- Transport
- Substrate utilization
  - PDH deficiency
    - ↑ pyruvate, Ala, lactate
      - = metabolic acidosis + lactic acidosis
- Krebs cycle
  - Fumarase deficiency
    - ↑ Fumarate, Succinate in urine
      - = encephalomyopathy
- Respiratory chain
  - ETC complexes
- Luft's Disease
  - "non thyroidal Hypermetabolism"
  - Defects of oxidative phosphorylation coupling
    - hypermetabolism - hyperthermia

Genetic

mt DNA

- MERRF
  - t-RNA gene mutation
- MELAS
- NARP
- LHON QQ
  - ↓efficiency of oxo-phs
    - Blindness

nDNA



Nuclear Lamina MHDE

1. Emery-Dreifuss muscular dystrophy
   - Emerin / Lamin A gene mutation
2. * Marie charcot Tooth type B21
   - muscle wasting
3. Hutchinson-Gilford progeria
   - Premature aging
4. Dunnigan-type partial Lipodystrophy

Lamin A Gene Mutation

Peroxisomes

1. Single peroxisomal enzyme deficiency
2. Zellweger Syndrome
   - PBDs (Peroxisomal Biogenesis Disorder)
     - PEX Gene mutation
3. XALD (X-Linked AdrenoleuKoDystrophy)
   - Defective VLCFA transport.

Vesicular Transport

Gricelli Syndrome

MYO-RAB-MLPH mutation

Lysosomes

1. Storage Diseases [Hydrolases deficiency]
   - Glycolipidoses - Oligosaccharidoses - Mucopolysaccharidoses
2. I-Cell Disease "MucoLipidosis IIA"
   - [Deficiency in tagging enzyme that mannose]
     - Psychomotor retardation _ Premature death

Actin Filaments

Muscular Dystrophy

- Duchenne (DMD)
  - Absent Dystrophin
  - Severe
- Becker (BMD)
  - Defective Dystrophin (Shorter)
  - Mild

Microtubules

Kinesin mutation

neurodegeneration

1. ALS (Amyotrophic Lateral Sclerosis) *
   - loss of muscle control
2. Alzheimer + Tau aggregation (MAPs)
   - dementia

Peripheral neuropathy

3. Charcot-Marie-tooth *

Intermediate Filaments

1. Epidermolysis bullosa Simplex
   - Keratin gene mutation
     - defective Skin
2. ALS (Lou Gehrig's disease) *
   - accumulation of Neurofilaments

Affects vessels, tendons, skin.

Lysyl oxidase mutation

Imperfect bone formation type I through type IV.

Osteogenesis imperfecta

Collagen Diseases

Type III EDS

- The most clinically important mutations are found in the gene of type III collagen.
- Since **type III collagen** is a major component of arteries, mutations affecting it result in fragile blood vessels.

Ehlers-Danlos syndrome

Chondrodysplasias

Mutations affecting **type II collagen** characterized by abnormal cartilage, which leads to bone and joint deformities.

Elastin:

Marfan's syndrome

- Due to mutated fibrillin
- Rupture of aorta.

Elastic fibers can stretch too much and rupture.

All result from defects in collagen synthesis and/or processing. collagens type I, III, or V or in the collagen processing enzymes like procollagen N-peptidase or lysyl hydroxylase.

Diseases caused by defective gap junctions and mutated connexins

- Marie-Charcot-Tooth disease
- Deafness
- Skin disorders
- Cataracts

An example of a tight junction protein: **Claudin**.
This protein can be associated with a cancer named: **Claudin-low breast cancer**(low expression of claudin) which is **characterized by being mesenchymal-like** (motile and elongated) **with low E-cadherin** expression, patients have **poor survival** (aggressive cancer) **and prognosis** (the outcome is bad: Death), **metastasis, and younger age of onset**.

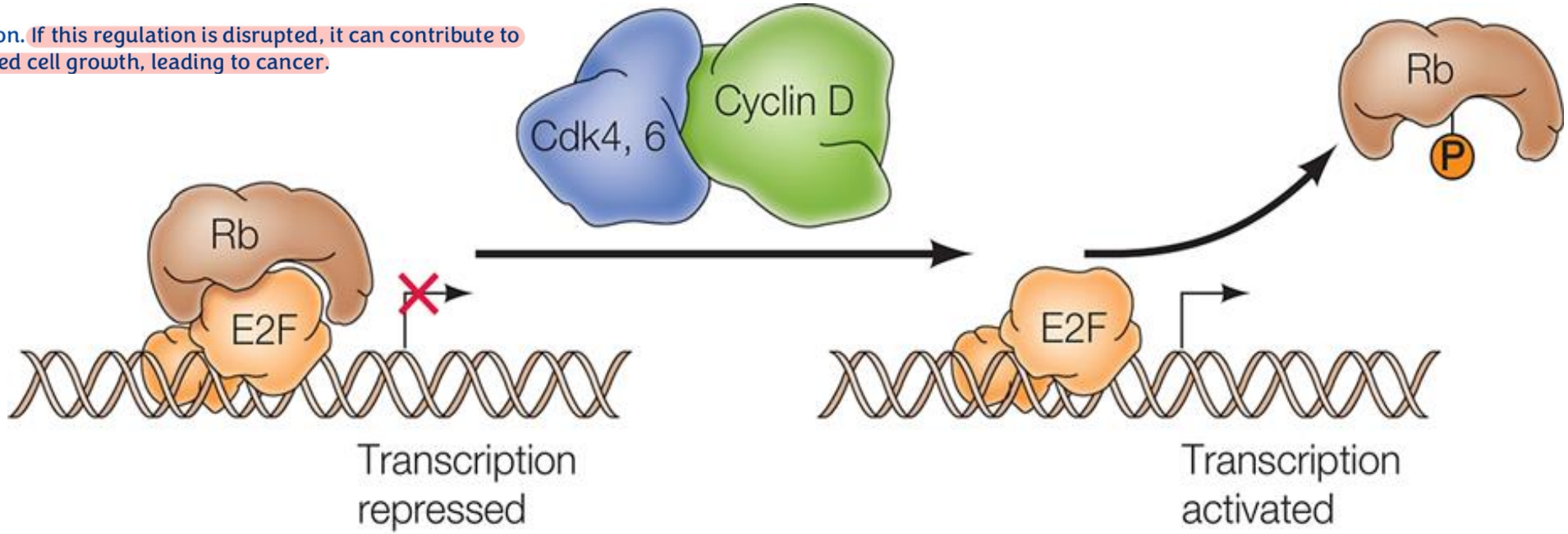
Hereditary deafnes
result from mutati
connexins, which
disrupt cellular
communication es
for hearing.

Retinoblastoma

Uncommon eye cancer usually affects children under 5, although it can affect children of any age

- When unphosphorylated, Rb protein binds to members of the E2F family of transcription factors repressing the transcription of many genes involved in cell cycle progression such as cyclin E.
- E2F is freed when Rb is phosphorylated by Cdk4,6/cyclin D stimulating cell cycle progression through restriction point.

proliferation. If this regulation is disrupted, it can contribute to uncontrolled cell growth, leading to cancer.



لَا حَوْلَ وَلَا قُوَّةَ إِلَّا بِاللَّهِ

Loss of balance + large BV

Ataxia-telangiectasia

- Defective ATM is responsible for the ataxia-telangiectasia, (defective nervous and immune systems and a high frequency of cancer.
  - Ataxia: uncoordinated movements, such as walking.
  - Telangiectasias: enlarged blood vessels (capillaries) below the surface of the skin.

Due to the replication of mutated or damaged DNA.