Lec 07: Platelets and Hemostasis

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**Platelets**

- **Platelets**: are small, irregularly shaped clear cell fragments (non-nucleated), **2–3 µm** in diameter.
- **Number**: **150,000 – 400,000/mm³**
- **Around** **10¹¹** platelets are produced each **day** by an average healthy adult.
- **Cell fragments bound to** **megakaryocytes** (**35-160 µm**) “Bud Off” → released → blood
- **The average lifespan of a platelet is normally just** **8-12 days**.
- Megakaryocyte and platelet production is regulated by thrombopoietin, a hormone usually produced by the liver and kidneys.
- Each megakaryocyte produces between 5,000 and 10,000 platelets.
- Discoid in shape have a mean volume of 7–11 fL.
- Old platelets are destroyed by phagocytosis in the spleen and by Kupffer cells in the liver.
- Reserve platelets are stored in the spleen, and are released when needed by sympathetically induced splenic contraction.
• If the number of platelets is too low, excessive bleeding can occur.

• However, if the number of platelets is too high, blood clots can form (thrombosis), which may obstruct blood vessels and result in such events as a stroke, myocardial infarction, pulmonary embolism or the blockage of blood vessels to other parts of the body, such as the extremities of the arms or legs.
• **thrombocytopenia** $\rightarrow$ low number of platelets

• **thrombasthenia** $\rightarrow$ a decrease in function of platelets

• **thrombocytosis** $\rightarrow$ an increase in the number of platelets

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**Glanzmann's thrombasthenia**

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**Thrombocytosis**
Platelet structure

1- **Surface coat** → mucopolysaccharide
   - **GPIb-IX-V**: It is the major platelet receptor for VWF.
   - **GPla** and **GPVI**: receptors for collagen.
   - **GPIIb-IIIa**: receptor for vWF.
   - Thromboxane A2 (TXA2) receptor.
   - ADP receptors: P2Y12 and P2Y1.

2- **Plasma membrane**: is formed of 3 layers and invaginates inside to form open membrane system and contain **Lipids** (phospholipids, cholesterol & glycolipids). **Carbohydrates** & **Proteins** (Glycoproteins).

This membrane is the basis structure of **platelet factor 3** (PF3). Responsible for the release of fatty acid derivatives: PGs, prostacyclins.
Platelet structure

Organelle zone
- Dense body
- Mitocondrion
- Glycogen
- Lysosome
- Alpha granules

Peripheral zone
- Glycocalyx
- Membrane

Membrane systems
- Open canalicular system
- Dense tubular system

Structural zone
- Microtubules
- Submembranous cytoskeleton
- Actin (G and F forms)
- Myosin
Structural Zone

- **Organized** network of **protein** filaments.
- **Maintain** shape of *resting* platelet—discoid.
- 3 principle types of filaments:
  a). **Microtubules**: → - Located beneath the cell membrane of resting platelet. Maintain discoid shape.
  b). **Microfilaments**: → - Mediate contractile events.
  c). **Intermediate** filaments.
Cell Membrane

• Structure and support.

1. Canalicular system
• Responsible for the secretion of granule contents. Provides a route for entry and secretion.

2. Dense Tubular System → Responsible for the storage of calcium. Major site of prostaglandin and thromboxane synthesis

• Receptors → For combining with collagen & fibrinogen.
• Precursors of substances like → Thromboxane A2, PG,LT & platelet factor 3,4 are also present.
Organelle Zone

- Secretion and storage.

**Mitochondria.** Power house of cell & Produce **ATP** & **ADP**.

- **Endoplasmic Reticulum** – **stores** large amount of calcium.

- **Glycogen particles**: support metabolic activities & Synthesizes various Enzymes.

- **lysosomes** which contain hydrolytic enzymes

- **Actin & Myosin** – same as those of contractile proteins of muscle. Responsible for **platelet contraction & clot retraction**.

- **Granules**: **dispersed** within the cytoplasm, which serve as **storage sites for proteins** → **platelet function**
Three types of granules

1. Dense granules (Delta) contain ADP, serotonin and calcium.

2. Specific (Alpha) granules contain platelet growth factor, beta thromboglobulin, fibrinogen, clotting factors as V, XIII, P-selectin, transforming growth factor-β1, platelet factor 4 (PF4) which is heparin antagonist factor.

3. Gamma granules contains calcium and may be site of synthesis of prostaglandin and thromboxane A2.
**Development:** From the pluripotent stem cells in the bone marrow.

- CFU-M Colony forming megakaryocytes
  - Megakaryoblast
  - Promegakaryocyte
  - Megakaryocytes
  - Platelets