

Chapter 3

Tissue Renewal

Def:- It's the process by which the body forms new cells to replace structures damaged in the pathological process

2 Types:-

1) Regeneration

- Healing by cells of the same type
- Occurs in tissues with high proliferative capacity (labile & stable cells)
- Requires a good number of stem cells and intact connective tissue matrix

2) Repair

- Occurs in tissues composed of permanent cells or with severe damage that causes decrease in number of stem cells and destruction of CT matrix
- involves combination of regeneration and scar formation (fibrosis)

Types of tissues according to the proliferation power

1) Labile cells -> proliferate throughout life with large number of stem cells

ex. epidermal cells, endometrial cells, GIT lining & bone marrow cells

2) Stable cells -> have lower level of multiplication under normal conditions

-> Can rapidly replicate if stimulated (when needed)

-> Spend most of their lives in G0 phase

ex. liver, kidney, endothelium, pancreatic cells, fibroblast, osteoblast & chondroblast

3) Non-dividing cells (permanent) -> don't multiply in postnatal life

ex. nerve, cardiac & smooth muscle cells

Stem Cells

Def:- undifferentiated cells that are characterized by

- 1) self-renewal capacity
- 2) ability to generate other differentiated cells

Types of division:-

- a) Symmetric -> one stem cell can replicate itself and create 2 stem cells
- b) Asymmetric -> one stem cell can divide into one similar stem cell & differentiated cell

Types of stem cells:-

- 1) Totipotent -> found after the fusion of oocyte (egg) & the sperm
-> differentiate into embryonic & extra-embryonic tissues (placenta).
Occurs in first 4 days
- 2) Embryonic -> are pluripotent cells that can differentiate into any cell except the placenta. Occurs during 5-7 days
- 3) Multipotent -> differentiate to a number of related cell types

4) Oligopotent -> differentiate to a few cell types as lymphoid or myeloid stem cells (more specified)

5) Unipotent -> Differentiate to only one cell type but still has the ability of self-renewal (way more specific)

Adult (somatic) stem cells : identified in many mature tissues as bone marrow, GIT, skin, liver and adipose tissue . They have a limited capacity of differentiation

Sources of stem cells : bone marrow , adipose tissue, blood and umbilical cord blood

When DNA is injured, the following could happen:-

- 1) Apoptosis (cell death)**
- 2) Repair by DNA repair gene**
- 3) Cancer if the DNA repair gene isn't working**
- 4) proliferation inhibition in checkpoint**

Cell cycle and regulation of cell replication

Cell cycle includes 5 phases:

- 1) G1 phase -> pre-synthetic phase**
- 2) S phase -> DNA Synthesis**
- 3) G2 phase -> pre-mitotic phase**
- 4) M phase -> Mitosis**
- 5) G0 phase -> Resting phase where stable cells spend most of their lives**

Characteristics of cell cycle:

- Labile cells can enter G1 phase directly after completing mitosis
- Stable cells can re-enter the cycle from G0 to G1 when needed
- Cell cycle has 2 check points (G1-S and G2-M) which act as surveillance for any DNA damage
- Cell cycle progression is controlled by cyclin & cyclin dependent kinases (CDKs) which control and signaling the cells that are ready to pass to the next phase

Control of cell growth:-

1) Growth stimulators -> polypeptide growth factor & cyclin-CDK complexes

a) Polypeptide growth factors (proteins secreted by certain cells to stimulate other cells to divide)

Growth Factor	Info about it
Platelet derived growth factor (PDGF)	<ul style="list-style-type: none">- found in platelet granules- produced by endothelial, macrophages and smooth muscle cells- Combines with a or B receptors- Causes migration and proliferation of fibroblast, monocytes & smooth muscle cells
Fibroblastic growth factor (FGF)	<ul style="list-style-type: none">- Act as a chemotactic and mitogenic factor for fibroblasts- Stimulates keratinocyte migration- Helps wound contraction

<p>Epidermal growth factor (EGF) & Transforming growth factor-a (TGF-a)</p>	<ul style="list-style-type: none"> - Stimulate mitosis in keratinocyte and fibroblast - stimulate granulation tissue repair - EGF receptors (EGFR) has 4 different transmembrane proteins with intrinsic tyrosinase activity - EGFR1 mutation & over expression causes malignancies - EGFR2 (also called HER-2 neu receptors) mutation & over expression causes poor prognosis of breast
<p>Transforming growth factor-B (TGF-B)</p>	<ul style="list-style-type: none"> - Is a chemotactic factor for inflammatory cells, fibroblast & smooth muscle cells - Helps angiogenesis
<p>Vascular endothelial growth factor (VEGF)</p>	<ul style="list-style-type: none"> - Increases vascular permeability - Stimulates mitosis in endothelial cells - Helps angiogenesis
<p>Cytokines secreted by macrophages and T lymphocytes</p>	<p style="text-align: center;">-</p>
<p>Hepatocyte growth factor</p>	<p style="text-align: center;">-</p>
<p>Tumor necrosis factor</p>	<p style="text-align: center;">-</p>

b) Cyclin-CDK complexes:-

-> are protein complexes formed by the association of an inactive cyclin-dependent kinase with a regulatory subunit (cyclin)

-> Control and signal the cells that are ready to pass to the next phase

2) Growth Inhibitors

- a) Histone deacetylase inhibitors**
- b) CDK inhibitors**
- c) Growth factor receptor inhibitors**

Extracellular Matrix (ECM):

- it's a collection of extracellular molecules that provide structural and biochemical support to the surrounding cells

**** It consist of:-**

- 1) Collagen and elastin for tensile strength and recoil**
- 2) Adhesive glycoproteins which connects the ECM elements together and to cells**
- 3) Lubricant gel of proteoglycan**

<> **Collagen: main structural protein in ECM for tensile strength, in order for it to work we need vitamin C**

Types:-

- Type 1 -> in skin, tendon and bone**
- Type 2 -> in cartilage**
- Type 4 -> in basement membrane**

<> **Elastin: allows tissues to retain\resume their shape after stretching**

<> Adhesive glycoproteins (causes adhesion between cells together and with the ECM) is classified into

- a) Immunoglobulin Family**
- b) Cadherins**
- c) Integrins**
- d) Fibronectin**
- e) Laminin**

<> Proteoglycans (hyaluronic acid):-

- ground substance of ECM**
- it's the filler material between cells**
- plays a role in regulating CT structure, permeability, and growth factor activity**