

# TISSUE REPAIR



## REPAIR

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- Maintenance of normal structure and function and survival of the organism
- Regeneration
- Healing: scar formation and fibrosis

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- Regeneration : growth of cells and tissue to replace lost structure
    - Tissue with high proliferative activity : hematopoietic tissue, epithelium
    - Intact connective scaffold
  
  - Healing : restore original structures involving collagen deposition and scar formation
    - Wound, inflammation, necrosis

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#### Factors involving tissue repair

- Tissue proliferative activity
- Stem cells
- Growth factors and chemical mediators
- Extracellular matrix

## REGENERATION

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- Regenerative capacity attributed to two main factors
  - The capacity of cell to reenter the cell cycle
  - Efficient differentiation of stem cells in area of injury
- Regeneration : Bone marrow, epithelium
- Liver regeneration
  - Compensatory hypertrophy and hyperplasia

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- Post hepatectomy : secretion of cytokine and growth factors
    - Secretion of **TNF, IL-6** →  $G_0 \rightarrow G_1$
    - TNF → Activation of **metalloproteinase**
    - Metalloproteinase → Secretion of **HGF, TGF- $\alpha$**
    - HGF, TGF- $\alpha$  →  $G_1 \rightarrow S$
    - **Norepinephrine, Insulin, Thyroid hormone**
  - TGF- $\beta$ , Activin

## HEALING, SCAR FORMATION AND FIBROSIS

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- Severe tissue injury
- Chronic injury
- Damage of parenchymal cells and stromal framework of the tissue

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- Inflammation
  - Angiogenesis
  - Migration and proliferation of fibroblasts
  - Scar formation
  - Connective tissue remodeling
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- Hallmark of healing : proliferation of fibroblasts and endothelial cell to form granulation tissue

## ANGIOGENESIS

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- Angiogenesis
  - Neovascularization
  - Endothelial precursor cells (EPCs) : vascular implants, ischemia
  - Pre-existing vessels

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- Vasodilation (NO) and increased vascular permeability (VEGF)
  - Degradation of basement membrane (metalloproteinase) and disruption of cell to cell contact (PA)
  - Migration and proliferation of endothelial cells
  - Maturation
  - Recruitment of periendothelial cells

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- Growth factors in angiogenesis

- Growth of endothelial cells

- Vascular endothelial growth factor (VEGF)
      - Inducing agents of VEGF : Hypoxia, TGF- $\beta$ , PDGF, TGF- $\alpha$
    - Fibroblast growth factor (FGF)

- Recruitment of pericytes and smooth muscle cells

- Angiopoietin
    - Platelet-derived growth factor (PDGF)

- Synthesis of extracellular matrix

- Transforming growth factor-  $\beta$  (TGF- $\beta$ )

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## CUTANEOUS WOUND HEALING

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- Inflammatory process
- Granulation formation and re-epithelialization
- Extracellular matrix deposition, wound contracture and tissue remodeling
  
- First intention wound
- Second intention wound

## HEALING BY FIRST INTENTION

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- 24 hr : migration of neutrophils, re-epithelialization
- Day 3 : migration of macrophages, granulation tissue formation, collagen synthesis

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- Day 5 : more granulation tissue formation and collagen synthesis, bridge in the incision, epidermis recover normal thickness
  - Week 2 : continue proliferation of fibroblasts and collagen deposition
  - 1 month : complete scar formation

## Growth factors and cytokines affecting in wound healing

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- Monocyte chemotaxis
- Fibroblast migration/replication
- Keratinocyte replication
- Angiogenesis
- Collagen synthesis
- Collagenase secretion
- Chemokines, TNF, PDGF, FGF, TGF- $\beta$
- PDGF, EGF, FGF, TGF- $\beta$ , TNF, IL-1
- HB-EGF, FGF-7, HGF
- VEGF, angiopoietins, FGF
- TGF- $\beta$ , PDGF
- PDGF, FGF, TNF; TGF- $\beta$  inhibits

### HEALING OF SECOND INTENTION

- More inflammatory process
- More granulation tissue formation
- More wound contracture : myofibroblasts
- Thinning of new epithelium

### WOUND STRENGTH

- 1 week : 10%
- 3 months : 70-80%



## **FACTORS THAT INFLUENCE WOUND HEALING**

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- **Local factors**
  - Infection
  - Physical factors
  - Foreign body
  - Type of tissue
- **Systemic factors**
  - Nutritional factors : protein, vitamin C
  - Metabolic status : DM
  - Blood circulation
  - Hormonal status

## **COMPLICATION IN CUTANEOUS WOUND HEALING**

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- Inadequate formation of granulation tissue and scar formation
- Excessive formation of the repair components
  - Hypertrophic scar
  - Keloid
  - Exuberant granulation
  - Aggressive fibromatosis
- Formation of contracture