GROWTH FACTORS in Wound Healing

The process of wound healing begins immediately following injury. Growth factors released in traumatized area promote cell migration into wound area (Chemotaxis); stimulate growth of Epithelial Cells, and Fibroblasts (mitogenesis), initiate formation of new blood vessels (angiogenesis) and stimulate matrix formation & remodelling of affected region.

Growth factors are classified as CYTOKINES which are proteins that act as internal cellular signals to allow cells to communicate with one another. Such cytokines regulate & modulate cellular activity & function via endocrine, paracrine, autocrine & intracrine mechanism.

Growth factors - that acts on Quiescent Cells in the G_0 phase of cell cycle have termed COMPETENCE FACTORS.

(I) eg: Platelet-derived growth factor (PDGF)
Fibroblast Growth factor (FGF) etc

(II) Other factors that acts on later in Cell Cycle - S & G_2 phases, they are termed PROGRESSION FACTORS

eg: Insulin-like Growth factors (IGFs)
Macrophage-derived Growth factor (MDGF) etc

Growth factors are POLYPEPTIDES, & those released from ACTIVATED MACROPHAGES are more imp^t.

1) Epidermal Growth factors (EGF) is mitogenic & maturation factor for variety of Epithelial cells & fibroblasts. It stimulates cell division by binding to Tyrosine Kinase Receptor on cell membrane.

Transforming Growth factor-alpha (TGF-α) is also have function closely similar to EGF.

(2) Platelet-derived Growth Factor (PDGF).

PDGF is stored in Platelet-Alpha Granules & released on Platelet activation, mainly by activated Macrophages.

PDGF cause both Migration & proliferation of Fibroblasts, Smooth Muscles Cells & Monocytes.

It is one of most potent COMPETENCE FACTORS in wounds & exert effects during first Two Phases of Repair.

It is Chemotactic for → Fibroblasts & Monocytes, as well as Mitogenic for → Fibroblasts & Vascular Smooth Muscle Cells.

PDGF acts both through Paracrine & Autocrine function

(3) Transforming Growth Factor-Beta (TGF-β)

TGF-β directly stimulate Collagen synthesis & decreases Extracellular Matrix degradation by Fibroblasts. & Increases synthesis of ECM proteins

It is released from Platelets & Macrophages at wound. TGF-β is profibrotic growth factor that accelerate wound repair at expense of ↑sed fibrosis.

TGF β act Autocrine fashion – to stimulate its own synthesis & secretion. TGF-β also as Chemoattractant for Fibroblasts & Macrophages to the wound.

(4) Fibroblast Growth Factor (FGF) :- are polypeptides with high affinity to HEPARIN & so do for the Basement Membrane

& basic FGF (bFGF) plays prominent role & in Angiogenesis, initiating release of Basement Membrane degrading enzymes that liberate Endothelial Cells before new vessel formation.

(5) Tumour Necrosis Factor-alpha (TNF-α)

released by Stimulated Macrophages and acts to stimulate Angiogenesis.

(6) Vascular Endothelial Growth factors (VEGF)

Glycoprotein with function similar to PDGF. It acts in paracrine Manner — AND — is potent ANGIOGENIC Stimulus.

Promotes blood vessel formation (angiogenesis) & has Central role in growth of new vessel formation.

It stimulates - Prolifn of Endothelial Cells after release from Platelets, Macrophages, Fibroblasts & Keratinocytes. It is also expressed in HYPOXIC Conditions of wounds.

(7) Keratinocyte Growth factor (KGF) is released by FIBROBLASTS & act in paracrine fashion to stimulate Keratinocyte division & differentiation AND thereby directly stimulate EPITHELIALIZATION.

(8) Insulin-like Growth factors - I (IGF-I) stimulate Collagen Synthesis by Fibroblasts. & facilitate fibroblast proliferation.

EXTRA CELLULAR MATRIX is a depository of Growth factors in LATENT FORMS under normal unwounded state. With injury & matrix destruction → inactive GFs are released in active form & assist in Initiating & Regulating the Repair process.