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Role of Growth Factors in Oral Tissues and Diseases

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ABSTRACT

Growth factors (GFs) are natural biological mediators that regulate key cellular eventsthat helps in tissue repair and regeneration such as mitogenesis, chemotaxis, differentiation, and metabolism.In recent concepts the areas of cellular and molecular biology explains the functions and their role in repair process.In vivo and vitro studies that proves the GFs can enhance the capacity of tissues to regenerate by regulating cell chemoattraction,differentiation and proliferation. In this review,explains the different role of growth factors in oral tissues and diseases.

Keywords: Oral Tissues, Biological Mediators, cells.

INTRODUCTION

Growth factors are signaling molecules utilize their effects on the neighbouring cells or cells located at a distance.These signalling molecules bind and acts on other molecules known as receptor molecules.On the cell surface there are specific growth factor receptor.The binding of growth factor to its growth receptor stimulates cell to grow in a process known as signal transduction[1].

Pathway of GF

Growth factor synthesized by an originating cell and bind to its receptor ,activate the target receptor and activates a series of cytoplasmic proteins called signal transducinng proteins and it present on its inner surface of plasma membrane[2,3].There are two important proteinsras and ab1 genes.ras binds with guanosine diphosphate (GDP),the cells remain in inactive state.Then the growth factor stimulates the inactive ras becomes active by releasing GDPand it binds to guanosine triphosphate.The active ras inturn activates cytoplasmic kinases and pass signals to nucleus for cell proliferation.

Signaling Molecules

The signals by growth and differentiation factors are transmitted from one cell to another by paracrine, autocrine, juxtacrine, and intracrine modes.

Paracrine

These signals target cells ,which are located in neighbourhood of emitting cell.

Autocrine

Synthesized by one cell, secreted in a soluble form outside the cell and then bind to surface receptors on the same cell to evoke an effect is an autocrine mode of action.

Juxtacrine

The adjacent cells should be in cell to cell physical contact.

Endocrine

These signals are called hormones,which travel through the blood to reach a distant place in the body[1].

Different types of growth factors ,effects and its sources5:

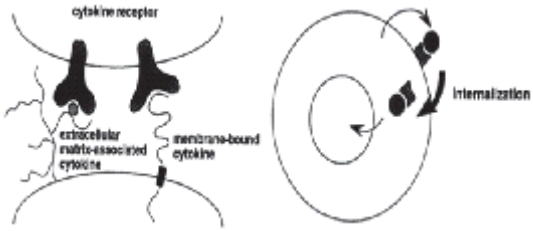
Growth Factors	Source	Target Cells / Effect
Epidermal growth factor (EGF)	Macrophages, platelets, epithelium	Mitogenic for epithelial tissues, fibroblasts, endothelial cells
Fibroblast growth factor (FGF)	Fibroblasts, endothelial cells, bone cells, macrophages	Endothelial cells, fibroblasts
Transforming growth factor (TGF-alpha)	Macrophages, eosinophils, keratinocytes, epithelial cells, platelets	Similar to EGF, but more potent angiogenesis factor
Transforming growth factor (TGF-beta)	Macrophages, lymphocytes, fibroblasts, keratinocytes, platelets, bone	Inhibits replication of most cells in vitro
Platelet derived growth factor (PDGF)	Endothelial cells, platelets, macrophages, fibroblasts	Mitogenic for vascular smooth muscles, fibroblasts, monocytes
Insulin-like growth factor (IGF I)	plasma, liver, fibroblasts	Mitogenic for fibroblasts, endothelial cells, fibroblasts, fetal tissues

Role of TGF in Tooth Development

Bell Stage

I. Histodifferentiation of odontoblasts and ameloblast take place. In addition, the mesenchymal cells differentiate into alveolar bone that forms the sockets for the teeth [10].

i.Paracrine **ii.Autocrine**



iii.juxtacrine **iv.Endocrine**

Secretion of growth factor by inner enamel epithelial cells

(TGF beta-1,BMP2,IGF)

↓

Bind to heparinsulphate proteoglycan

Ectomesenchymal cells differentiate to odontoblasts

Core binding factor alpha-1 appears in the mesenchyme (Early bell stage)

Mesenchyme respond to signals from the epithelium

Once the signals reaches cbfa-1 disappears

↓

Odontoblast differentiation start secreting dentin matrix

Gradual disintegration of basement membrane (MMPs & Proteases)

Preameloblasts interact directly with odontoblasts

Initiation of enamel matrix secretion

Role ofTGF-β2 during bell stage

TGF beta -2 shifts to inner enamel epithelial cells

Induces differentiation of odontoblasts

Induces differentiation of ameloblasts

Role of TGF in Oral diseases

Role of TGF-β in cancer

TGF-β exists in three isoforms (TGF-â1, TGF-â2, and TGF-â3), but the extended superfamily includes more than 30 additional cytokines, classified into several subfamilies [e.g., bone morphogenetic proteins (BMPs) and activins]. Cancer cells secrete and respond toTGF-â in an autocrine manner[11].

cytokine induces

cytostatic effect on many epithelial cell types

Receptors

(Heterotetrameric serine/threonine kinases,) control proliferation, differentiation, and programmed cell death

Receptors play an important role in apoptosis by signaling through the SMAD pathway

SMAD pathway

TGF-β dimers bind to a type II receptor,

phosphorylation

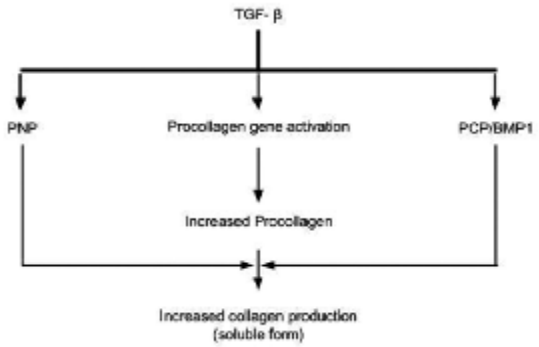
type Ireceptor.

Receptor-regulatedSMAD (R-SMAD)

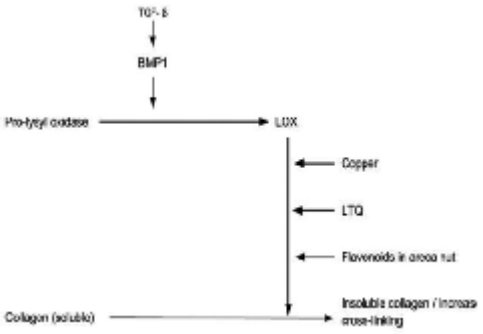
Prevents the ability of cells to progressthrough the cell cycle, and it stimulates apoptosis or differentiation[12].

Role of TGF-β in oral submucous fibrosis

Collagen synthesis regulated by TGF-β



Mechanism involved in increased collagen cross-linking[13]



Role of TGF-β in periodontal regeneration

Three major activities of TGF-ß include:

a) Inhibition of cell proliferation,

b) Enhancement of extracellular matrix deposition and

c) The exhibition of complex immune regulatory properties.

It can stimulate or inhibit the cell growth ,differentiation and also modulate other GFs like PDGF, EGF and FGF. It inhibits epithelial cell proliferation and stimulates mesenchymal cells. Primarily,it is found in the platelets and osseous tissue.

TGF-β

Recruiting and stimulating osteoprogenitor cells

proliferate and desire supporting periodontal wound healing and regeneration[2,14].

CONCLUSION

The present study mainly focus the role of transforming growth factors and other growth factors in odontogenesis,oral cancer,oral submucous fibrosis , periodontium

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