Role of Growth Factors in Oral Tissues and Diseases

S. LEENA SANKARI, L. MALATHI, M. KASTHURI* and N. BALACHANDER

Department of Oral Pathology, Sree Balaji Dental College and Hospital, Bharath University, Pallikaranai, Chennai - 600100, India.

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ABSTRACT

Growth factors (GFs) are natural biological mediators that regulate key cellular events that 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 neighboring 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.

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 transducing proteins and it present on its inner surface of plasma membrane. There are two important protein ras 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 GDP and it binds to guanosine triphosphate. The active ras intern 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.

Different types of growth factors, effects and its sources:

<table>
<thead>
<tr>
<th>Growth Factors</th>
<th>Source</th>
<th>Target Cells / Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ecdsinal growth factor (IGF)</td>
<td>Mesenchymal cells, alveolar bone, bone, epithelial cells</td>
<td>Stimulates proliferation of mesenchymal cells, osteoblasts, osteoclasts</td>
</tr>
<tr>
<td>Epidermal growth factor (EGF)</td>
<td>Epidermis, epithelial cells, bone cells, smooth muscles</td>
<td>Stimulates cell proliferation and differentiation</td>
</tr>
<tr>
<td>Transforming growth factor (TGF-α)</td>
<td>Microvilli, mesenchymal cells, epithelial cells, keratinocytes</td>
<td>Similar to EGF, but more potent to epidermal cells</td>
</tr>
<tr>
<td>Transforming growth factor (TGF-β)</td>
<td>Microvilli, mesenchymal cells, epithelial cells, keratinocytes</td>
<td>Inhibits proliferation of mesenchymal cells</td>
</tr>
<tr>
<td>Fibroblast growth factor (FGF)</td>
<td>Mesenchymal cells, fibroblasts, epithelial cells, endothelial cells</td>
<td>Stimulates proliferation of fibroblasts, osteoblasts, endothelial cells</td>
</tr>
<tr>
<td>Insulin-like growth factor (IGF-I)</td>
<td>Placenta, liver, fibroblasts</td>
<td>Stimulates proliferation of fibroblasts, endothelial cells, fibroblasts, epithelial cells</td>
</tr>
</tbody>
</table>

Role of TGF in Tooth Development

Bell Stage

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

Odontoblast differentiation start secreting dentin matrix

Gradual disintegration of basement membrane (MMPs & Proteases)

Preameloblasts interact directly with odontoblasts

Initiation of enamel matrix secretion

Role of TGF-β2 during bell stage

TGF beta-2 shifts to inner enamel epithelial cells

Induces differentiation of odontoblasts

Induces differentiation of ameloblasts

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 reach cbfa-1 disappears

Role of TGF-β

Paracrine

Autocrine

Juxtacrine

Endocrine
Role of TGF in Oral diseases

Role of TGF-β in cancer

TGF-β exists in three isoforms (TGF-α1, TGF-α2, and TGF-α3), 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 to TGF-α in an autocrine manner.

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 I receptor.

Receptor-regulated SMAD (R-SMAD)
Prevents the ability of cells to progress through the cell cycle, and it stimulates apoptosis or differentiation.

Role of TGF-β in oral submucous fibrosis

Collagen synthesis regulated by TGF-β

Mechanism involved in increased collagen cross-linking

Role of TGF-β in periodontal regeneration

Three major activities of TGF-β 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.

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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