

Serum and in situ expression of transforming growth factor *beta* 1 in Psoriasis

Thesis

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ABSTRACT

Psoriasis vulgaris is a skin disease characterized by hyperproliferation of epidermal keratinocytes, capillary elongation, accompanied by inflammatory cell infiltrate. Keratinocytes hyperproliferation could be explained by dysregulation of growth factors controlling epidermal proliferation and by altered metabolism of their receptors in affected skin.

Transforming growth factor beta 1 regulates the proliferation and differentiation of cells, wound healing, and angiogenesis. It is a potent inhibitor of cells as it arrests the cell cycle in the G1 to S phases. It shows a multitude of effects on cellular differentiation and growth.

KEY WORDS: Psoriasis, Transforming growth factor beta 1.

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LIST OF ABBREVIATIONS

α	alpha
AA	arachidonic acid
α-E β7	alpha E Beta 7
ALA	alpha linolenic acid
AP-1	activator protein-1
APC	antigen-presenting cell
β	beta
BMP	bone morphogenic protein
cAMP	cyclic adenosine monophosphate
c-JNK	c-Jun amino terminal kinase
CLA	cutaneous lymphocyte-associated antigen
CTGF	connective tissue growth factor
CTL	cutaneous T lymphocytes
CTLA4	cytotoxic T lymphocyte antigen 4
DC	dendritic cell
DHA	docosahexaenoic acid
DPC4	deleted in pancreatic carcinoma 4
EGF	epidermal growth factor
EGF-R	epidermal growth factor receptor
ELISA	enzyme linked immunosorbant assay

EPA	eicosapentaenoic acid
γ	gamma
G1	GAP 1
GM-CSF	granulocyte-macrophage colony-stimulating factor
HB-EGF	heparin binding epidermal growth factor
HERVs	human endogenous retroviruses
HGF	hepatocyte growth factor
HIV	human immunodeficiency virus
HLA	Human leucocyte antigen
H₂O₂	hydrogen peroxide
HSP	heat shock protein
ICAM	intercellular adhesion molecule
INF	interferon
iNOS	inducible nitric oxide synthase
Ig	immunoglobulin
IL	interleukin
IRF1	interferon regulated factor 1
K	keratin
Kb	kilobase
KC	keratinocyte
Kd	kilodalton
KGF	keratinocyte growth factor
LAK	lymphokine activated killer cell

LAP	latency associated peptide
LDL	low density lipoprotein
LFA	lymphocyte function antigen
LTB4	leukotriene B4
MHC	major histocompatibility complex
MIG	monokine induced by interferon gamma
NFKB	nuclear factor Kappa Beta
NGF	nerve growth factor
NK	natural killer
NO	nitric oxide
ODC	ornithine decarboxylase
PAI-1	plasminogen activator inhibitor-1
PASI	psoriasis area and severity index
PLA2	phospholipase A2
PUFA	polyunsaturated fatty acid
PMN	polymorphonuclear cells
RT-PCR	reverse transcriptase polymerase chain reaction
SCC	squamous cell carcinoma
ScF	scatter factor
SD	standard deviation
Smad	Derived from Sma and MAD gene homologues in Caenorhabditis elegans and Drosophila melanogaster

S phase	synthesis
sICAM	serum intercellular adhesion molecule
SLeX	sialyl Lewis X
STAT1	Signal transducer and activator of transcription 1
TCR	T cell receptor
TGase K	keratinocyte transglutaminase
TGF-α	transforming growth factor-alpha
TGF-β	transforming growth factor-beta
TGF-β R	transforming growth factor-beta receptor
Th	T-helper
Tie	tyrosine kinase
TLR	Toll like receptor
TNF-α	tumor necrosis factor-alpha
t-PA	Tissue-plasminogen activator
TSP-1	trhombospondin-1
u-PA	Urokinase-plasminogen activator
VC	Verrucous carcinoma
VCAM	vascular cell adhesion molecule
VEGF	Vascular endothelial growth factor
VLA-4	very late antigen-4
VLDL	Very low density lipoprotein

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Psoriasis is derived from the Greek word "*psora*" meaning "*to itch*". Although psoriasis was first recognized as a distinct disease as early as 1808, its pathogenic mechanisms have eluded investigators for decades. Recently, it has attracted the attention of molecular genetics having fallen under the somewhat elusive descriptor "complex disease" (**Tagami, 1997**).

Psoriasis is a common disease with a prevalence up to two percent in the world population (**He et al., 2005**). It is defined as a clinical entity affecting skin, nails, mucous membranes and joints. The usual presentation is that of a sharply demarcated erythematous, hyperkeratotic, and sometimes pustular lesions of varying extent, distributed symmetrically over the skin, however there are many varieties of lesions; different sizes, shapes and patterns. Occasionally, the entire skin can become involved, leading to erythroderma or exfoliative dermatitis (**Bos et al., 1999**).

The pathogenesis of psoriasis is diverse, it includes Cellular alterations in the skin with marked hyperplasia of the epidermis, altered keratinocytes differentiation and angiogenesis The infiltrate is composed of skin-infiltrating Cutaneous leukocyte associated antigen (CLA+) memory T cells predominantly showing a T helper (Th1) Phenotype, neutrophils, macrophages, and increased numbers of dendritic cells (**Chamian et al., 2005**).

Transforming growth factor beta (TGF- β) belong to a family of growth factors with inhibitory effects on epithelial cell proliferation as well as immunosuppressive effects. TGF- β s inhibit the growth of many cell types, including keratinocytes (KC) and they stimulate the differentiation of KC in culture. Three isoforms of TGF- β s have been identified in various human tissues: TGF- β 1, TGF- β 2 and TGF- β 3 (*Doi et al., 2003*).

Aim of Work:

The aim of the work was to evaluate the expression of TGF- β 1 in patients with psoriasis in order to define its role in this inflammatory hyperproliferative skin disease.