Role of Estrogen and Matrix Metalloproteinase–1 in Skin Aging and Photoaging

Thesis

Submitted for partial fulfillment of Master degree in Dermatology, Venereology and Anderology

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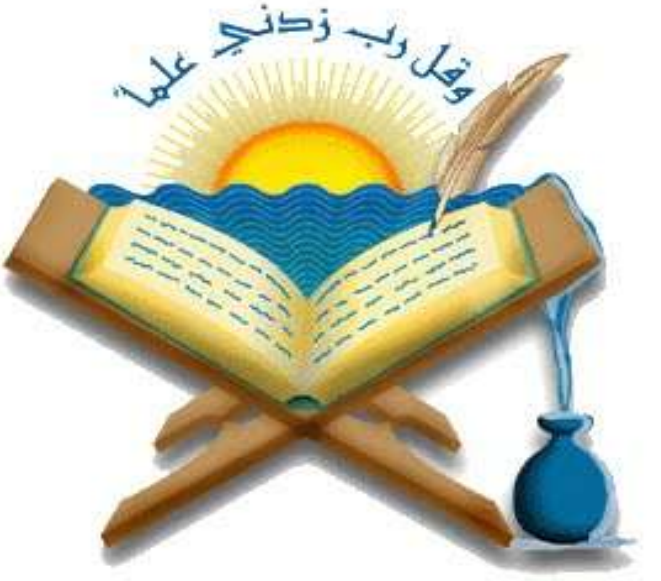
بسم الله الرحمن الرحيم



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Contents

List of Abbreviations

AP-1	Activator protein-1
APCs	Antigen presenting cells
ATP	Adenosine triphosphate
BCC	Basal cell carcinoma
bFGF	Basic fibroblast growth factor
Cdk	Cyclin dependent kinases
CyR61	Cysteine rich growth regulatory factor
DEJ	Dermo-epidermal junction
DHEA	Dehydroepiandrostrone
ECM	Extracellular matrix
EGF	Epidermal growth factor
ER	Estrogen receptor
FSH	Follicle stimulating hormone
GAGs	Glycosaminoglycans
GM-CSF	Granulocyte macrophage colony stimulating factor
H&E	Hematoxylin and Eosin
HRT	Hormone replacement therapy
HSD	Hydroxysteroid dehydrogenase
IGF	Insulin-like growth factor
IGFBP	Insulin-growth factor binding protein
IL	Interleukin
LCs	Langerhans cells
LDL	Low density lipoproteins
LH	Luteinzing hormone
MED	Minimal erythema dose
MIF	Macrophage migration inhibitory factor
MMPs	Matrix metalloproteinases
mt DNA	Mitochondrial DNA
MT-MMPs	Membrane type MMPs
NF-kβ	Nuclear factor kβ
PDGF	Platelet derived growth factor
ROS	Reactive oxygen species
SCC	Squamous cell carcinoma
SERMs	Selective ER modulators
TGF	Transforming growth factor
TIMPs	Tissue inhibitors of matrix metalloproteinases
TNF α	Tumour necrosis factor α
UV	Ultraviolet
VEGF	Vascular endothelial growth factor

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Protocol

Role of Estrogen and Matrix Metalloproteinase–1 in Skin Aging and Photoaging

Protocol for Thesis

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Role of Estrogen and Matrix Metalloproteinase–1 in Skin Aging and Photoaging

Introduction

Human skin, like all other body organs undergoes chronological aging. In addition, unlike other organs, skin is exposed to ultraviolet (UV) irradiation and, therefore, undergoes aging as a consequence of sun exposures (photoaging) ***(Fisher et al., 2002).***

Clinically, naturally aged skin is smooth, pale and finely wrinkled. In contrast; photoaged skin is coarsely wrinkled and associated with pigmentation and telangiectesia ***(Gilchrest, 1989).*** Alteration in collagen, which is the major structural component of skin, have been suggested to be the cause of clinical changes, such as skin wrinkling and loss of elasticity, observed in naturally aged and photoaged skin ***(Fisher et al., 1997).***

UV irradiation activates growth factors and cytokine receptors on the surface of keratinocytes and fibroblasts. Activated receptors stimulate signal transduction cascades that induce the transcription factor; Activator Protein1 (AP-1), which stimulates transcription of matrix metalloproteinases (MMPs) secreted from keratinocytes and fibroblasts ***(Ullrich and Schlessinger, 1990).***

MMPs are a family of zinc dependant endoproteinases that has pivotal role in the dynamic remodeling of extracellular matrix (ECM). MMP-1 is the most abundant MMPs and is produced by fibroblasts. It initiates cleavage of fibrillar collagen at single site within its central triple helix. Once cleaved by MMP-1, collagen can be further degraded by elevated levels of MMP-3 and MMP-9. Thus, MMPs mediate collagen damage in photoaged skin ***(Sternlicht and Werb, 2001).***

Estrogen and estrogen like compounds work to reverse the effects of both intrinsic aging and photoaging in the skin, by functioning as both antioxidants and signaling molecules ***(Kang et al., 2003)***. They mediate their activity by interaction and activation of specific intracellular receptor proteins; Estrogen Receptors (ERs). There are two types of estrogen receptors: ERα and ERβ.

ERβ were found to show strong expression in the epidermis, dermal fibroblasts, blood vessels, and hair follicles of male and female adult scalp skin, but no specific staining of ER-α was observed ***(Thornton et al., 2003; Pelletier and Ren, 2004).***

Estrogens were found to increase the activity of transforming growth factor beta (TGF-β), which increases the production of collagen. On the other hand, they reduce the concentration of reactive oxygen species (ROS). ROS were found to increase signaling pathways that inhibit collagen production and also increase MMPs activity, resulting in a net result of decreased collagen content. Thus, a good part of the changes in collagen, seen in aging, were found to be associated with decreased level of estrogen ***(Kang et al., 2003).***

Aim of work

The aim of the work is to study the expression of ERβ and MMP-1 in premenopausal and postmenopausal women, both in sun-exposed and sun-protected skin, to find out their role in skin aging and photoaging.

Subjects and Methods,

The study will include 20 female subjects comprising two groups:
- Group I: 10 premenopausal women
- Group II: 10 postmenopausal women

Both groups will be subjected to the following:
- History with emphasis on outdoor activities and smoking.
- Examination

- Skin biopsies: 2 skin biopsies will be taken from each subject, one from sun protected skin and one from sun exposed skin. Each biopsy will be processed and stained by :
- Hematoxylin and Eosin (H&E) for routine histopathological examination.
- Immunoperoxidase technique to study the expression of both ERβ and MMP1 by immunohistochemistry.

The study will include:

_ Introduction and aim of the work.
_ Review of literature.
_ Subjects and Methods.
_ Results.
_ Discussion .
_ Summary and Conclusions.
_ References.
_ Arabic Summary.

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