STUDY OF SERUM LEVELS AND SKIN EXPRESSION OF S100B PROTEIN IN PSORIASIS

Thesis

Submitted for partial fulfillment of master degree in

Dermatology, Venereology and Andrology

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2013

دراسة مستوى بروتين S100B فى مصل الدم و ظهوره فى الجلد فى مرض الصدفية

رسالة مقدمة من

أمنية أسامة الحاجري

بكالوريوس الطب والجراحة – كلية الطب ، جامعة عين شمس

توطئة للحصول على درجة الماجستير في الأمراض الجلدية و التناسلية و الذكورة

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2013

ACKNOWLEGEMENT

Thanks to ***God*** first and foremost. I feel always indebted to God, the most kind and the most merciful.

I would like to express my great gratitude and respect to ***Prof. Dr. Samar Abdalla Salem*** *, Professor of Dermatology, Venereology and Andrology, Ain Shams University*, for giving me the privilege of being under her supervision in this thesis, and thank her for her outstanding encouragement, advice and her sincere endless support throughout this work, ***Dr. Ekramy El Khateeb****, Lecturer of Dermatology, Venereology and Anndrology, Ain Shams University*, for his great care and patience, sincere guidance, tremendous effort and continuous valuable advice through out this work.

I am deeply indebted ***to Prof. Dr. Hnaa Imam****, Professor in Dermatology and Venereology, National Research Centre*, for her great continuous cooperation and supervision all to the end of this thesis, ***Pof. Dr. Wafaa Abdelaal****, Professor of Pathology, National Research Centre*, ***Dr. Reham El Nemr****, Assistant Professor of Pathology, National Research Centre*, *and* ***Prof. Dr. Mervat Harvy****, Professor of Medical Biochemistry, National Research Centre,* for their remarkable efforts, considerable help, and continuous supervision and guidance which were the major factors behind the completion of this thesis.

CONTENTS

LIST OF ABBREVIATIONS

ABC	Avidin–biotin–peroxidase complex
APC	Antigen presenting cell
Ca^{2+}	Calcium
CLA	Cutaneous lymphocyte antigen
CNS	Central nervous system
Cu^{2+}	Copper
CXC	Chemokines
DAB	Diaminobenzidine
DC	Dendritic cell
EDC	Epidermal differentiation complex
ER	Endoplasmic reticulum
GFAP	Glial fibrillary acidic protein
GH	Growth hormone
GM-CSF	Granulocyte-macrophage colony stimulating factor
HLA	Human leukocytic antigen
HRP	Horseradish peroxidase
ICAM-1	Intercellular adhesion molecule-1
IFN-γ	Interferon gamma
IgG1	Immunoglobulin G (subtype 1)
IL-1β	Interleukin-1 beta
IL-2	Interleukin-2
IL-8	Interleukin-8
IP-10	Inducible protein-10
IP-10	Inducible protein-10
kDa	Kilo Dalton
LFA-1	Lymphocyte functional associated antigen-1
MHC	Major histocompatibility complex
MIF	Macrophage migrating inhibiting factor
MIG	Monokine induced by interferon gamma
NEF	Neurite extension factor
NKT	Natural killer cell

OR	Odds ratio
PASI	Psoriasis Area Severity Index
PBS	Phosphate Buffered Saline
PRA	Prolactin receptor associated protein
PRL	Prolactin
PSORS	Psoriasis susceptibility locus
PUVA	Psoralin + ultraviolet rays type A
RA	Rheumatoid arthritis
RAGE	Receptor for advanced glycation endproducts
RANTES	Regulated upon Activation, Normal T-cell Expressed, and Secreted
RT	Room temperature
STAT4	Signal transducer and activator of transcription 4
T-AP interactions	T-cell/APC interactions
T-bet	T cell-associated transcription factor
TGF- β	Transforming growth factor -βbeta
Th	T helper
TMB	Tetramethylbenzidine
TNF-α	Tumor necrosis factor α alfa
T-reg	T-regulatory cell
UVB	Ultraviolet rays type B
VCAM-1	Vascular cell adhesion molecule-1
VEGF	Vascular endothelial growth factor
VEG-F	Vascular endothelial growth factor
VLA-4	Very late antigen-4
Zn^{2+}	Zinc
5-HT_{1A}	5-hydroxytryptamine (serotonin) receptor 1A

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INTRODUCTION

Psoriasis is a chronic relapsing skin condition affecting the population worldwide characterized by epidermal hyperplasia and parakeratosis **(*Raut et al, 2013*)**. The etiology includes genetic and environmental factors **(*Weigle and McBane 2013*)**. Sharply demarcated margins with clear-cut borders are the hallmark of psoriatic lesions. Additional morphological features include erythema and scaling. Sometimes, pustular lesions coexist. Scaling predominates in stable chronic plaque psoriasis, whereas erythema is the dominant feature of unstable progressing lesions. Lesions may sting, itch and bleed easily **(*Naldi and Gambini, 2007*)**.

Psoriasis represents T-cell mediated autoimmune disorder. In spite of significant advances in understanding the pathogenesis of psoriasis, the exact etiology of the disease remains unknown **(*Raut et al, 2013*)**. Numerous immunologic, bioregulatory and biochemical changes accompanying this disease were described **(*Ghoreschi et al, 2007*)**.

The S-100 family of proteins are acidic calcium and zinc binding low molecular weight proteins mainly present in astrocytes and in a population of oligodendrocytes of the CNS

(*Hattinger et, 2013*). Thay are found exclusively in vertebrates with at least 25 members found to date in human. They constitute the largest subfamily of the EF-hand proteins **(*Santamaria-Kisiel et al, 2006*)**.

S100 proteins are proposed to have intracellular and extracellular roles in the regulation of many diverse processes such as protein phosphorylation, cell growth and motility, cell-cycle regulation, transcription, differentiation, Ca^{2+} homeostasis and cell survival **(*Santamaria-Kisiel et al, 2006*)** by serving as calcium sensor proteins that, upon activation, regulate the function and/or subcellular distribution of specific target proteins **(*Donato, 1999*)**. They play a role in the pathogenesis of epidermal diseases, as selected S100 proteins are markedly overexpressed in psoriasis, wound healing, skin cancer, inflammation, cellular stress, and other epidermal states **(*Eckert et al, 2004*)**.

S100B protein is normally present in the epidermis in Langerhans' cell and melanocytes and in dermis in Schwann cells, sensory corpuscles and sweat glands. On the other hand, it is abnormally expressed in melanocytic lesions, such as, nevi, melanoma and melanoma metastases **(*Boni et al, 1997*)**. In general, it is expressed in dendritic cells and cells of neurogenic origin. Increased circulating S100B levels have been also demonstrated in

gastrointestinal cancer, neurological diseases including minor and severe head trauma, subarachnoid hemorrhage and cerebral infarction, neurodegenerative processes, peripheral nervous system lesion and/or impairment, cardiopulmonary bypass surgery, cerebrovascular or cardiovascular ischemic disease, and cardiac arrest **(*Undén et al, 2004*)**.

Studies showed that there is elevation of S100B protein level in the sera of psoriatic patients which is directly correlated with the severity of psoriasis by PASI score **(*Paradisi et al, 2007*)**.

AIM OF THE WORK

The aim of this thesis is to evaluate the level of S100B in psoriasis through immunohistochemical and serological studies to assess its possible involvement in the pathogenesis of psoriasis.