

**A study of melanocytes, melanocyte precursor
cells and stem cell factor in responding and
resistant lesions of vitiligo before and after
photochemotherapy**

Thesis

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ABSTRACT

Introduction and background: PUVA therapy has long been considered a standard line of treatment for vitiligo that can stimulate melanogenesis. The response to PUVA therapy has always been deficient in some anatomical sites including hands, feet and periorificial areas. Treatment of these areas has always been a therapeutic challenge.

Aim of work: To clarify causes of resistance at those sites, by studying the expression of stem cell factor on keratinocytes and c-kit receptor on melanocytes in both resistant and responding lesions of vitiligo before and after photochemotherapy.

Patients and methods: The study included twenty patients of generalized active vitiligo. Four skin biopsies: 2 biopsies (1 lesional and 1 perilesional) from areas expected to respond and 2 biopsies (1 lesional and 1 perilesional) from areas expected to resist were taken from each patient before PUVA and as soon as repigmentation starts other four skin biopsies were taken in the same pattern. Immunohistochemical staining was done for each section by Hematoxylin & Eosin, Melan-A, stem cell factor, c-kit protein.

Results: Before PUVA therapy, there was increased expression of SCF and absence of c-kit from lesional skin in both groups. Areas resistant to treatment showed significantly lower hair follicle density, epidermal melanocyte density by Melan-A staining, lesional SCF expression as well as perilesional c-kit expression. After PUVA therapy there was a significant decrease in SCF expression in both groups but significant rise in c-kit expression was noted only in responding lesions.

Conclusion: Areas resistant to treatment in vitiligo show lower numbers of hair follicles, melanocytes and lower expression of SCF as well as c-kit compared to responding areas. These differences could be behind the resistance to PUVA therapy. A defect in SCF/c-kit system interaction that fails to be corrected by PUVA could be suggested.

Key words: vitiligo- resistance-SCF/c-kit-photochemotherapy.

List of abbreviations

ADF	Adult T-cell leukemia-derived factor.
aFGF	alpha fibroblastic growth factor.
AIDS	Acquired immunodeficiency syndrome.
AIRE	Auto-immune regulator gene.
AP	Antioxidant pool.
APECED	Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy.
BB-UVB	Broad band ultraviolet B.
bFGF	Basic fibroblast growth factor.
Ca ²⁺	Calcium.
cAMP	Cyclic AMP.
CMV	cytomegalovirus
CAT	Catalase.
CREB	cAMP-response element binding protein
CRE	cAMP response element.
DOPA	Dihydroxyphenylalanine.
DRG	Dorsal root ganglia.
EDN	Endothelins.
EDN1	Endothelin-1.

EDN2	Endothelin-2.
EDN3	Endothelin-3.
EDNRA	Endothelin receptor A.
EDNRB	Endothelin receptor B.
EGF	Epidermal growth factor.
FGF-1	Fibroblastic growth factor-1.
GISTs	Gastrointestinal stromal tumors.
GM-CSF	Granulocyte macrophage colony stimulating factor.
H2O2	Hydrogen peroxide.
Hcy	Homocysteine .
HGF	Hepatocyte growth factor.
HIV	Human immunodeficiency virus.
HLA	Human leucocyte antigen
IL-1	Interleukin-1.
IL-6	Interleukin-6.
LIF	Leukaemia inhibitory factor.
LIFRa	Leukaemia inhibitory factor receptor a.
Mcs	Melanocytes
MC1R	Melanocortin 1 receptor.

MHC	Major histocompatibility complex.
MITF	Microphthalmia-associated transcription factor.
MK	Mono-aminophosphate kinase.
MMP	Matrix metalloproteinase.
mRNA	Messenger RNA.
mSCF or SCF-2	Membrane-bound SCF.
MSH	Melanocyte stimulating hormone.
PAR-2	Protinease-activated receptors 2.
PGE2	Prostaglandin E2.
PGF2a	Prostaglandin F2a.
PC (KUS)	Pseudocatalase (KUS)
PKA	protein kinase A.
PNS	Peripheral nervous system.
PUVA	Psoralen and UVA.
RTKs	Receptor tyrosine kinases.
SCF	Stem cell factor.
sSCF or SCF-1	Soluble SCF.
Th1	T-helper 1.
Th17	T-helper 17.
Th2	T-helper 2.

TIM	Topical immunomodulators.
TNF α	Tumor necrosis factor- alpha.
TRP	Tyrosine related protein.
UVA	Ultraviolet A.
UVB	Ultraviolet B.
UVR	Ultraviolet radiation.
VAMA	Vitiligo-associated melanocyte antigens.

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