بسم الله الرحمن الرحيم

تم رفع هذه الرسالة بواسطة / سامية زكى يوسف

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسؤولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد
Investigating the effect of phototherapy on gene expression of CXCR3-B in Vitiligo

Thesis
Submitted for Partial Fulfilment of master’s degree in medical Biochemistry & Molecular biology

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قالوا:
"سبحانك إلا علمنا لتأمل إلَّا ما علمتنا إنك أنتَ الحكيم العليم الأكيم.

صدّ الله العظيم

سورة البقرة الآية: 21"
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<td>BB-UVB</td>
<td>Broad-band ultraviolet B</td>
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<tr>
<td>CRH</td>
<td>Corticotropin releasing hormone</td>
</tr>
<tr>
<td>CRHR 1</td>
<td>Corticotropin releasing hormone receptor 1</td>
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<tr>
<td>CTLA-4</td>
<td>Cytotoxic T lymphocyte antigen-4</td>
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<td>CXCR3</td>
<td>C-X-C motif chemokine receptor 3</td>
</tr>
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<td>CXCR3-alt</td>
<td>Chemokine receptor 3-alternative</td>
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<td>DAMPs</td>
<td>Damage-associated molecular patterns</td>
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<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>GPR9</td>
<td>G protein-coupled receptor 9</td>
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<tr>
<td>GWAS</td>
<td>Genome-Wide Association Studies</td>
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<tr>
<td>HLA</td>
<td>Human leukocyte antigen</td>
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<td>HMGB-1</td>
<td>High-mobility group box chromosomal protein 1</td>
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<td>HS</td>
<td>Highly significant</td>
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<td>IFN</td>
<td>Interferon</td>
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<td>IL-17</td>
<td>Interleukin-17</td>
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<td>IQR</td>
<td>Inter-quartile range</td>
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<tr>
<td>mAb</td>
<td>Monoclonal antibodies</td>
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<td>MBEH</td>
<td>Monobenzyle Ether of Hydroquinone</td>
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<tr>
<td>MED</td>
<td>Minimal erythematous dose</td>
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<td>MITF</td>
<td>Melanocyte Inducing Transcription Factor</td>
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<td>mRNA</td>
<td>Messenger Ribonucleic acid</td>
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<td>NADH</td>
<td>Nicotinamide adenine dinucleotide</td>
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<td>NB-UVB</td>
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<td>Nrf2</td>
<td>Nuclear factor E2-related factor 2</td>
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<td>Nrf2-ARE/HO-1</td>
<td>Nuclear factor E2-related factor 2-antioxidant response element/heme oxygenase-1</td>
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<td>NS</td>
<td>Non significant</td>
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<td>NSV</td>
<td>Non-segmental vitiligo</td>
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<td>POMC</td>
<td>Pro-opiomelanocortin gene</td>
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<td>PTPN22</td>
<td>Protein tyrosine phosphatase non-receptor type 22</td>
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<td>PUVA</td>
<td>Psoralen + UVA</td>
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<tr>
<td>PUVA</td>
<td>Psoralen ultraviolet A</td>
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<tr>
<td>RNA</td>
<td>Ribonucleic acid</td>
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<td>ROC</td>
<td>Receiver-operating characteristic</td>
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<td>S</td>
<td>Significant</td>
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<td>SPSS</td>
<td>Statistical Package for Social Science</td>
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<td>SV</td>
<td>Segmental vitiligo</td>
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<td>Th17</td>
<td>T helper type 17</td>
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<tr>
<td>TM</td>
<td>Transmembrane</td>
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<tr>
<td>TRM</td>
<td>Tissue Resident Memory cell</td>
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<td>TRPM2</td>
<td>transient receptor potential M member 2</td>
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Introduction

Vitiligo is an acquired disease affecting skin characterized by the selective loss of melanocytes which results in typical nonscaly, chalky-white macules. It is common with worldwide prevalence about 0.5%-2% (Bergqvist et al., 2020).

Vitiligo has significant psychological impact leading to social isolation, discrimination and low self-esteem (Hamidizadeh et al., 2020). A recent metaanalysis showed that 23% vitiligo patients, suffer from anexity disorder and is significantly higher in females than in males. Many patients consider skin depigmentation as an impenetrable barrier for finding a suitable job or getting married and suffer from more discrimination in daily life (Liu et al., 2021).

Vitiligo is classified clinically into non-segmental vitiligo (NSV) and segmental vitiligo (SV). Non-segmental vitiligo includes acrofacial, mucosal, generalized or common, universal, mixed and rare forms. Segmental vitiligo may affect one, two or multiple segments of the body and even have bilateral segmental distribution with leukotrichia (Taïeb and Picardo, 2019).

That exact etiolog of vitiligo is unclear. Theories about its pathogenesis include T cell mediated autoimmune distruption, that maybe triggered by oxidative stress, with an underlying genetic predisposition (Gianfaldoni and Lotti, 2019).
Vitiligo relapses occur at the same site after cessation of treatment, indicating an autoimmune memory of the skin cells that allows disease exacerbation after treatment is stopped. The presence of melanocyte-specific TRM (Tissue Resident Memory cell) is clearly demonstrated in vitiligo, a disease that may be seen now as a memory skin disease. In addition, chemokine receptors signaling appears important to drive TRM into the appropriate tissue environment for their formation and maintenance, as shown for the chemokine receptors CXCR3 in vitiligo (Cavalié et al., 2015, Boniface et al., 2019).

C-X-C motif chemokine receptor 3 (CXCR3) is gene coding for a chemokine receptor that is highly expressed on effector T cells and plays an important role in T cell trafficking and function. The CXCR3 gene is located on the long arm of chromosome X in region (Nazari et al., 2020).

Deficiency in CXCR3 reduces the overall number of TRM cells in the skin and monoclonal antibodies (mAb)-mediated CXCR3 blockade can prevent TRM formation (Zaid et al., 2017, Fernandez-Ruiz et al., 2016).

CXCR3 has three isoforms in human: CXCR3A, CXCR3B and CXCR3Alt. Importantly, the isoform B is absent in rodents. Signaling through CXCR3-A stimulates proliferation and cell migration, while CXCR3-B signals inhibit angiogenesis, proliferation, and migration but can stimulate apoptosis in tumor cells. The role of CXCB
stimulation in vitiligo has not been reviled yet \cite{Nazari et al., 2020, Tulic et al., 2019}.

Phototherapy including psoralen ultraviolet A (PUVA), excimer lamp and laser, and narrowband UVB (NBUVB) is used to treat vitiligo. Excimer is a targeted therapy that works well for localized disease, but NBUVB is preferable for widespread vitiligo (greater than 5\% of the body surface area). Narrow band UVB (311nm) is now one of the most effective treatment modalities for vitiligo, but its mechanisms of action are not well understood \cite{Zubair and Hamzavi, 2020, Ibrahim et al., 2019}.
Aim of the Work

The primary aim of the work was to investigate the effect of phototherapy (NBUVB and excimer laser) on CXCR3B expression in vitiligo.

The secondary aim was to find a possible causal relationship between CXCR3B levels and vitiligo in an attempt to evaluate CXCR3B role in the pathogenesis of vitiligo.
Chapter 1
VITILIGO

1.1 Definition
It is a chronic depigmentary disorder presented by white patches due to destruction of melanocytes of epidermis (Taïeb and Picardo, 2019).

1.1. Prevelance and Gender Distribution
Vitiligo is common with worldwide prevalence about 0.5%–1% appearing at any age but most cases before the age of 20, with almost equal gender distribution (Gianfaldoni and Lotti, 2019).

1.2. Clinical Types and Differential Diagnoses
Vitiligo is clinically presented by pale or milk-white macules or patches due to the selective destruction of melanocytes (Picardo et al., 2015).

Clinically, vitiligo is classified into two major types: segmental and Non-segmental vitiligo. Non-segmental vitiligo (NSV) is much more common with asymmetrical distribution usually has a gradual onset and progressive course. Segmental vitiligo (SV) follows a characteristic dermatomal distribution whether unilateral or bilateral. It’s less common and often patients are presented with a rapid onset and stationary course (Zailaie, 2017).

However, there is a form of mixed vitiligo involving the combination of both SV and NSV in the same patient (Speeckaert et al., 2020).