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Vitiligo Guidelines

Mauro Picardo
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Rome, Italy

epidemiology

definition

classification

assessment

pathogenesis

therapy

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PubMed vitiligo treatment

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See 101 articles about Mitf (**VITILIGO**) gene function
See also: Mitf (**VITILIGO**) microphthalmia-associated transcription factor in the Gene database

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1. Modern **vitiligo** genetics sheds new light on an ancient disease.
Spritz RA.
J Dermatol. 2013 May;40(5):310-8. doi: 10.1111/1346-8138.12147.
PMID: 23668538 [PubMed - in process]

2. Melanocytes transplantation in patients with **vitiligo** using needling micrografting technique.
Sharquie KE, Noaimi AA, Al-Mudaris HA.
J Drugs Dermatol. 2013 May 1;12(5):e74-8.
PMID: 23652963 [PubMed - in process]

3. Inflammatory Mediators are Inhibited by a Taurine Metabolite in CpG Oligodeoxynucleotide and IFN-r Activated Macrophage Cell Line.
Kim BS, Spinner DS, Kascsak RJ, Park SY, Cho IS, Schuller-Levis G, Park E.
J Drugs Dermatol. 2013 May 1;12(5):551-7.
PMID: 23652950 [PubMed - in process]

4. The therapeutic effects of a topical tretinoin and corticosteroid combination for **vitiligo**: a placebo-controlled, paired-comparison, left-right study.
Kwon HB, Choi Y, Kim HJ, Lee AY.
J Drugs Dermatol. 2013 Apr 1;12(4):E63-e67.
PMID: 23652908 [PubMed - in process]

5. Reversible Cardiomyopathy Associated with Autoimmune Polyendocrine Syndrome Type II.
Karavelioglu Y, Baran A, Karapinar H, Küçükdurmaz Z, Yilmaz A.
Intern Med. 2013;52(9):981-5. Epub 2012 Mar 1.
PMID: 23648718 [PubMed - in process] Free Article

6. Basic evidence for epidermal H2O2/ONOO--mediated oxidation/nitration in segmental **vitiligo** is supported by repigmentation of skin and eyelashes after reduction of epidermal H2O2 with topical NB-UVB-activated pseudocatalase PC-KUS.
Schallreuter KU, Salem MA, Holtz S, Panske A.

Poor outcomes sharing
Poor criteria (diagnosis and effectiveness) sharing
Variable duration treatment
Home-made trial design

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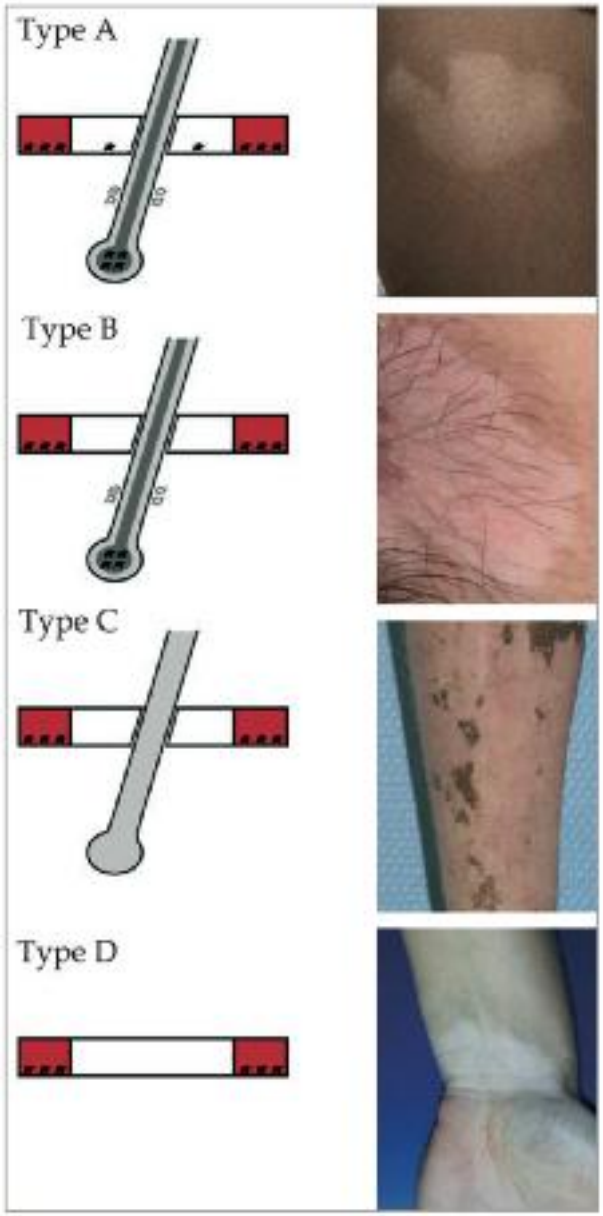

Fig 1. The relationship between the clinical type of vitiligo and the remaining melanocytes (*printed asterisks in skin diagrams) from the follicular and epidermal reservoir.

Repigmentation and melanocyte reservoir: different vitiligo?

How to define and measure disease?

How to compare effectiveness?

Gauthier, 2013

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Clinical dermatology • **Original article**

CED
Clinical and Experimental Dermatology

Broadband ultraviolet B vs. psoralen ultraviolet A in the treatment of vitiligo: a randomized controlled trial

M. El Mofty, M. Bosseila, H. M. Mashaly, H. Gawdat and H. Makaly

Phototherapy Unit, Dermatology Department, Cairo University, Cairo, Egypt

Clinical and Experimental Dermatology (2013) **0**, pp1–6

doi:10.1111/ced.12099

Journal of Dermatological Treatment, 2013; Early Online: 1–4

ISSN: 0954-6634 print / 1471-1753 online
DOI: 10.3109/09546634.2013.777381

informa
healthcare

ORIGINAL ARTICLE

Comparison of efficacy of narrow band UVB therapies with UVB alone, in combination with calcipotriol, and with betamethasoneand calcipotriol in vitiligo

Necmettin Akdeniz[1], Ibrahim Halil Yavuz[2], Serap Gunes Bilgili[3], Goknur Ozaydın Yavuz[2] & Omer Calka[3]

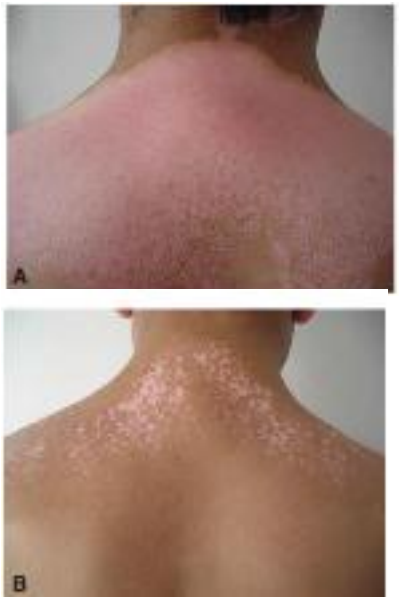

Figure 1. (A) The patient before treatment with betamethasone plus calcipotriol plus narrow-band UVB therapies. (B) The patient after treatment with betamethasone plus calcipotriol plus narrow-band UVB therapies.

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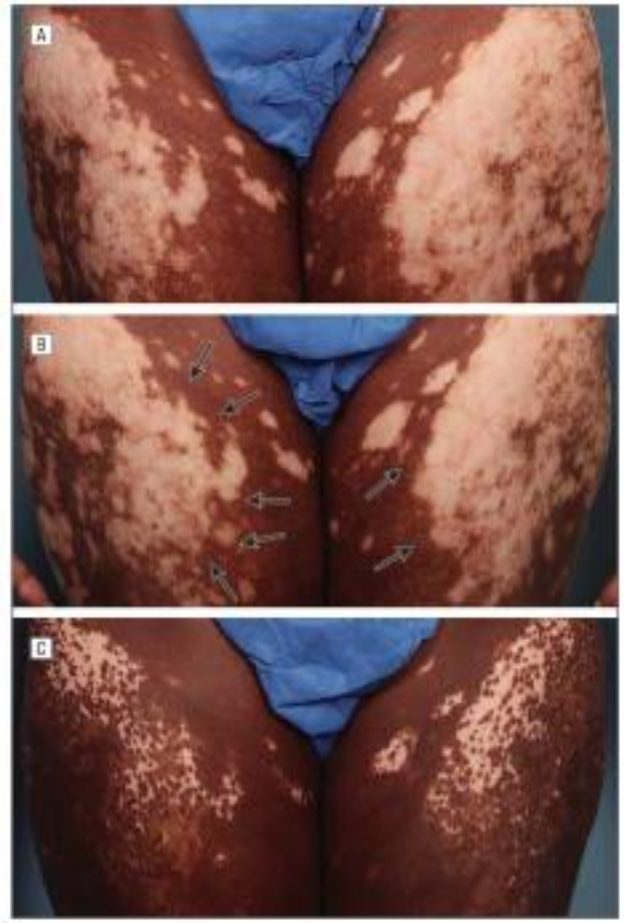
OBSERVATION

ONLINE FIRST

The Efficacy of Afamelanotide and Narrowband UV-B Phototherapy for Repigmentation of Vitiligo

Pearl E. Grimes, MD; Iltefat Hamzavi, MD; Mark Lebwohl, MD; Jean Paul Ortonne, MD; Henry W. Lim, MD

JAMA Dermatol. 2013;149(1):68-73.
Published online October 15, 2012.
doi:10.1001/2013.jamadermatol.386



DEPIGMENTATION

CLINICAL PRACTICE

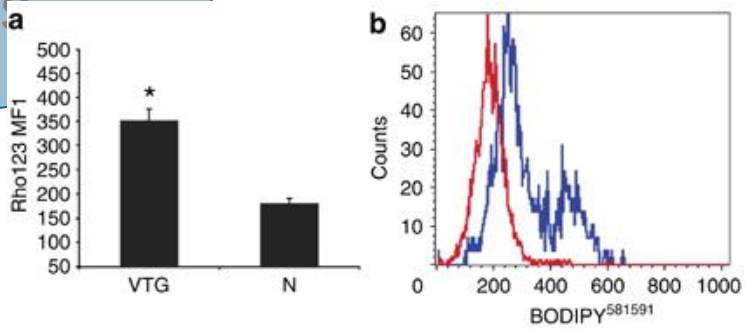
degenerative process

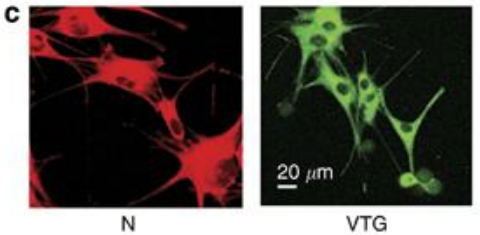
immune process

toxic damage

detachment

metabolic defect





ETIOLOGIC APPROACH

DEGENERATION

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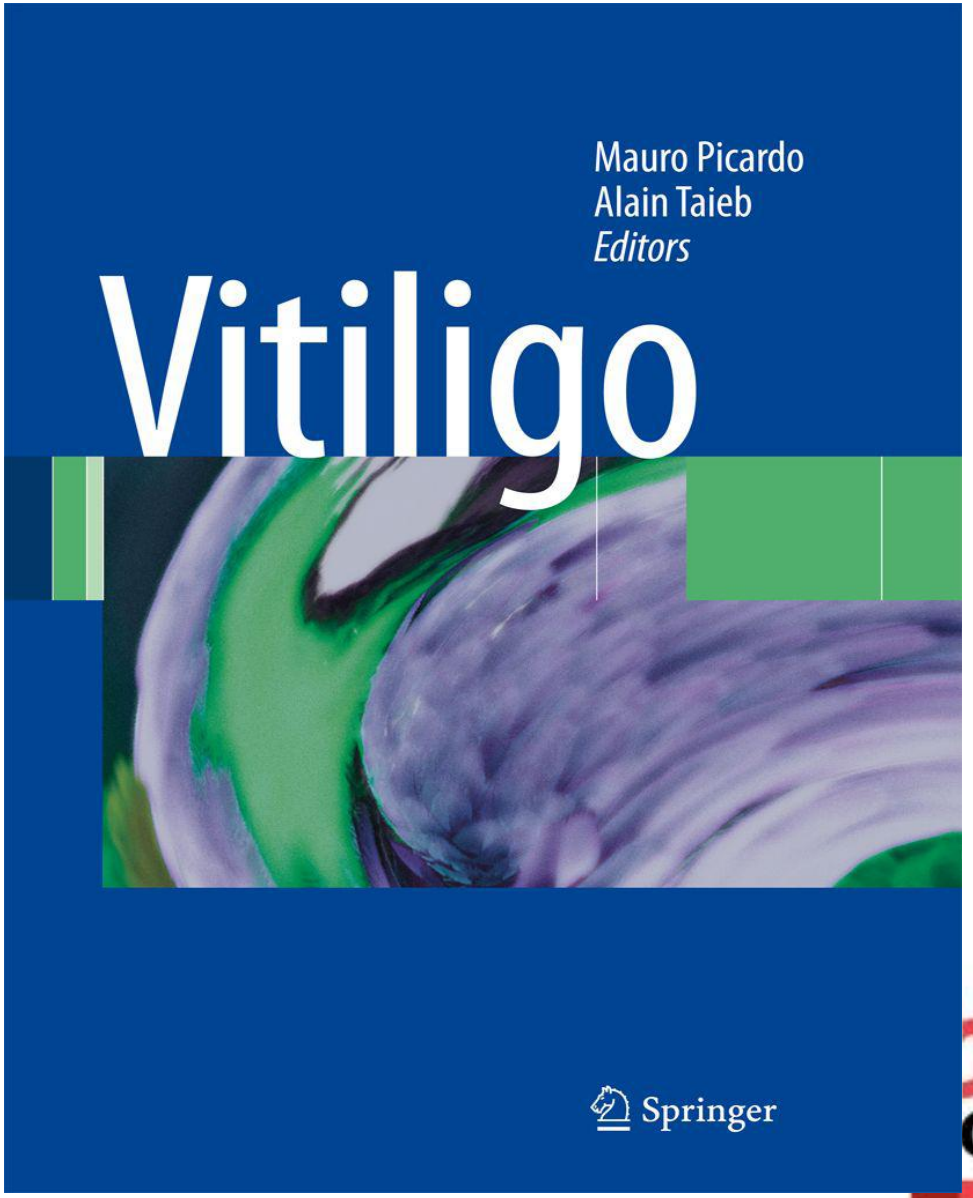
EU EXPERTS DISCUSSION & IDEAS SHARING

Courtesy of Vitiligo International



VEFT Authors

Taieb, A. Alomar, M. Böhm, M.L. Dell'Anna, A.dePase, V. Eleftheriadou, K. Ezzedine, Y. Gauthier, D. Gawkrodger, N. van Geel, G. Leone, T. Jouary, S. Moretti, TL. Nieuweboer-Krobotova, M.J. Olsson,T. Passeron, D. Parsad, A. Tanew, W. van derVeen, M. Whitton, A. Wolkerstorfer,

M. Picardo.

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Aims

- *What is already known about this topic?* Vitiligo is a disease lacking definitive and completely effective therapies. Phototherapy and combined treatments are the most effective treatments.
- *What is the goal of the treatment in vitiligo?* Therapy should stop the progression of the lesions and provide complete or almost complete repigmentation to be satisfactory for the patient. The results should be maintained over time.
- *What does this study add?* The criteria for treatment have been critically reviewed. Evidence-based recommendations (S1) for the treatment of vitiligo have been made. A proposal for clinical evaluation, treatment and follow-up has been outlined.

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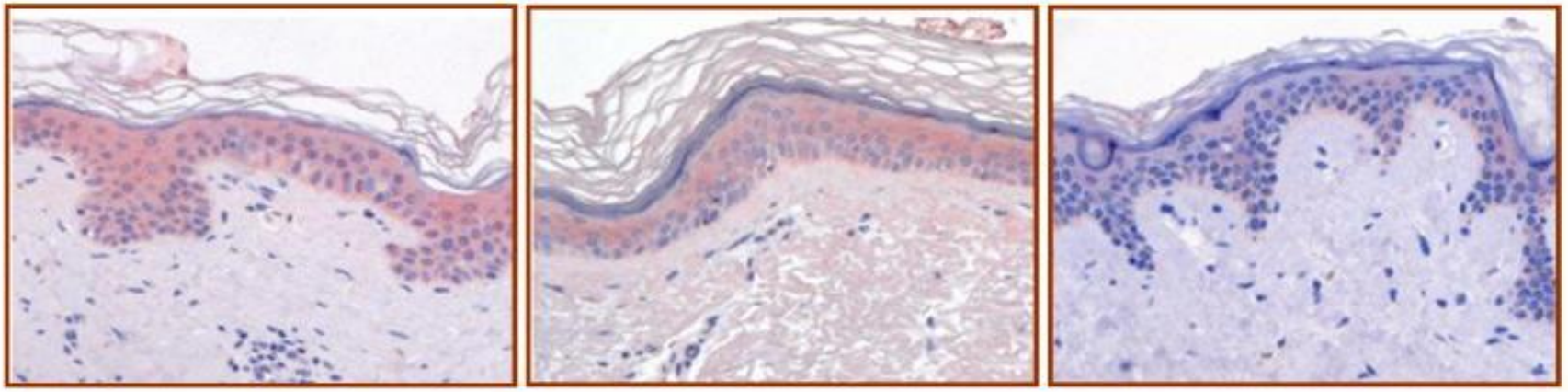
infiammazione: IL1β e NALP1

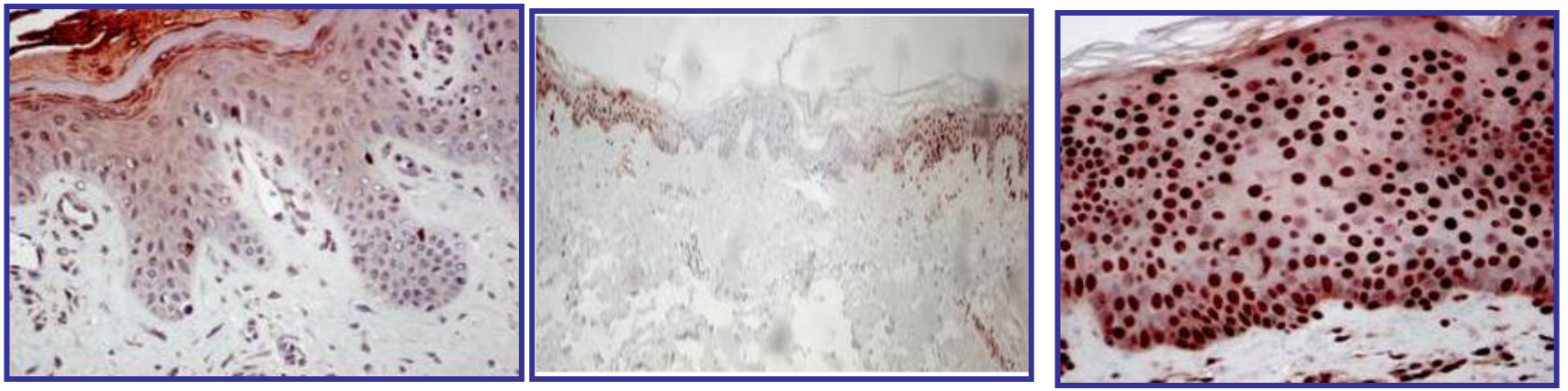
Lesional/periesional skin | Lesional skin | Non lesional skin

IL1b



IL1beta appeared to be expressed more in samples overlapping the border of the lesion and in perilesional and lesional samples than in non lesional vitiligo skin.

NALP1



1. Topical corticosteroids

- Limited, extra-facial involvement- potent TCS, once daily for 3 months or 15 days/month for 6 months
- First and safest choice-potent TCS rather than super potent
- If systemic absorption-consider mometasone furoate or methylprednisolone aceponate
- For facial lesions- consider topical calcineurin inhibitors rather than TCS

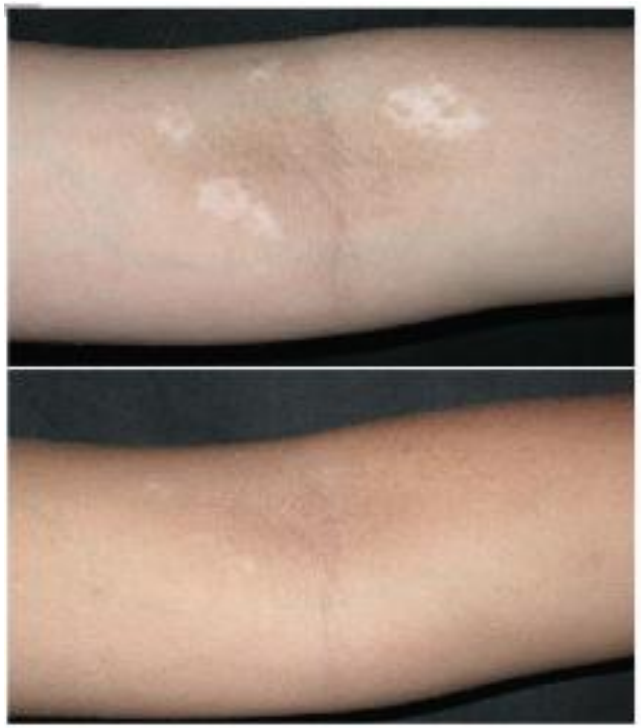
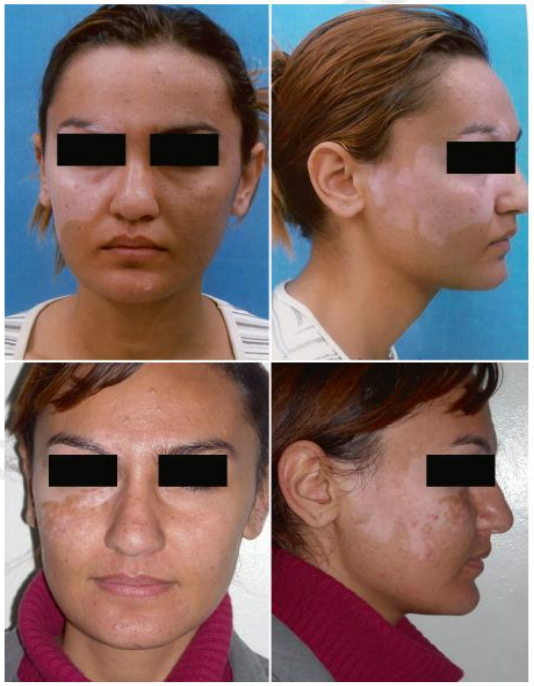


Fig. 3.2.1.1 Patient treated with betamethasone: before (*up*) and after (*down*) the therapy

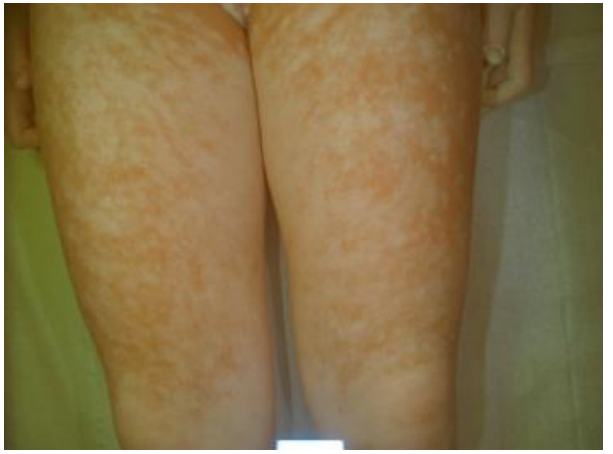
2. Calcineurin inhibitors

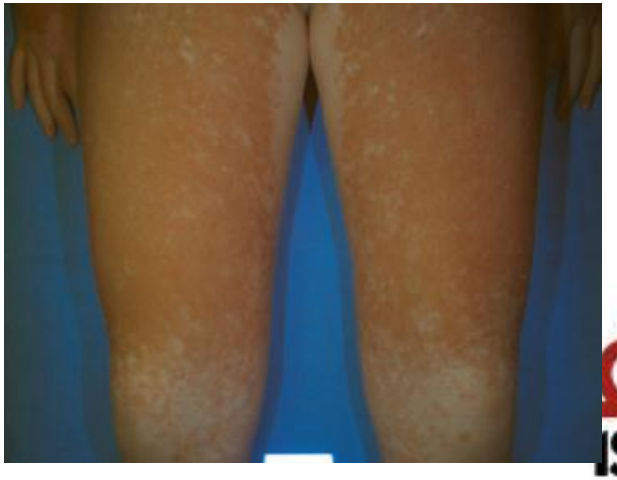


- For new and actively spreading lesions and face/neck areas
- Twice daily, initially for 6 months, for both adults and children
- Safety profile is better concerning risk of skin atrophy
- During the treatment- moderate but daily sun exposure
- If effective consider prolonged treatment (⇧12 months)

NB-UVB and targeted phototherapies

- Total body NB UVB for NSV- arrest and repigment vitiligo
- Targeted phototherapies for localized vitiligo, recent onset & childhood vitiligo
- Maximum cycle duration- 1 year for adults and 6 months for children. One year interruption between cycles
- Stop treatment: if no results in 3 months or if ⇩ 25% repigmentation in 6 months
- Maintenance treatment-not recommended. Regular follow- ups necessary



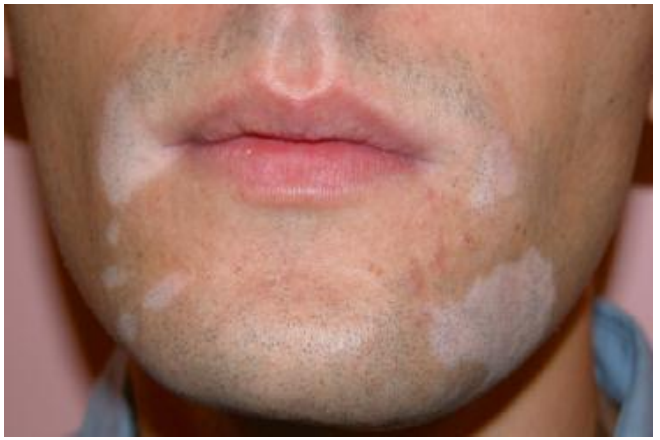


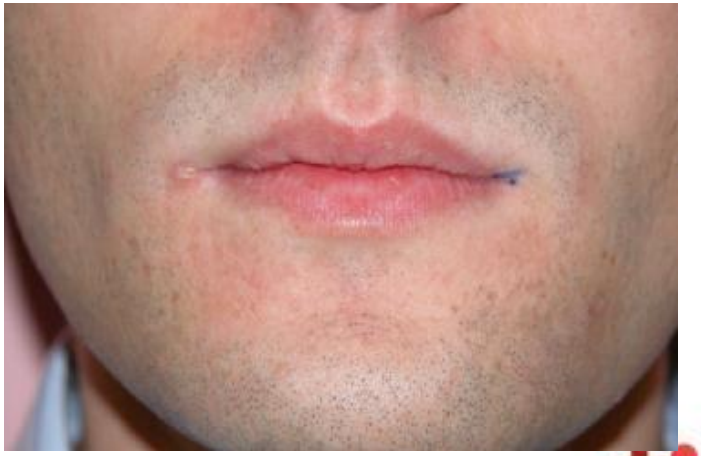
PUVA and photochemotherapy

- Oral PUVA-second line therapy in adults
- 12 to 24 months therapy
- Topical PUVA-very low dosage psoralens creams

4. Combination treatments (1/3)

- Topical steroids and phototherapy
- For difficult to treat areas such as bony prominences
- Highly potent topical steroids once a day (3 weeks out of 4) for the 3 first months of phototherapy





4. Combination treatments (2/3)

Topical calcineurin inhibitors and phototherapy

- Effective and provides better results that the two treatments alone
- Should be used only in controlled or experimental settings due to ? carcinogenicity
- Use of adequate photoprotection due to the lack of data on long term safety (or not) of combination of TCI and UV

4. Combination treatments (3/3)

Vitamin D analogues and phototherapy

- Not recommended

Phototherapy and other treatment

- Phototherapy+oral antioxidants- possibly beneficial

Phototherapy after surgery

- NB-UVB or PUVA should be used for 3-4 weeks after skin surgery

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5. Oral steroids/other immunosuppressants (1/2)

Oral Mini Pulse

- Stable vitiligo-not useful
- Fast spreading vitiligo- weekend OMP (2.5 mg/day) of dexamethasone before phototherapy (based on author's experience)
- Optimal duration of OMP to stop vitiligo progression is 3-6 months

5. Other immunosuppressants and biologics

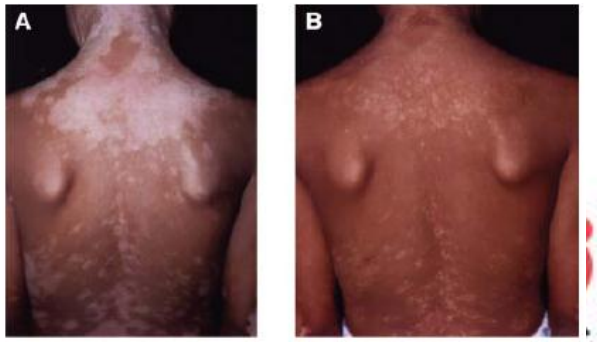
- Cyclophosphamide, Cyclosporine & Anti-TNF-α

Not recommended due to lack of data and for the possible side effects

6. Other systemic interventions: antioxidants

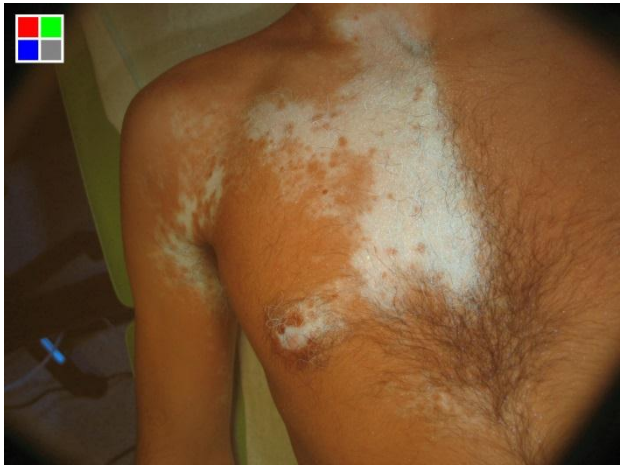
- Vitamin E, vitamin C, ubiquinone, lipoic acid, Polypodium Leucotomos, Ginko biloba etc.

- Antioxidant supplementation could be useful during UV therapy and reactivation phases

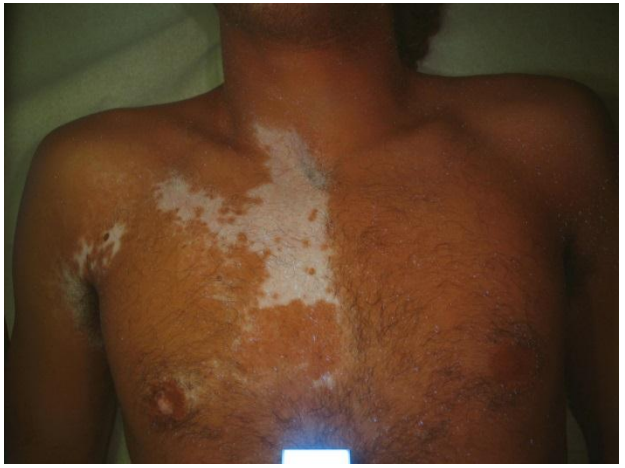


7. Surgery

- For NSV- patients with stable disease and negative Koebner phenomenon



- Risk of relapse



- For SV and other localized forms-after failure of medical interventions

8. Other interventions (1/3)

Camouflage

Self-tanners
- Lasts 3-5 days, stain free, waterproof
- Sea water makes them fade away quickly

Highly pigmented cover creams
- easy to apply, fragrance free, waterproof
- Fixing spray
- applied and removed daily with caution to avoid Koebner's phenomenon

Dermal pigmentation, cosmetic tattoos
- for lips, nipples especially in black people
- in other areas to be used with caution

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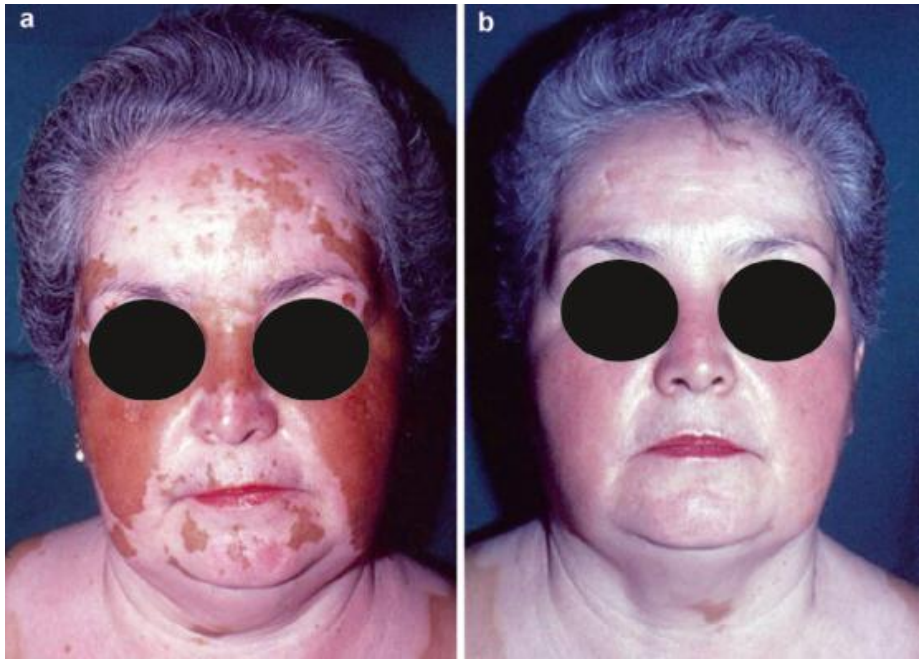
8. Other interventions (2/3)

for extensive disfiguring vitiligo & after exploring other therapies



Depigmentation with:

- Monobenzone
- Q-switched ruby laser alone or in combination with methoxyphenol,
- Cryotherapy

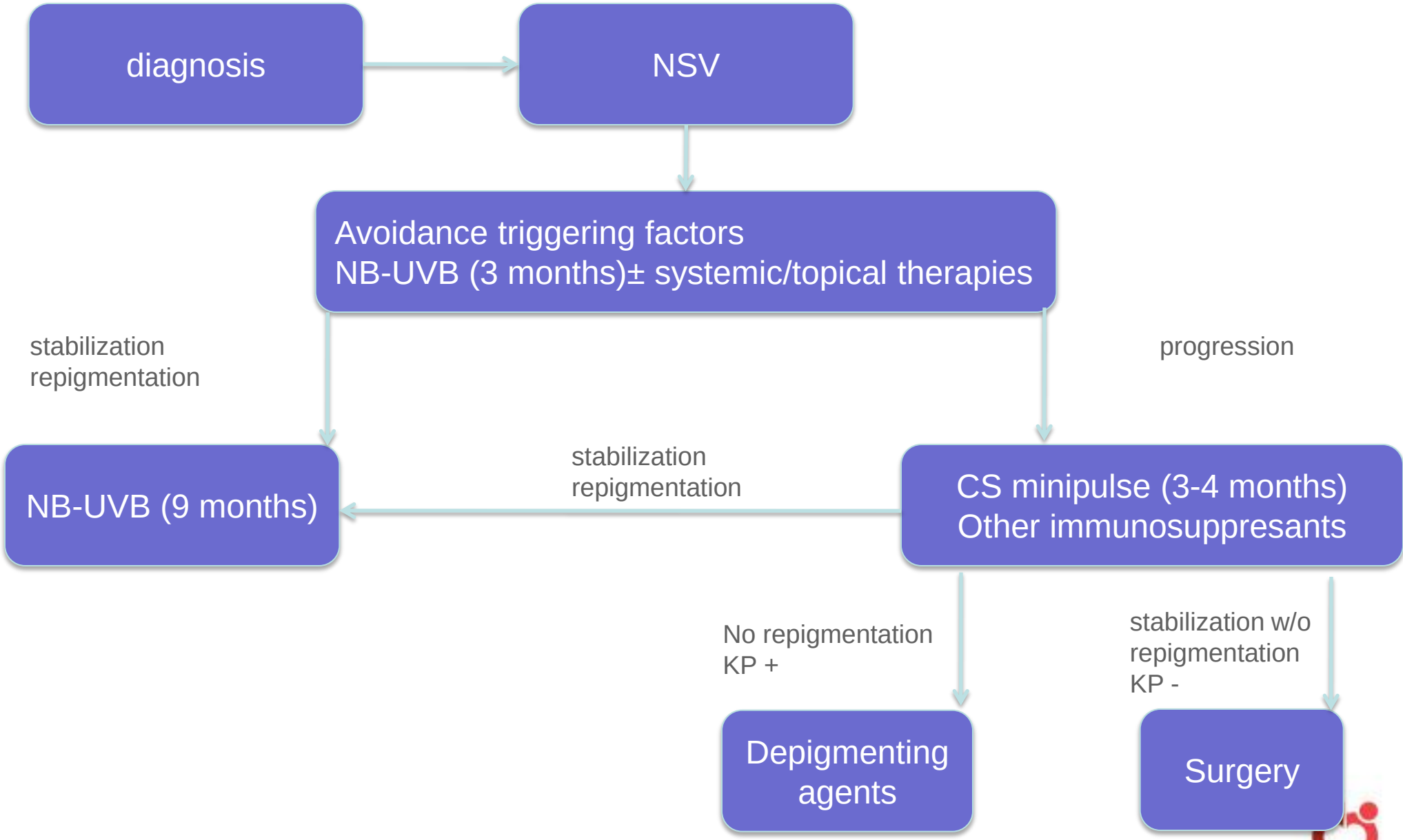
8. Other interventions (3/3)

Psychological interventions

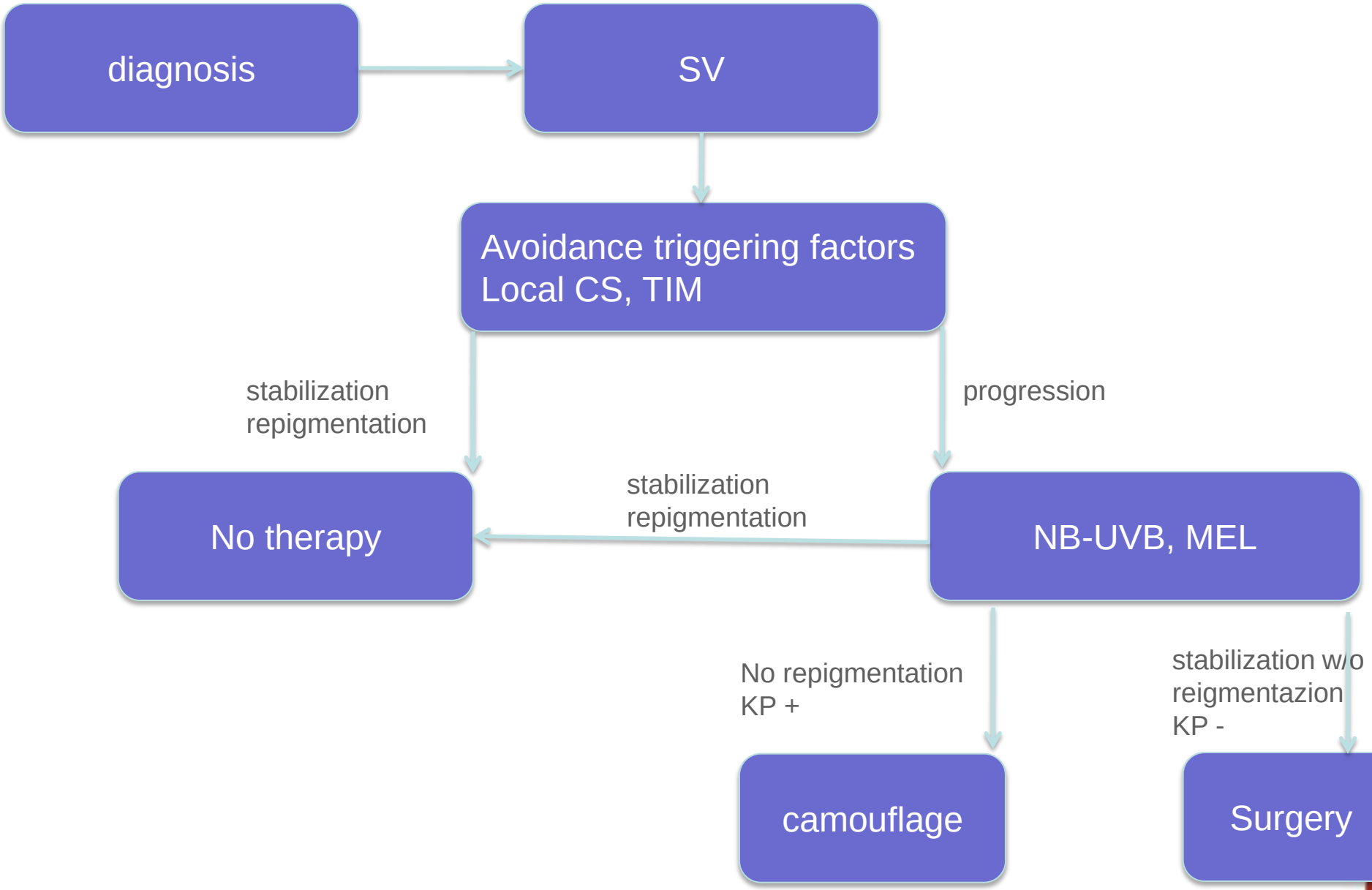
•Subjective assessment- DLQI, QoL questionnaire or Patient-defined outcome questionnaire for vitiligo

•Psychological support and community interventions may be needed

•Adolescents and dark skinned individuals- often stigmatised



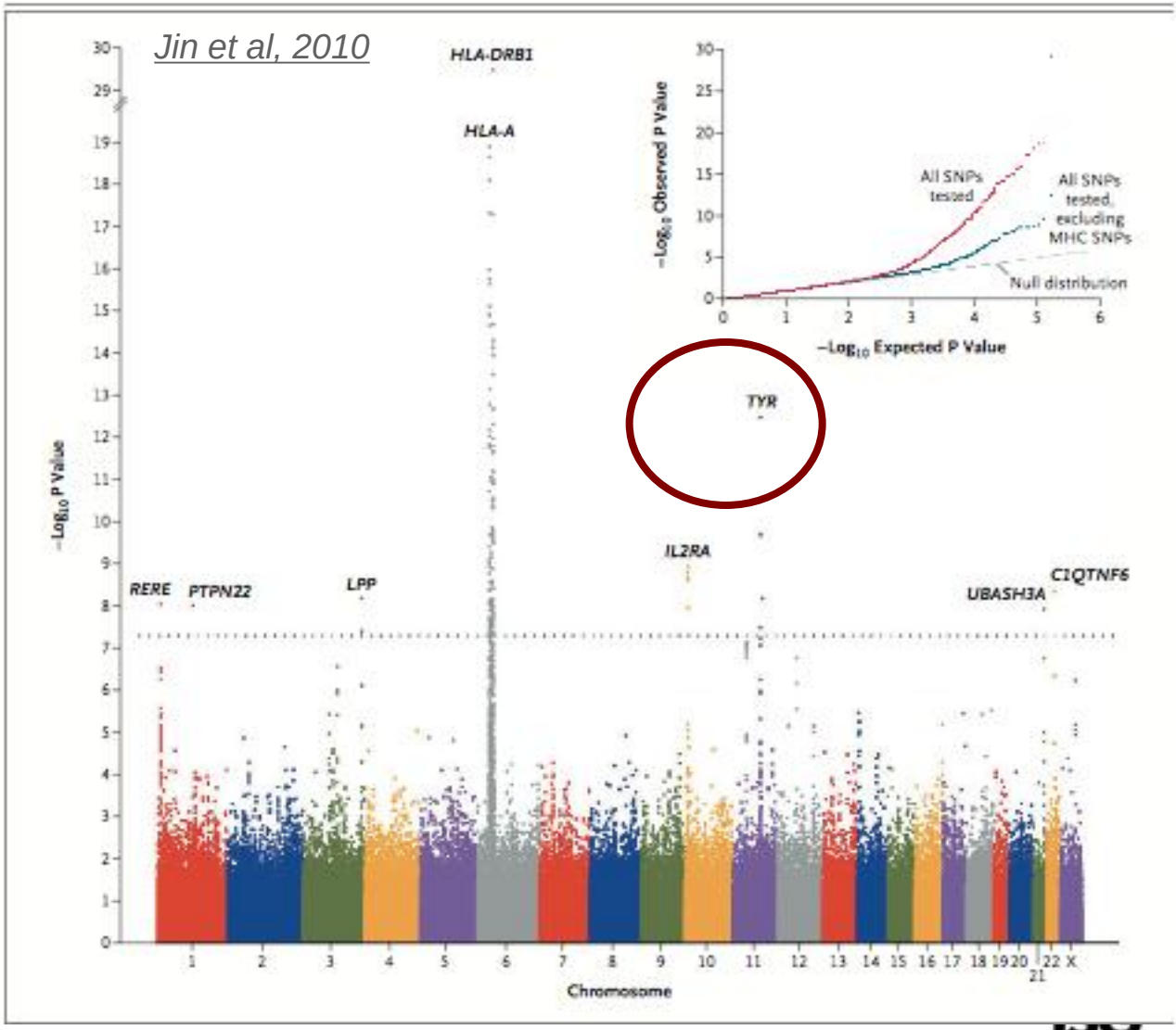
Algorithm for NSV



Algorithm for SV

The genetic background for immune and redox deregulation

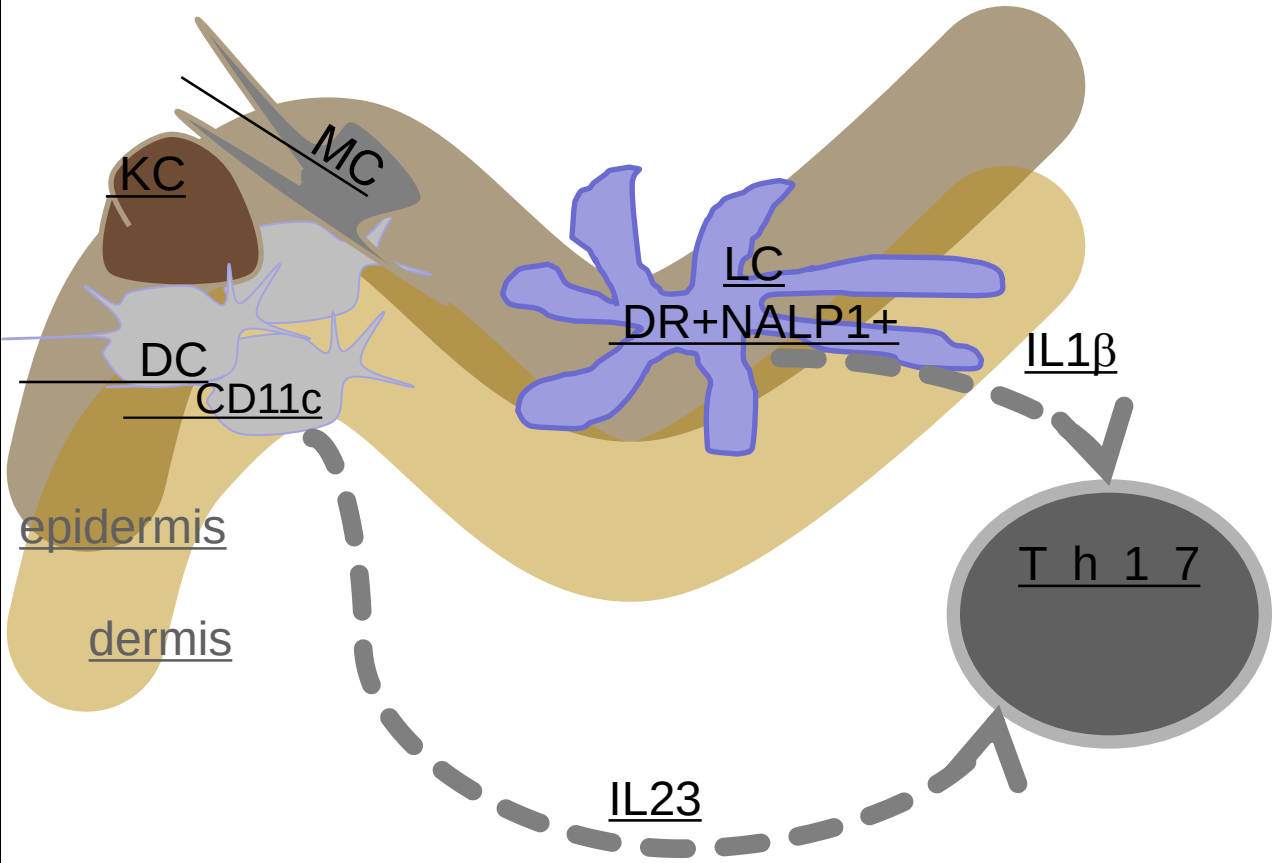
Genomewide association analysis indicate 10 independent SNP: in MHC loci (6p21.3), in seven regions related to autoimmnune diseases, and in 11q14.3 (**TYR**)

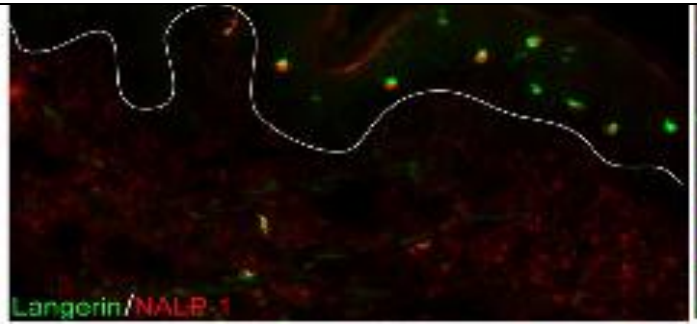


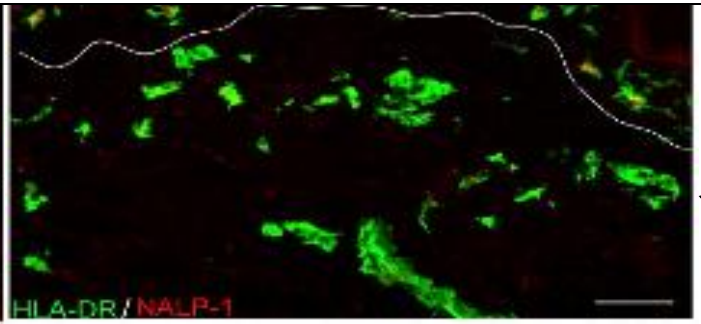
Variant thermosensitive, aberrantly glycosilated, retained in ER

Th17 and Dendritic Cells

Wang, 2001

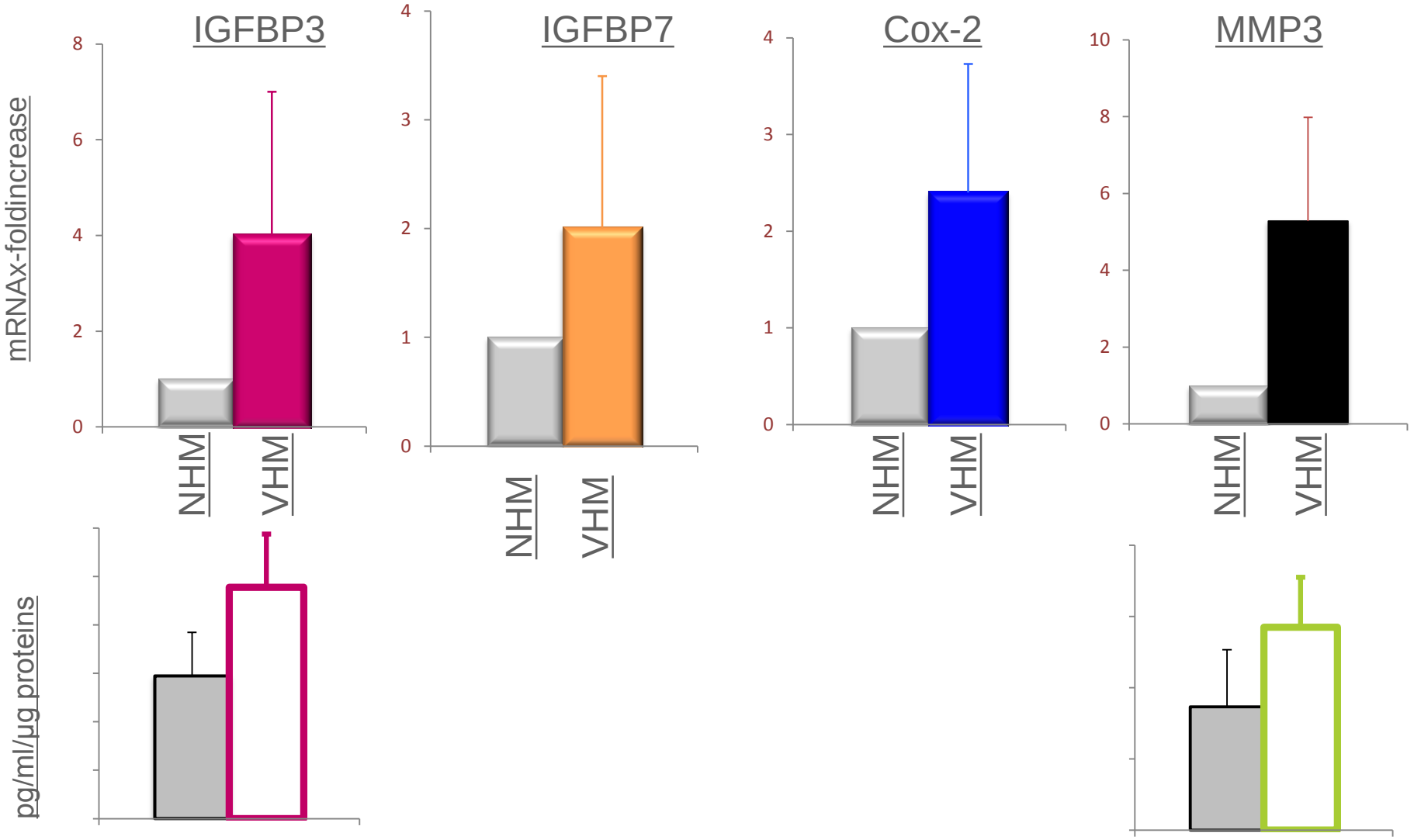




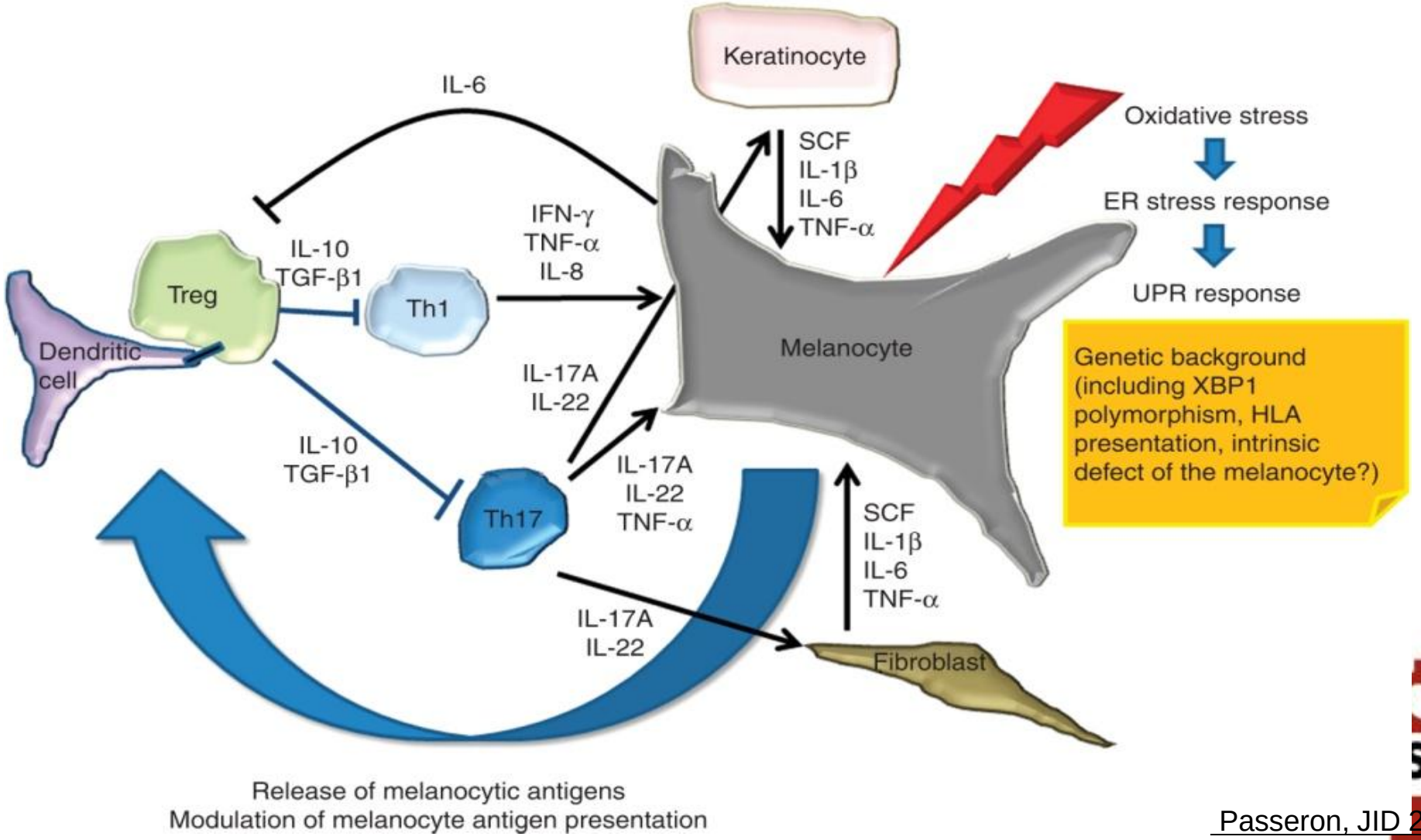


LC in half lower epidermis

SASP factors

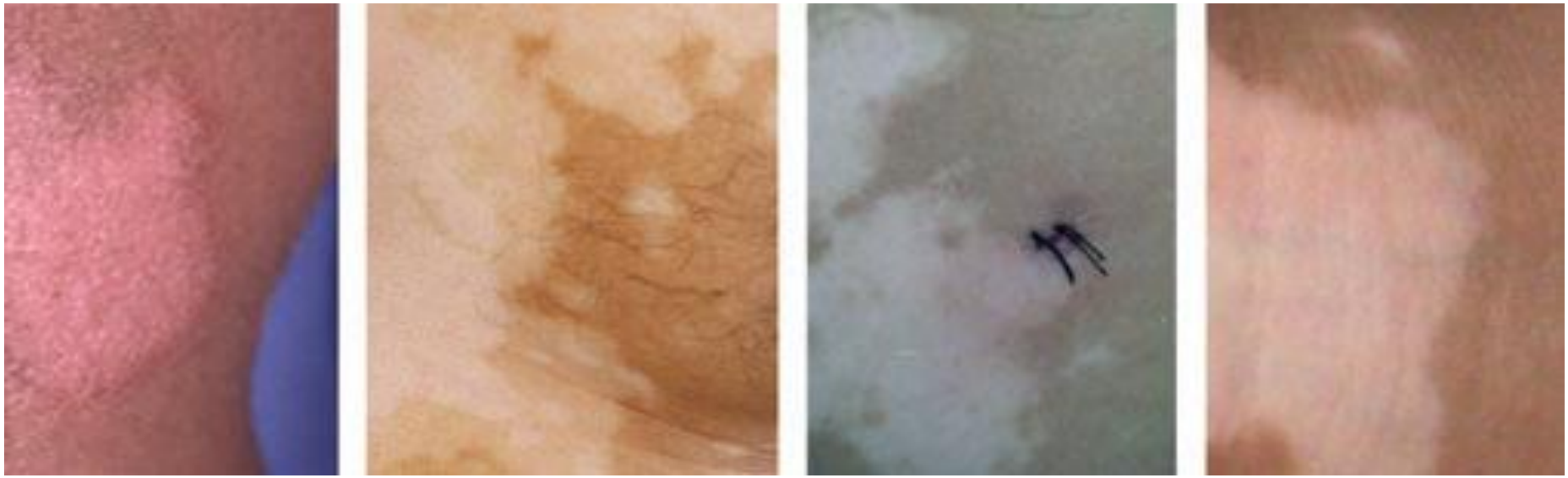


How we link oxidative stress and inflammation?



Passeron, JID 2012

Clinical type of VTG lesions



(a) Inflammatory lesion with raised borders.
(b) Trichrome vitiligo.
(c) Hypomelanotic lesion with poorly defined borders.
(d) Amelanotic lesion with sharply demarcated borders.

Clinical features are indicators of activity in common vitiligo, L. Benzekri *et al.*

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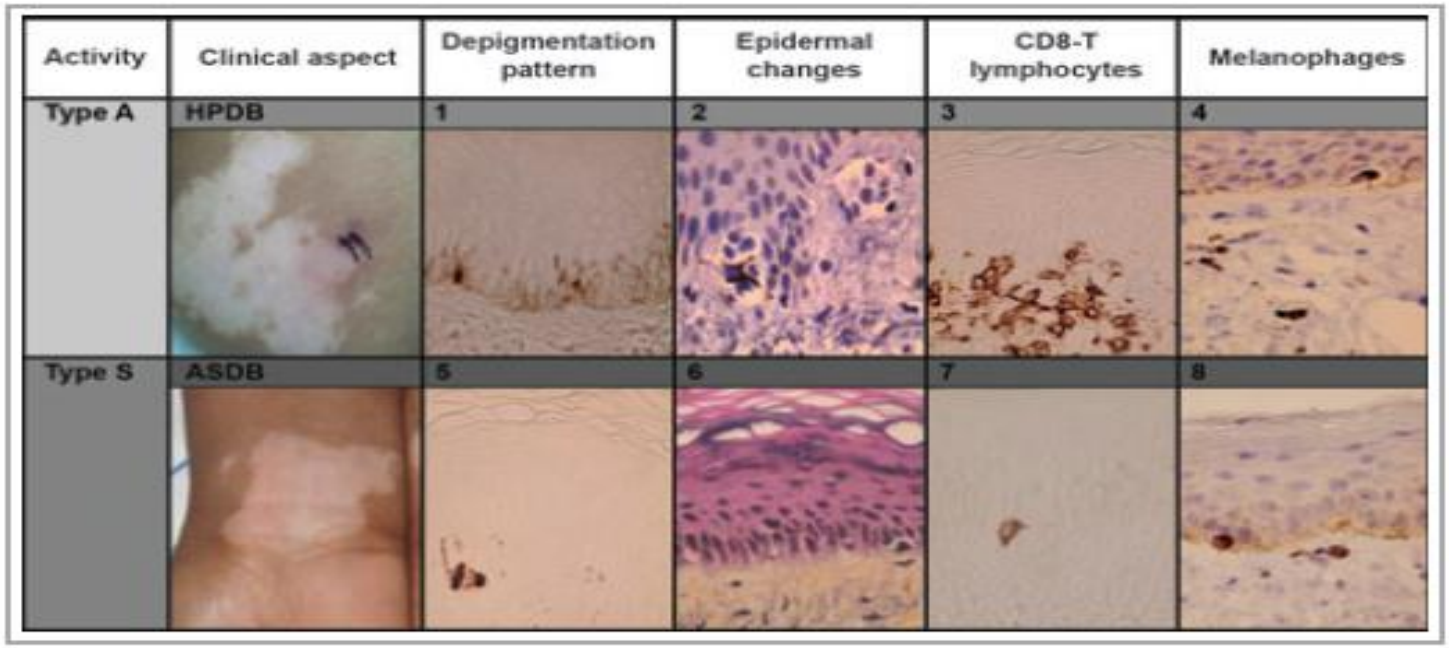
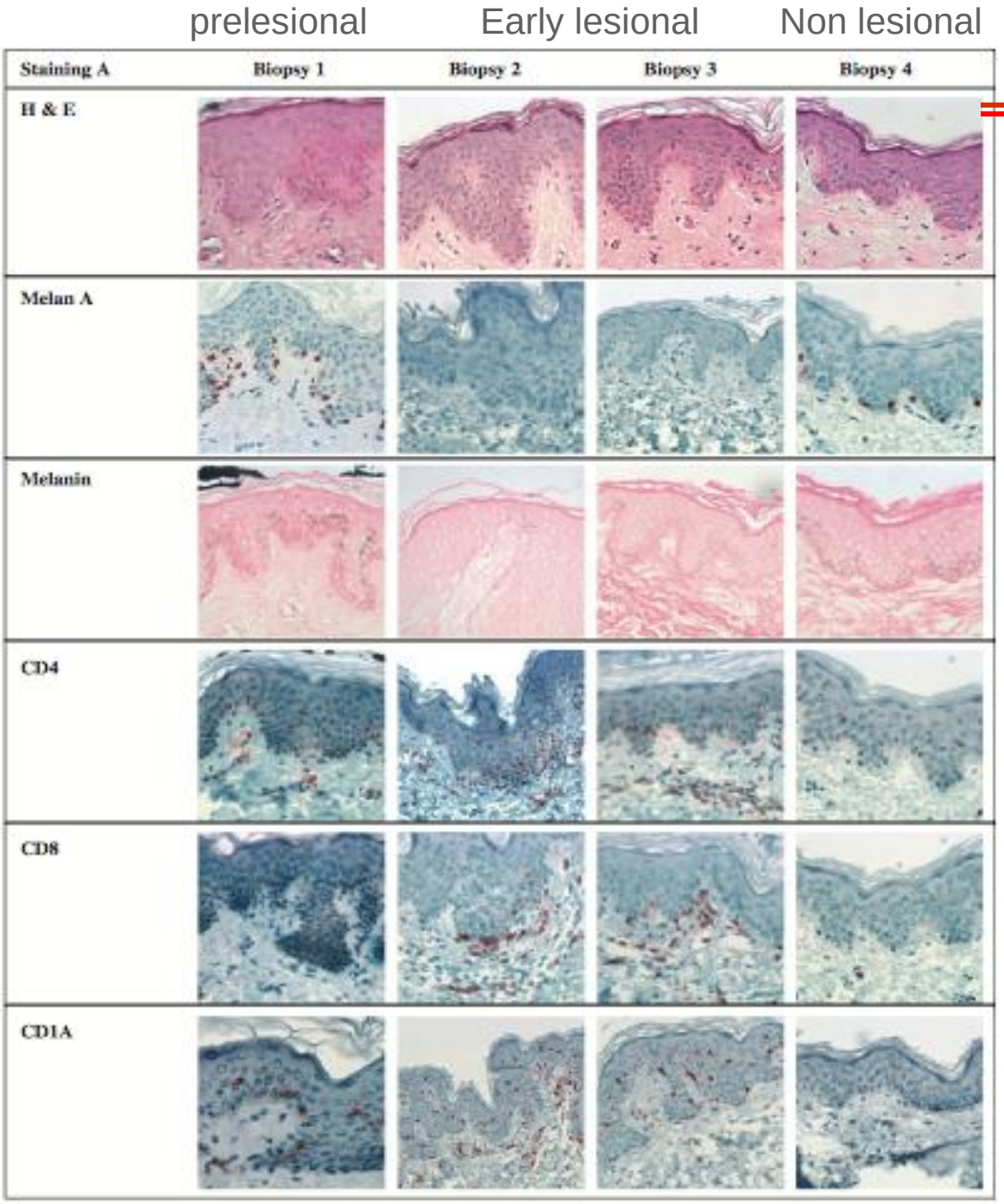
Table 4 The relationship between the clinical aspect and activity of vitiligo lesions

Clinical aspect	Activity of the lesion						
	Actively spreading			Stable			P value
Hypomelanotic lesion with poorly defined borders H.P.D.B N = 28	Yes	n = 26	92·85%	Yes	n = 2	7·15%	<0·001
	No	n = 2	7·15%	No	n = 26	92·85%	
Amelanotic lesion with sharply demarcated borders A.S.D.B N = 20	Yes	n = 3	15%	Yes	n = 17	85%	<0·001
	No	n = 17	85%	No	n = 3	15%	

N, number of patients; n = number of lesions studied.





SV and inflammation

Reduced Treg (FOXP3)
In lesional vs non lesional

High melanocyte specific T

Halo nevi occurrence as basis for the Ag exposure and immune damage

(Histology relevance)

Van Geel, 2010

Pigment Cell Melanoma Res. 2013 May;26(3):367-76. doi: 10.1111/pcmr.12077. Epub 2013 Mar 15.

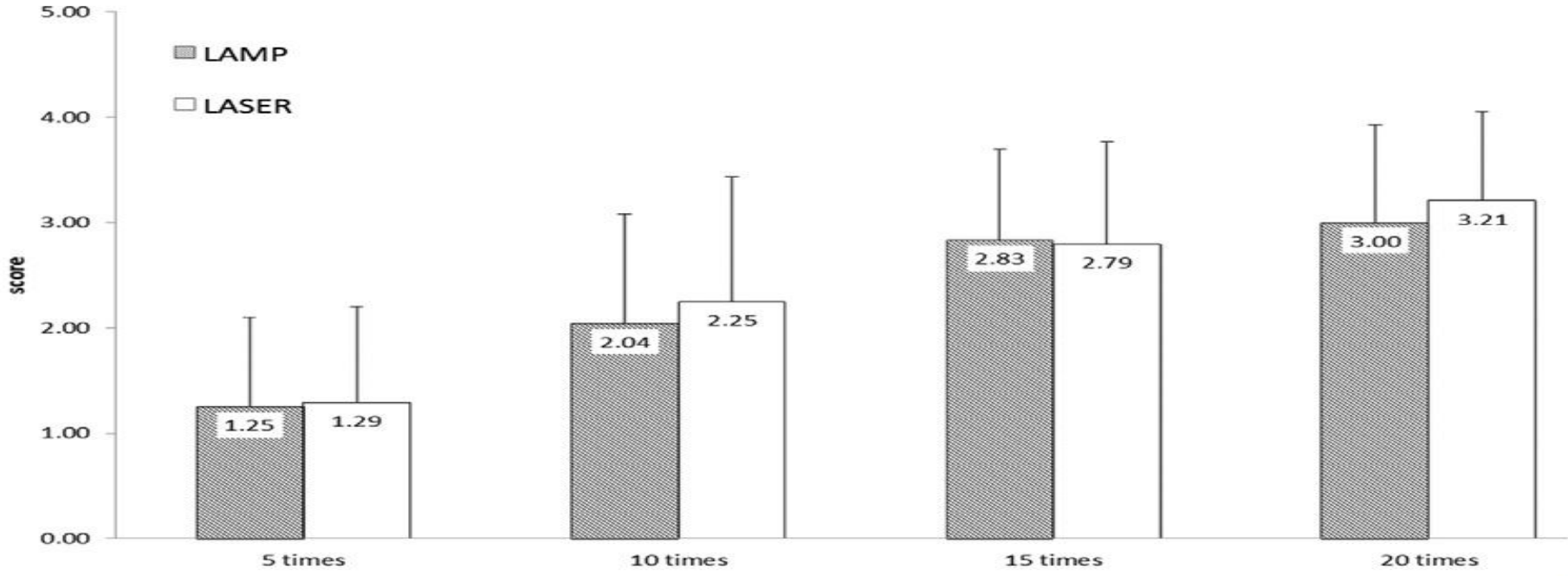
Irradiance, but not fluence, plays a crucial role in UVB-induced immature pigment cell development: new insights for efficient UVB phototherapy.

Lan CC, Yu HS, Lu JH, Wu CS, Lai HC.

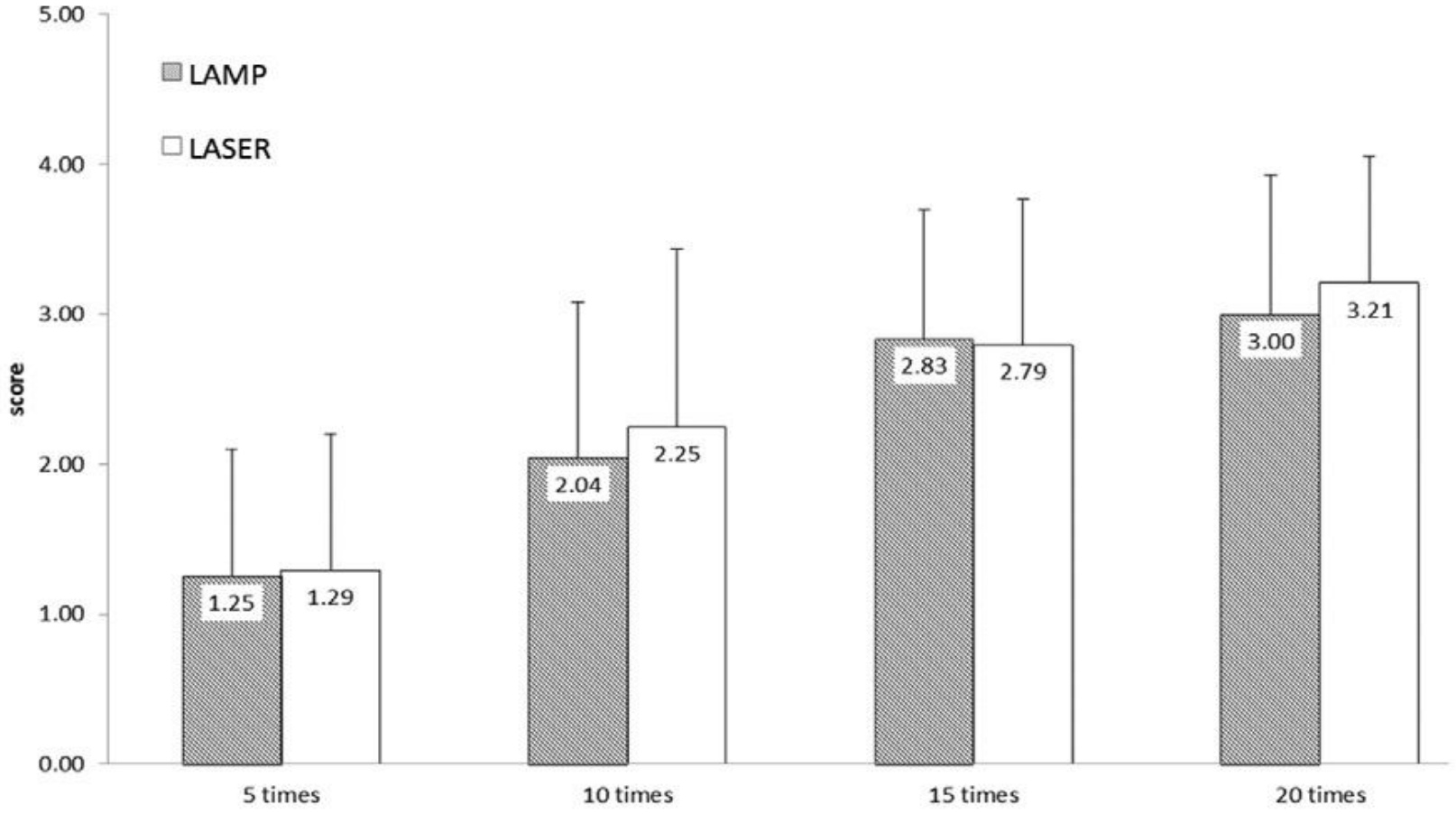
Department of Dermatology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; Department of Dermatology, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan; Department of Dermatology, Kaohsiung Municipal Ta-Tung Hospital, Kaoshiung Medical University, Kaohsiung, Taiwan.

Abstract

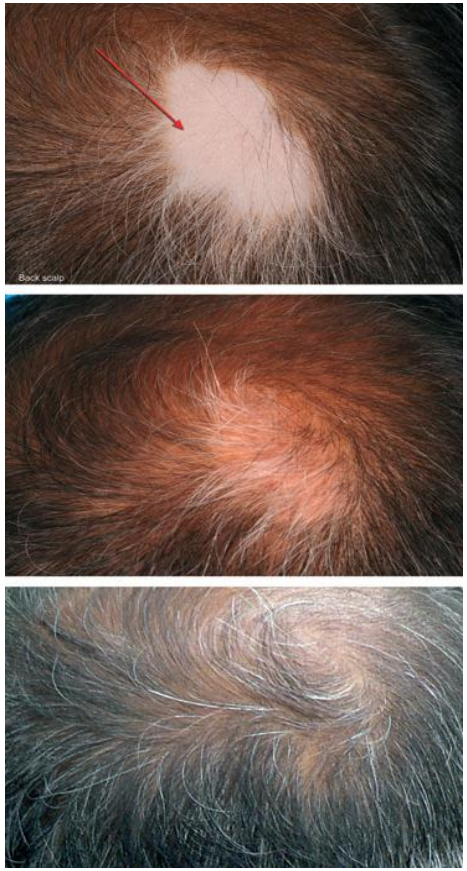
Light exposure modulates development of living organisms. In the field of medicine, light has frequently been used for regenerative purposes. Excimer light (308 nm) has demonstrated superior efficacy in treating **vitiligo**, a condition requiring development of melanoblasts and a model for studying nerve cell regeneration, as compared to narrow-band ultraviolet B (NBUVB; 311 nm). Using mouse-derived melanoblast cells to examine the pro-differentiation effects of these two light sources, we demonstrated that at equivalent fluence, excimer light induces melanoblast differentiation, while NBUVB failed to so. Mechanistically, activation of aryl hydrocarbon receptor pathway and nuclear translocation of epidermal growth factor receptor are involved in pro-differentiation effects of excimer light. Reduction in irradiance by filter abrogated the effects of excimer light in melanoblasts, even when equivalent fluence was delivered by the same light source. As ultraviolet B (UVB) irradiation is closely associated pigment cell development, future therapy employing UVB for pigmentation purposes should incorporate irradiance as a crucial specification.



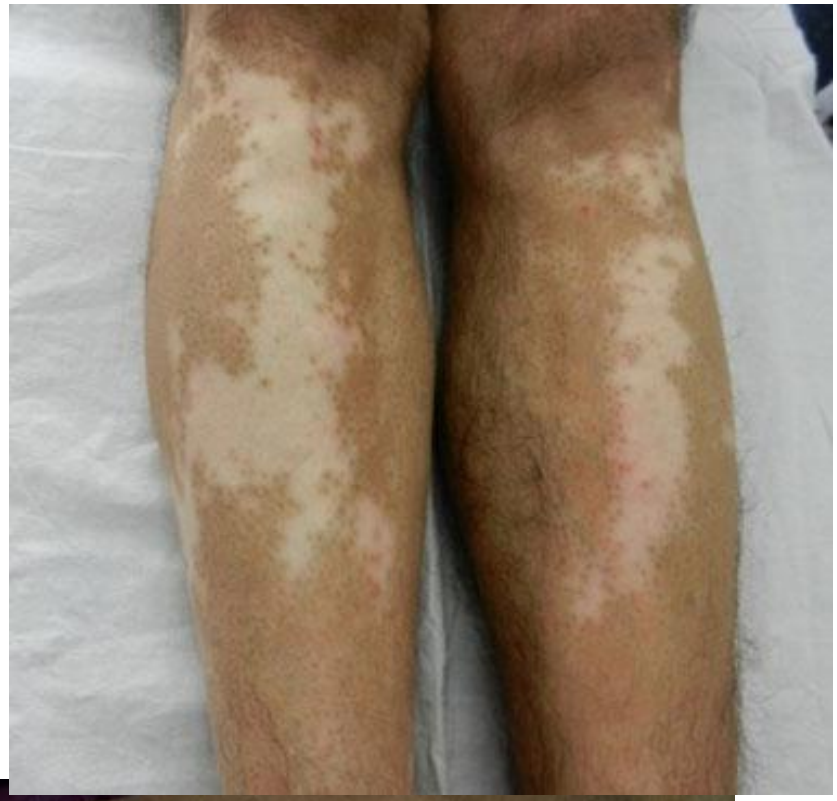
Comparison between eximer laser and light

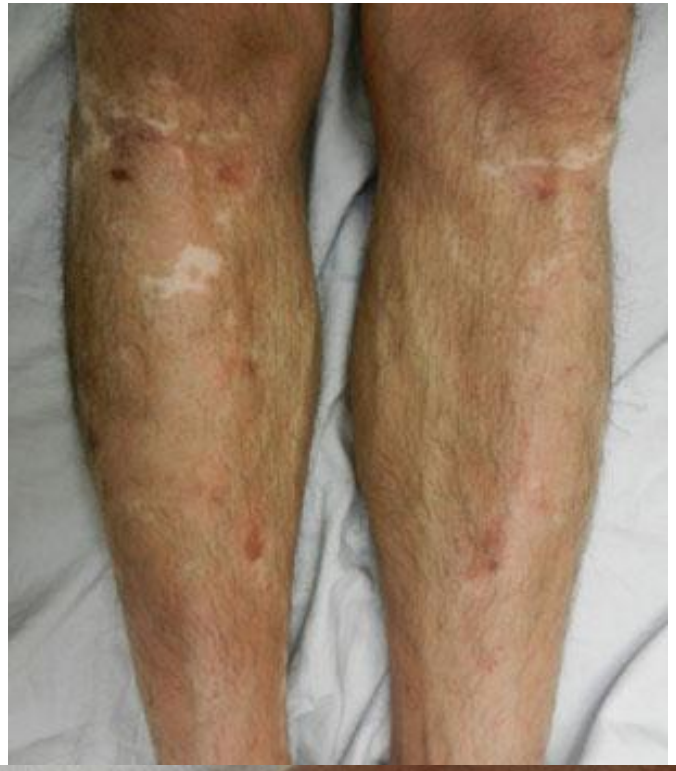


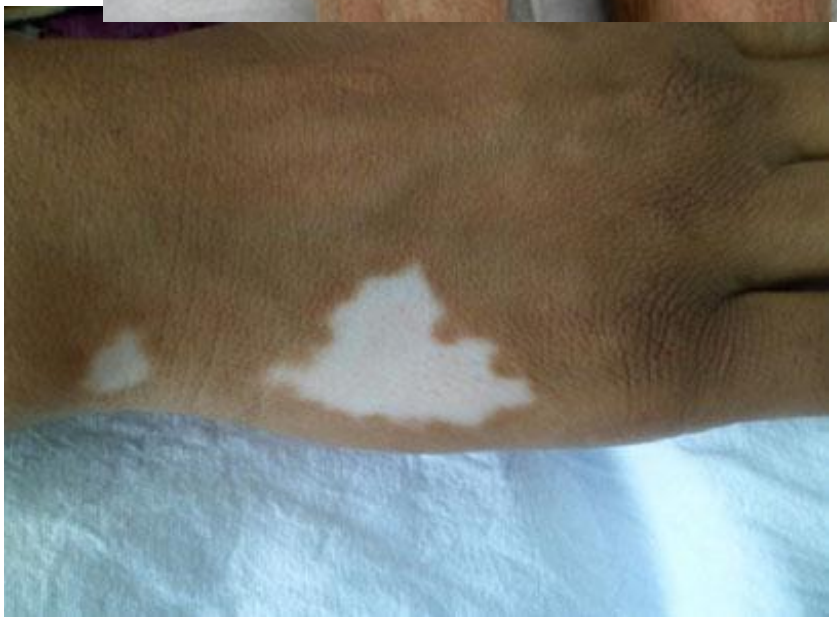
Leucotrichia repigmentation with noncultured cellular grafting

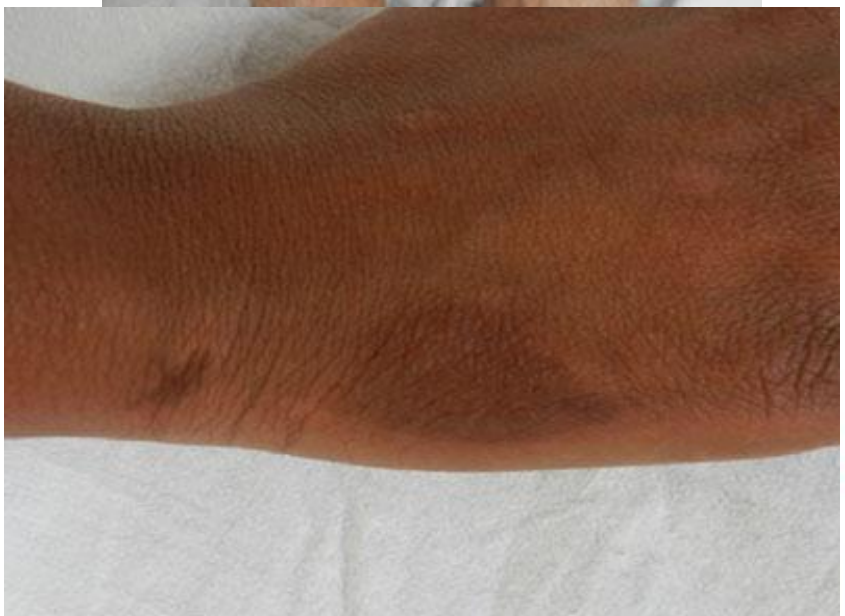


, E.Y. Gan et al. 2011





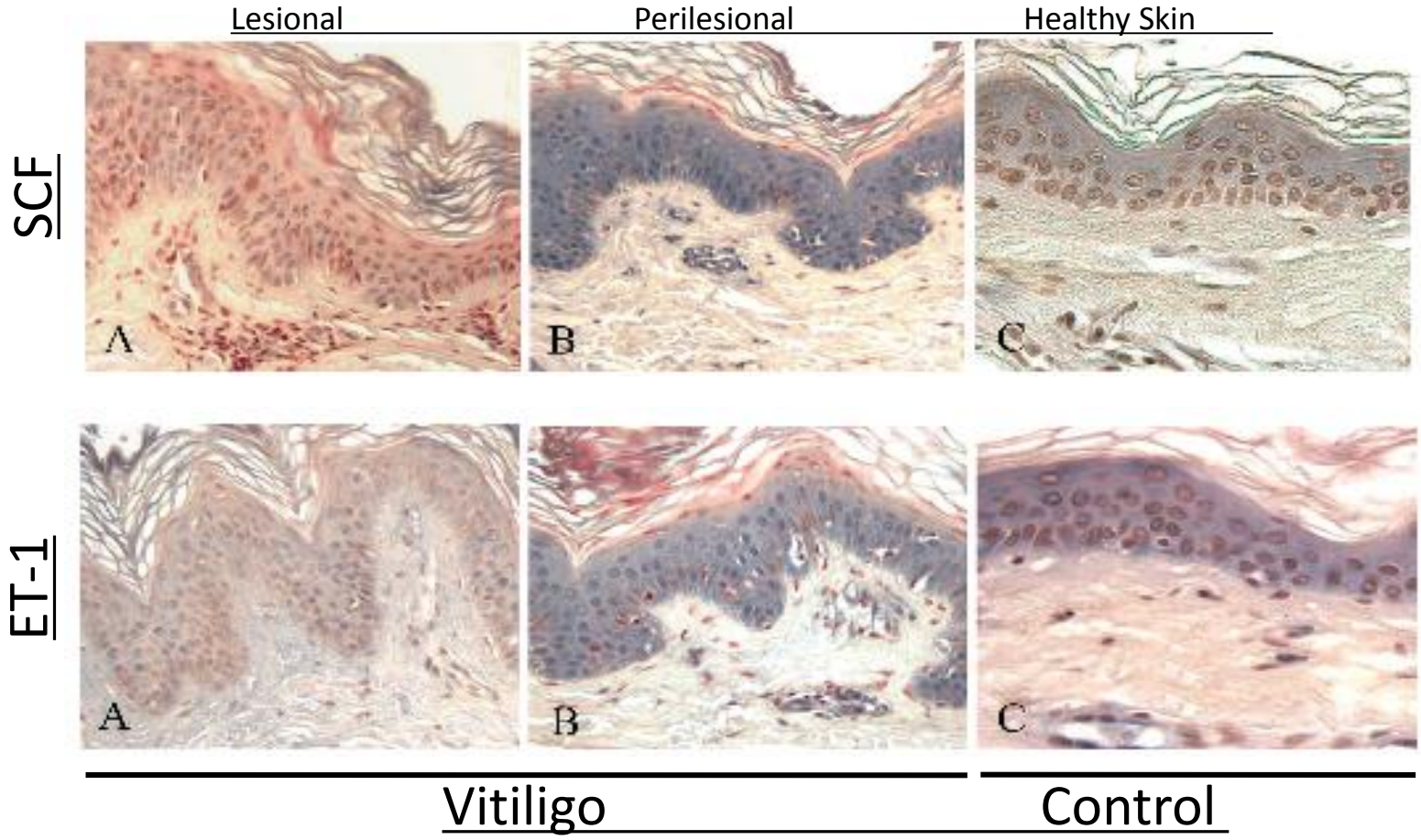




ISG

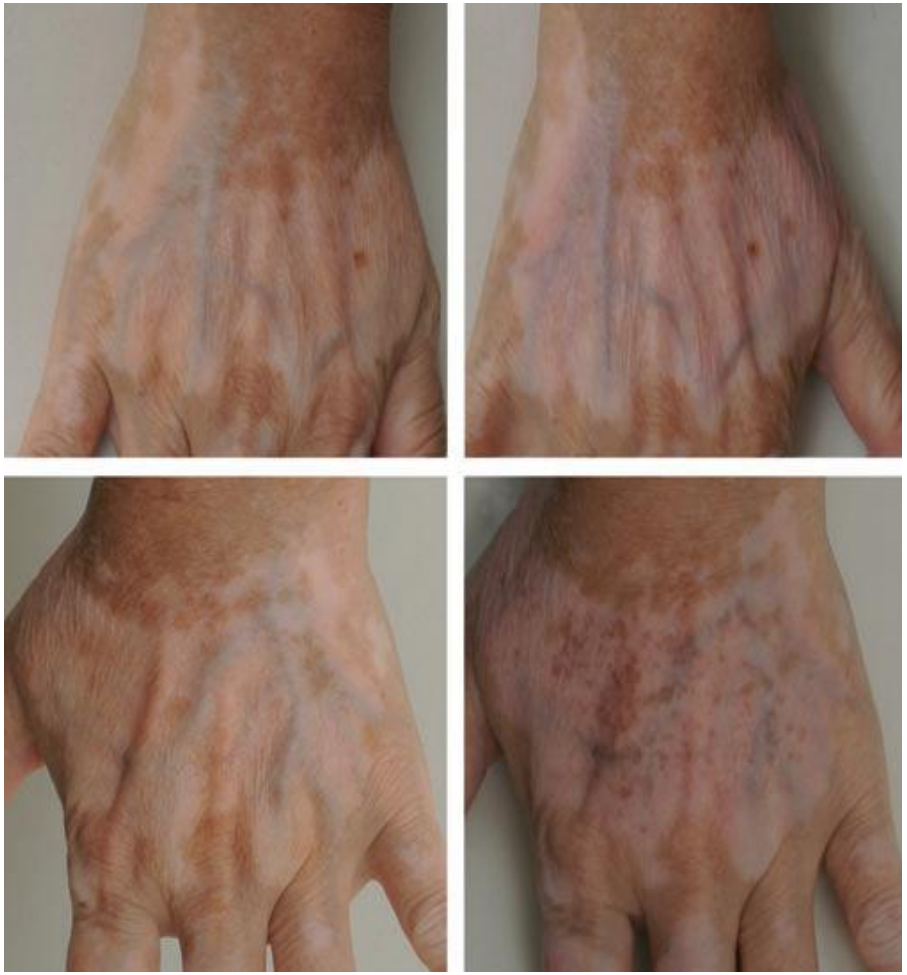
Microenvironment alteration contributes to melanocyte dysfunction in vitiligo

The melanocyte-stimulating cytokines SCF and ET-1 show a lower expression in vitiligo skin

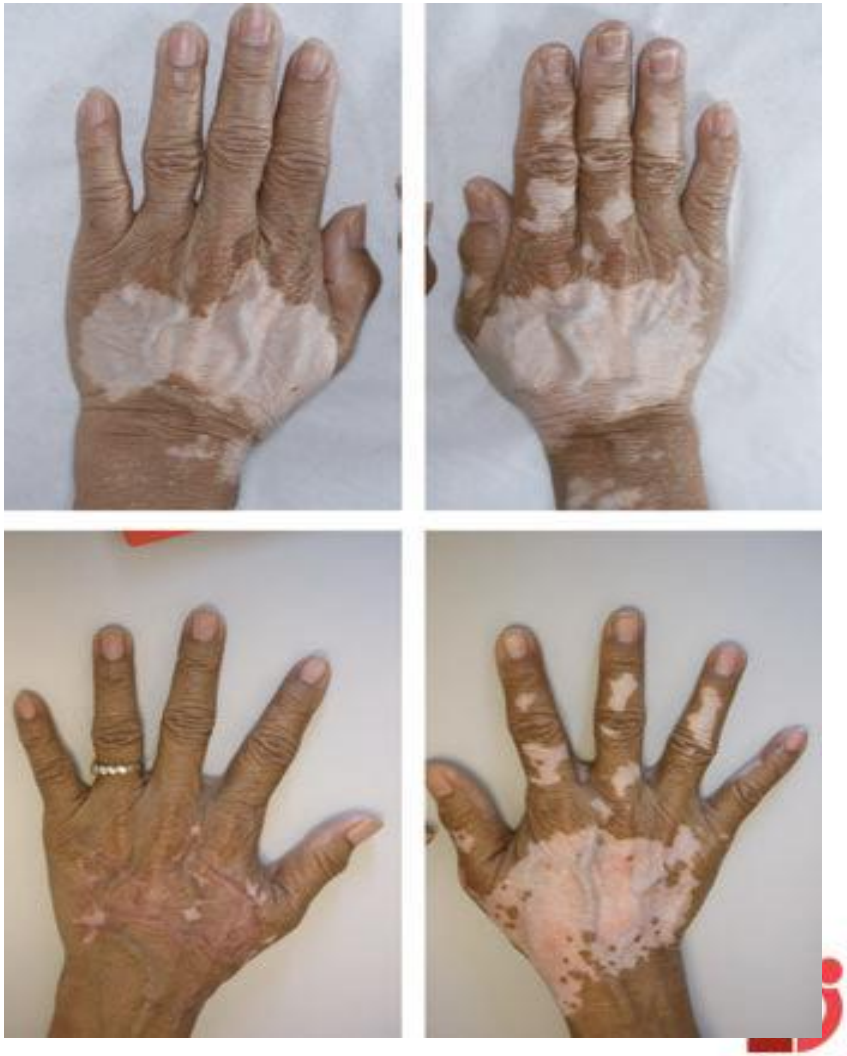


Moretti et al., 2009

Laser plus NBUVB



Co2



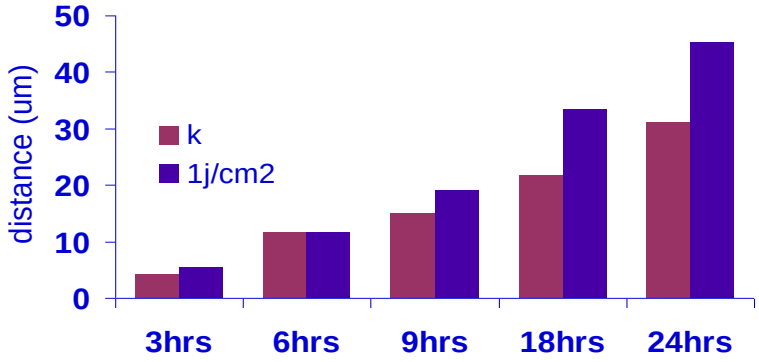
Erbium

He-neon

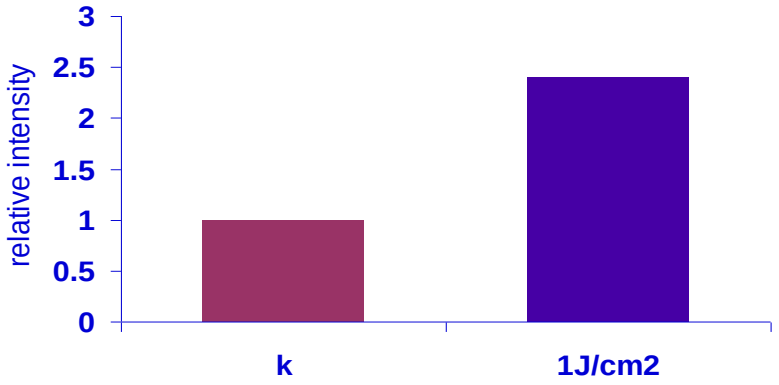
Growth factors release
Signal transduction induction
ATP production
KER/FIBRO proliferation
MEL migration
Melanin production

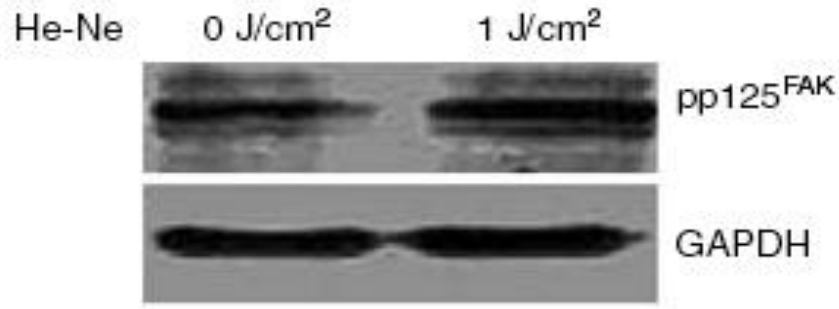
repigmetation

migration



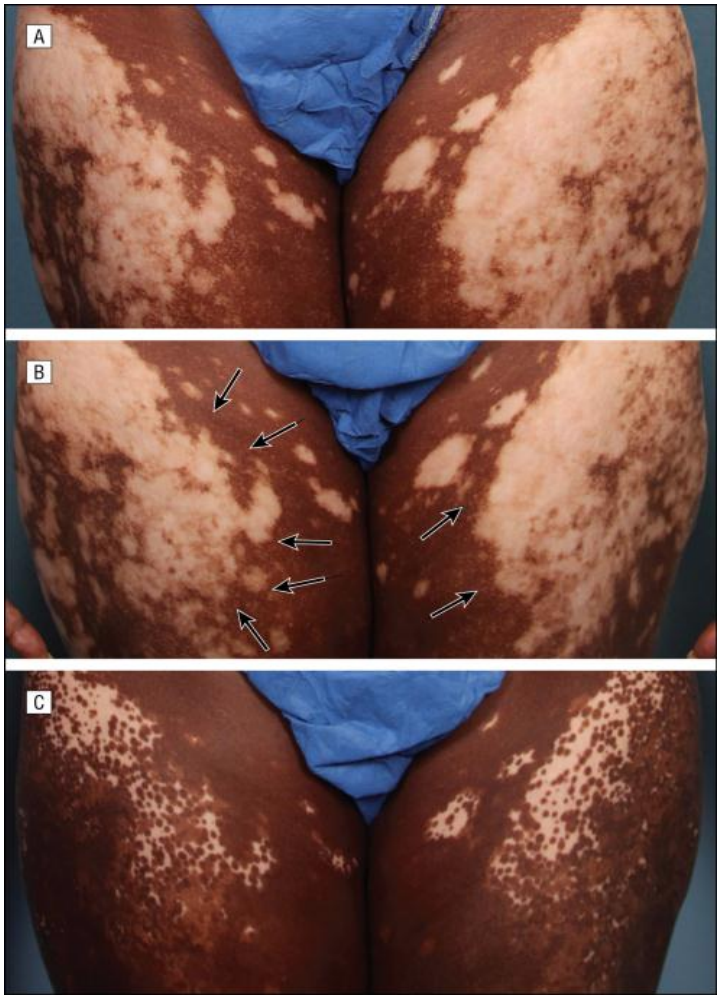
FAK expression



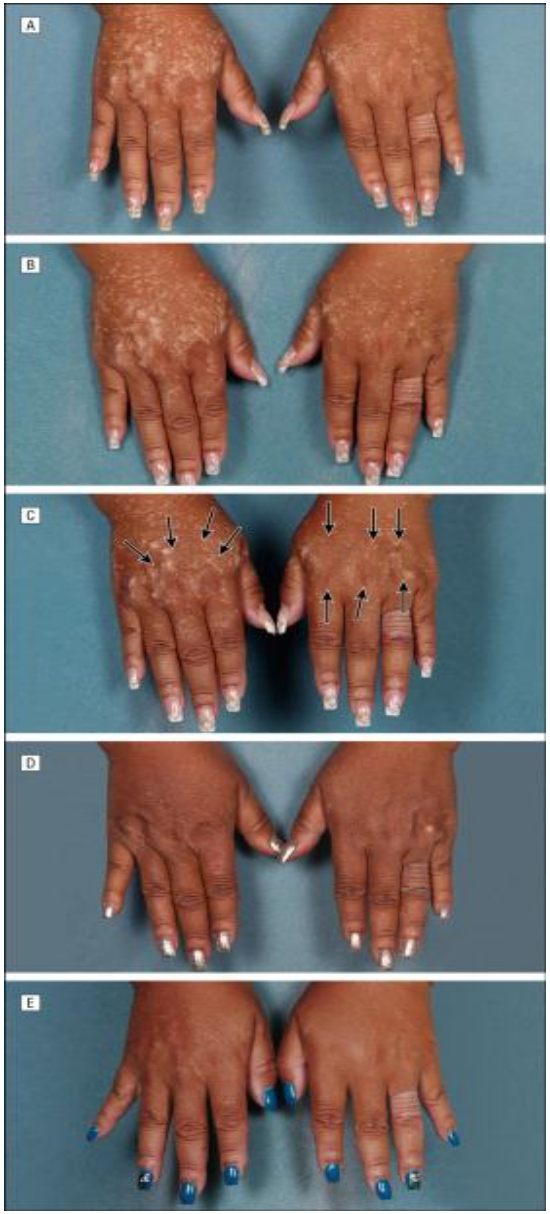


Lan, 06

Afamelanotide plus NB-UVB



14 days of treatment



persistence of repigmentation
after not implant for 5 months

JAMA Dermatol.2013;149(1):68-73

ISG

Types and Therapies

Arrest of the progression

ROTATIONAL THERAPY

Induction of proliferation and migration of differentiated melanocytes

SEQUENTIAL THERAPY

COMBINATORY THERAPY

Improve of melanocyte survival

ISG

SPRUSD
Setting **P**riorities & **R**educing **U**ncertainties for People with **S**kin **D**isease

International consensus on core outcomes set for vitiligo research

Dr Viktoria Eleftheriadou MD PhD
Centre of Evidence Based Dermatology
University of Nottingham
28/02/2013

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