VITILIGO AS SYSTEMIC DISEASE

Istanbul Master Class
Prof Sibel Alper- President
November 2014

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DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

- - President World Health Academy Publishing House, Zurich, CH
- - Editor, Dermatologic Therapy, Wiley-Blackwell
- - Chief Medical Officer, BIOSKIN EVOLUTION ®
- - Consultant, EVLaser
- - Consultant, GLG, USA
- - Consultant, Advance Medical, USA
- - Scientific Director, Dolce Aqua® , Italy
- - Consultant, CLINUVEL , Australia
- - Chief Medical Officer, Applied Biology, Inc , Irvine, CA , USA
- - Executive, Vitiligo Research Foundation, USA
- - Editor in Chief, Journal of Pigmentary Disorders, 2014

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Multimedia Center Production - Rome

Vitiligo or Vitiligos ?

Vitiligo: Systemic disease

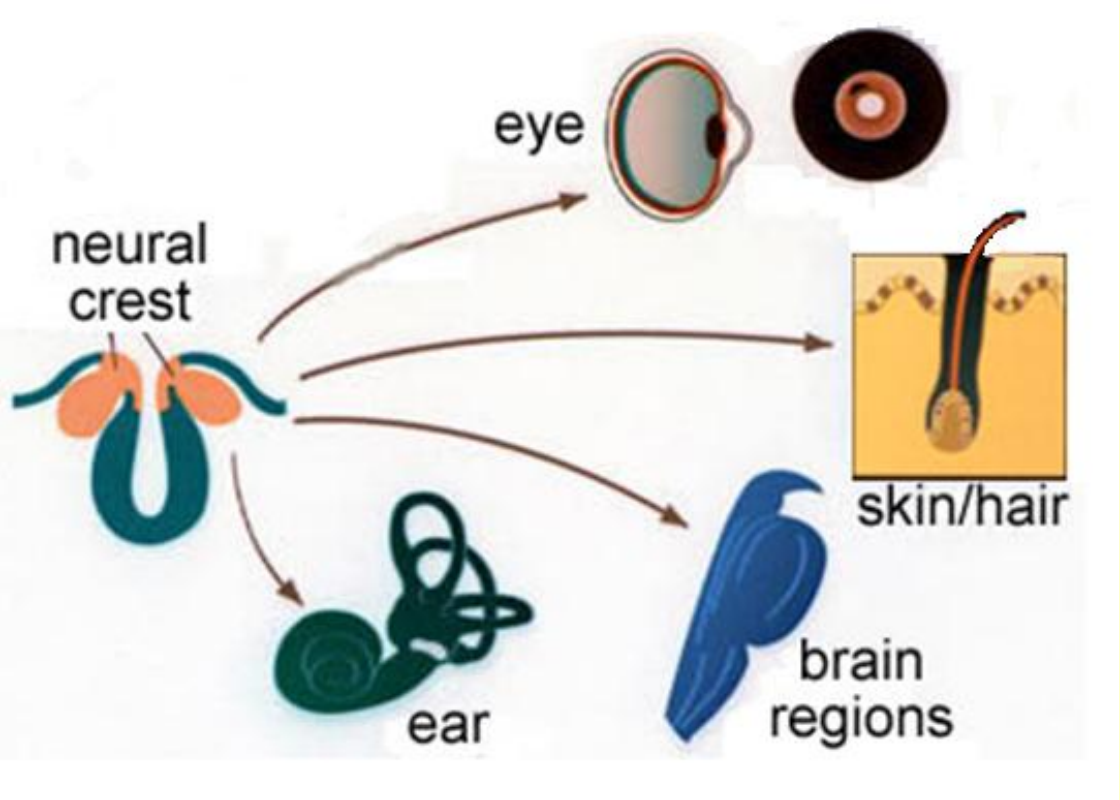
- Melanocytes Biology
- Systemic investigations
- Stop progression – spreading
- Systemic treatments
- Support patients
- Educate patients and Scientific Community

- Melanocytes migration -

Melanocytes precursors, knew as melanoblasts, are formed in the the neural crest: in the 11th week of fetal life, they migrate to various sites, where they proliferate and then differentiate into mature melanocyte.

Melanocytes reside in:

- **skin** (epidermis and hair follicle)
- **inner ear**
- **eye** (choroid and retina)
- **brain** and leptomeninges



Locations and functions of melanocytes

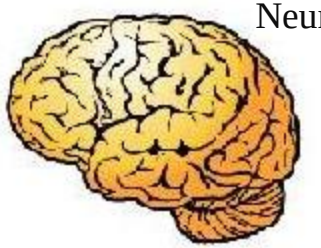
EYE

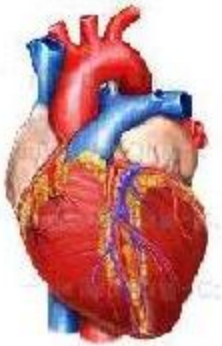
Choroid: Constitutive eye pigmentation, protection against UV

Retinal pigment epithelium: vision, metabolism of rod outer segments and retinoids

BRAIN

Neuroendocrine function and detoxification





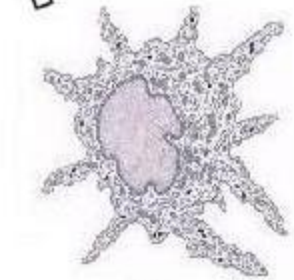
HEART

unknown

EAR

Inner ear: balance

Cochlea: hearing



ADIPOSE TISSUE

Anti-inflammation, reduction/binding of ROS

HAIR FOLLICLE

Melanocyte stem cell reservoir for skin. Hair pigmentation, Removal of toxic byproducts

EPIDERMIS

Constitutive skin pigmentation.

Responses to and protection against the environment (primarily UV)

Vitiligo: Systemic approach- Diagnosis

Clin Dermatol. 2014 May-Jun;32(3):430-4. doi: 10.1016/j.clindermatol.2013.11.011. Epub 2013 Nov 22.

Vitiligo as a systemic disease.

Lotti T[1], D'Erme AM[2].

Author information

Abstract

Vitiligo is an acquired depigmentary skin disorder of unknown etiology. Vitiligo is not only a disease of melanocytes of the skin. Human melanocytes are derived from the neural crest and are located on various parts of the body. The involvement of skin melanocytes is the most visible one, but a systemic involvement of melanocytes can be observed. Some types of vitiligo (nonsegmental vitiligo) may also be associated with various diseases, mainly with autoimmune pathogenesis. Vitiligo represents a spectrum of many different disorders with different etiologies and pathogeneses, causing a common phenotype: the loss of melanocytes and/or their products. This phenotype is always consistent with a systemic involvement.

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PMID: 24767192 [PubMed - in process]

Vitiligo: Systemic investigation

- Thyroid
- Auto-immune gastritis
- Pernicious anaemia
- DM Type -1
- Poly glandular syndrome type 2
- Metabolic disorders
- Others

Vitiligo: Systemic therapeutic approach

- Minocycline : 2011- Parsad
- Statins: 2013- Harris
- Immuno-suppresives
- Low dose cytokines
- Others

Neovir® as monotherapy for progressing vitiligo: a clinical study

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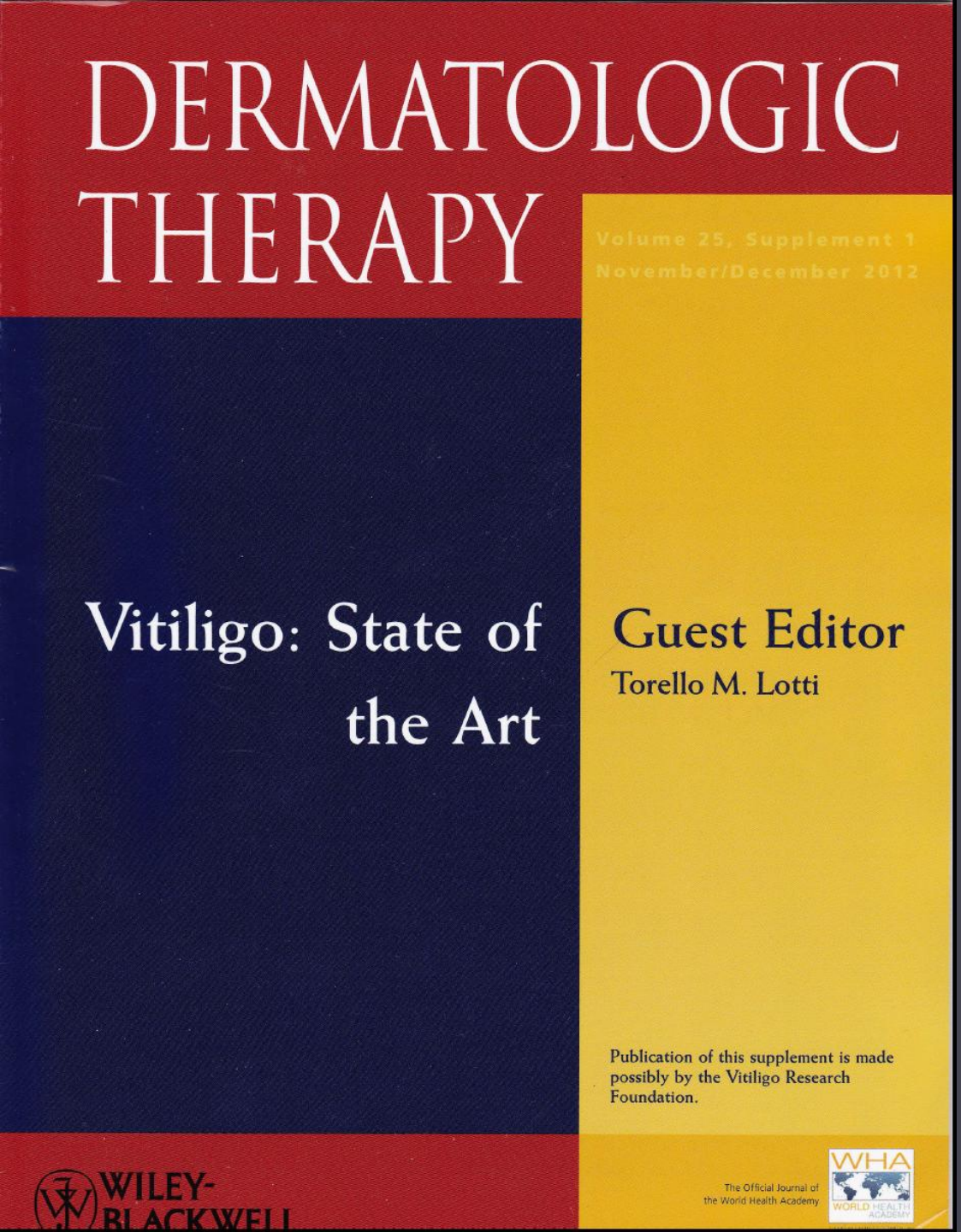
DERMATOLOGIC THERAPY
ISSN 1396-0296

THERAPEUTIC HOTLINE

Acridone acetic acid, sodium salt, as an agent to stop vitiligo progression: a pilot study

IGOR V. KOROBKO* & KONSTANTIN M. LOMONOSOV†
**VR Foundation, New York, New York and †Department of Skin and Venereal Diseases, I.M. Sechenov First Moscow State Medical University, Moscow, Russia*

Deramatologic Therapy, 2014



WHAT'S NEW

Effective and safe systemic treatments for stopping vitiligo progression and inducing repigmentation

- bFGF
- IL-10
- IL-4
- Low dose oral treatment

Prof. Dr. Davinder Parsad, MD, PhD

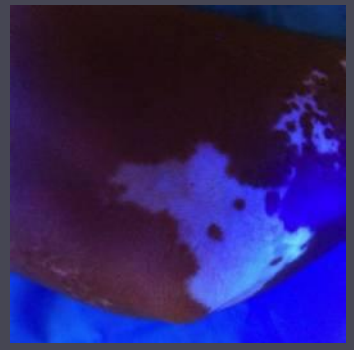
- Dr John Harris, PhD

ON GOING RESEARCH

Effects of low dose cytokines on co-coluteres of keratinocytes and melanocytes in Vitiligo (University of Florence, G. Marconi University-Rome, Scientific Departement of Guna)

Presently under evaluation the clinical effects of low dose GUNA-FGF, GUNA ANTI IL-1, GUNA IL-10, GUNA IL-4

… my personal long way in Vitiligo treatment



CXCL10 is required for progression and maintenance of vitiligo

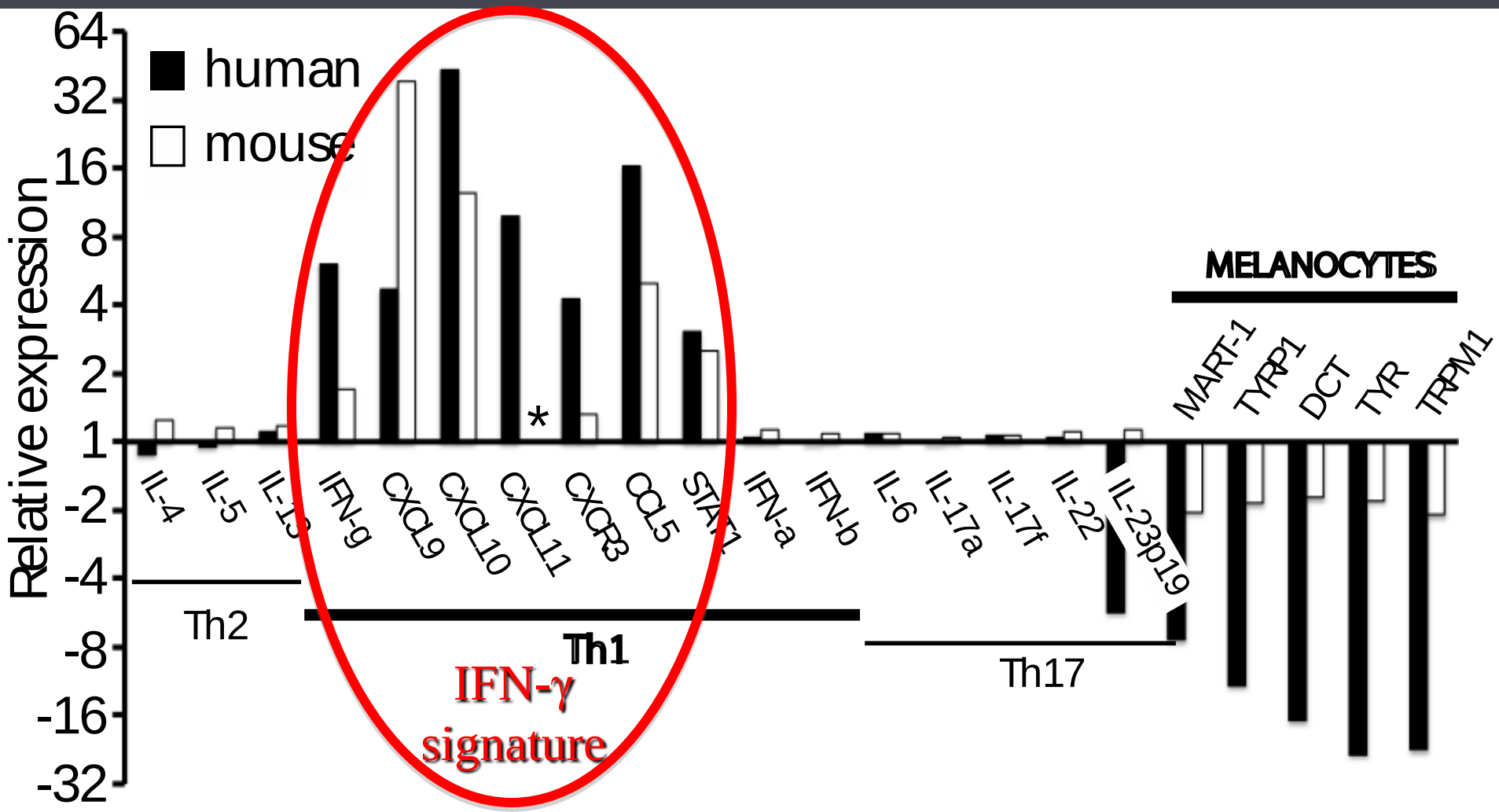
Proposed by : John E. Harris, MD, PhD

Assistant Professor of Medicine

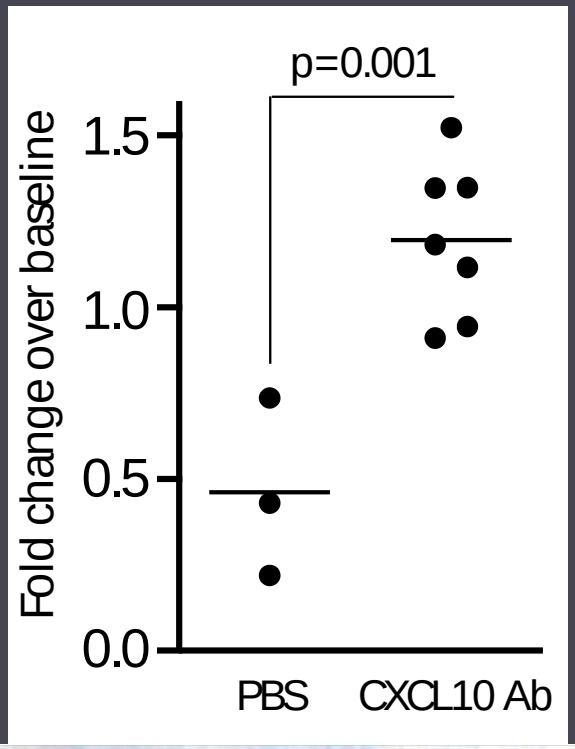
Division of Dermatology

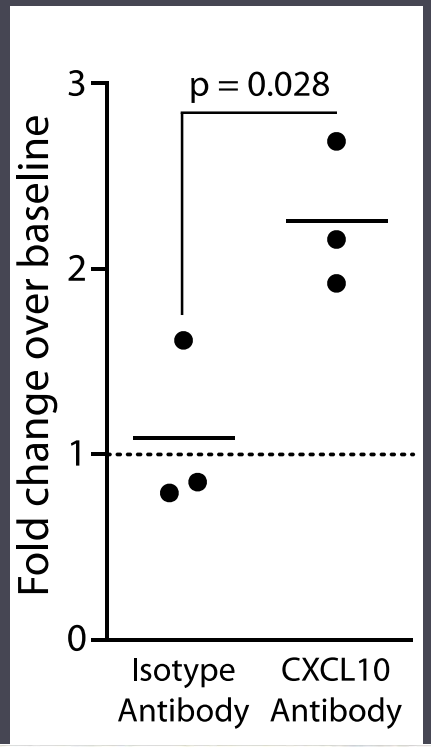
University of Massachusetts Medical School

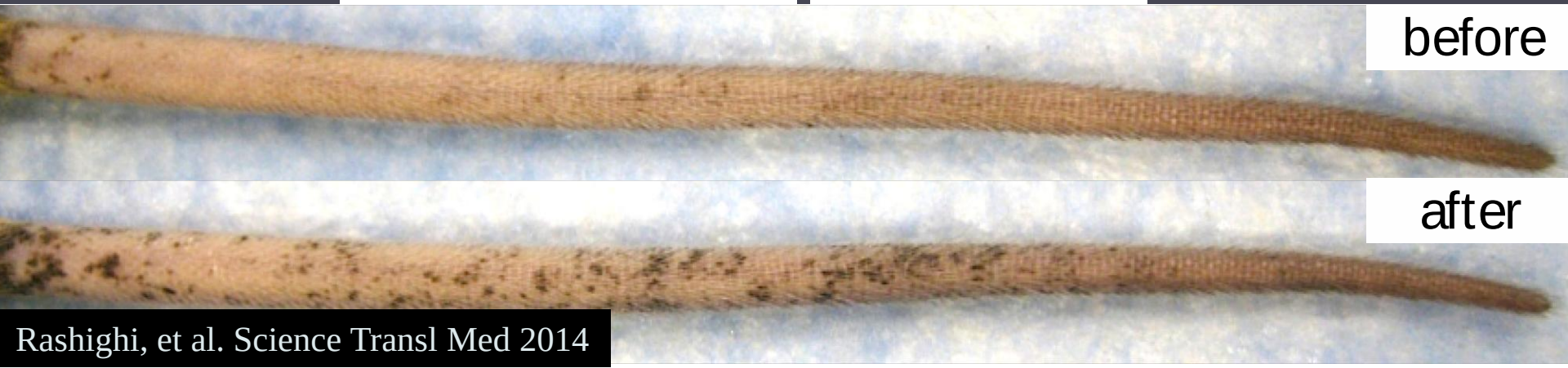
Gene expression is similar in mouse and human vitiligo



Neutralization of CXCL10 reverses vitiligo in mice







Rashighi, et al. Science Transl Med 2014

- Classification of **vitiligo**: a challenging endeavor.

- Hercogová J, Schwartz RA, Lotti TM.
- Dermatol Ther. 2012 Nov;25 Suppl 1:S10-6. doi: 10.1111/dth.12010.

Clinical Classification

- **Localized**
  - Focal: one or more macules in one area but not clearly in a segmental distribution;
  - Unilateral/segmental: one or more macules involving a unilateral segment of the body – lesions stop abruptely at the midline;
  - Mucosal: mucous membranes alone.

- **Generalized**
  - Vulgaris – scattered patches that are widely distributed;
  - Acrofacialis – distal extremities and face;
  - Mixed – acrofacialis and vulgaris;
- **Universalis**
  - Complete or nearly complete depigmentation.

Working Classification of Vitiligo

- Clinical
- Genetic
- Pathobiological
- Epidemiological
- Multisystem organ dysfunction based
- Trigger based
- **Practical implications**

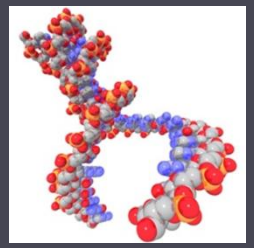
Working Classification of Vitiligo

- **Clinical**
- Localized (focal, segmental, mucosal)
- Generalized (vulgaris, acrofacialis, mixed)
- Universalis
- Special forms (trichrome, quadrichrome)
- Inflammatory
- **Practical implications**
- Localized – stable, regressive
- Generalized – progressive, systemic, autoimmune
- Universalis – comorbidities (eye, inner ear etc.)

Working Classification of Vitiligo

- **Genetic**
- Inherited in non-Mendelian, multifactorial and polygenic pattern
- Monozygotic twins with identical DNA have only 23 % concordance in developing vitiligo
- HLA haplotypes associated with ethnicities and autoimmune diseases
- PTPN22 nucleotide polymorfism – autoimmune diseases
- **Practical implications**
- Delineate patients subgroups prone to develop selected comorbidities
- Personalized treatment

Chromosome	Gene	Protein	Function	GV susceptibility variant[a]	Other autoimmune disease associations
1p36.23	*RERE*	Atrophin-like protein 1	Regulates apoptosis		
1p13.2	*PTPN22*	Lymphoid-specific protein tyrosine phosphatase nonreceptor type 22	Regulates T cell receptor signaling	R620W	Type 1 diabetes, SLE, Graves' disease, rheumatoid arthritis, Addison's disease, psoriasis, inflammatory bowel disease
2q33.2	*CTLA4*[b]	Cytotoxic T-lymphocyte antigen 4	Inhibits T cells		Type 1 diabetes, Graves' disease, Hashimoto's thyroiditis, inflammatory bowel disease, SLE
3p13	*FOXP1*	Forkhead box P1	Regulates lymphoid cell development		
3q28	*LPP*	LIM domain-containing preferred translocation partner in lipoma	Unknown		Celiac disease, rheumatoid arthritis
5q22.1	*TSLP*	Thymic stromal lymphoprotein	Regulates T cell and dendritic cell maturation		
6p21.3	MHC class I (*HLA-A*)	Human leukocyte antigen α chain	Presents peptide antigens	*02	Many
	MHC class II[c]	Unknown			Many
	MHC class III	Unknown			Many
6q27	*CCR6*	C−C chemokine receptor type 6	Regulates B cell differentiation, function of dendritic and Th17 cells		Inflammatory bowel disease, rheumatoid arthritis, Graves' disease
10p15.1	*IL2RA*	Interleukin-2-receptor α chain	Regulates lymphocyte response to bacteria *via* IL2		Type 1 diabetes, Graves' disease, multiple sclerosis, rheumatoid arthritis, SLE
11q14.3	*TYR*	Tyrosinase	Key enzyme of melanin biosynthesis	R402Q	
14q12	*GZMB*	Granzyme B	Mediates target cell apoptosis by cytotoxic T cells and natural killer cells and activation-induced cell death of effector Th2 cells		
17p13.2	*NLRP1*	NACHT, LRR, and PYD domains-containing protein 1			Type 1 diabetes, Addison's disease, celiac disease, systemic sclerosis
21q22.3	*UBASH3A*	Ubiquitin-associated and SH3 domain-containing A	Regulates T cell receptor signaling		Type 1 diabetes
22q12.1	*XBP1*	X-box binding protein 1	Regulates expression of MHC class II genes, IL6, B cell and plasma cell differentiation		Crohn's disease
22q13.1	*C1QTNF6*	C1q and tumor necrosis factor-related protein 6	Unknown		Type 1 diabetes, rheumatoid arthritis
Xp11.23	*FOXP3*	Forkhead box P3	Regulates regulatory T cells		IPEX



Spritz RA. J Genet Genomics. 2011, 20;38(7):271-8

Working Classification of Vitiligo

- **Pathobiological**
- Autoimmune
- Neurohumoral
- Autocytotoxic
- Biochemical
- Oxydative
- Melanocytorrhagy
- Decreased melanocyte lifespan
- **Practical implication**
- Understand the origin in the single subject
- Personalized treatment

ETIOPATHOGENESIS

GENETIC PREDISPOSITION

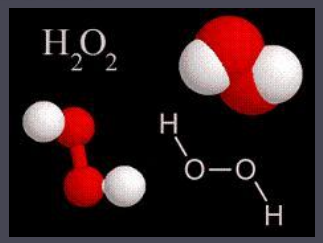
Autoimmune Susceptibility Locus (AI

NEURAL HYPOTHESIS

AUTOIMMUNE HYPOTHESIS

MELANOCYTE DESTRUCTION

AUTOCYTOTOXIC/ RADICALIC HYPOTHESIS

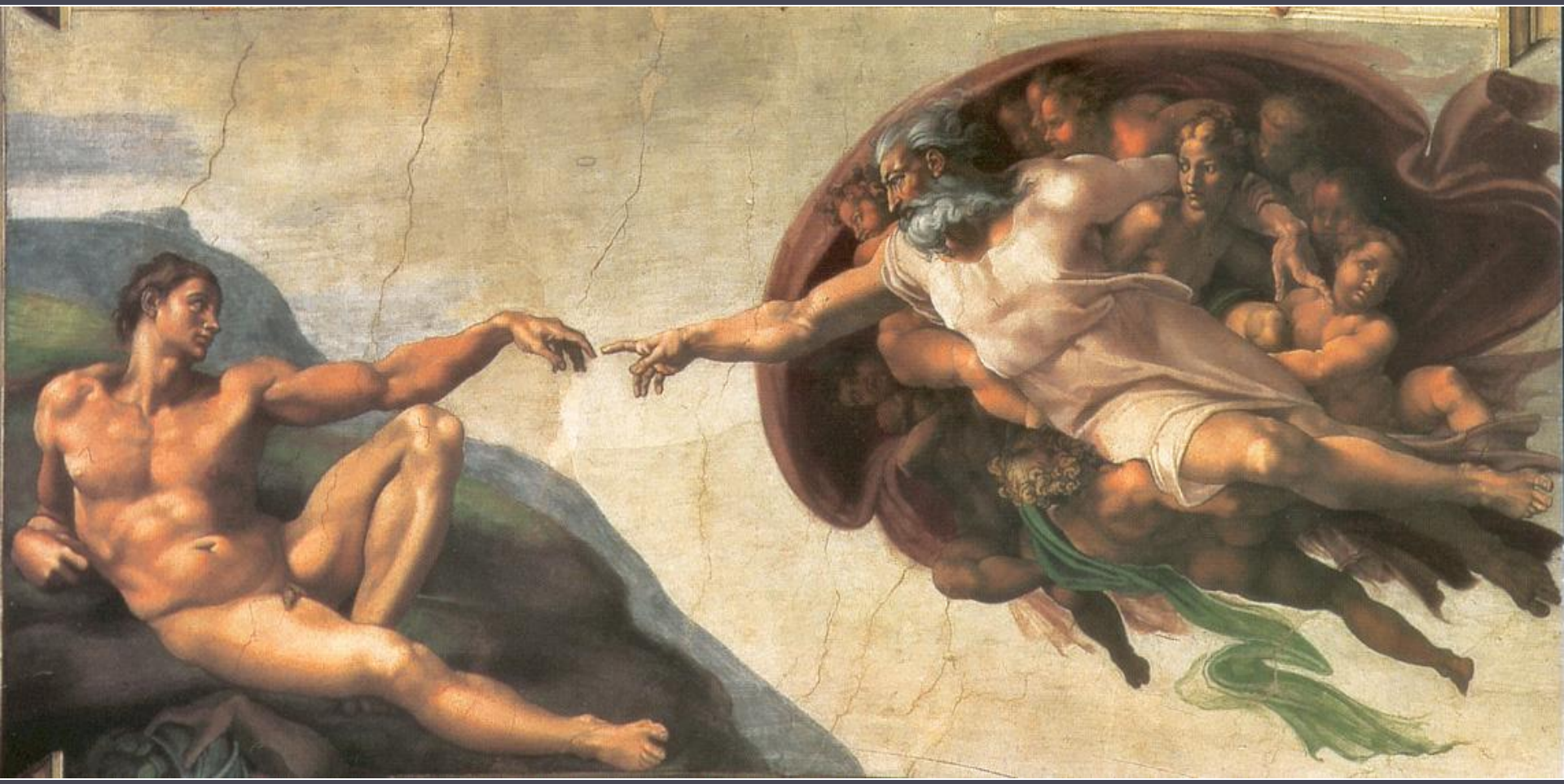


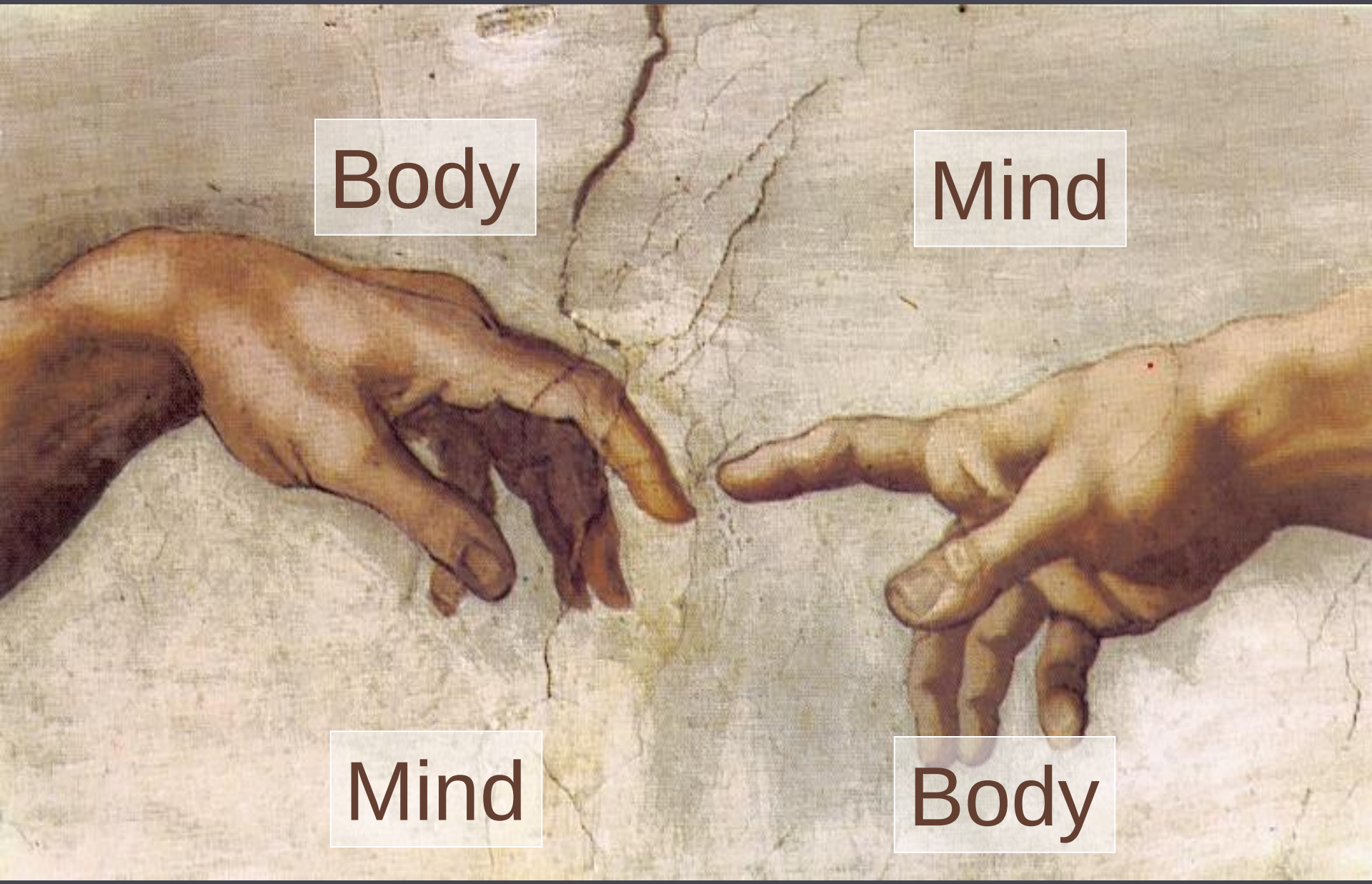
ECLECTIC HYPOTHESIS
MELANOCYTORRAGY
SYNERGISTIC THEORY

Working Classification of Vitiligo

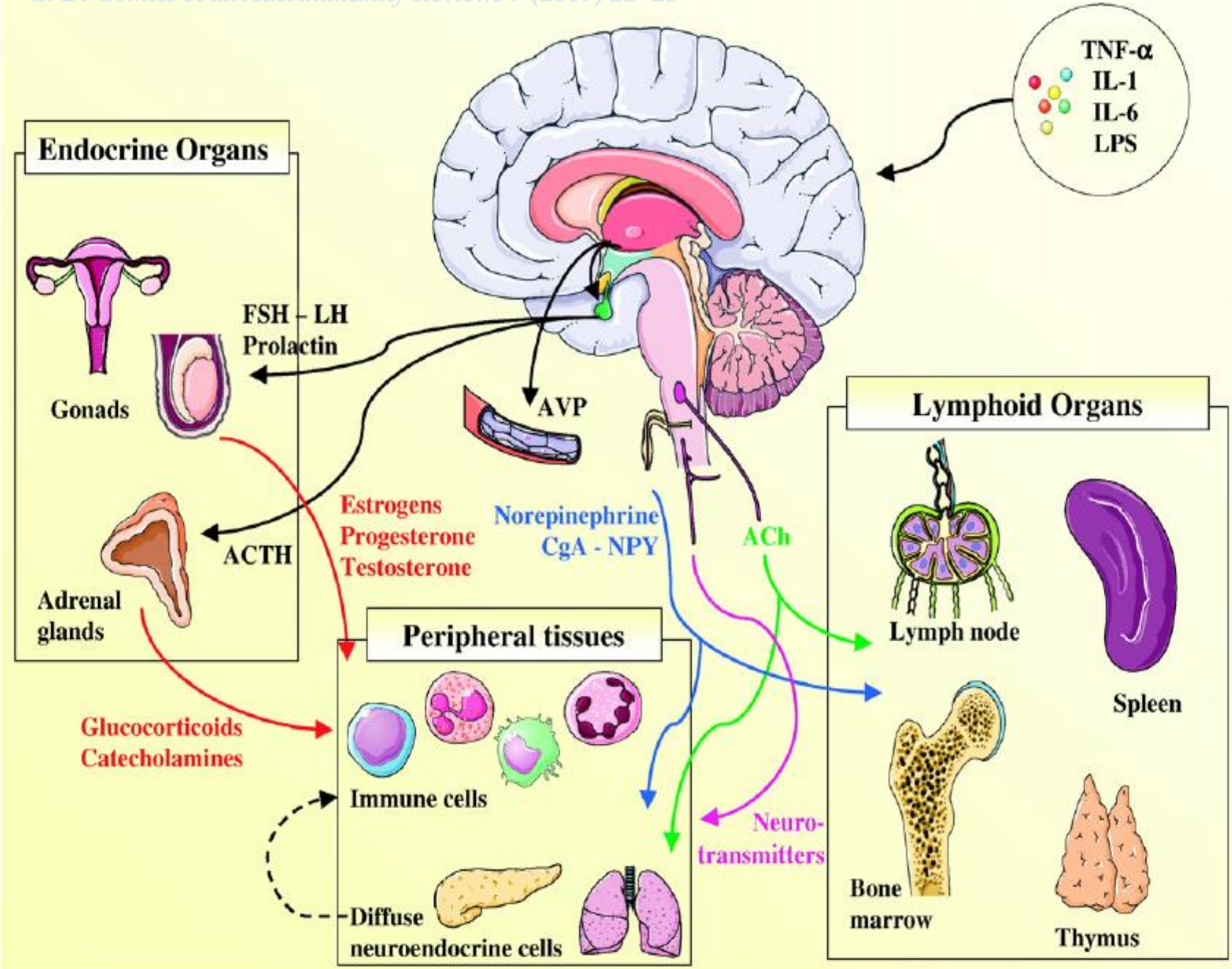
- **Epidemiological**
- Prevalence from 0.3 % to 8.8 %
- Role of environmental factors
- Monozygotic twins with identical DNA have only a 23 % concordance in developing vitiligo
- **Practical implication**
- Discover environmental factors
- Personalized treatment

The Neuro Immune Cutaneous Endocrine Network relationship between Mind and Skin




Body
Mind
Mind
Body

G. Di Comite et al. Autoimmunity Reviews 7 (2007) 23–29



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DERMATOLOGIC THERAPY
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The neuro-immuno-cutaneous-endocrine network: relationship between mind and skin

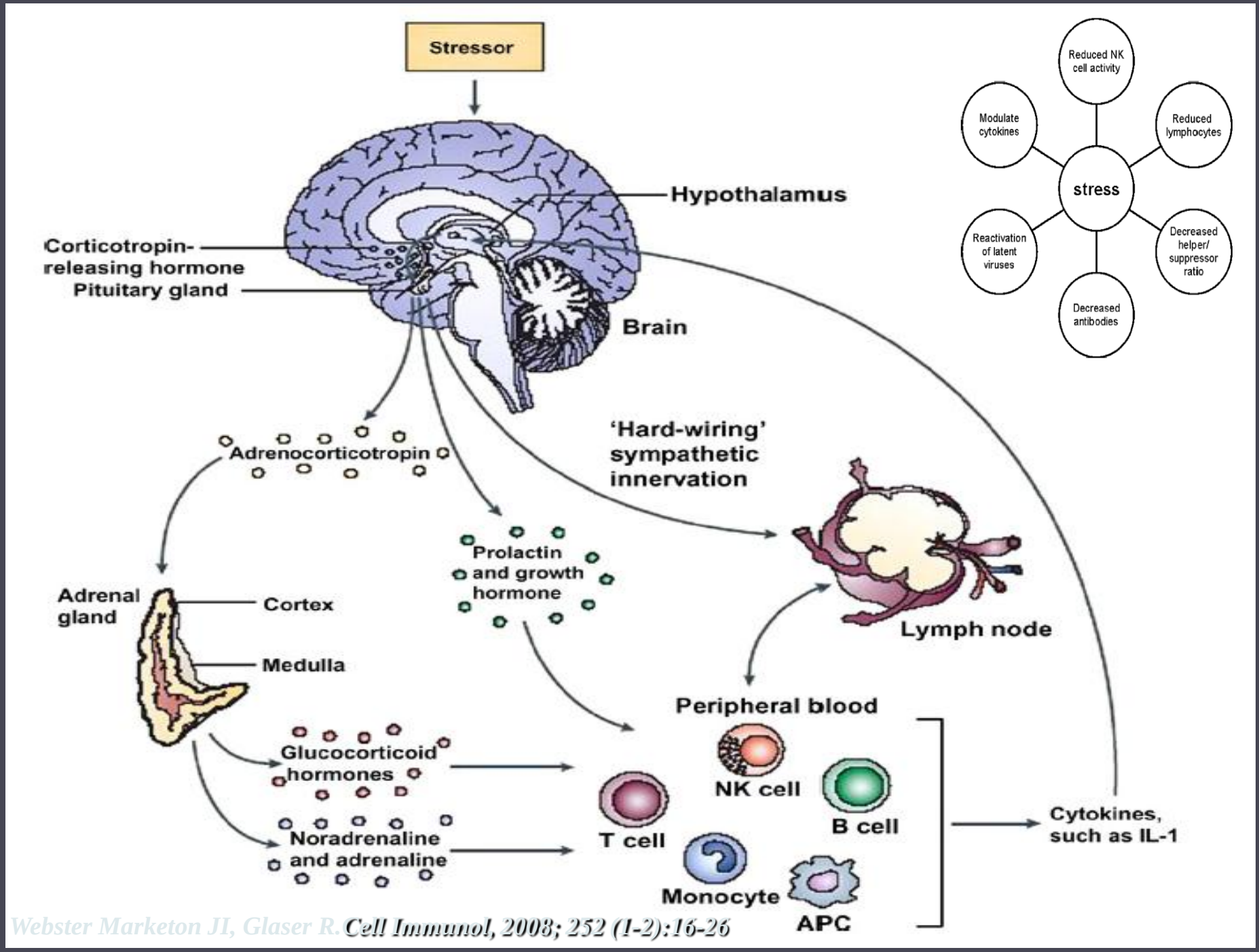
BENEDETTA BRAZZINI,* ILARIA GHERSETICH,* JANA HERCOGOVA,† & TORELLO LOTTI*
**Department of Dermoscience, University of Florence, Florence, Italy, and*
†Department of Dermatology, Charles University, Prague, Czech Republic

CLINICAL REVIEW

Neuropeptides in skin

Torello Lotti, MD,[a] Giuseppe Hautmann, MD,[b] and Emiliano Panconesi, MD[b]
Siena and Florence, Italy

Neuropeptides are a heterogeneous group of more than 50 molecules that play a role in various cutaneous functions and diseases; they act as neuromodulators, neurotransmitters, neurohormones, and hormones. In the skin, neuropeptides are synthesized locally (i.e., in keratinocytes and in endothelial cells) and are transported by nerve fibers or immune cells (i.e., lymphocytes, monocytes, and polymorphonuclear cells). Specific receptors and binding sites for neuropeptides have been described in different cell lines in the skin (keratinocytes, endothelial cells, immune cells, fibroblasts). Many different biologic actions of neuropeptides have been demonstrated. Depletion of cutaneous neuropeptides (i.e., with capsaicin cream) or therapeutic use of neuropeptide agonists and/or antagonists may aid in the treatment of skin diseases. (J AM ACAD DERMATOL 1995;33:482-96.)



Webster Marketon JI, Glaser R. Cell Immunol, 2008; 252 (1-2):16-26

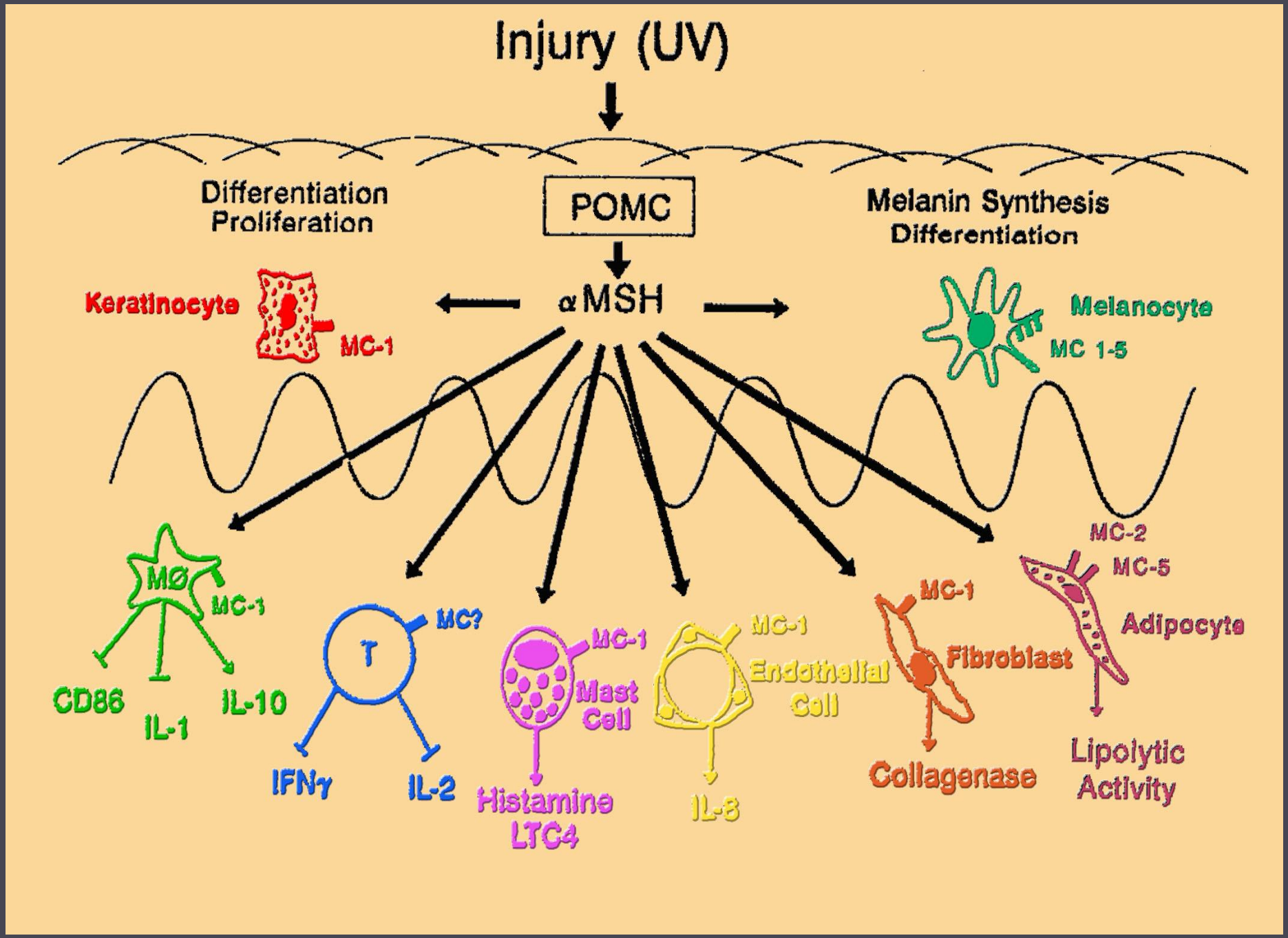
International Journal of Dermatology

International Journal of Dermatology 2002, **41**, 311–318

Review

Can the brain inhibit inflammation generated in the skin? The lesson of α-melanocyte-stimulating hormone

Torello Lotti, MD, Beatrice Bianchi, PhD, Ilaria Ghersetich, MD, Benedetta Brazzini, MD, and Jana Hercogova, MD


Injury (UV)
Differentiation
Proliferation
POMC
Melanin Synthesis
Differentiation
Keratinocyte
MC-1
αMSH
Melanocyte
MC 1-5
MØ
MC-1
CD86
IL-1
IL-10
T
MC?
IFNγ
IL-2
MC-1
Mast
Cell
Histamine
LTC4
MC-1
Endothelial
Cell
IL-8
MC-1
Fibroblast
Collagenase
MC-2
MC-5
Adipocyte
Lipolytic
Activity

Lotti T et al. International Journal of Dermatology 2002, 41, 311–318

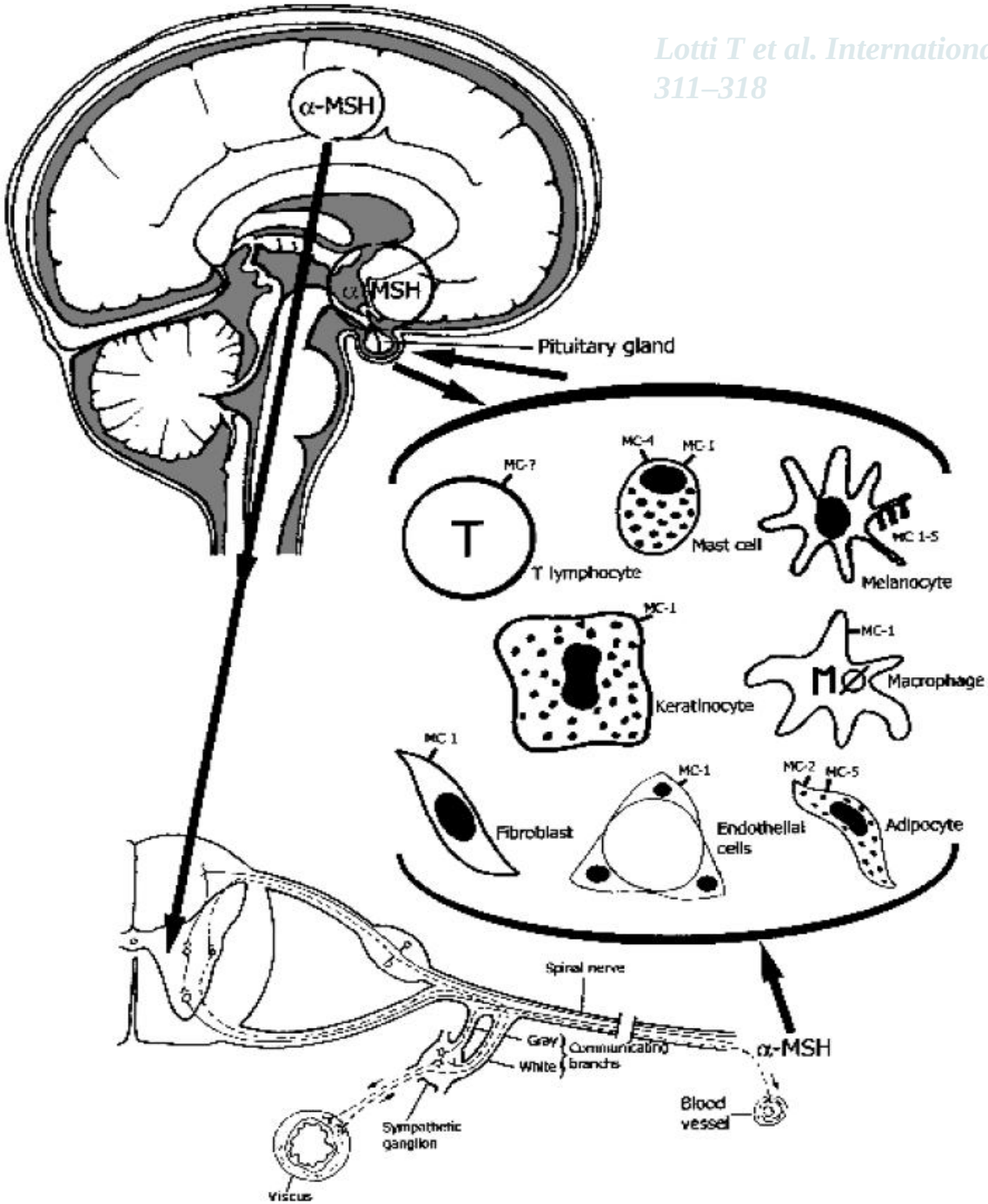


Figure 1 In the brain α-melanocyte stimulating hormone is synthetized predominantly in the pituitary gland. When administered into the cerebral ventriculi (in mice) α-MSH inhibits the cutaneous inflammation induced by application of topical irritants and intradermal injection of cytokines. This action is related to the integrity of the spinal cord descending neurogenic pathways and of β2 receptors in the periphery. α-melanocyte stimulating hormone is also released in the plasma by the pituitary gland and by different cells, including keratinocytes, melanocytes, monocytes, macrophages, endothelial cells, adipocytes, fibroblasts and mast cells. Membrane receptors for α-MSH are present both in the brain and on nearly all the cells that produce and release α-MSH and participate in cutaneous inflammation mainly by reducing and terminating the same flogistic reactions

Autoimmune markers in vitiligo patients appear correlated with obsession and phobia

S. Moretti,[†] M. Arunachalam,[†,*] R. Colucci,[†] S. Pallanti,[‡] J.A. Kline,[§] S. Berti,[†] F. Lotti,[†] T. Lotti[†]

[†]Department of Critical Care Medicine and Surgery, Division of Dermatology, University of Florence, Florence, Italy
[‡]Department of Psychiatry, University of Florence, Florence, Italy
[§]Department of Emergency Medicine Research, Carolinas Medical Center, Charlotte, NC, USA

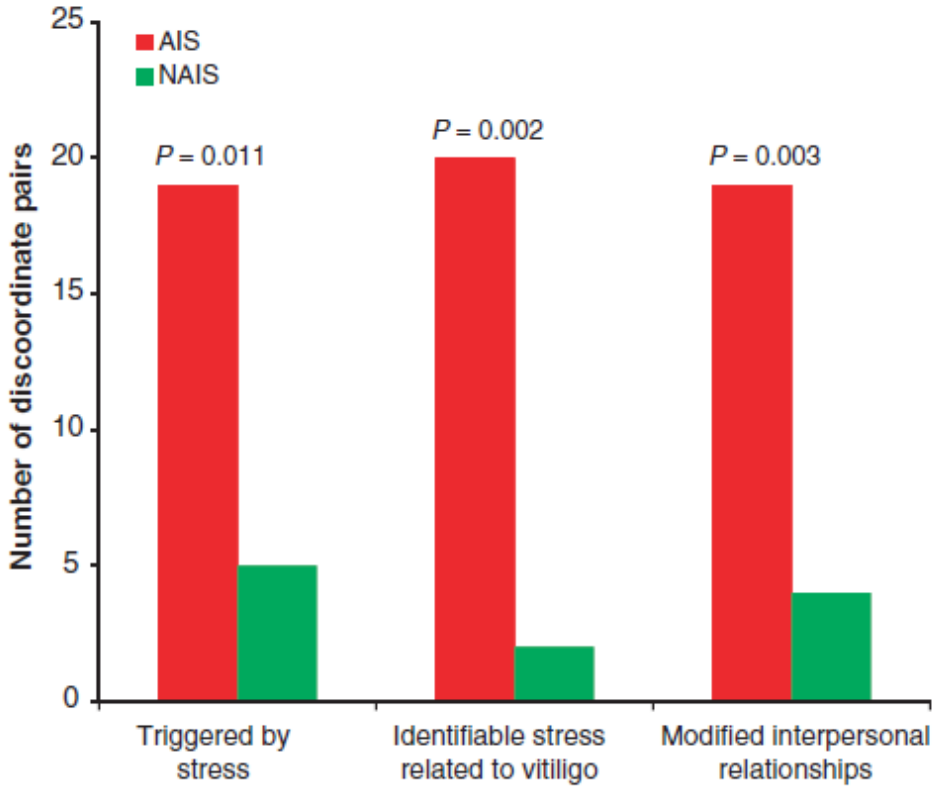
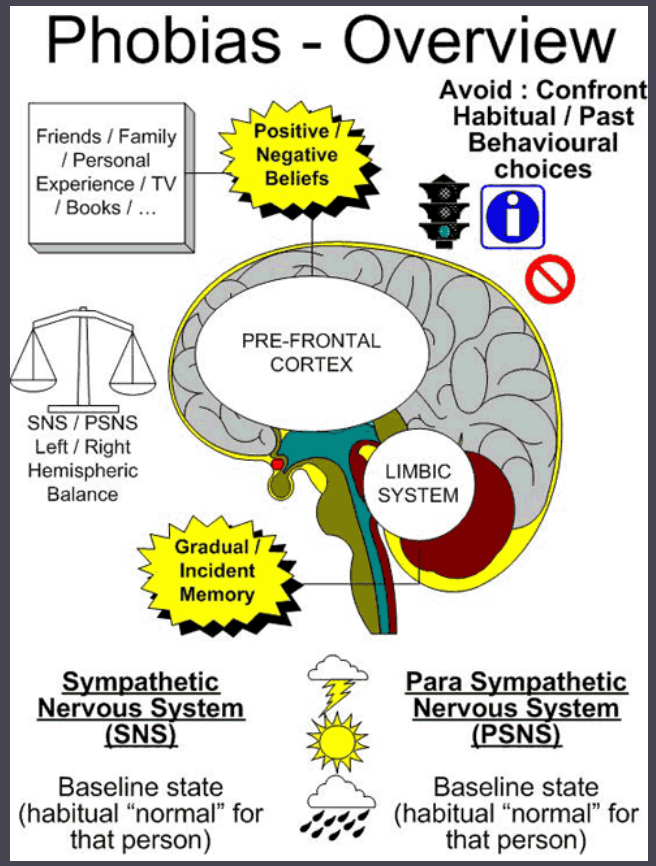


Figure 1 Psychological discomfort factors and social aspects shown in the graph are significantly higher in autoimmune markers vs. negative autoimmune markers vitiligo patients.



Working Classification of Vitiligo

- **Multisystem organ dysfunction**
- Many disorders or syndromes are variably associated
- Most of such cases are discovered at birth or during infancy
- **Practical implications**
- Great help for pediatricians and geneticists
- Discover yet unidentified causes of vitiligo
- Personalized treatment

Vitiligo: Disease Association

More common associations
- Addison disease
- Alopecia areata
- Atopic dermatitis
- Autoimmune thyroid disease
- Chronic urticaria
- Diabetes mellitus
- Halo nevi
- Hypoacusis
- Hypoparathyroidism
- Ichthyosis
- Ocular abnormalities
- Pernicious anemia
- Psoriasis
- Rheumatoid arthritis

Less common associations
- Acrokeratosis paraneoplastica Bazex
- Alezzandrini syndrome
- APECED syndrome
- Asthma
- Ataxia-telangiectasia
- Deafness
- DOPA-responsive dystonia
- Dysgammaglobulinemia
- HIV
- Inflammatory bowel disease
- Kabuki syndrome
- Kaposi sarcoma
- Melanoma
- MELAS syndrome
- Morphea
- Multiple sclerosis
- Myasthenia gravis
- Nonmelanoma skin cancer
- Pemphigus vulgaris
- Sarcoidosis
- Schmidt syndrome
- Systemic lupus erythematosus
- Turner syndrome
- Twenty-nail dystrophy
- Vogt-Koyanagi-Harada syndrome

Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. J Am Acad Dermatol. 2011;65(3):473-91.

Working Classification of Vitiligo

- **Trigger based**
- Vitiligo, leukodermas, depigmented patches
- Trichrome, quadrichrome vitiligos
- Inflammatory vitiligo
- **Practical implications**
- Leukodermas and special triggers will facilitate understanding and treating the individual patient since childhood

CHEMICALLY INDUCED LEUKODERMA

Most potent phenol/catechol derivatives
- Monobenzyl ether of hydroquinone (MBH)
- Hydroquinone
- *p-tert*-Butylcatechol (PTBC)
- *p-tert*-Butylphenol (PTBP)
- *p-tert*-Amylphenol (PTAP)

Additional phenol/catechol derivatives
- Monomethyl ether of hydroquinone (MMH)
- Monoethyl ether of hydroquinone (MEH)
- *p*-Phenylphenol
- *p*-Octylphenol
- *p*-Cresol

Sulfhydryls
- Cysteamine
- Sulfanolic acid
- Cystamine dihydrochloride

Miscellaneous
- Mercurials
- Arsenic
- Cinnamic aldehyde
- PPD
- Corticosteroids
- Chloroquin
- Soymilk and derived protein Thiotepa (inhibits PAR-2) (Miyamoto and Taylor[4] and Ortonne[1])
- Tretinoin
- Benzoyl peroxide
- Ammoniated mercury
- Azelaic acid
- Fluorouracil
- Briilliant lake red R

Ghosh S.cIndian J Dermatol. 2010;55(3):255-8.

Working Classification of Vitiligo

- **Molecular**
- Genome-wide linkage and genome-wide association studies of generalized vitiligo have indentified multiple loci which contribute both to vitiligo susceptibility and to other autoimmune diseases (PTPN22 nucleotide polymorphism)
- Most genes encode molecules relevant for vitiligo
- **Practical implications**
- “Vitilogenic molecules” specific for individuals/subgroups
- Limited number of molecules, same phenotype
- Personalized treatment/ common way treatment

Working Classification of Vitiligo

- **Vitiligo:**
- Spectrum of diseases with different clinical presentations, unknown etiology, fragmented genetic data and pathogenetical hypothesis
- Our working classification is proposed as a fertile ground to the scientific community
- The phenotypic manifestation is not a disease!
- **TAKE HOME MESSAGE FOR VITILIGO**

- Treatments of **vitiligo**: what's new at the horizon.
- Lotti TM, Hercogová J, Schwartz RA, Tsampau D, Korobko I, Pietrzak A, Mitrevska NT, Valle Y, Buggiani G.
- Dermatol Ther. 2012 Nov;25 Suppl 1:S32-40. doi: 10.1111/dth.12011.

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DOI:10.1089/ars.2009.2779

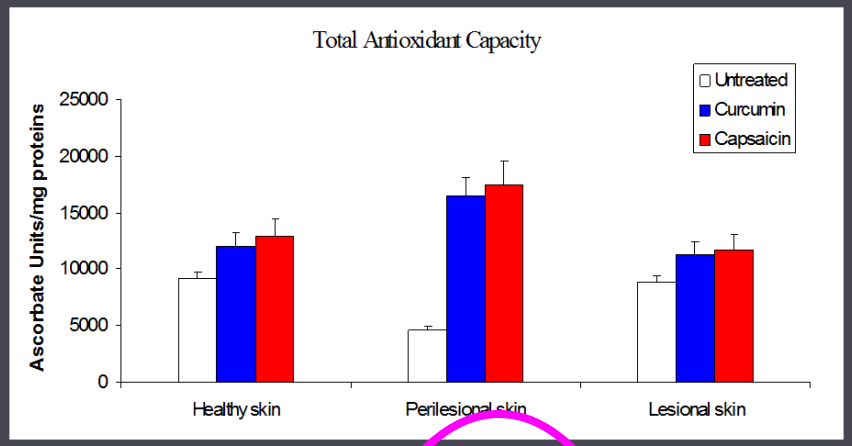
ORIGINAL RESEARCH COMMUNICATION

The Involvement of Smac/DIABLO, p53, NF-kB, and MAPK Pathways in Apoptosis of Keratinocytes from Perilesional Vitiligo Skin: Protective Effects of Curcumin and Capsaicin

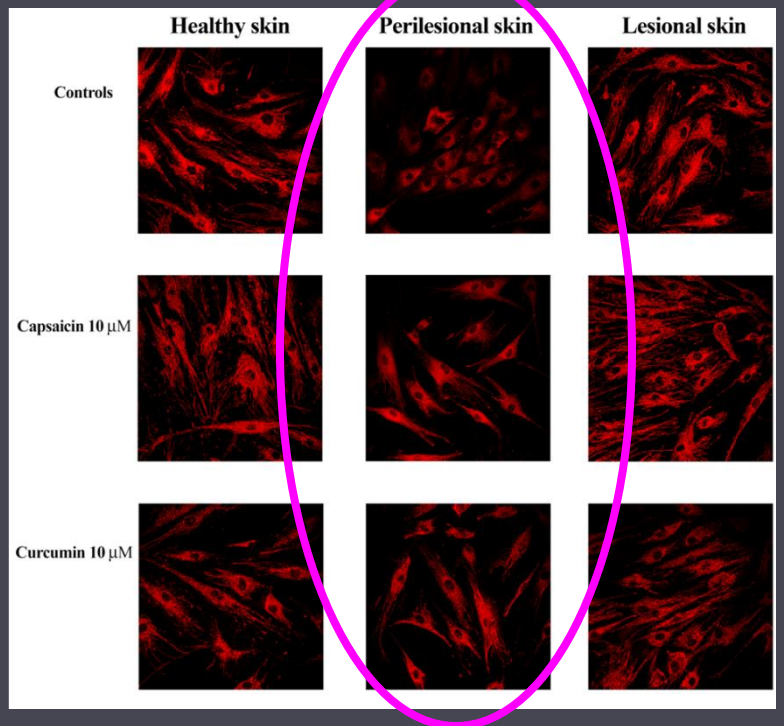
Matteo Becatti,[1] Francesca Prignano,[2] Claudia Fiorillo,[1] Leonardo Pescitelli,[2] Paolo Nassi,[1] Torello Lotti,[2] and Niccolò Taddei[1]

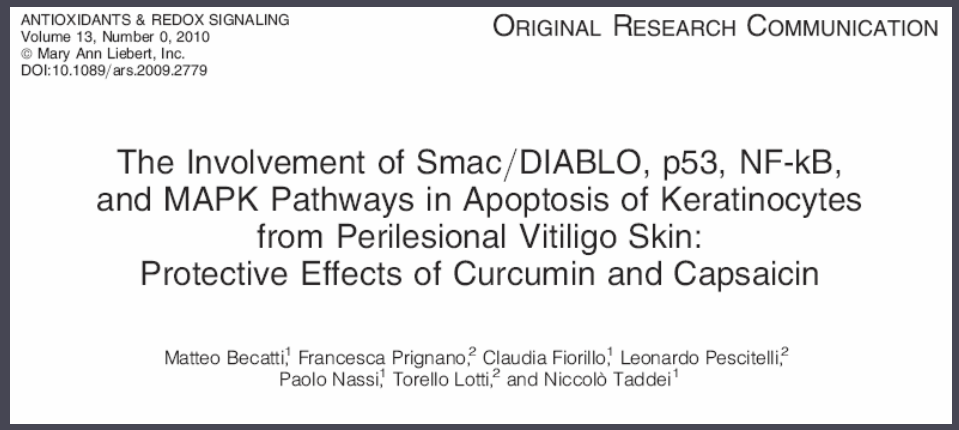
Positive effects of the supplementation of antioxidants in cultured cells

- Total Antioxidant Capacity (marker of cellular scavenging activity)



- Mitochondrial membrane depolarization (marker of mitochondrial and cellular integrity)





ANTIOXIDANTS & REDOX SIGNALING
Volume 13, Number 0, 2010
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ORIGINAL RESEARCH COMMUNICATION

The Involvement of Smac/DIABLO, p53, NF-kB, and MAPK Pathways in Apoptosis of Keratinocytes from Perilesional Vitiligo Skin: Protective Effects of Curcumin and Capsaicin

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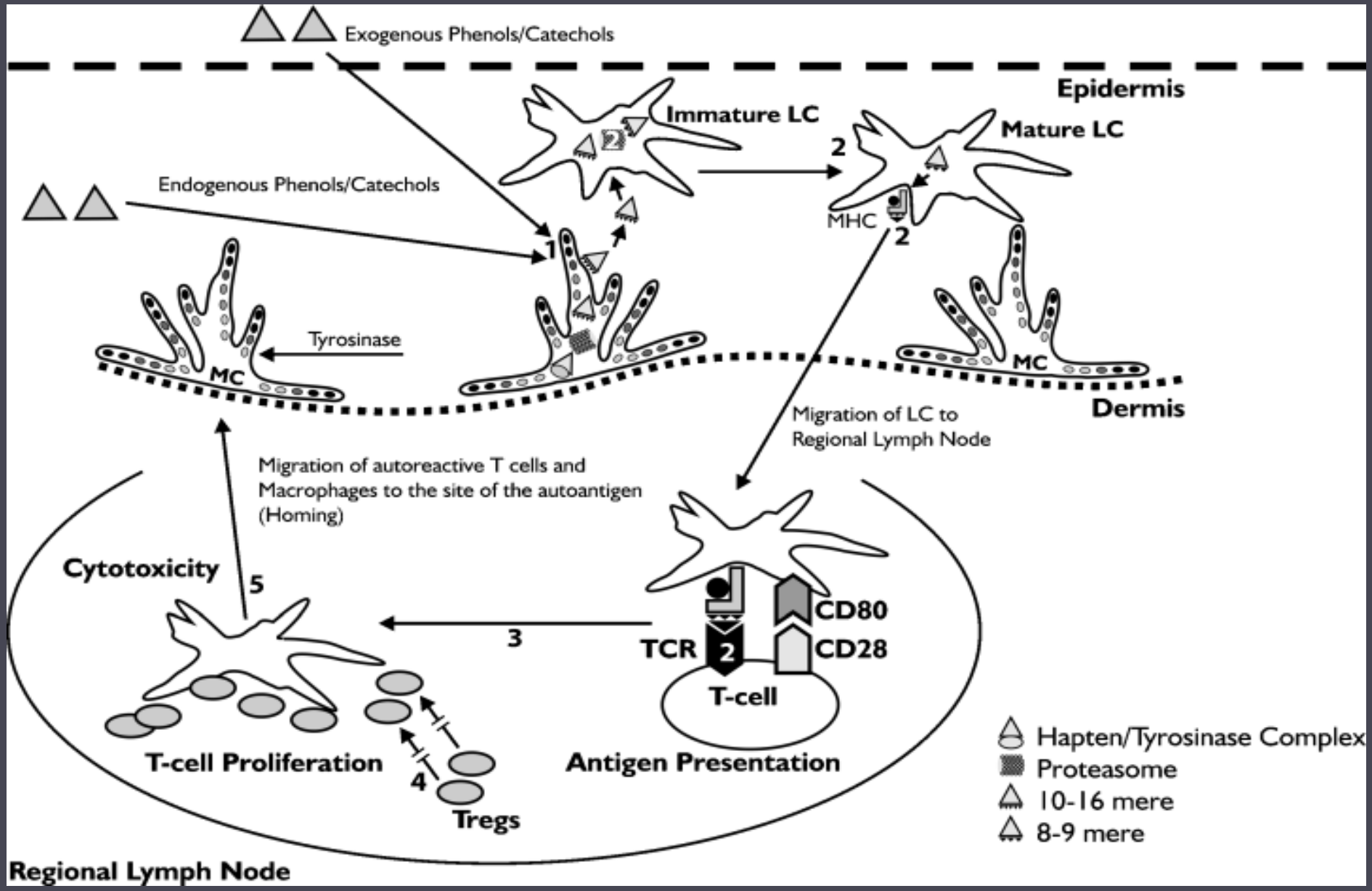
Vitiligo Road Map.

Lee BW, Schwartz RA, Hercogová J, Valle Y, Lotti TM.

Dermatol Ther. 2012 Nov;25 Suppl 1:S44-56. doi: 10.1111/dth.12006.

Convergence Theory



Westerhof, D'Ischia. Vitiligo puzzle: the pieces fall in place. Pigment Cell Res 2007 20; 345-359

Vitiligo is a systemic disease

Lotti T.

D’Erme E.

Hercogova J.

Dermatol Clin 2014

Metabolic syndrome in **vitiligo**.

Pietrzak A, Bartosińska J, Hercogová J, Lotti TM, Chodorowska G. Dermatol Ther. 2012 Nov;25 Suppl 1:S41-3. doi: 10.1111/dth.12012.

VITILIGO:
NOT ONLY A MELANOCYTIC DISEASE

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Ultrastructural and functional alterations of mitochondria in perilesional vitiligo skin

Francesca Prignano [a,*], Leonardo Pescitelli [a], Matteo Becatti [b], Paola Di Gennaro [a], Claudia Fiorillo [b], Niccolò Taddei [b], Torello Lotti [a]

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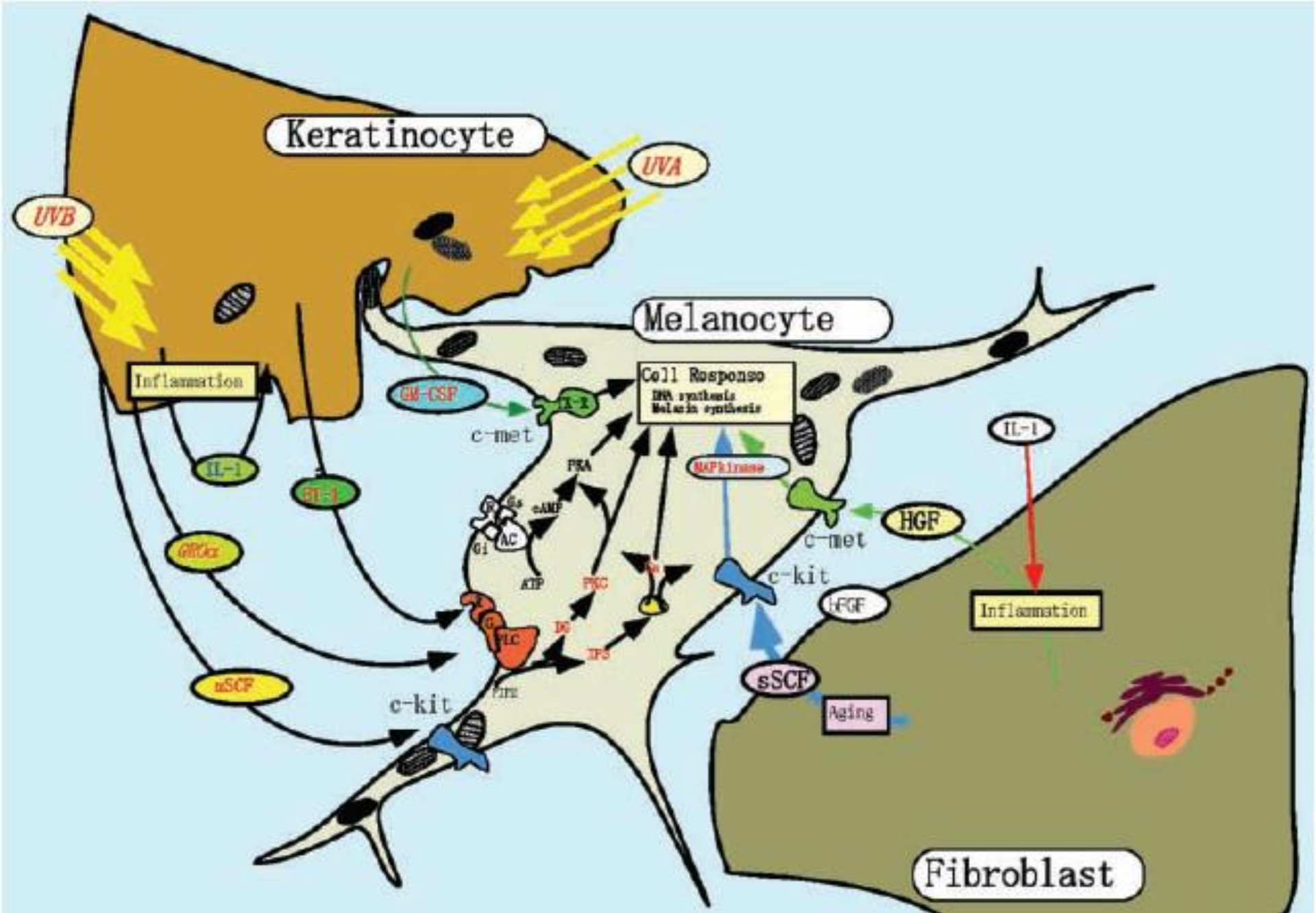
Arch Dermatol Res
DOI 10.1007/s00403-010-1109-5

ORIGINAL PAPER

Dendritic cells: ultrastructural and immunophenotypical changes upon nb-UVB in vitiligo skin

Francesca Prignano · F. Ricceri · B. Bianchi · D. Guasti · V. Bonciolini · T. Lotti · N. Pimpinelli



Imokawa G. Autocrine and paracrine regulation of melanocytes in human skin and in pigmentary disorders. Pigment Cell Res 2004

Vitiligo: recent insights and new therapeutic approaches.

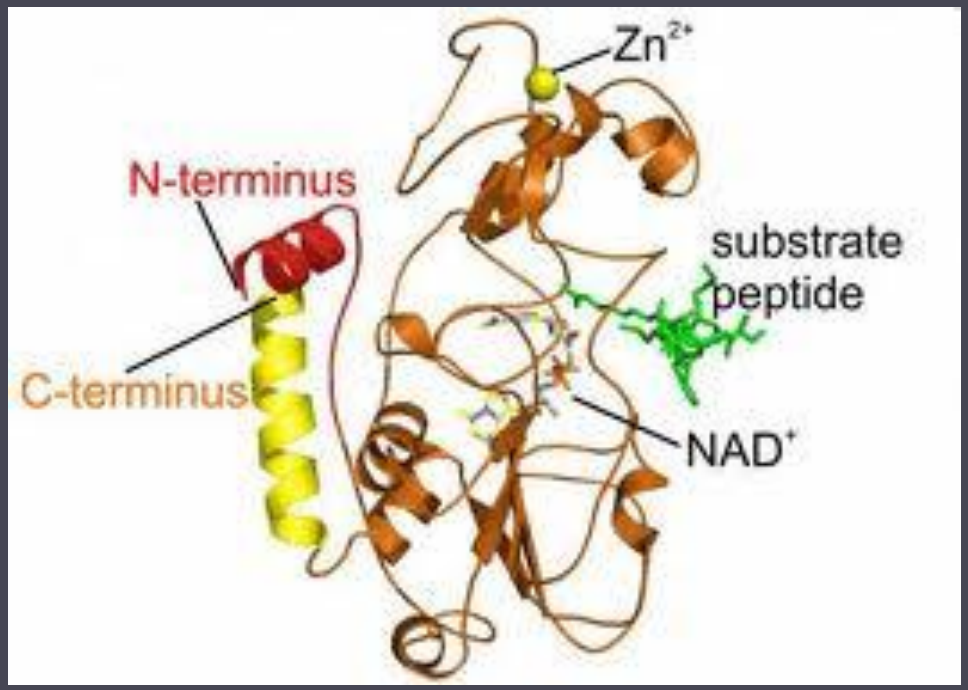
Lotti TM, Berti SF, Hercogova J, Huggins RH, Lee BW, Janniger CK, Schwartz RA. G Ital Dermatol Venereol. 2012 Dec;147(6):637-47.

Treatment of vitiligo at the Dead Sea: An integrated concept research and practice

J Cell Mol Med. 2014 Jan 10. doi: 10.1111/jcmm.12206. [Epub ahead of print]

SIRT1 regulates MAPK pathways in vitiligo skin: insight into the molecular pathways of cell survival.

Becatti M, Fiorillo C, Barygina V, Cecchi C & Lotti T



Abstract
Vitiligo is an acquired and progressive hypomelanotic disease that manifests as circumscribed depigmented patches on the skin. The aetiology of vitiligo remains unclear, but recent experimental data underline the interactions between melanocytes and other typical skin cells, particularly keratinocytes. Our previous results indicate that keratinocytes from perilesional skin show the features of damaged cells. Sirtuins (silent mating type information regulation 2 homolog) 1, well-known modulators of lifespan in many species, have a role in gene repression, metabolic control, apoptosis and cell survival, DNA repair, development, inflammation, neuroprotection and healthy ageing. In the literature there is no evidence for SIRT1 signalling in vitiligo and its possible involvement in disease progression. Here, biopsies were taken from the perilesional skin of 16 patients suffering from non-segmental vitiligo and SIRT1 signalling was investigated in these cells. For the first time, a new SIRT1/Akt, also known as Protein Kinase B (PKB)/mitogen-activated protein kinase (MAPK) signalling has been revealed in vitiligo. SIRT1 regulates MAPK pathway via Akt-apoptosis signal-regulating kinase-1 and down-regulates pro-apoptotic molecules, leading to decreased oxidative stress and apoptotic cell death in perilesional vitiligo keratinocytes. We therefore propose SIRT1 activation as a novel way of protecting perilesional vitiligo keratinocytes from damage.
© 2013 The Authors. Journal of Cellular and Molecular Medicine published by John Wiley & Sons Ltd and Foundation for Cellular and Molecular Medicine.
KEYWORDS:
MAPK , Akt, SIRT1, oxidative stress, vitiligo
PMID 24410795
[PubMed - as supplied by publisher]

J Clin Exp Cardiolog. 2012 Nov;3(11). pii: 216.

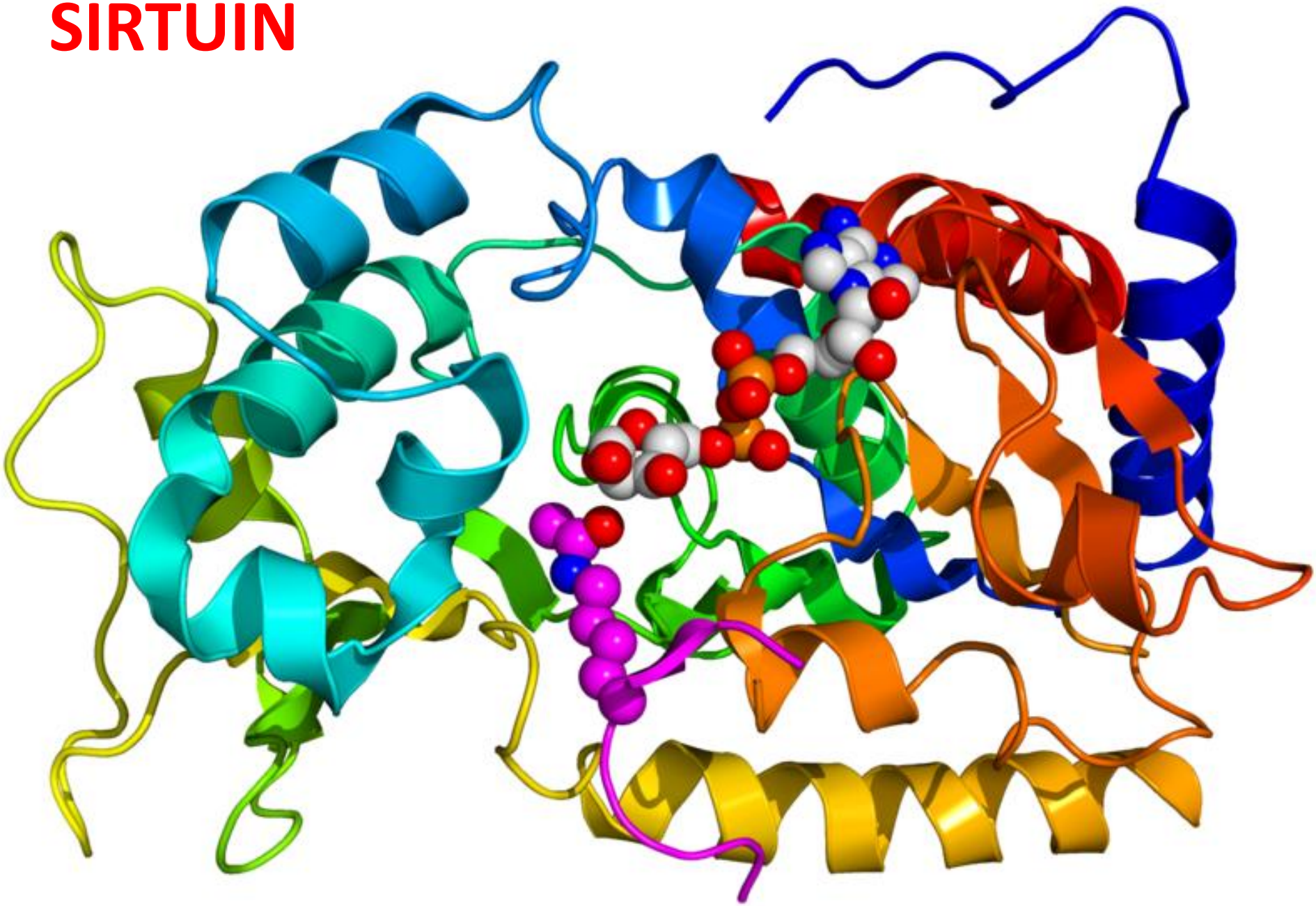
The Sirtuin System: The Holy Grail of Resveratrol?

Mohar DS, Malik S.

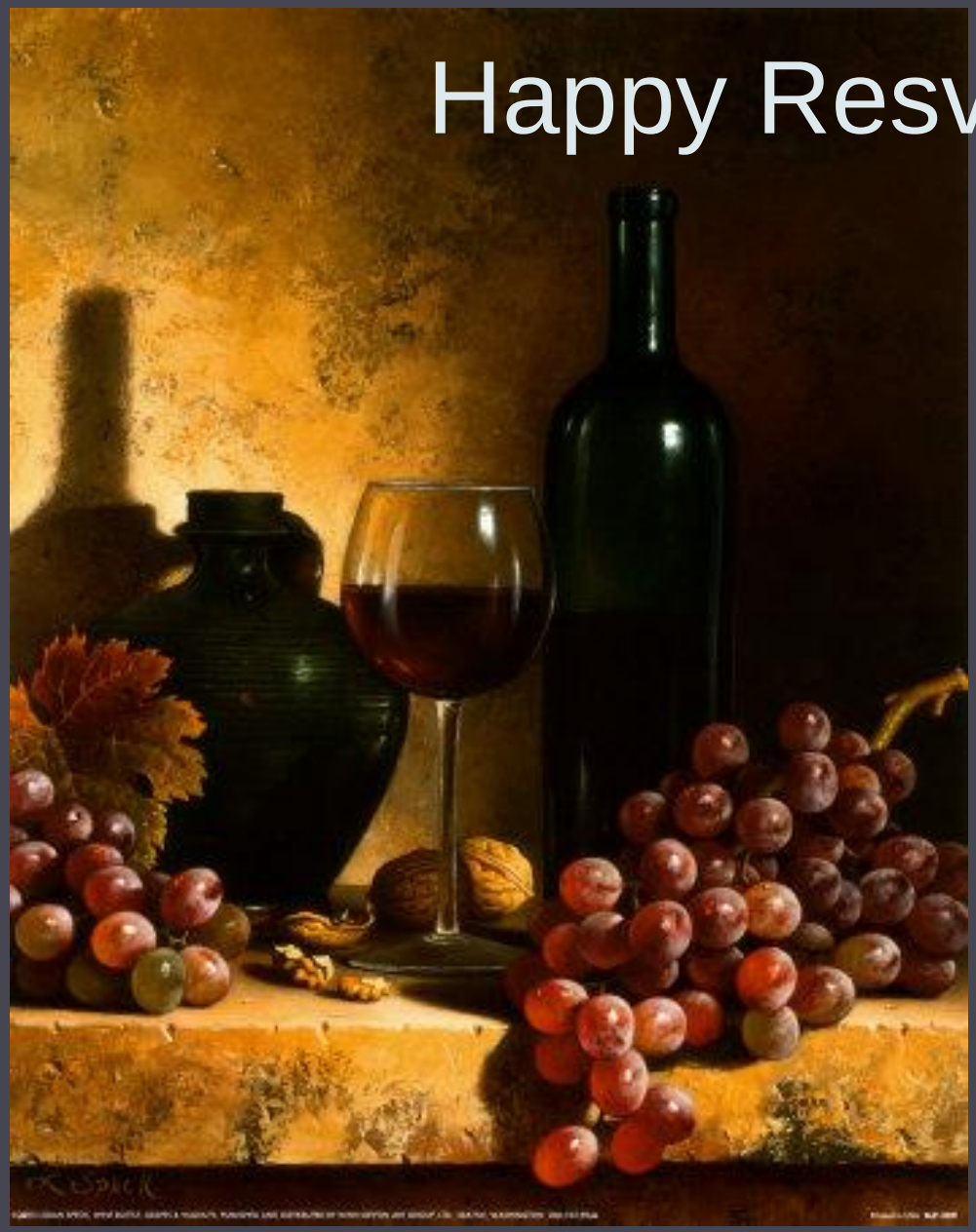
Abstract

The oxidative stress theory has been associated with atherosclerosis and has prompted a multitude of studies to evaluate the effects of antioxidants on cardiovascular disease prevention. Resveratrol, a relatively new antioxidant has gained considerable curiosity. This polyphenol stilbene identified in grape skin, is believed to be the main component contributing to the anti-atherosclerotic benefits linked to red wine consumption. It has demonstrated the ability to protect endothelial cells from lipid damage, promote vasodilation via modulation of nitric oxide synthesis, and inhibit platelet aggregation and smooth muscle proliferation. Although the complete mechanism of Resveratrol has yet to be fully elucidated, the Sirtuin system, consisting of 7 highly conserved families of regulator genes, are thought to be instrumental in establishing the various health benefits. In this article we assess the current applications, mechanism, pharmacokinetics, bioavailability, and safety profile of the novel antioxidant Resveratrol and provide an in-depth review of the influence of the Sirtuin system on the Resveratrol mechanism of action. We resolve that while early data on Resveratrol are promising, the anti-oxidative and ultimately, anti-atherosclerotic potential depends on further clarification of the intricate and complex relationship between Resveratrol and the Sirtruin system.

SIRTUIN



Happy Resveratrol



Br J Dermatol. 2014 Oct;171(4):786-98. doi: 10.1111/bjd.13286. Epub 2014 Oct 1.

High prevalence of circulating autoantibodies against thyroid hormones in vitiligo and correlation with clinical and historical parameters of patients.

Colucci R[1], Lotti F, Dragoni F, Arunachalam M, Lotti T, Benvenga S, Moretti S.

⊕ **Author information**

Abstract

BACKGROUND: Autoantibodies against thyroid hormones (THAbs) directed towards triiodothyronine (T3-Ab) and/or thyroxine (T4-Ab) are very rare in the general population. They are increased in some nonthyroidal autoimmune diseases, where they seem to predict autoimmune thyroid disorders (ATDs). So far, their presence in patients with vitiligo has not been evaluated, but it might have a possible predictive role.

OBJECTIVES: To assess the prevalence of THAbs in a group of vitiligo patients and to correlate their presence with clinical and historical parameters.

METHODS: In total 79 patients with nonsegmental vitiligo and 100 controls were examined. Clinical characteristics of vitiligo and family and personal medical history were evaluated. Antinuclear autoantibodies, thyroid hormones and thyroid autoantibodies were measured. IgM T3-Ab, IgG T3-Ab, IgM T4-Ab and IgG T4-Ab were assayed by a radioimmunoprecipitation technique. Fisher's test, Student's t-test and $\chi(2)$ -test were used for statistical analysis.

RESULTS: Overall 77 of 79 patients (97%) had at least one type of THAb (11 T3-Ab, 10 T4-Ab, 56 both). In the control group, only one person (1%) had THAbs. In patients with vitiligo, T3-Abs were significantly associated with leucotrichia (IgM+IgG, $P = 0{\cdot}033$; IgG, $P = 0{\cdot}039$; IgM, $P = 0{\cdot}005$) and thyroglobulin autoantibodies (IgM+IgG, $P = 0{\cdot}031$; IgG, $P = 0{\cdot}058$), while the absence of T3-Ab was related to personal history of cancer (IgM+IgG, $P = 0{\cdot}021$; IgG, $P = 0{\cdot}039$). T4-Abs were significantly associated with vitiligo activity (IgM+IgG, $P < 0{\cdot}001$; IgM, $P = 0{\cdot}037$) and duration (IgG, $P = 0{\cdot}013$).

CONCLUSIONS: The surprisingly high prevalence of THAb in patients with vitiligo and their associations suggest a possible pathogenetic role in the disease and stress the tight link between vitiligo and ATDs. Further evaluation in a larger group of patients and an adequate follow-up are needed to define their potential predictive role.

Take Home Message 2014

Wien Med Wochenschr. 2014 Jul;164(13-14):278-85. doi: 10.1007/s10354-014-0288-7. Epub 2014 Jul 25.

Vitiligo: what's new in the psycho-neuro-endocrine-immune connection and related treatments.

Lotti T[1], Zanardelli M, D'Erme AM.

Author information

Abstract

Vitiligo is an acquired depigmentary skin disorder of unknown origin characterized by well-demarcated, white macules of varying size and distribution. Despite relevant new research and progresses, why melanocytes disappear to induce the characteristic achromic lesions of vitiligo is not fully understood. In spite of recent findings implicating genetic, immune and oxidative stress factors, the exact pathogenesis of vitiligo remains obscure. An innovative concept based on a functional cross-talk between the nervous and immune system is emerging. Neuropeptides released from peripheral nerve endings could synergize with new cytokines to adversely affect melanocyte function and viability. Evidence is increasing regarding the role of neuropeptides in the pathogenesis of vitiligo and a new winning approach to vitiligo therapy based on neuropeptides regulation is at the horizon.

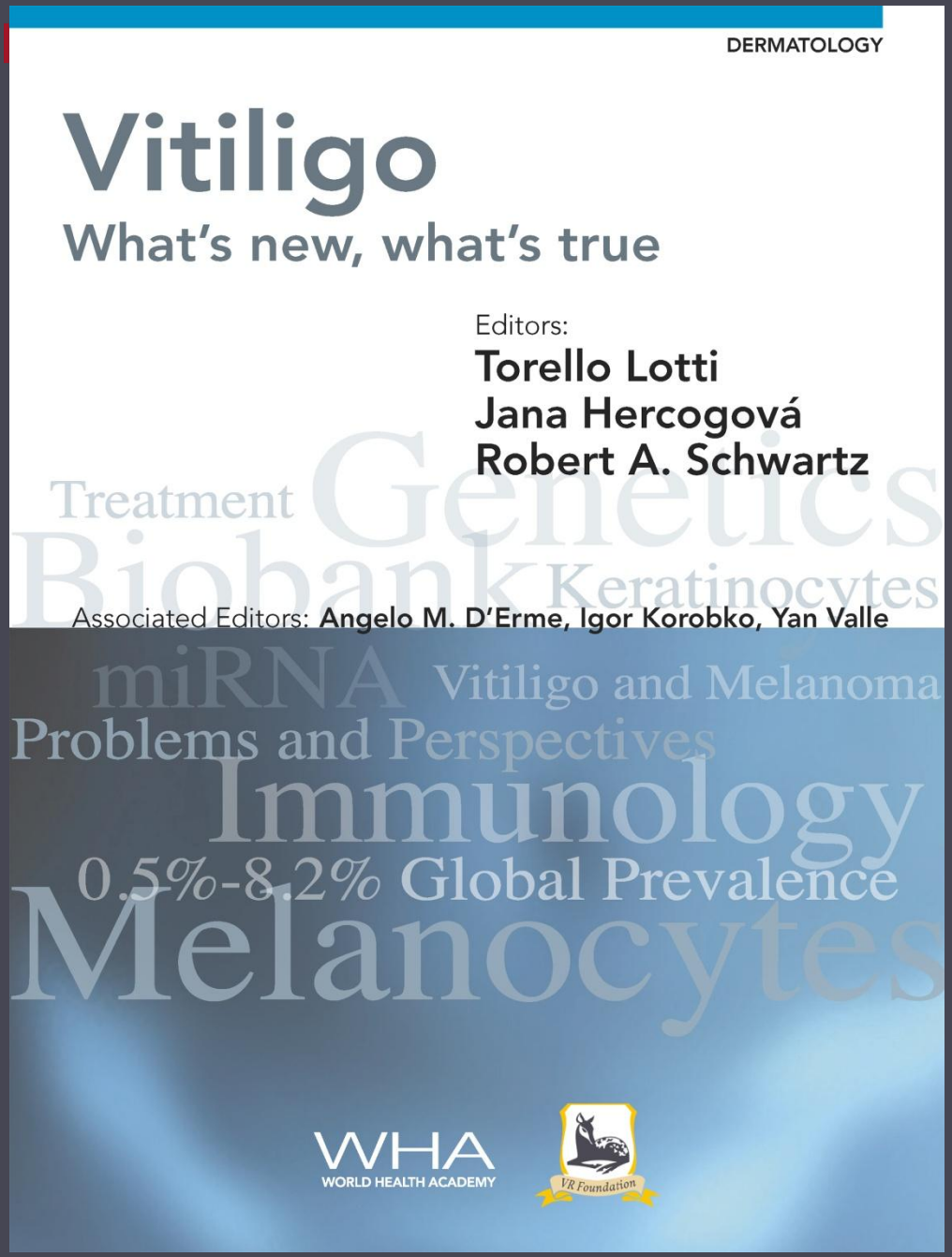
PMID: 25059737 [PubMed - in process]

Future Take Home Message::
Low dose cytokines and systemic neuropeptidergic regulation

Pigmentary Disorders and Vitiligo VRF MasterClass , Amristar, India

November 28 -30, 2014

President: Prof. Davinder Parsad



2014 News

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Cattedra di Dermatologia e Venereologia
Dir. Prof. Torello Lotti

Università degli Studi Guglielmo Marconi

Thank you for your attention

Pigmentary Disorders and Vitiligo VRF MasterClass , Istambul, Turkey,

November 21 -23, 2014

President: Prof. Sibel Alper

Thank You
Prof
Sibel Alper