

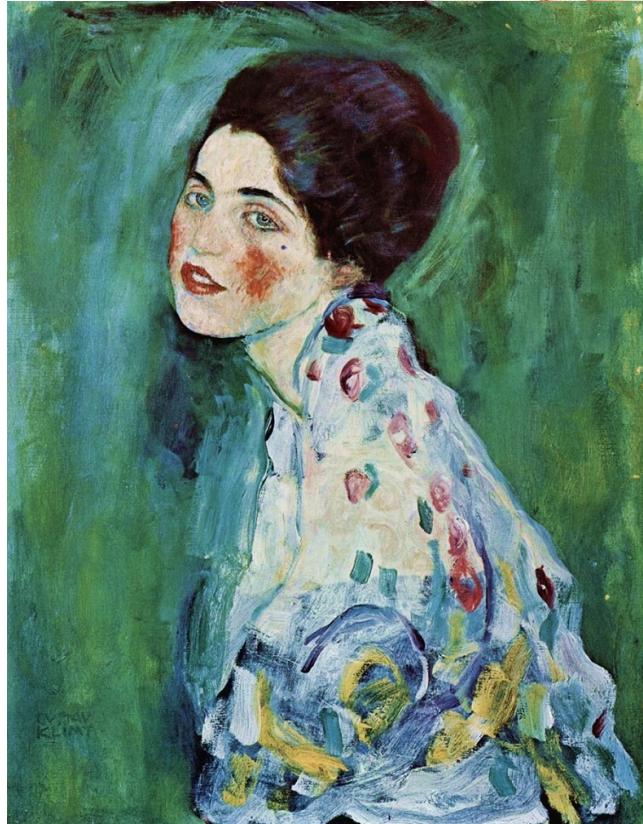
AC-FE ACNE FERRARA 2017

14° MEETING DI AGGIORNAMENTO SU ACNE E DERMATOSI CORRELATE
FERRARA 24-25 NOVEMBRE 2017

PATOGENESI DELLA ROSACEA

DOTT.SSA ELISA MOLINELLI
UNIVERSITA' POLITECNICA DELLE MARCHE
OSPEDALI RIUNITI DI ANCONA

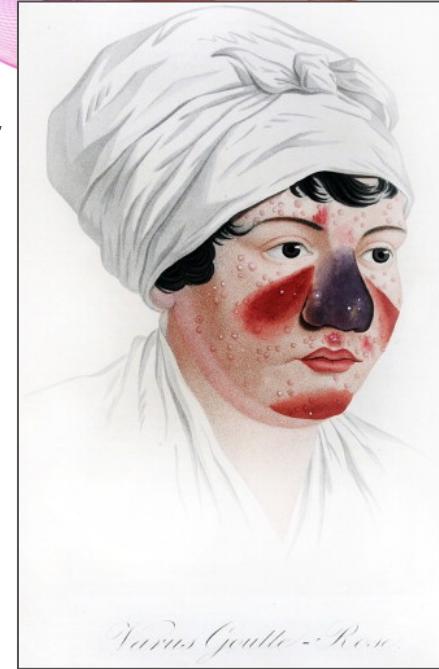
Direttore: Prof.ssa Annamaria Offidani



Gustav Klimt, Ritratto di Signora, 1898

DEFINIZIONE

...DAL LATINO ROSACEUS: COLORATO DI ROSA...



**DERMATOSI INFAMMATORIA CRONICA BENIGNA
INTERESSANTE LE AREE CONVESSE
CENTRALI DEL VOLTO**

DAL 2002

MANIFESTAZIONI CLINICHE E CLASSIFICAZIONE



SOTTOTIPO I:
ERITEMATO-
TELEANGECTASICA



S
PAPU

MEDICAL DERMATOLOGY

BJD
British Journal of Dermatology

Updating the diagnosis, classification and assessment of rosacea: recommendations from the global ROSacea COnsensus (ROSCO) panel

J. Tan,¹ L.M.C. Almeida,² A. Bewley,^{3,4} B. Cribier,⁵ N.C. Dlova,⁶ R. Gallo,⁷ G. Kautz,⁸ M. Mannis,⁹ H.H. Oon,¹⁰ M. Rajagopalan,¹¹ M. Steinhoff,¹² D. Thiboutot,¹³ P. Troielli,¹⁴ G. Webster,¹⁵ Y. Wu,¹⁶ E.J. van Zuuren,¹⁷ and M. Schaller¹⁸

REVIEW

Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee

Richard L. Gallo, MD, PhD,^a Richard D. Granstein, MD,^b Sewon Kang, MD,^c Mark Mannis, MD,^d Martin Steinhoff, MD, PhD,^{e,f} Jerry Tan, MD,^g and Diane Thiboutot, MD^h
San Diego and Sacramento, California; New York, New York; Baltimore, Maryland; Doha, Qatar;
Dublin, Ireland; Windsor, Ontario, Canada; and Hershey, Pennsylvania



SOTTOTIPO IV:
OCULARE

...AL 2017...

CLASSIFICAZIONE

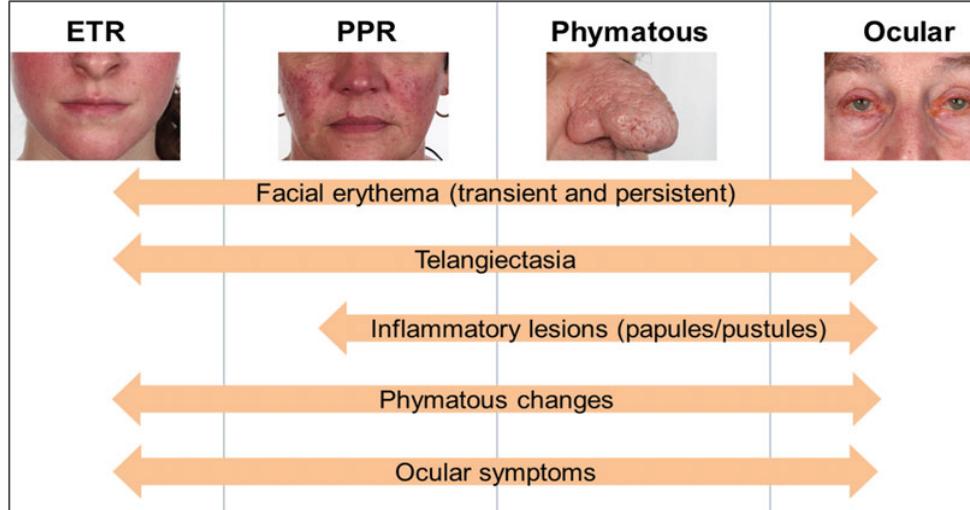


MEDICAL DERMATOLOGY

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...AL 2017...

CLASSIFICAZIONE



REVIEW

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San Diego and Sacramento, California; New York, New York; Baltimore, Maryland; Doha, Qatar; Dublin, Ireland; Windsor, Ontario, Canada; and Hershey, Pennsylvania

Table I. Phenotypes of rosacea

Diagnostic*	Major [†]	Secondary
Fixed centrofacial erythema in a characteristic pattern that may periodically intensify	Flushing Papules and pustules Telangiectasia	Burning sensation Stinging sensation Edema Dryness
Phymatous changes	Ocular manifestations <ul style="list-style-type: none">• Lid margin telangiectasia• Interpalpebral conjunctival injection• Spade-shaped infiltrates in the cornea• Scleritis and sclerokeratitis	Ocular manifestations <ul style="list-style-type: none">• “Honey crust” and collarette accumulation at the base of the lashes• Irregularity of the lid margin• Evaporative tear dysfunction (rapid tear breakup time)

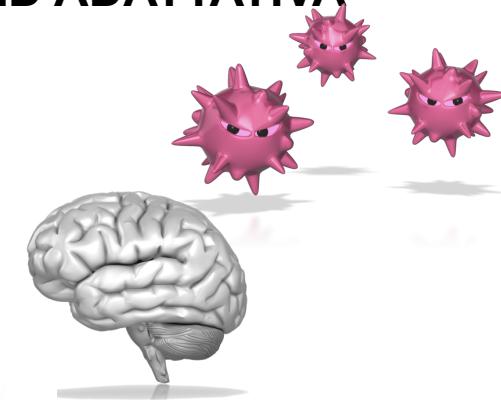
CLASSIFICAZIONE: ALTRE VARIANTI?



- Rosacea *fulminans* (pioderma faciale)
- Rosacea conglobata
- Rosacea granulomatosa (acne agminata)
- Rosacea da corticosteroide
- Dermatite periorifiziale granulomatosa dell'infanzia



- DISREGOLAZIONE DELL'IMMUNITÀ INNATA ED ADATTATIVA
- DISMICROBISMO
- MECCANISMI NEUROCUTANEI E VASOATTIVI
- PREDISPOSIZIONE GENETICA

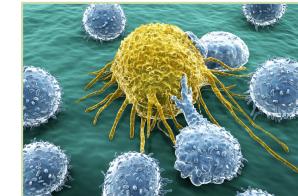


PATOGENESI: FATTORI DI RISCHIO AMBIENTALI

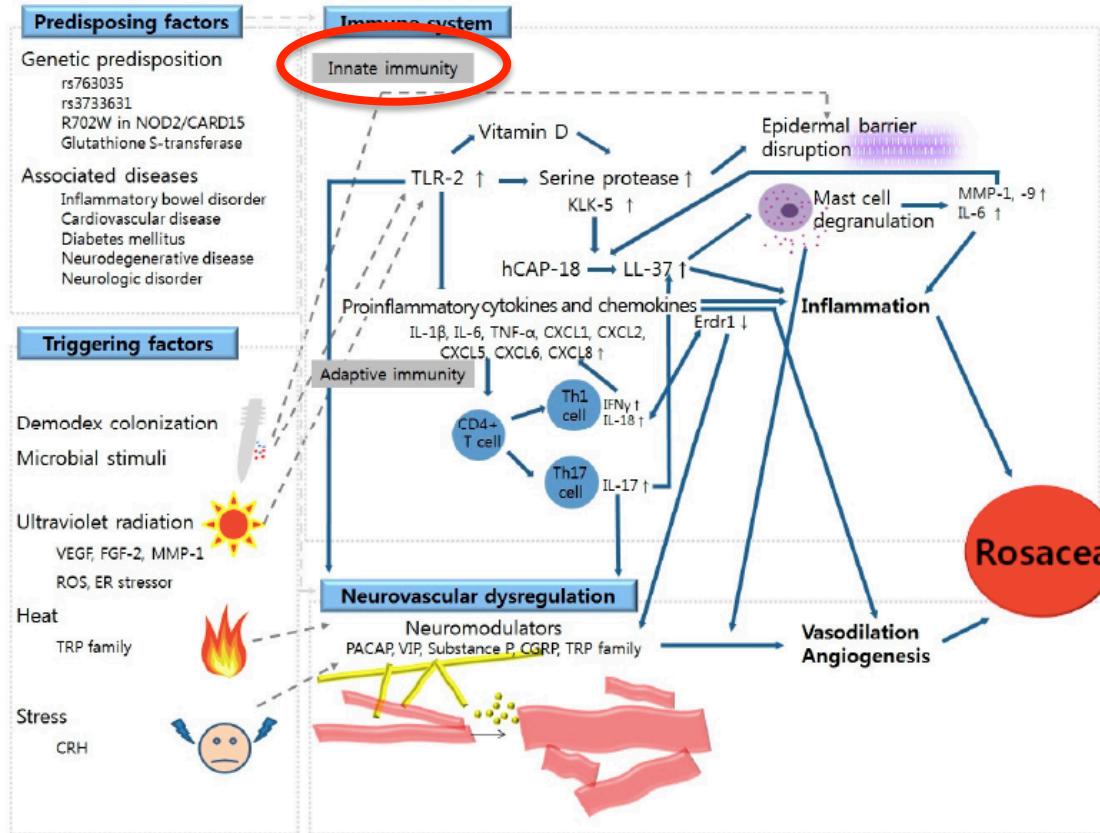
- RADIAZIONI ULTRAVIOLETTE
- ELEVATI LIVELLI DI VITAMINA D
- ALCOLICI
- CONSUMO DI SPEZIE
- STRESS, ESERCIZIO FISICO
- DISMICROBISMO CUTANEO
- DISMICROBISMO GASTRO-INTESTINALE



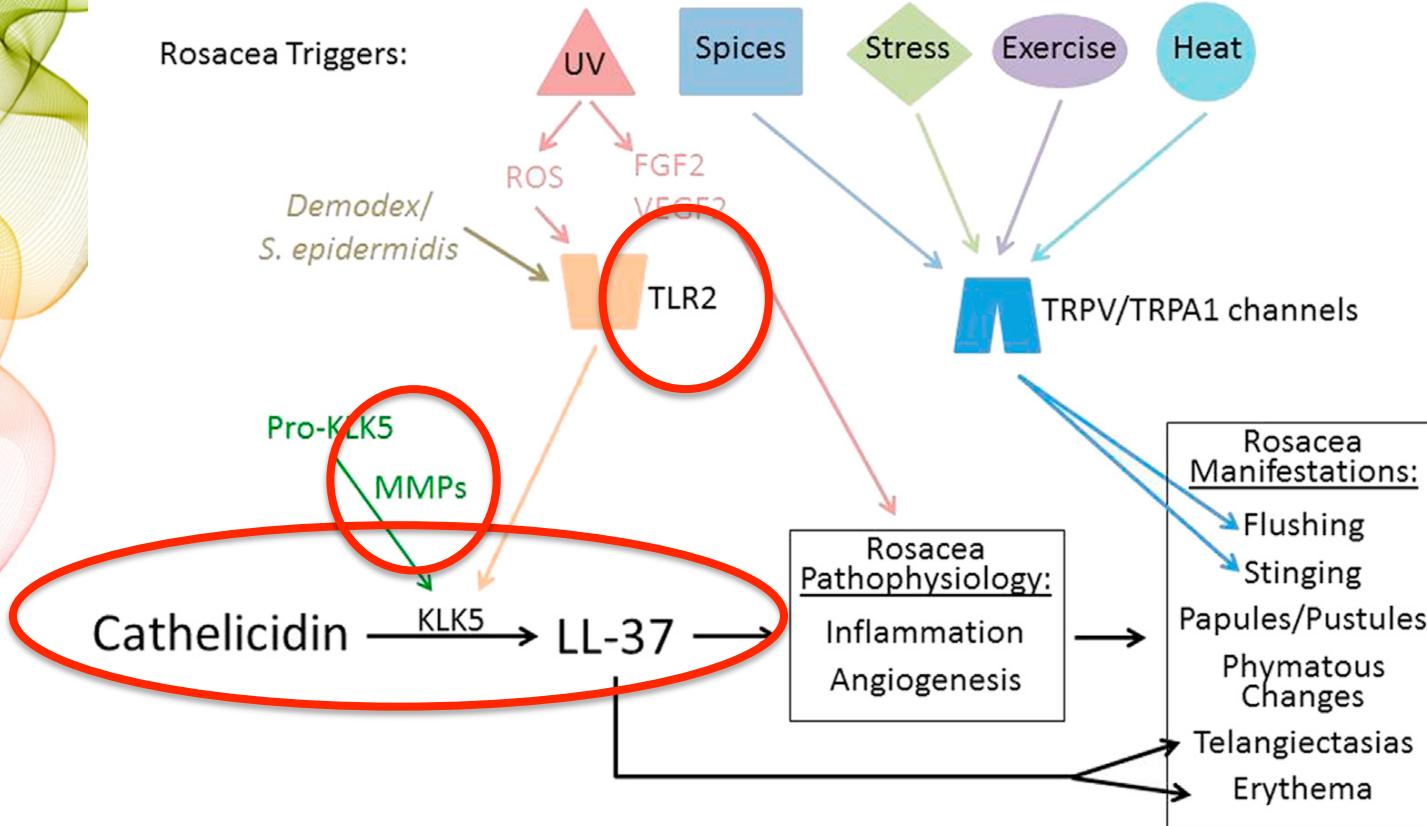
FUMO: RUOLO PROTETTIVO!

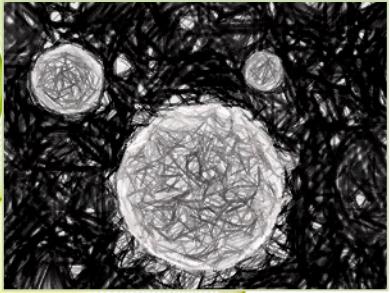


PATOGENESI: TRIGGER E MEDIATORI



PATOGENESI: IMMUNITA' INNATA





PATOGENESI: RUOLO DEI MASTOCITI

J Invest Dermatol. 2014 November ; 134(11): 2728–2736. doi:10.1038/jid.2014.222.

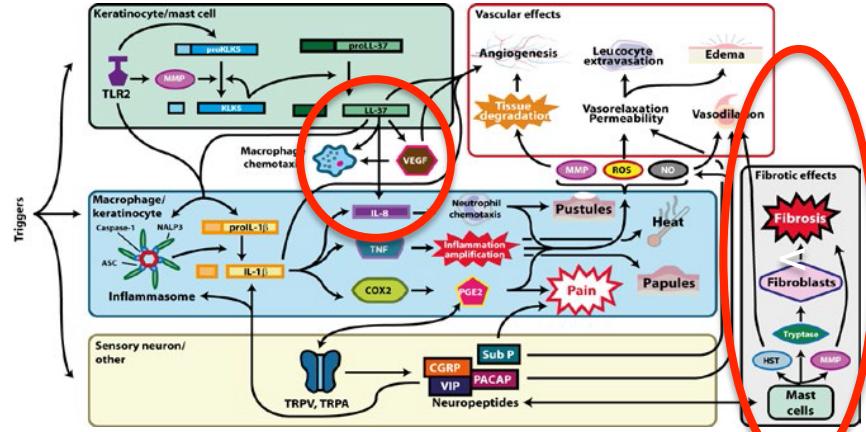


Mast cells are key mediators of cathelicidin initiated skin inflammation in rosacea

Yumiko Muto, Zhenping Wang, Matthieu Vanderberghe, Aimee Two, Richard L. Gallo, and Anna Di Nardo

Division of Dermatology, Department of Medicine, University of California, San Diego

- Iperesprese nella cute affetta da rosacea
- Sono principale fonte di catelicidine e serin-proteasi
- Sono attivate loro stesse da LL-37 (via TPRV4)
- Contribuiscono all'attivazione dell'immunità adattativa (rilascio di TNF, chemochine) e alla fibrosi (attivazione fibroblasti)

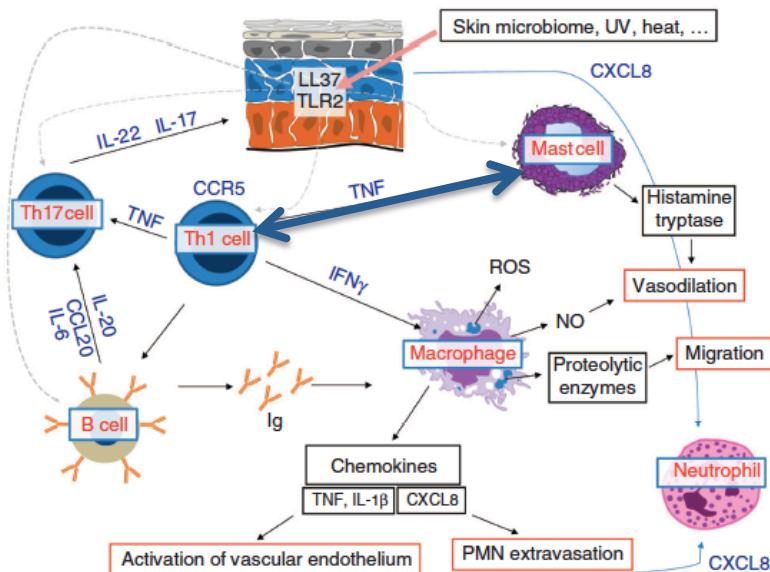


PATOGENESI: IMMUNITA' ADATTATIVA



Molecular and Morphological Characterization of Inflammatory Infiltrate in Rosacea Reveals Activation of Th1/Th17 Pathways

Timo Buhl^{1,2,3,7}, Matthias Sulk^{3,4,7}, Paweł Nowak^{4,7}, Jörg Budenkotte⁴, Ian McDonald², Jérôme Aubert⁵, Isabelle Carlavan⁵, Sophie Déret⁵, Pascale Reiniche⁵, Michel Rivier⁵, Johannes J. Voegeli³ and Martin Steinhoff^{2,3,6}



**Domina risposta Th1
CD4+
Soprattutto ET e PP**

**Ruolo marginale linfociti B
Plasmacellule
Soprattutto in Fimatosa e Oculare**

PATOGENESI: DISMICROBISMO



Potential role of microorganisms in the pathogenesis of rosacea

Anna D. Holmes, PhD
Fort Worth, Texas

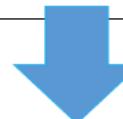
DISMICROBISMO CUTANEO



DEMODEX FOLLICULORUM

HEALTHY SKIN

- Low numbers of mites
- Evasion of immune system by expression/release of immunomodulatory molecules
- Decreased reactivity of immune cells
- Absence of inflammation



INFLAMED SKIN

- Genetically susceptible individuals
 - Large numbers of mites
- Mechanical disruption of hair follicle and upregulation of TLR expression
- Release of chitin fragments, proteases and endogenous bacteria from decaying mites
 - Activation of Host Immune system
- Chemokine release and inflammatory cell infiltrate
- Clinical lesion (inflammatory papules and pustules)

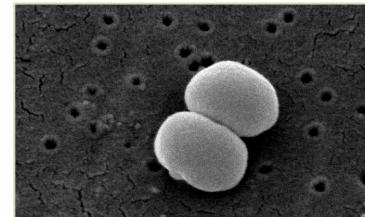
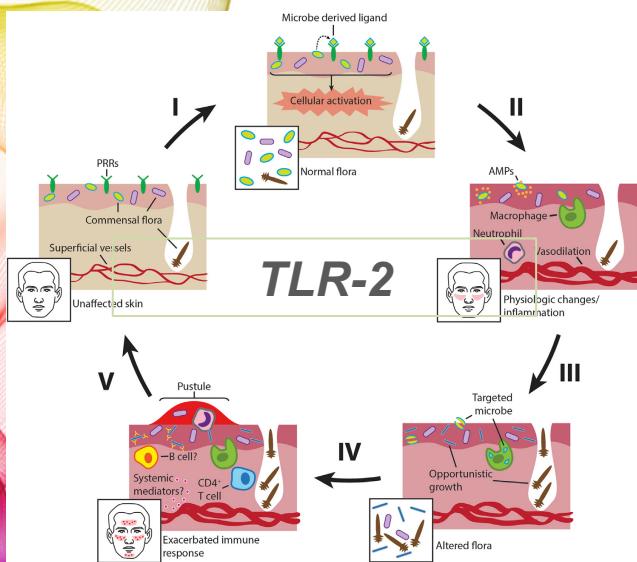


DENSITA' AUMENTATA SIA NELLE FORME ETR CHE PRP

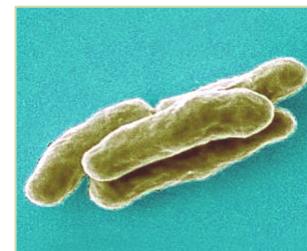
PATOGENESI: DISMICROBISMO



DISMICROBISMO CUTANEO



**STAPHYLOCOCCUS EPIDERMIDIS
(PPR)**



**BACILLUS OLERONIUS
(PPR ed OCULARE)**

CLAMYDOPHILA PNEUMONIAE??

Holmes AD et al. J Am Acad Dermatol, 2013

PATOGENESI: DISMICROBISMO

EPIDEMIOLOGY

BJD

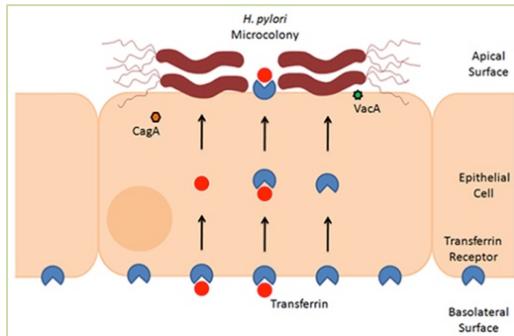
British Journal of Dermatology

Rosacea and gastrointestinal disorders: a population-based cohort study

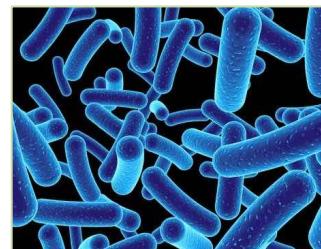
A. Egeberg,¹ L.B. Weinstock,² E.P. Thyssen,² G.H. Gislason^{3,4,5} and J.P. Thyssen¹



DISMICROBISMO GASTRO-INTESTINALE



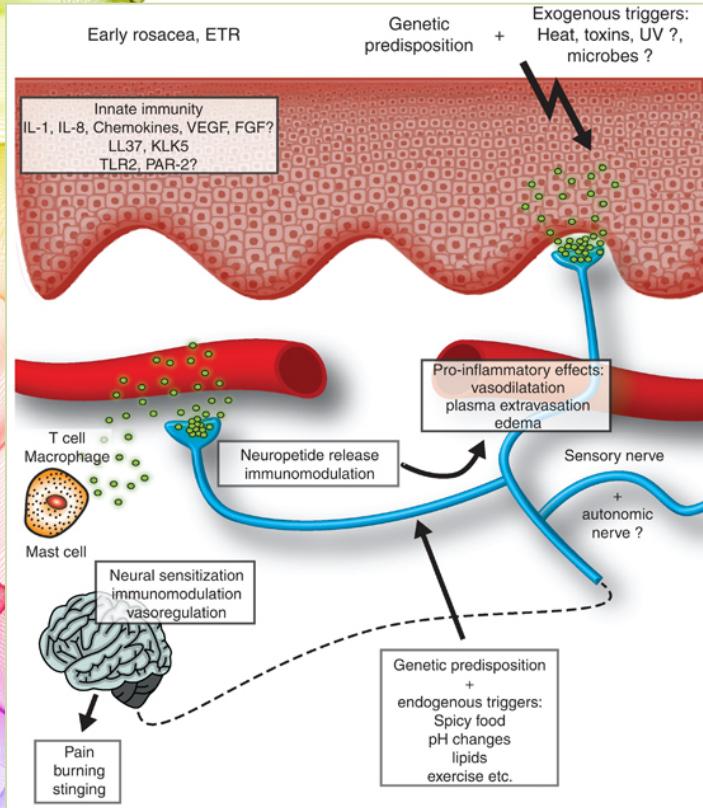
SIBO
(PPR)



**HELICOBACTER PYLORI
(ETR)**

Associazione con fattore di virulenza Cag-A

PATOGENESI: DISREGOLAZIONE NEURO-VASCOLARE



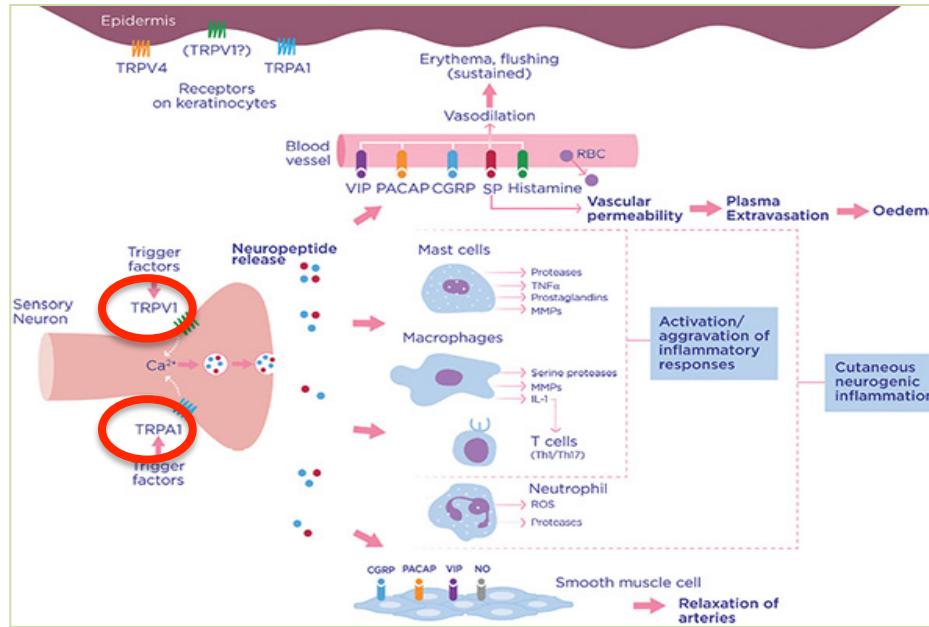
3 MECCANISMI

- Instabilità vaso-motoria
- Rilascio di neuropeptidi pro-infiammatori
- Danno neuronale diretto

2 RECETTORI

- ***Transient Receptor Potential Vanilloid Family (TRPV)***
- ***Transient Receptor Potential Ankyrin Family (TRPA)***

PATOGENESI: DISREGOLAZIONE NEURO-VASCOLARE



**DISREGOLAZIONE DELL'UNITÀ NEURO-IMMUNOLOGICA
(VASI + FIBRE NERVOSE SENSITIVE + MAST CELLS)**



Assessment of the Genetic Basis of Rosacea by Genome-Wide Association Study

Anne Lynn S. Chang¹, Inbar Raber¹, Jin Xu¹, Rui Li¹, Robert Spitale¹, Julia Chen¹, Amy K. Kiefer², Chao Tian², Nicholas K. Eriksson², David A. Hinds² and Joyce Y. Tung²

- Predisposizione genetica influisce 46% nella manifestazione di malattia
- Familiarità 50% dei casi
- Polimorfismi individuati: gene GST, TACR3, BTNL2
- Associazione con HLA-DRB1, HLA-DQB1 e HLA-DQA1



COMORBIDITA'

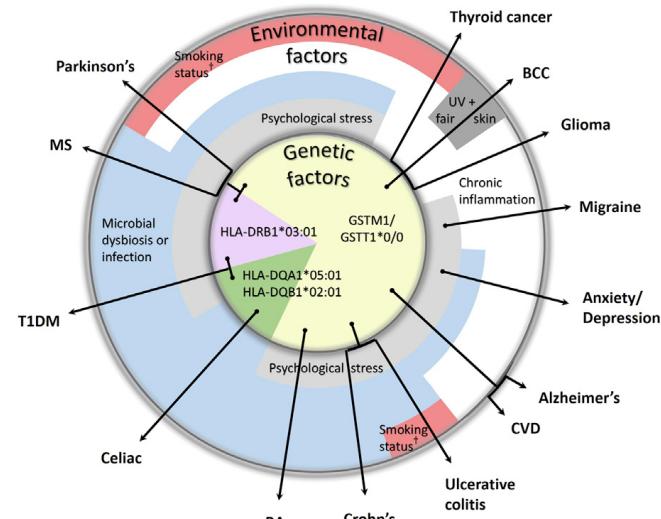
REVIEW

Comorbidities in rosacea: A systematic review and update

Roger Haber, MD,^{a,b} and Maria El Gemayel, MD^{c,d}



Comorbidity	Screening considerations
CVD	Screen personal and family history of CVD, calculate BMI, check blood pressure, and fasting lipid panel, fasting glucose or HbA1c level at least once in patients older than 45 y Encourage weight loss, exercise, and avoidance of smoking and alcohol consumption when applicable
Gastrointestinal	Suggest aspirin or low-dose doxycycline in patients with several risk factors Ask about gastrointestinal symptoms in the review of systems. Refer early to a gastroenterologist if symptoms of IBD, IBD, GERD, <i>Helicobacter pylori</i> infection, or celiac disease are present
Depression/anxiety	Ask about symptoms of depression and anxiety in the review of systems and refer for management if such symptoms are identified
Neurologic	Ask about symptoms or look for physical signs of dementia, Parkinson disease, migraine, glioma, multiple sclerosis, or facial dystonia, and refer to neurologist for management if any of these symptoms are identified
Malignancy	Follow screening recommendations for the general population and consider yearly or periodic skin and a thyroid check for patients with a family history of cancers or high exposure to UV light
Others	Ask about symptoms of rheumatoid arthritis and refer to specialist if present



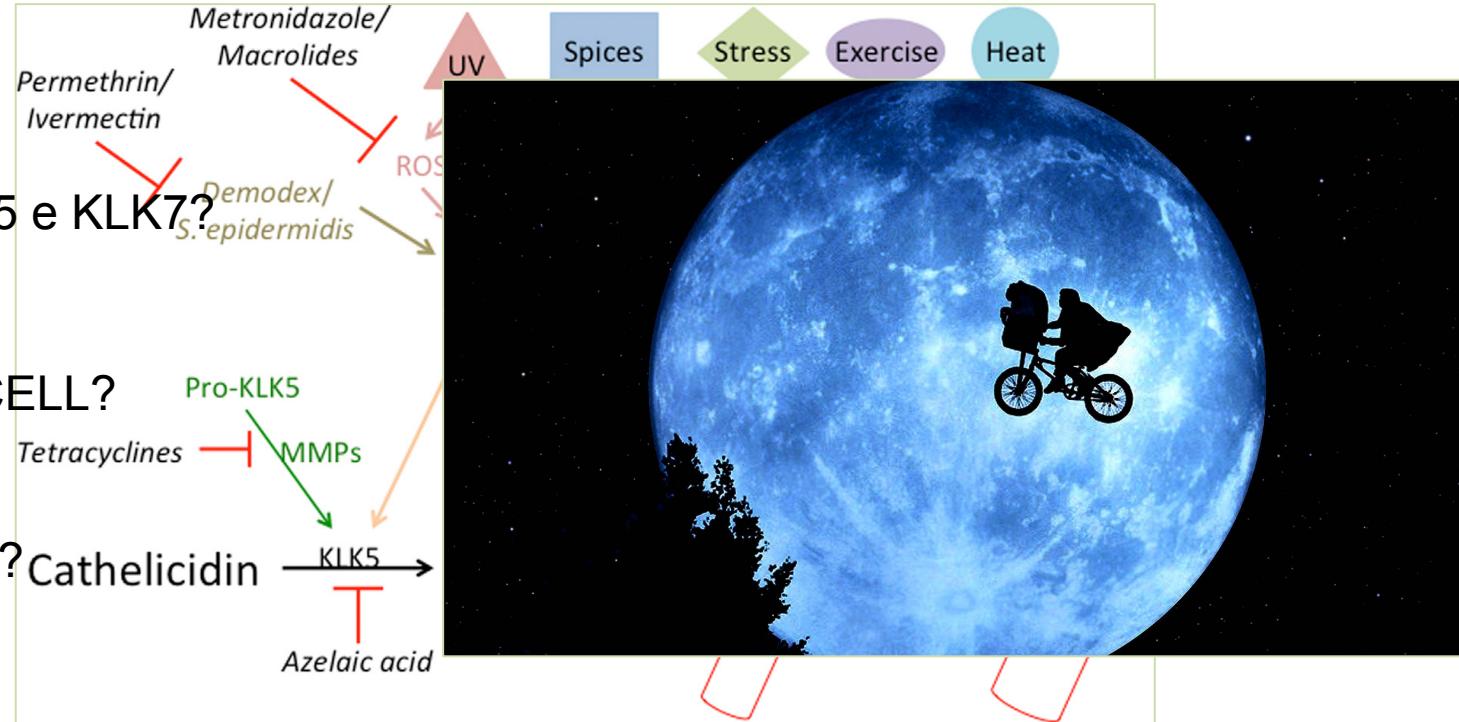
PATOGENESI e TERAPIA

TRPA?

KLK-5 e KLK7?

MAST CELL?

TRPV? Cathelicidin



E NEL FUTURO....?



GRAZIE PER L'ATTENZIONE