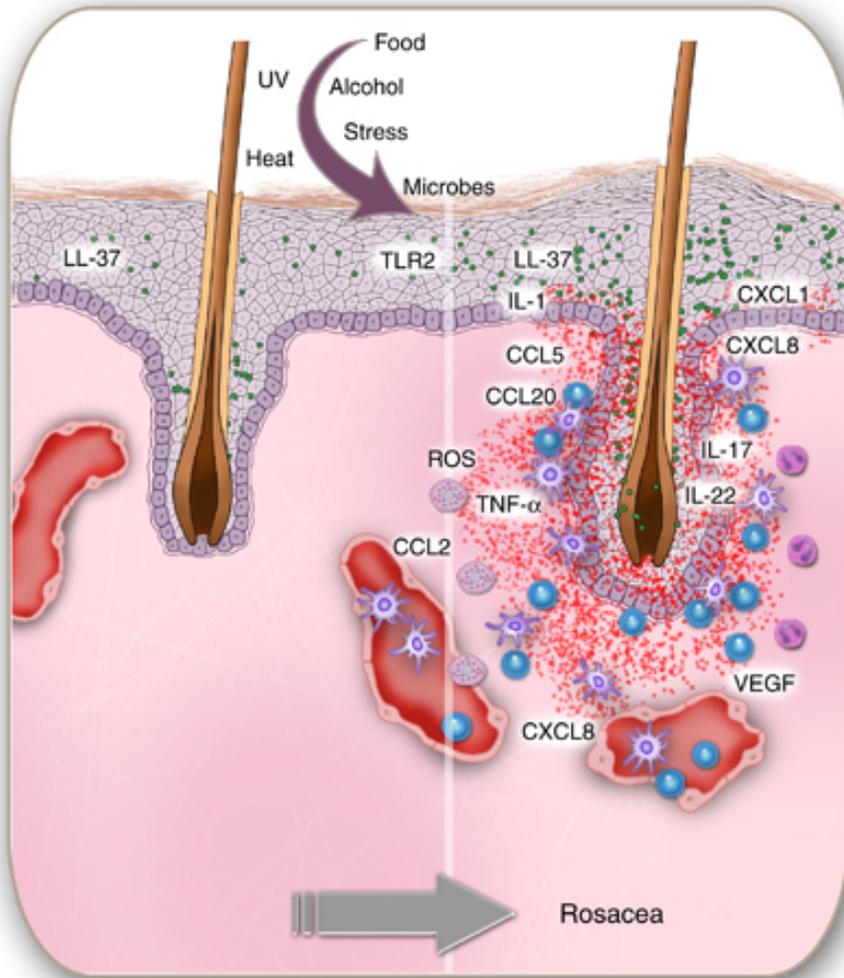


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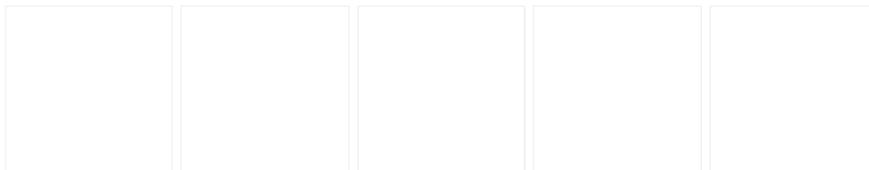
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Cytokines and chemokines are key effectors of rosacea trigger factors. Rosacea trigger factors such as UV radiation, heat, spicy food, alcohol, stress, or microbes induce primary proinflammatory cytokines such as tumor necrosis factor (TNF)-alpha and IL-1 family members, as well as LL-37 through Toll-like receptor 2 (TLR2) signaling or other mechanisms. Subsequently, a first wave of chemokines is produced that leads to the recruitment of T cells into the perifollicular space. Subsequently, T cell-derived cytokines such as IL-17 and IL-22, together with UV radiation, activate keratinocytes to produce CCL20, CXCL1, and CXCL8. CCL20 attracts additional T-helper 17 (TH17) cells, whereas CXCL1 and CXCL8 recruit abundant neutrophils, leading to the formation of pustules. Simultaneously, IL-17 promotes angiogenesis via the induction of vascular endothelial growth factor (VEGF). Additional angiogenic mediators include CCL2, CXCL1, CXCL8 and reactive oxygen species (ROS).

[Source publication](#)



**Rosacea: the Cytokine and Chemokine Network**

[Article](#) [Full-text available](#)

Dec 2011

● Peter Arne Gerber · ● Bettina Alexandra Buhren · ● Martin Steinhoff · ● Bernhard Homey

Rosacea is one of the most common dermatoses of adults. Recent studies have improved our

Rosacea is one of the most common dermatoses of adults. Recent studies have improved our understanding of the pathophysiology of rosacea. Current concepts suggest that known clinical trigger factors of rosacea such as UV radiation, heat, cold, stress, spicy food, and microbes modulate Toll-like receptor signaling, induce reactive oxygen species, as...

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#### Contexts in source publication

##### Context 1

... rosacea, activation of TLR2 leads to the expression of abnormally high levels of the antimicrobial peptide cathelicidin, which has been shown to promote leukocyte trafficking through the induction of CXCL8 and induce angiogenesis ( De et al., 2000;Koczulla et al., 2003;Yamasaki et al., 2007). In particular, the induction of CXCL8 by the cationic cathelicidin peptide LL-37 in keratinocytes is regarded as a crucial event for the recruitment of neutrophils and hence the formation of pustules (Zhang et al., 2011). Moreover, a recent study on the role of *Propionibacterium acnes* (P. ...

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##### Context 2

... our current understanding of the involvement of cytokines and chemokines is insufficient and further systematic research is required. Nevertheless, a model for the cytokine and chemokine network of rosacea may be postulated by extrapolating from known clinical trigger factors and current pathophysiological concepts: external and internal trigger factors induce primary proinflammatory cytokines such as TNF- $\alpha$  and IL-1 family members through TLR2 signaling or other mechanisms ( Figure 1 ). Subsequently, a first wave of chemokines is produced that leads to the recruitment of T cells into the perifollicular space. ...

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#### Citations

... 6.[8][9][10] Trigger factors for rosacea such as ultraviolet radiation and stress alter Toll-like receptor (TLR) signaling, inducing reactive oxygen species and augmenting downstream cytokine and chemokine inflammatory responses. 11 TLR activation is thought to lead to the synthesis of pro-inflammatory cytokines and secretion of antimicrobial peptides such as cathelicidin and chemokines with TLR2 in particular being highly expressed in the skin of rosacea patients. 12 This is consistent with findings that rosacea patients have increased expression of enzymes responsible for activating cathelicidin, the antimicrobial peptide LL-37. ...

##### Rosacea and the cardiovascular system

[Article](#)

Jul 2020 · [J Cosmet Dermatol](#)

 Tamara Searle ·  Firas Al-Niimi ·  Faisal R. Ali

Rosacea and the cardiometabolic syndrome are both associated with chronic inflammation and a pro-inflammatory phenotype. Emerging clinical evidence supports the relationship between rosacea and cardiometabolic syndrome hypertension and obesity. This article...

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... Therapeutic methods (radiation and cryotherapy) applied to the head-and-neck region may induce leukocyte activation and thus the formation of histopathological changes of AR by stimulating the inflammatory process in the skin. [40] In our study, we found 1.7 times more AR prevalence in those who had a local treatment of head-and-neck region. Treatment In our study, the AR prevalence in the primary and lower education levels was higher than the university graduates. ...

##### Assessment of acne rosacea prevalence and quality of life between individuals aged 18 years and over in mahmudiye district center, Eskisehir, Turkey (A population-...

Jan 2020

GulsumOzturk Emiral · Ozkan Ozay · ● Didem Arslantas · Alaettin Unsal · HilalKaya Erdogan

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... Consistent with the anti-inflammatory effects of ART in some reports [20,28], IL-1 $\beta$ , IL-6 and TNF $\alpha$  were also repressed by ART in rosacea-like mouse. Moreover, ART repressed the expression of CCL2 (monocyte chemokine), CXCL2 (neutrophil chemokine) in LL37-induced mouse model, which could exert chemotaxis on macrophages and neutrophils in rosacea [9]. Thus, as demonstrated in histologic analysis and Immunofluorescence in mouse lesions, rosacea-like dermatitis and subcutaneous inflammatory cell infiltration including macrophages and neutrophils were significantly suppressed by ART. ...

### Artemisinin, a potential option to inhibit inflammation and angiogenesis in rosacea

Article [Full-text available](#)

Sep 2019 · BIOMED PHARMACOTHER

Xin Yuan · Ji Li · Yangfan Li · ● Zhili Deng · ● Hongfu Xie

Background: Rosacea is a facial chronic inflammatory skin disease with dysfunction of immune and vascular system. Artemisinin (ART), an anti-malaria drug, was reported to have several effects including anti-inflammation and anti-angiogenesis activities. Howev...

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... Initially, AMPs were identified as endogenous antibiotics due to their potential to kill various pathogens such as gram-positive and gram-negative bacteria, viruses and fungi [5]. In addition to its antimicrobial activity, LL37 can also induce a series of inflammatory processes, including mast cell activation and release of chemokines and cytokines from keratinocytes and other local cells [8][9][10]. In a reported animal model, intradermal injection of human cathelicidin LL37 induced a series of inflammatory responses similar to the features of rosacea patients [7]. ...

### Thalidomide ameliorates rosacea-like skin inflammation and suppresses NF- $\kappa$ B activation in keratinocytes

Article [Full-text available](#)

May 2019

Mengting Chen · ● Hongfu Xie · Zhaohui Chen · San Xu · ● Zhili Deng

Background: Rosacea is a chronic inflammatory skin disorder of uncertain etiology. Evidence suggests the underlying pathogenesis is modulated by abnormal inflammatory and vascular responses. Thalidomide is a synthetic derivative acid with anti-inflammator...

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... 5,28 For instance, IL-6 and TNF- $\alpha$  are pro-inflammatory cytokines that are upregulated in rosacea and also involved in obesity-induced inflammation. 29, 30 Above all, obesity is a key feature of MetS, where increased visceral adiposity leads to insulin resistance and consequently atherosclerotic CVD due to chronic low-grade inflammation. 31 With respect to cardiovascular risk, rosacea is associated with hyperlipidemia, smoking, alcohol, and hypertension. ...

### Association between rosacea severity and relative muscle mass: A cross-sectional study

Article

Oct 2018 · J DERMATOL

Jae-Hui Nam · Junghwa Yang · Jiho Park · Je Hyun Seo · ● Won-Serk Kim

Rosacea is thought to be associated with factors involved in metabolic syndrome (MetS). Muscle mass has a beneficial role in preventing MetS, but its link to rosacea remains unknown. We sought to investigate the association between rosacea severity and relativ...

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... A significant role in the development and course of rosacea belongs to an impairment of the immunological reactivity of the patient 1,3,6 . The study of cytokines' role in the regulation of pathological processes in chronic dermatoses, particularly rosacea, by determining the nature of changes in the serum content of interleukins, is relevant [11][12][13][14] [15] [16] . Interleukins are secretory Résultats. ...

### **Interleukin-17A and Interleukin-18 level in the blood serum of patients with different clinical course of Rosacea**

Article [Full-text available](#)

Sep 2018

Maryna V. STOROZHUK · OIha I. DENYSENKO

Introduction. Rosacea is a common chronic dermatosis characterized by lesions of open areas of the skin (face) and torpidity to treatment. The objective of our study was to determine and analyze the content of proinflammatory cytokines – interleukin-17A (IL-17...

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... Rosacea is a common, chronic inflammatory disease of the skin, which can cause prominent redness and sometimes permanent deformations. Genetic factors, immune system, microorganisms, such as *Helicobacter pylori* and *Demodex folliculorum*, ultraviolet (UV) light, neurovascular disorder, disruption of skin barrier, and various environmental factors are considered to play a role in the etiopathogenesis of this disease [1, 11, 15,18,29]. The proinflammatory effect of UV and the role of oxidative stress and immune response to demodex mite are considered to contribute to the development of inflammation in rosacea [3,25,30,31]. ...

### **The investigation of the relationships of demodex density with inflammatory response and oxidative stress in rosacea**

Article

Aug 2018 · [ARCH DERMATOL RES](#)

● Tuğba Falay Gur · ● Aslı Vefa Erdemir · ● Mehmet Salih Gurel · ● Abdurrahim Kocyigit · ● Duygu Erdil

The relationships of demodex density with systemic oxidative stress, inflammatory response, and clinical severity in rosacea are not clear. This study aimed to (a) analyze the levels of systemic oxidative stress, antioxidant capacity, inflammatory parameters, and...

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... 9 Similarly, these cytokines have been found to be increased in patients with rosacea as a result of an aberrant innate immune system and toll-like receptor activation. 10 In our cases, initiation of the aromatase inhibitor may have disrupted the calcium homeostasis and, in the setting of ongoing inflammation, precipitated the formation of small calcifications. This course from inflammation, trigger exposure, calcification, and finally ossification requires further investigation. ...

### **Two cases of treatment with aromatase inhibitors and development of miliary osteoma cutis—Is there an association?**

Article [Full-text available](#)

Aug 2018

● Eric D. Schadler · Stephanie L. Mehlis · Thomas L. Cibull · Bernhard Ortel

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... The density of the sensory neuron is increased in the ETR subtype [73]. In

addition, the density of TRP ion channels is increased on the sensory neurons and blood vessels as well as immune cells in all subtypes of rosacea [74, 75]. Dermal immunolabeling of TRPV2 and TRPV3 and gene expression of TRPV1 are significantly increased in ETR. ...

### Skin neurogenic inflammation

[Article](#)

Apr 2018 · [SEMIN IMMUNOPATHOL](#)

● Jae Eun Choi · ● Anna Di Nardo

The epidermis closely interacts with nerve endings, and both epidermis and nerves produce substances for mutual sustenance. Neuropeptides, like substance P (SP) and calcitonin gene-related protein (CGRP), are produced by sensory nerves in the dermis;...

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... Koo et al. also demonstrated the elevated levels of pro-inflammatory cytokines IL-7, IL-12 and IL-17 in patients' tears in demodex blepharitis, which were normalized after TTO treatment (Koo et al. 2012). Furthermore IL-17 can affect the expression of the antimicrobial protein LL-37 in human epidermal keratinocytes (Woo et al. 2016), induce angiogenesis in rosacea through VEGF (vascular endothelial growth factor) (Gerber et al. 2011) and stimulate the inflammatory and allergic reaction which further enhances the expression of IL-6, MMP-1 and MMP-9 (Woo et al. 2016). This may indicate the potential targeting mechanism of TTO in treating facial rosacea. ...

### Can the tea tree oil (Australian native plant: *Melaleuca alternifolia* Cheel) be an alternative treatment for human demodicosis on skin?

[Article](#) [Full-text available](#)

Apr 2018 · [Parasitology](#)

● Nelson Siu Kei Lam · ● Xin Xin Long · ● Robert C Griffin · ● Mu-Kai Chen · ● James CG Doery

Australian tea tree oil (TTO) and its extract terpinen-4-ol (T4O) are found to be effective in moderating demodex-related diseases. Their possible effects are lowering the mite counts, relieving the demodex-related symptoms and modulating the immune system especially...

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