

Gut microbiota and nutrient interactions with skin in psoriasis: A comprehensive review of animal and human studies

Giovanni Damiani, Nicola Luigi Bragazzi, Thomas S McCormick, Paolo Daniele Maria Pigatto, Sebastiano Leone, Alessia Pacifico, Danica Todorovic, Sveva Di Franco, Aniello Alfieri, Marco Fiore

ORCID number: Giovanni Damiani (0000-0002-2390-6505); Nicola Luigi Bragazzi (0000-0001-8409-868X); Thomas S McCormick (0000-0002-3294-0326); Paolo Daniele Maria Pigatto (0000-0001-6599-9538); Sebastiano Leone (0000-0001-7852-4101); Alessia Pacifico (0000-0003-0348-0620); Danica Todorovic (0000-0002-1157-1402); Sveva Di Franco (0000-0003-0399-2677); Aniello Alfieri (0000-0002-1330-5968); Marco Fiore (0000-0001-7263-0229).

Author contributions: Damiani G and Fiore M designed the study; Todorovic D, Di Franco S and Alfieri A performed the research; Bragazzi NL and Pigatto PDM supervised the manuscript; Leone S and Pacifico A provided critical reviews; Damiani G and Fiore M wrote the manuscript; McCormick TS revised the manuscript in order to improve and polish the language.

Conflict-of-interest statement: The authors declare no conflict of interest.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the

Giovanni Damiani, Thomas S McCormick, Department of Dermatology, Case Western Reserve University, Cleveland, OH 44106, United States

Giovanni Damiani, Paolo Daniele Maria Pigatto, Clinical Dermatology, IRCCS Istituto Ortopedico Galeazzi, Milan 20122, Italy

Giovanni Damiani, Paolo Daniele Maria Pigatto, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan 20122, Italy

Nicola Luigi Bragazzi, Postgraduate School of Public Health, Department of Health Sciences, University of Genoa, Genoa 16132, Italy

Sebastiano Leone, Department of Medicine, Division of Infectious diseases, "San Giuseppe Moscati" Hospital, Avellino 83100, Italy

Alessia Pacifico, San Gallicano Dermatological Institute, IRCCS, Rome 00144, Italy

Danica Todorovic, Dermatology Clinic, Medical Faculty, Nis University, Nis 18000, Serbia

Sveva Di Franco, Aniello Alfieri, Marco Fiore, Department of Women, Child and General and Specialized Surgery, University of Campania "Luigi Vanvitelli", Naples 80138, Italy

Corresponding author: Marco Fiore, MD, Academic Fellow, Department of Women, Child and General and Specialized Surgery, University of Campania "Luigi Vanvitelli", Piazza L Miraglia 2, Naples 80138, Italy. marco.fiore@unicampania.it

Abstract

The intestinal tract (*i.e.*, the gut), is where the body's nutrients are absorbed, and is simultaneously inhabited by numerous microbes. An increasing body of literature suggests a crucial role for the gut microbiome in modulating systemic inflammatory disease. Psoriasis is a chronic systemic inflammatory disease and its pathogenesis is related to the interaction between genetic susceptibility, immune response and environmental triggers. The omics era has allowed physicians to assess different aspects of psoriasis pathogenesis such as the microbiome, infectome, and autoinfectome. Furthermore, diet appears to play an important role in modulating disease activity, perhaps by influencing gut microbes. Given these observations, we aimed to summarize the current knowledge regarding skin-microbiome-gut-nutrients and psoriasis.

Key words: Gut; Microbiota; Nutrients; Endotypes; Exposome; Psoriasis

original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited Manuscript

Received: December 10, 2019

Peer-review started: December 10, 2019

First decision: January 13, 2020

Revised: February 25, 2020

Accepted: March 9, 2020

Article in press: March 9, 2020

Published online: March 26, 2020

P-Reviewer: Rhoads J, Serban ED

S-Editor: Ma YJ

L-Editor: Webster JR

E-Editor: Liu JH



©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Psoriasis is a chronic systemic inflammatory disease and its pathogenesis is related to the interaction between genetic susceptibility, immune response and environmental triggers. The omics era has allowed physicians to study psoriasis pathogenesis from different perspectives such as the microbiome, infectome, and autoinfectome. Furthermore, diet appears to play an important role in modulating disease activity. Given these observations, this review aimed to summarize the current knowledge on skin-microbiome-gut-nutrients and psoriasis.

Citation: Damiani G, Bragazzi NL, McCormick TS, Pigatto PDM, Leone S, Pacifico A, Todorovic D, Di Franco S, Alfieri A, Fiore M. Gut microbiota and nutrient interactions with skin in psoriasis: A comprehensive review of animal and human studies. *World J Clin Cases* 2020; 8(6): 1002-1012

URL: <https://www.wjnet.com/2307-8960/full/v8/i6/1002.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v8.i6.1002>

INTRODUCTION

Psoriasis is alternatively regarded as an inflammatory^[1], pruritic^[2], autoimmune^[3,4], or even autoinflammatory^[5] systemic chronic disease affecting not only the skin but the whole body, providing a potential explanation for the numerous comorbidities discovered in relation to this disease^[6-12]. The biomarker research performed in the past decades identified substantial inadequacies in describing the wide spectrum of psoriasis^[13-15], and failed to explain the complexity of psoriasis endotypes^[16]. The genetic background of psoriasis patients reveals that deficiency of the interleukin 1 (IL-1) receptor antagonist and deficiency of the IL-36 receptor antagonist are the only recognized mutations^[17], conversely other psoriatic forms are considered complex diseases, due to the intricate interaction between inherited susceptibility alleles and environmental triggers^[18]. In addition, epigenetic modifications seem to play a pivotal role in developing psoriasis, establishing environmental triggers as potential modulatory factors^[19] as well as in response to anti-psoriatic therapies^[20]. These new findings provide a rationale for observed treatment loss-of-response and biologically justify switching to alternative treatments in patient management^[21-24]. Furthermore, an increased body of evidence suggests a crucial role for the gut microbiome in modulating psoriasis; linking the skin and gut microbiome^[25]. The gut is the site where nutrients are absorbed and at the same time is inhabited by nutrient-modifying microbes. The Skin-Microbiome-Gut-Nutrient interaction is still only partially understood; therefore, this review aimed to summarize the current knowledge in this field.

PSORIASIS, DIET AND CIRCADIAN RHYTHM

Psoriasis is associated with metabolic and cardiovascular disease^[6,26,27]. It has been widely demonstrated that genetic and environmental factors including nutrition, may strongly influence psoriatic pathogenesis and disease progression^[28,29]. Increased body mass and a high fat diet may trigger as well as exacerbate psoriasis^[29]. Moderate to severe psoriasis is frequently associated with numerous metabolic disorders including obesity, diabetes, dyslipidemia, metabolic syndrome and non-alcoholic fatty liver disease^[30]. Fatty acids are increased in obese patients, leading to augmented inflammation and insulin resistance. Furthermore, obesity may also affect drug pharmacokinetics and pharmacodynamics^[29]. The option to treat psoriasis patients with phototherapy is affected by body mass index; obese patients require an excessive amount of photosensitizing drug which may lead to toxicities. Obesity is also an important risk factor for psoriasis, given that the relationship between obesity and psoriasis is mutually interdependent^[29]. Recent evidence has suggested an additional role of vitamin D in the pathogenesis of several inflammatory skin diseases including psoriasis^[31]. An association between low levels of vitamin D and psoriasis has been described^[31]. Vitamin D also participates in keratinocyte proliferation and maturation. Nevertheless, the potential value of vitamin D supplementation for psoriasis is still

under debate^[31]. Dietary antioxidants including omega 3 polyunsaturated fatty acids derived from fish oil, vitamin B12, vitamin D and selenium have the capacity to decrease oxidative stress and consequently lower reactive oxygen species production, and this could be relevant in the pathogenesis of psoriasis. Based on these findings, the Mediterranean diet has been proposed to slow disease progression^[32,33]. All of these endogenous factors contribute to the composition of the so-called “exposome”, a measure of the whole complex of endogenous, ingested and not ingested, substances that interact with the body that are capable of perturbing, modifying and modulating vital functions^[34]. Exposures capable of modulating psoriasis include tobacco, which increases severity, flare frequency, and even the incidence of the psoriasis^[35], alcohol^[36] and pollutants^[37], even if the role of both alcohol and pollutants in psoriasis is still debatable. Interestingly, the use of marijuana was recently related to secukinumab resistance in a cohort of erythrodermic patients, focusing the attention on addiction screening during intake medical history of psoriatic patients^[38]. Anti-psoriatic drugs are also capable of modulating taste, and consequently, the patient’s diet, as recently described for both methotrexate^[39] and apremilast^[40].

Since the melatoninergic system was discovered in the epidermis, circadian rhythm has been regarded as a possible modulator of inflammation^[41], healing^[42], aging^[43], neuroendocrine^[44], and neoplastic conditions^[45]. The cyclic nature of sunlight which influences the suprachiasmatic nucleus (central clock) also influences other peripheral tissue, including skin (peripheral clock), in different ways that are slowly beginning to be understood by examining the mechanism(s) of their dysfunction^[46,47]. The shift in circadian rhythm may be occasional and transitory, as in the case of jet-lag during intercontinental flights^[48], or in the case of the Ramadan fasting months for Muslims^[49,50], or more chronic, as in night shift workers^[51,52]; however this effect is particularly evident in psoriatic patients. Interestingly, night-shift workers exhibited not only an increase in severity of psoriatic flares, but also an increased incidence of psoriasis, suggesting that shifting the circadian rhythm (*i.e.*, sleep and diet) may be a risk factor for psoriasis^[52]. Sunlight, in the form of narrow band UVB (NB-UVB), may also be curative for psoriatic skin, allowing a reprogramming of the circadian clock and inhibition of autoimmune phenomena^[53], however skin may also marginally adapt to NB-UVB, an outcome termed photoadaptation^[54]. Thus, sunlight is considered an integral part of the exposome.

PSORIASIS, NUTRIENTS AND SKIN CANCER

The possible influence of nutrients on gene expression and clinical progression or remission of psoriasis is not fully explored and may represent the main challenge in approaching complementary therapy for psoriasis. It is reported that many dietetic factors may exert beneficial effects, while others can aggravate inflammatory and immune networks, thus leading to psoriasis comorbidities^[55]. Previous studies have reported the positive effects of low-energy diets, vegetarian diets, formula diet weight loss programs, gluten-free or very low-calorie carbohydrate-free diet. It is believed that certain vitamins (*e.g.*, A, E and C), and oligo-elements (*e.g.*, iron, copper, manganese, zinc, and selenium) are anti-oxidants, leading to a reduction in oxidative stress and decreased production of reactive oxygen species^[55]. In fact, the disruption of cell redox signaling and involvement of oxidative stress in the pathogenesis of psoriasis was previously suggested, indicating that the potential therapeutic use of dietary antioxidants in psoriasis may represent a novel complementary strategy^[56]. Although limited data exist regarding the role of specific diet regimens in psoriasis, the main goal for clinicians is to reduce cardiac risk factors and obesity-related comorbidities.

Interestingly, psoriatic patients displayed a higher risk of cancer compared to the general population; furthermore, this increase is not fully explained by anti-psoriatic immunosuppressive therapies, so several real-life or ecological studies have suggested an intimate relation with diet^[57]. This theory is supported by the evidence that different foods modify microRNA expression in psoriatic patients^[28]. The influence of a restrictive caloric diet was documented to be beneficial in relapsing plaque psoriasis, and may also decrease the risk of cancer^[58-60]. Some lipid components, such as omega-3 polyunsaturated fatty acids may protect cells against UV-induced DNA damage by increasing the expression of tumor-suppressor protein p53, thus promoting cell cycle arrest and preventing melanoma development^[61-63]. Solid cancers in psoriasis have been reported, especially those linked to alcohol and smoking. A higher risk of non-melanoma skin cancers, especially squamous cell carcinoma has been shown, possibly as a result of previous exposure to 8-methoxypsoralen-ultraviolet-A (PUVA), cyclosporin, tumor necrosis factor-inhibitors

and/or methotrexate^[64-66]. Consideration of malignancy risk associated with individual treatments and personal nutritional phenotype may help clinicians to make optimal therapeutic decisions for individual patients.

MOUSE MODEL OF PSORIASIS AND DIET

The "omics" era has provided researchers with new powerful techniques (*e.g.*, metagenomics) and has elucidated a myriad of dysregulated immune responses that are heavily associated with the gut microbiota. Previous research suggested that ingested nutrients heavily affect the body's microbial composition and community. This has led to experimental approaches in mouse models of psoriasis. In recent years, nutrition and microbial influence has been heavily implicated in psoriasis onset and disease severity. The contribution of nutrients in mouse models has provided valuable insight into human disease regulation. For instance, 12-O-tetradecanoylphorbol-13-acetate (TPA), a known inflammatory signal transducer, can induce psoriasis-like skin lesions in mice, while lesions and proinflammatory cytokine expression were significantly reduced in TPA-induced psoriasis by tangerine-derived nutrient flavonoids: Nobiletin (Nob) and 5-hydroxy-6,7,8,3',4'-pentamethoxyflavone (5-HPMF)^[67]. In addition, obesity, a result of poor nutrition, has been shown to exacerbate the severity of psoriasiform dermatitis in imiquimod-induced rodent models^[68]. Collectively, these results support the need to elucidate nutritional impact on psoriasis severity. Research has suggested that monounsaturated fatty acid-rich diets, such as the Mediterranean Diet have anti-inflammatory effects and slow the progression of psoriasis in patients^[33]. Poor nutrition has been associated with dysregulated metabolic functions and even more so, has been shown to be critical in skin disease metabolic homeostasis compared to healthy individuals. Previous research has shown evidence for biochemical skin barrier restoration through topical administration of solenopsin, a compound of fire ant venom chemically similar to ceramides, and its derivatives by reducing inflammatory markers and improving acanthosis in KC-Tie2 mice, an established rodent-model of psoriasis^[69].

PSORIASIS AND THE MICROBIOME

Several lines of evidence confirmed the relationship between skin microorganisms and psoriatic lesions, such as *Group A β-hemolytic streptococcal infections* linked to guttate psoriasis^[70]. Other microorganisms including *Staphylococcus aureus*, *Malassezia* and *Candida albicans* also appear to be involved in psoriasis pathogenesis^[71]. The deep inter-relationship between the mycobiome and microbiome seem to act as a disease-modifier in psoriatic patients. Although it is well known that the gut and skin microbiome deeply interact, sparse information is available on the gut and skin mycobiome. Using high-throughput 16S rRNA gene sequencing, Alekseyenko *et al*^[72], found that psoriatic plaques had an abundance of the following bacteria: *Corynebacterium*, *Propionibacterium*, *Staphylococcus*, and *Streptococcus*. Baker *et al*^[73], found that peptidoglycan, a cell wall component of Gram-positive bacteria including *Streptococci* and *Staphylococci*, acts as a T cell activator in psoriasis. The authors observed that dermal papillae and cellular infiltrates of guttate and chronic plaque skin lesions had higher numbers of peptidoglycan-containing cells compared to non-lesional psoriatic skin. Psoriatic dermal *Streptococcal*- and *Staphylococcal*-specific CD4+ T cell lines proliferated and produced IFN- α in response to the *respective* peptidoglycan structures. Overall, these results suggest that peptidoglycans may be responsible for T cell activation in psoriasis. Moreover, some studies have linked gut microbiota and psoriasis.

Up to 10% of patients with inflammatory bowel disease (IBD) are diagnosed with psoriasis^[74]. Patients with psoriasis have a 3-fold higher risk of developing Crohn's disease as compared to the general population; and Crohn's disease patients have a 7-fold higher risk of developing psoriasis^[75]. Recently, Scher *et al*^[76], using pyrosequencing, found that patients with psoriatic arthritis and patients with skin psoriasis had a decreased bacterial diversity and a reduced relative abundance of some bacterial taxa such as *Akkermansia*, *Ruminococcus*, and *Pseudobutyriovibrio*, as compared to healthy controls. Among the risk factors for psoriatic diseases summarized in **Table 1**, overall, the alteration of gut microbiota may translate into physiological consequences including poor regulation of intestinal immune responses that may then affect distant organ systems^[77-85]. Given the gut microbiome's influence on the Gut-Skin axis, probiotic supplementation may have a promising role in the management of psoriatic patients. On this point, Gueniche *et al*^[77], in a randomized

double-blind placebo-controlled clinical study, showed that oral supplementation with the probiotic strain *Lactobacillus paracasei* decreased skin sensitivity and increased the rate of barrier function recovery.

INFECTOMICS AND AUTOINFECTOMICS IN PSORIASIS

The term “exposome” defines all environmental factors, including infectious and non-infectious agents, to which a human is exposed over a lifetime^[80]. The “microbiota” is a term used to describe the 10-100 trillion symbiotic microbes harbored by each human; the “microbiome” consists of the genes that these microbes harbor^[81]; the “infectome” is a part of the microbiome, referring to the collection of human exposure to infectious agents; the “autoinfectome” describes a part of the microbiome that includes the infectious agents linked to the presence of autoimmune diseases^[82]. **Figure 1** summarizes the main interactions between the exposome, microbiome, infectome and autoinfectome. Recently a systematic review, which included 933 psoriatic arthritis patients and 1611 controls, aimed to evaluate the link between infections (viral and bacterial infections) and the risk of psoriatic arthritis and reported a controversial result that exhibited a trend but failed to achieve significance^[83]. However, differences exist between infection, colonization and dysbiosis, as suggested by several studies highlighting a different mycobiome and microbiome in psoriasis, psoriatic arthritis and control subjects^[84]. In fact, a dysregulation in the ratio of *Firmicutes/Bacteroidetes* was highlighted in the gut microbiome of psoriatic patients; furthermore, *Actinobacteria* was reduced in the gut of psoriatic patients. Gut dysbiosis was also found to be related to skin dysbiosis as decreased beta-diversity in psoriatic skin microbiome is related to an increased risk of developing psoriatic arthritis, and skin flora are now regarded as possible sensitive and specific biomarkers to predict comorbidities in psoriatic patients^[84]. The skin microbiota in psoriasis patients seems to be less diverse when compared to healthy persons with a decrease in *Coprococcus* species^[76], and more recently *Akkermansia muciniphila*^[85]. The characteristic proinflammatory mediators of psoriatic skin lesions have been reported to be the innate antimicrobial peptides and proteins (AMPs). AMPs are a diverse group of small molecules (12–100 amino acid residues) that constitute the primary effector system of innate immunity against microbes^[86]. Although medical history certainly plays a crucial role in psoriasis management, it has some limitations such as recall bias. In particular, it has already been demonstrated that not all infections or even dysbiosis that are not clinically evident are still capable of triggering an immune/autoimmune response. Currently, there is limited, evolving information suggesting some benefit from fecal microbiota transplantation, although durability of response is a concern and currently under investigation^[87,88].

TREATMENT OF PSORIASIS: TAKING INTO ACCOUNT INTERACTIONS WITH DIET AND MICROBIOME

Drug therapies are an important consideration for alteration of the cutaneous and gut microbiome^[78,89] as well as the mycobiome; however, few studies have explored this topic, and are summarized in **Table 2**.

To date IL-17/IL-17RA signaling has been demonstrated to be a key component in regulating *Candida* in the gut microbiome^[79]. Furthermore, psoriatic arthritis and IBD have genetic and environmental similarities, highlighting that microbiome dysbiosis may affect autoimmune diseases^[78]. T-cell activation is an important mechanism of psoriasis, and dysbiosis has been associated with the differentiation of T-cells into effector T cells with fewer regulatory T-cells resulting in changes in the levels of cytokines. In particular, Th17 inhibitors produced the best response compared to patients treated with tumor necrosis factor- α and IL-23 inhibitors^[78]. It is interesting to note that this Th-17 mediated response may not translate to the skin, as the skin microbiome could prevent the development of psoriatic plaques in these individuals^[3,79]. It is possible that transplanting fecal microbiota could improve or resolve the dysbiosis present in psoriatic arthritis^[79]. Fecal microbiota transplants have been used with success in IBD. In fact, Kraggsnaes *et al*^[90] are currently exploring fecal microbiota transplantation (FMT) in patients with psoriatic arthritis currently on methotrexate to examine their treatment response. Evaluating evidence of the efficacy of FMT is likely due to be complicated by various factors including antibiotic use, prior psoriasis therapy, subtype of psoriasis and comorbidities which similarly affect the gut or skin microbiome^[91]. Future studies are needed to identify potential

Table 1 Synthesis of psoriasis risk factors reporting reference number, first author surname, year of publication, population risk factors reported in each study and the type of psoriasis

Ref.	Year	Studied population	Psoriasis risk factors	Type of psoriasis
Barrea et al ^[29]	2016	Human	Obesity	Not specified
Kanemaru et al ^[68]	2015	Animal - Mice	Obesity	Psoriasiform dermatitis
Dauden et al ^[30]	2018	Human	Metabolic disorders	Not specified
Barrea et al ^[31]	2017	Human	Reduction vitamin D	Not specified
Lin et al ^[56]	2016	Human	Oxidative stress	Not specified
Yang et al ^[67]	2018	Animal - Mice	12-O-tetradecanoylphorbol-13-acetate administration	Psoriasis-like skin lesions
Ottman et al ^[70]	2012	Human	<i>Beta-hemolytic streptococcal</i> infections	Guttate psoriasis
Zeng et al ^[71]	2017	Human	<i>Staphylococcus aureus</i> , <i>Malassezia</i> and <i>Candida albicans</i> infections	Not specified
Alekseyenko et al ^[72]	2013	Human	<i>Corynebacterium</i> , <i>Propionibacterium</i> , <i>Staphylococcus</i> , and <i>Streptococcus</i> infections	Psoriatic plaques
Baker et al ^[73]	2006	Human	Higher numbers of peptidoglycan-containing cells	Guttate and chronic plaques
Oliveira Mde et al ^[75]	2015	Human	Inflammatory bowel disease (i.e., Crohn's disease)	Not specified
Scher et al ^[76]	2015	Human	Significant reduction in <i>Akkermansia</i> , <i>Ruminococcus</i> , and <i>Pseudobutyrvibrio</i> in gut microbiota	Psoriatic arthritis
Tan et al ^[85]	2018	Human	Reduction of <i>Coprococcus</i> species and <i>Akkermansia muciniphila</i> in gut microbiota	Psoriatic arthritis

modulators of the gut and skin microbiome, and identify which medications would be optimal for a patient's individual microbiome signature.

CONCLUSION

The interaction of Microbiome-Gut-Nutrients in psoriasis is beginning to be understood with the advent of improved omics technologies and their possible integration with each other in order to more precisely separate psoriasis patient endotypes. The transition from immune-targeted therapy to precision-based therapy will be based on the mix between biological signature, the endotype, and potential specific interaction within the exposome.

Table 2 Synthesis of psoriasis proposed treatments including reporting reference number, first author surname, year of publication, population risk factors reported in each study and the type of psoriasis

Ref.	Year	Study type	Studied population	Proposed treatment	Type of psoriasis
Barrea <i>et al</i> ^[32] , Phan <i>et al</i> ^[33]	2015, 2018	Cohort	Human	Dietary antioxidants (omega 3 polyunsaturated fatty acids derived from fish oil, vitamin B12, vitamin D and selenium)	Not specified
Subbiah <i>et al</i> ^[55]	2010	Review	-	Low-energy diets, vegetarian diets, formula diet weight loss programs, gluten-free or very low-calorie carbohydrate-free diet	Not specified
Subbiah <i>et al</i> ^[55] , Lin <i>et al</i> ^[85]	2010, 2016	Review	-	Dietary antioxidants: Vitamins (A, E and C), and oligo-elements (iron, copper, manganese, zinc, and selenium)	Not specified
Murzaku <i>et al</i> ^[61] , Upala <i>et al</i> ^[62] , Morken <i>et al</i> ^[63]	2014, 2017, 2011	Review, systematic review, pilot study	Human	Omega-3 polyunsaturated fatty acids	Not specified
Yang <i>et al</i> ^[67]	2018	RCT	Animal – mice	Nobiletin (Nob) and 5-hydroxy-6,7,8,3',4'-pentamethoxyflavone (5-HPMF)	Not specified
Arbiser <i>et al</i> ^[69]	2017	RCT	Animal - mice	Topical administration of solenopsin analogs	Not specified
Gueniche <i>et al</i> ^[77]	2014	RCT	Human	Oral supplementation with the probiotic <i>Lactobacillus paracasei</i>	Not specified
Eppinga <i>et al</i> ^[78]	2014	Review	-	Th17, TNF- α and IL-22 inhibitors	Psoriatic arthritis
Castelino <i>et al</i> ^[79]	2014	Review	-	Transplant of fecal microbiome	Psoriatic arthritis

RCT: Randomized controlled trial; TNF: Tumor necrosis factor; IL: Interleukin 1.

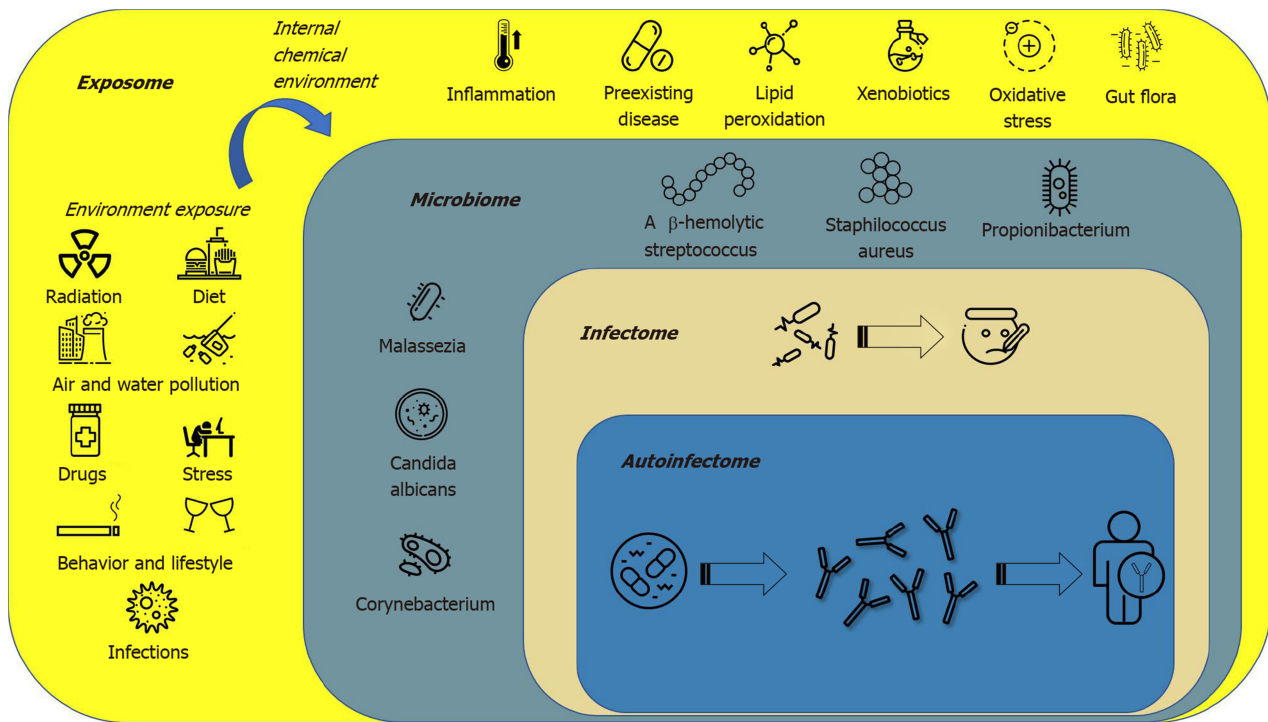


Figure 1 The figure describes the complex panorama of the exposome. The exposome represent all environmental exposures, from infectious and noninfectious causes. Environmental exposure changes the internal chemical environment that can lead to alterations in the microbiome. The microbiome is the number of all genes of symbiotic microbes harbored by each human. The fraction of the microbiome concerning the collection of human exposure to infectious agents is represented by the infectome. The autoinfectome is the part of the infectome that contains the infectious agents causing autoimmune diseases.

REFERENCES

- 1 Greb JE, Goldminz AM, Elder JT, Lebwohl MG, Gladman DD, Wu JJ, Mehta NN, Finlay AY, Gottlieb AB. Psoriasis. *Nat Rev Dis Primers* 2016; **2**: 16082 [PMID: 27883001 DOI: 10.1038/nrdp.2016.82]
- 2 Damiani G, Cazzaniga S, Conic RR, Naldi L; Psocare Registry Network. Pruritus Characteristics in a Large Italian Cohort of Psoriatic Patients. *J Eur Acad Dermatol Venereol* 2019; **33**: 1316-1324 [PMID: 31736536 DOI: 10.1111/jdv.15539]
- 3 Lande R, Botti E, Jandus C, Dojcinovic D, Fanelli G, Conrad C, Chamilos G, Feldmeyer L, Marinari B, Chon S, Vence L, Riccieri V, Guillaume P, Navarini AA, Romero P, Costanzo A, Piccolella E, Gilliet M, Frasca L. The antimicrobial peptide LL37 is a T-cell autoantigen in psoriasis. *Nat Commun* 2014; **5**: 5621 [PMID: 25470744 DOI: 10.1038/ncomms6621]
- 4 Arakawa A, Siewert K, Stöhr J, Besgen P, Kim SM, Rühl G, Nickel J, Vollmer S, Thomas P, Krebs S, Pinkert S, Spannagl M, Held K, Kammerbauer C, Besch R, Dornmair K, Prinz JC. Melanocyte antigen triggers autoimmunity in human psoriasis. *J Exp Med* 2015; **212**: 2203-2212 [PMID: 26621454 DOI: 10.1084/jem.20151093]
- 5 Liang Y, Sarkar MK, Tsoi LC, Gudjonsson JE. Psoriasis: a mixed autoimmune and autoinflammatory disease. *Curr Opin Immunol* 2017; **49**: 1-8 [PMID: 28738209 DOI: 10.1016/j.coi.2017.07.007]
- 6 Al-Mutairi N, Al-Farag S, Al-Mutairi A, Al-Shiltawy M. Comorbidities associated with psoriasis: an experience from the Middle East. *J Dermatol* 2010; **37**: 146-155 [PMID: 20175849 DOI: 10.1111/j.1346-8138.2009.00777.x]
- 7 Santus P, Rizzi M, Radovanovic D, Airoldi A, Cristiano A, Conic R, Petrou S, Pigatto PDM, Bragazzi N, Colombo D, Goldust M, Damiani G. Psoriasis and Respiratory Comorbidities: The Added Value of Fraction of Exhaled Nitric Oxide as a New Method to Detect, Evaluate, and Monitor Psoriatic Systemic Involvement and Therapeutic Efficacy. *Biomed Res Int* 2018; **2018**: 3140682 [PMID: 30345297 DOI: 10.1155/2018/3140682]
- 8 Fiore M, Leone S, Maraolo AE, Berti E, Damiani G. Liver Illness and Psoriatic Patients. *Biomed Res Int* 2018; **2018**: 3140983 [PMID: 29546055 DOI: 10.1155/2018/3140983]
- 9 Della Valle V, Maggioni M, Carrera C, Cattaneo A, Marzano AV, Damiani G. A mysterious abdominal pain during active psoriasis. *Intern Emerg Med* 2018; **13**: 889-892 [PMID: 29086113 DOI: 10.1007/s11739-017-1765-y]
- 10 Damiani G, Radaeli A, Olivini A, Calvara-Pinton P, Malerba M. Increased airway inflammation in patients with psoriasis. *Br J Dermatol* 2016; **175**: 797-799 [PMID: 26991762 DOI: 10.1111/bjd.14546]
- 11 Malerba M, Damiani G, Radaeli A, Ragnoli B, Olivini A, Calzavara-Pinton PG. Narrowband ultraviolet B phototherapy in psoriasis reduces proinflammatory cytokine levels and improves vitiligo and neutrophilic asthma. *Br J Dermatol* 2015; **173**: 1544-1545 [PMID: 26130316 DOI: 10.1111/bjd.13988]
- 12 Watad A, Bragazzi NL, McGonagle D, Damiani G, Comaneshter D, Cohen A, Amital H. Systemic Sclerosis is Linked to Psoriasis and May Impact on Patients' Survival: A Large Cohort Study. *J Clin Med* 2019; **8** [PMID: 30995800 DOI: 10.3390/jcm8040521]
- 13 Villanova F, Di Meglio P, Nestle FO. Biomarkers in psoriasis and psoriatic arthritis. *Ann Rheum Dis* 2013; **72** Suppl 2: ii104-ii110 [PMID: 23532439 DOI: 10.1136/annrheumdis-2012-203037]
- 14 Asa'ad F, Fiore M, Alfieri A, Pigatto PDM, Franchi C, Berti E, Maiorana C, Damiani G. Saliva as a

- Future Field in Psoriasis Research. *Biomed Res Int* 2018; **2018**: 7290913 [PMID: 29888276 DOI: 10.1155/2018/7290913]
- 15 **Diani M**, Perego S, Sansoni V, Bertino L, Gomasasca M, Faraldi M, Pigatto PDM, Damiani G, Banfi G, Altomare G, Lombardi G. Differences in Osteoimmunological Biomarkers Predictive of Psoriatic Arthritis among a Large Italian Cohort of Psoriatic Patients. *Int J Mol Sci* 2019; **20** [PMID: 31717649 DOI: 10.3390/ijms20225617]
- 16 **Menter MA**, Griffiths CE. Psoriasis: the future. *Dermatol Clin* 2015; **33**: 161-166 [PMID: 25412790 DOI: 10.1016/j.det.2014.09.012]
- 17 **Cowen EW**, Goldbach-Mansky R. DIRA, DITRA, and new insights into pathways of skin inflammation: what's in a name? *Arch Dermatol* 2012; **148**: 381-384 [PMID: 22431779 DOI: 10.1001/archdermatol.2011.3014]
- 18 **Capon F**. The Genetic Basis of Psoriasis. *Int J Mol Sci* 2017; **18** [PMID: 29186830 DOI: 10.3390/ijms18122526]
- 19 **Zhao M**, Lu Q. The Aberrant Epigenetic Modifications in the Pathogenesis of Psoriasis. *J Investig Dermatol Symp Proc* 2018; **19**: S81-S82 [PMID: 30471758 DOI: 10.1016/j.jisp.2018.09.007]
- 20 **Ovejero-Benito MC**, Reolid A, Sánchez-Jiménez P, Saiz-Rodríguez M, Muñoz-Aceituno E, Llamas-Velasco M, Martín-Vilchez S, Cabaleiro T, Román M, Ochoa D, Daudén E, Abad-Santos F. Histone modifications associated with biological drug response in moderate-to-severe psoriasis. *Exp Dermatol* 2018; **27**: 1361-1371 [PMID: 30260532 DOI: 10.1111/exd.13790]
- 21 **Kerdel F**, Zaiac M. An evolution in switching therapy for psoriasis patients who fail to meet treatment goals. *Dermatol Ther* 2015; **28**: 390-403 [PMID: 26258910 DOI: 10.1111/dth.12267]
- 22 **Damiani G**, Conic RRZ, de Vita V, Costanzo A, Regazzini R, Pigatto PDM, Bragazzi NL, Pacifico A, Malagoli P. When IL-17 inhibitors fail: Real-life evidence to switch from secukinumab to adalimumab or ustekinumab. *Dermatol Ther* 2019; **32**: e12793 [PMID: 30515970 DOI: 10.1111/dth.12793]
- 23 **Damiani G**, Cazzaniga S, Naldi L; PsoReal Study Group. Use of fumaric acid derivatives (FADs) in Italian reference centres for psoriasis. *G Ital Dermatol Venereol* 2019 [PMID: 30636394 DOI: 10.23736/S0392-0488.18.06032-7]
- 24 **Damiani G**, Conic RRZ, Pigatto PDM, Bragazzi NL, Pacifico A, Malagoli P; Young Dermatologists Italian Network. From randomized clinical trials to real life data. An Italian clinical experience with ixekizumab and its management. *Dermatol Ther* 2019; **32**: e12886 [PMID: 30942952 DOI: 10.1111/dth.12886]
- 25 **Yan D**, Issa N, Afifi L, Jeon C, Chang HW, Liao W. The Role of the Skin and Gut Microbiome in Psoriatic Disease. *Curr Dermatol Rep* 2017; **6**: 94-103 [PMID: 28804689 DOI: 10.1007/s13671-017-0178-5]
- 26 **Conic RR**, Damiani G, Schrom KP, Ramser AE, Zheng C, Xu R, McCormick TS, Cooper KD. Psoriasis and Psoriatic Arthritis Cardiovascular Disease Endotypes Identified by Red Blood Cell Distribution Width and Mean Platelet Volume. *J Clin Med* 2020; **9** [PMID: 31936662 DOI: 10.3390/jcm9010186]
- 27 **Seth D**, Ehler AN, Golden JB, Damiani G, McCormick TS, Cameron MJ, Cooper KD. Interaction of Resistin and Systolic Blood Pressure in Psoriasis Severity. *J Invest Dermatol* 2019 [PMID: 31734188 DOI: 10.1016/j.jid.2019.07.727]
- 28 **Kocic H**, Damiani G, Stamenkovic B, Tirant M, Jovic A, Todorovic D, Peris K. Dietary compounds as potential modulators of microRNA expression in psoriasis. *Ther Adv Chronic Dis* 2019; **10**: 2040622319864805 [PMID: 31431821 DOI: 10.1177/2040622319864805]
- 29 **Barrea L**, Nappi F, Di Somma C, Savanelli MC, Falco A, Balato A, Balato N, Savastano S. Environmental Risk Factors in Psoriasis: The Point of View of the Nutritionist. *Int J Environ Res Public Health* 2016; **13** [PMID: 27455297 DOI: 10.3390/ijerph13070743]
- 30 **Dauden E**, Blasco AJ, Bonanad C, Botella R, Carrascosa JM, González-Parra E, Jodar E, Joven B, Lázaro P, Oliveira A, Quintero J, Rivera R. Position statement for the management of comorbidities in psoriasis. *J Eur Acad Dermatol Venereol* 2018; **32**: 2058-2073 [PMID: 29992631 DOI: 10.1111/jdv.15177]
- 31 **Barrea L**, Savanelli MC, Di Somma C, Napolitano M, Megna M, Colao A, Savastano S. Vitamin D and its role in psoriasis: An overview of the dermatologist and nutritionist. *Rev Endocr Metab Disord* 2017; **18**: 195-205 [PMID: 28176237 DOI: 10.1007/s1154-017-9411-6]
- 32 **Barrea L**, Balato N, Di Somma C, Macchia PE, Napolitano M, Savanelli MC, Esposito K, Colao A, Savastano S. Nutrition and psoriasis: is there any association between the severity of the disease and adherence to the Mediterranean diet? *J Transl Med* 2015; **13**: 18 [PMID: 25622660 DOI: 10.1186/s12967-014-0372-1]
- 33 **Phan C**, Touvier M, Kesse-Guyot E, Adjibade M, Hercberg S, Wolkenstein P, Chosidow O, Ezzedine K, Sbidian E. Association Between Mediterranean Anti-inflammatory Dietary Profile and Severity of Psoriasis: Results From the NutriNet-Santé Cohort. *JAMA Dermatol* 2018; **154**: 1017-1024 [PMID: 30046840 DOI: 10.1001/jamadermatol.2018.2127]
- 34 **Vermeulen R**, Schymanski EL, Barabási AL, Miller GW. The exposome and health: Where chemistry meets biology. *Science* 2020; **367**: 392-396 [PMID: 31974245 DOI: 10.1126/science.aay3164]
- 35 **Naldi L**. Psoriasis and smoking: links and risks. *Psoriasis (Auckl)* 2016; **6**: 65-71 [PMID: 29387595 DOI: 10.2147/PTT.S85189]
- 36 **Svanström C**, Lonne-Rahm SB, Nordlind K. Psoriasis and alcohol. *Psoriasis (Auckl)* 2019; **9**: 75-79 [PMID: 31687362 DOI: 10.2147/PTT.S164104]
- 37 **Puri P**, Nandar SK, Kathuria S, Ramesh V. Effects of air pollution on the skin: A review. *Indian J Dermatol Venereol Leprol* 2017; **83**: 415-423 [PMID: 28195077 DOI: 10.4103/0378-6323.199579]
- 38 **Damiani G**, Pacifico A, Russo F, Pigatto PDM, Bragazzi NL, Bonifati C, Morrone A, Watad A, Adawi M. Use of Secukinumab in a Cohort of Erythrodermic Psoriatic Patients: A Pilot Study. *J Clin Med* 2019; **8** [PMID: 31159169 DOI: 10.3390/jcm8060770]
- 39 **Duhra P**, Foulds IS. Methotrexate-induced impairment of taste acuity. *Clin Exp Dermatol* 1988; **13**: 126-127 [PMID: 3214955 DOI: 10.1111/j.1365-2230.1988.tb00677.x]
- 40 **Damiani G**, Bragazzi NL, Grossi E, Petrou S, Radovanovic D, Rizzi M, Atzeni F, Sarzi-Puttini P, Santus P, Pigatto PD, Franchi C. Severe bitter taste associated with apremilast. *Dermatol Ther* 2019; **32**: e12876 [PMID: 30882959 DOI: 10.1111/dth.12876]
- 41 **Lyons AB**, Moy L, Moy R, Tung R. Circadian Rhythm and the Skin: A Review of the Literature. *J Clin Aesthet Dermatol* 2019; **12**: 42-45 [PMID: 31641418]
- 42 **Vorotelyak EA**, Malchenko LA, Rogovaya OS, Lazarev DS, Butorina NN, Brodsky VY. Melatonin Stimulates Epithelium Migration in Wound Models In Vitro and In Vivo. *Bull Exp Biol Med* 2019; **168**: 242-246 [PMID: 31776954 DOI: 10.1007/s10517-019-04683-x]

- 43 **Nanzadsuren T**, Myatav T, Dorjkhuu A, Byamba K. Association between serum melatonin and skin aging in an urban population of Mongolia. *J Cosmet Dermatol* 2019 [PMID: 31566872 DOI: 10.1111/jocd.13166]
- 44 **Bocheva G**, Slominski RM, Slominski AT. Neuroendocrine Aspects of Skin Aging. *Int J Mol Sci* 2019; **20** [PMID: 31181682 DOI: 10.3390/ijms20112798]
- 45 **Pourhanifeh MH**, Mahdavinia M, Reiter RJ, Asemi Z. Potential use of melatonin in skin cancer treatment: A review of current biological evidence. *J Cell Physiol* 2019; **234**: 12142-12148 [PMID: 30618091 DOI: 10.1002/jcp.28129]
- 46 **Plikus MV**, Van Spyk EN, Pham K, Geyfman M, Kumar V, Takahashi JS, Andersen B. The circadian clock in skin: implications for adult stem cells, tissue regeneration, cancer, aging, and immunity. *J Biol Rhythms* 2015; **30**: 163-182 [PMID: 25589491 DOI: 10.1177/0748730414563537]
- 47 **Bragazzi NL**, Sellami M, Salem I, Conic R, Kimak M, Pigatto PDM, Damiani G. Fasting and Its Impact on Skin Anatomy, Physiology, and Physiopathology: A Comprehensive Review of the Literature. *Nutrients* 2019; **11** [PMID: 30678053 DOI: 10.3390/nu11020249]
- 48 **Damiani G**, Bragazzi NL, Garbarino S, Chattu VK, Shapiro CM, Pacifico A, Malagoli P, Pigatto PDM, Conic RRZ, Todorovic D, Watad A, Adawi M. Psoriatic and psoriatic arthritis patients with and without jet-lag: does it matter for disease severity scores? Insights and implications from a pilot, prospective study. *Chronobiol Int* 2019; **36**: 1733-1740 [PMID: 31645138 DOI: 10.1080/07420528.2019.1678629]
- 49 **Adawi M**, Damiani G, Bragazzi NL, Bridgewood C, Pacifico A, Conic RRZ, Morrone A, Malagoli P, Pigatto PDM, Amital H, McGonagle D, Watad A. The Impact of Intermittent Fasting (Ramadan Fasting) on Psoriatic Arthritis Disease Activity, Enthesitis, and Dactylitis: A Multicentre Study. *Nutrients* 2019; **11** [PMID: 30871045 DOI: 10.3390/nu11030601]
- 50 **Damiani G**, Watad A, Bridgewood C, Pigatto PDM, Pacifico A, Malagoli P, Bragazzi NL, Adawi M. The Impact of Ramadan Fasting on the Reduction of PASI Score, in Moderate-To-Severe Psoriatic Patients: A Real-Life Multicenter Study. *Nutrients* 2019; **11** [PMID: 30691245 DOI: 10.3390/nu11020277]
- 51 **Li WQ**, Qureshi AA, Schernhammer ES, Han J. Rotating night-shift work and risk of psoriasis in US women. *J Invest Dermatol* 2013; **133**: 565-567 [PMID: 22931920 DOI: 10.1038/jid.2012.285]
- 52 **Cohen JM**, Jackson CL, Li TY, Wu S, Qureshi AA. Sleep disordered breathing and the risk of psoriasis among US women. *Arch Dermatol Res* 2015; **307**: 433-438 [PMID: 25676527 DOI: 10.1007/s00403-015-1536-4]
- 53 **Chen X**, Yang M, Cheng Y, Liu GJ, Zhang M. Narrow-band ultraviolet B phototherapy versus broad-band ultraviolet B or psoralen-ultraviolet A photochemotherapy for psoriasis. *Cochrane Database Syst Rev* 2013; CD009481 [PMID: 24151011 DOI: 10.1002/14651858.CD009481.pub2]
- 54 **Pacifico A**, Damiani G, Iacovelli P, Conic RR, Scarabello A, Filoni A, Malagoli P, Bragazzi NL, Pigatto PD, Morrone A. Photoadaptation to UVB TL01 in psoriatic patients. *J Eur Acad Dermatol Venereol* 2020 [PMID: 31967696 DOI: 10.1111/jdv.16209]
- 55 **Subbiah MT**. Application of nutrigenomics in skin health: nutraceutical or cosmeceutical? *J Clin Aesthet Dermatol* 2010; **3**: 44-46 [PMID: 21103317]
- 56 **Lin X**, Huang T. Oxidative stress in psoriasis and potential therapeutic use of antioxidants. *Free Radic Res* 2016; **50**: 585-595 [PMID: 27098416 DOI: 10.3109/10715762.2016.1162301]
- 57 **Geller S**, Xu H, Lebwohl M, Nardone B, Lacouture ME, Kheterpal M. Malignancy Risk and Recurrence with Psoriasis and its Treatments: A Concise Update. *Am J Clin Dermatol* 2018; **19**: 363-375 [PMID: 29260411 DOI: 10.1007/s40257-017-0337-2]
- 58 **Castaldo G**, Galdo G, Rotondi A, Cereda E. Very low-calorie ketogenic diet may allow restoring response to systemic therapy in relapsing plaque psoriasis. *Obes Res Clin Pract* 2016; **10**: 348-352 [PMID: 26559897 DOI: 10.1016/j.orcp.2015.10.008]
- 59 **Fontana L**, Klein S, Holloszy JO. Long-term low-protein, low-calorie diet and endurance exercise modulate metabolic factors associated with cancer risk. *Am J Clin Nutr* 2006; **84**: 1456-1462 [PMID: 17158430 DOI: 10.1093/ajcn/84.6.1456]
- 60 **Nagui N**, El Nabarawy E, Mahgoub D, Mashaly HM, Saad NE, El-Deeb DF. Estimation of (IgA) anti-gliadin, anti-endomysium and tissue transglutaminase in the serum of patients with psoriasis. *Clin Exp Dermatol* 2011; **36**: 302-304 [PMID: 21418272 DOI: 10.1111/j.1365-2230.2010.03980.x]
- 61 **Murzaku EC**, Bronsnick T, Rao BK. Diet in dermatology: Part II. Melanoma, chronic urticaria, and psoriasis. *J Am Acad Dermatol* 2014; **71**: 1053.e1-1053.e16 [PMID: 25454037 DOI: 10.1016/j.jaad.2014.06.016]
- 62 **Upala S**, Yong WC, Theparee T, Sanguankeo A. Effect of omega-3 fatty acids on disease severity in patients with psoriasis: A systematic review. *Int J Rheum Dis* 2017; **20**: 442-450 [PMID: 28261950 DOI: 10.1111/1756-185X.13051]
- 63 **Morken T**, Bohov P, Skorve J, Ulvik R, Aukrust P, Berge RK, Livden JK. Anti-inflammatory and hypolipidemic effects of the modified fatty acid tetradecylthioacetic acid in psoriasis--a pilot study. *Scand J Clin Lab Invest* 2011; **71**: 269-273 [PMID: 21338276 DOI: 10.3109/00365513.2011.559552]
- 64 **Lee JH**, Kim HJ, Han KD, Kim HN, Park YM, Lee JY, Park YG, Lee YB. Cancer risk in 892 089 patients with psoriasis in Korea: A nationwide population-based cohort study. *J Dermatol* 2019; **46**: 95-102 [PMID: 30443930 DOI: 10.1111/1346-8138.14698]
- 65 **Fiorentino D**, Ho V, Lebwohl MG, Leite L, Hopkins L, Galindo C, Goyal K, Langhoff W, Fakharzadeh S, Srivastava B, Langley RG. Risk of malignancy with systemic psoriasis treatment in the Psoriasis Longitudinal Assessment Registry. *J Am Acad Dermatol* 2017; **77**: 845-854.e5 [PMID: 28893407 DOI: 10.1016/j.jaad.2017.07.013]
- 66 **Pouplard C**, Brenaut E, Horreau C, Barnette T, Misery L, Richard MA, Aractingi S, Aubin F, Cribier B, Joly P, Jullien D, Le Maître M, Ortonne JP, Paul C. Risk of cancer in psoriasis: a systematic review and meta-analysis of epidemiological studies. *J Eur Acad Dermatol Venereol* 2013; **27** Suppl 3: 36-46 [PMID: 23845151 DOI: 10.1111/jdv.12165]
- 67 **Yang G**, Li S, Yang Y, Yuan L, Wang P, Zhao H, Ho CT, Lin CC. Nobiletin and 5-Hydroxy-6,7,8,3',4'-pentamethoxyflavone Ameliorate 12- O-Tetradecanoylphorbol-13-acetate-Induced Psoriasis-Like Mouse Skin Lesions by Regulating the Expression of Ki-67 and Proliferating Cell Nuclear Antigen and the Differentiation of CD4⁺ T Cells through Mitogen-Activated Protein Kinase Signaling Pathways. *J Agric Food Chem* 2018; **66**: 8299-8306 [PMID: 30058806 DOI: 10.1021/acs.jafc.8b02524]
- 68 **Kanemaru K**, Matsuyuki A, Nakamura Y, Fukami K. Obesity exacerbates imiquimod-induced psoriasis-like epidermal hyperplasia and interleukin-17 and interleukin-22 production in mice. *Exp Dermatol* 2015; **24**: 436-442 [PMID: 25777289 DOI: 10.1111/exd.12691]
- 69 **Arbiser JL**, Nowak R, Michaels K, Skabytska Y, Biedermann T, Lewis MJ, Bonner MY, Rao S, Gilbert

- LC, Yusuf N, Karlsson I, Fritz Y, Ward NL. Evidence for biochemical barrier restoration: Topical solenopsin analogs improve inflammation and acanthosis in the KC-Tie2 mouse model of psoriasis. *Sci Rep* 2017; **7**: 11198 [PMID: 28894119 DOI: 10.1038/s41598-017-10580-y]
- 70 **Ottman N**, Smidt H, de Vos WM, Belzer C. The function of our microbiota: who is out there and what do they do? *Front Cell Infect Microbiol* 2012; **2**: 104 [PMID: 22919693 DOI: 10.3389/fcimb.2012.00104]
- 71 **Zeng J**, Luo S, Huang Y, Lu Q. Critical role of environmental factors in the pathogenesis of psoriasis. *J Dermatol* 2017; **44**: 863-872 [PMID: 28349593 DOI: 10.1111/1346-8138.13806]
- 72 **Alekseyenko AV**, Perez-Perez GI, De Souza A, Strober B, Gao Z, Bihan M, Li K, Methé BA, Blaser MJ. Community differentiation of the cutaneous microbiota in psoriasis. *Microbiome* 2013; **1**: 31 [PMID: 24451201 DOI: 10.1186/2049-2618-1-31]
- 73 **Baker BS**, Laman JD, Powles A, van der Fits L, Voerman JS, Melief MJ, Fry L. Peptidoglycan and peptidoglycan-specific Th1 cells in psoriatic skin lesions. *J Pathol* 2006; **209**: 174-181 [PMID: 16493599 DOI: 10.1002/path.1954]
- 74 **Salem I**, Ramser A, Isham N, Ghannoum MA. The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. *Front Microbiol* 2018; **9**: 1459 [PMID: 30042740 DOI: 10.3389/fmicb.2018.01459]
- 75 **Oliveira Mde F**, Rocha Bde O, Duarte GV. Psoriasis: classical and emerging comorbidities. *An Bras Dermatol* 2015; **90**: 9-20 [PMID: 25672294 DOI: 10.1590/abd1806-4841.20153038]
- 76 **Scher JU**, Ubeda C, Artacho A, Attur M, Isaac S, Reddy SM, Marmon S, Neimann A, Brusca S, Patel T, Manasson J, Pamer EG, Littman DR, Abramson SB. Decreased bacterial diversity characterizes the altered gut microbiota in patients with psoriatic arthritis, resembling dysbiosis in inflammatory bowel disease. *Arthritis Rheumatol* 2015; **67**: 128-139 [PMID: 25319745 DOI: 10.1002/art.38892]
- 77 **Gueniche A**, Philippe D, Bastien P, Reuteler G, Blum S, Castiel-Higounenc I, Breton L, Benyacoub J. Randomised double-blind placebo-controlled study of the effect of *Lactobacillus paracasei* NCC 2461 on skin reactivity. *Benef Microbes* 2014; **5**: 137-145 [PMID: 24322879 DOI: 10.3920/BM2013.0001]
- 78 **Eppinga H**, Konstantinov SR, Peppelenbosch MP, Thio HB. The microbiome and psoriatic arthritis. *Curr Rheumatol Rep* 2014; **16**: 407 [PMID: 24474190 DOI: 10.1007/s11926-013-0407-2]
- 79 **Castelino M**, Eyre S, Upton M, Ho P, Barton A. The bacterial skin microbiome in psoriatic arthritis, an unexplored link in pathogenesis: challenges and opportunities offered by recent technological advances. *Rheumatology (Oxford)* 2014; **53**: 777-784 [PMID: 24067887 DOI: 10.1093/rheumatology/ket319]
- 80 **Bogdanos DP**, Smyk DS, Invernizzi P, Rigopoulou EI, Blank M, Pouria S, Shoenfeld Y. Infectome: a platform to trace infectious triggers of autoimmunity. *Autoimmun Rev* 2013; **12**: 726-740 [PMID: 23266520 DOI: 10.1016/j.autrev.2012.12.005]
- 81 **Turnbaugh PJ**, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. The human microbiome project. *Nature* 2007; **449**: 804-810 [PMID: 17943116 DOI: 10.1038/nature06244]
- 82 **Bogdanos DP**, Smyk DS, Rigopoulou EI, Sakkas LI, Shoenfeld Y. Infectomics and autoinfectomics: a tool to study infectious-induced autoimmunity. *Lupus* 2015; **24**: 364-373 [PMID: 25801879 DOI: 10.1177/0961203314559088]
- 83 **Thrastardottir T**, Love TJ. Infections and the risk of psoriatic arthritis among psoriasis patients: a systematic review. *Rheumatol Int* 2018; **38**: 1385-1397 [PMID: 29124396 DOI: 10.1007/s00296-017-3873-4]
- 84 **Benhadou F**, Mintoff D, Schnebert B, Thio HB. Psoriasis and Microbiota: A Systematic Review. *Diseases* 2018; **6** [PMID: 29865237 DOI: 10.3390/diseases6020047]
- 85 **Tan L**, Zhao S, Zhu W, Wu L, Li J, Shen M, Lei L, Chen X, Peng C. The *Akkermansia muciniphila* is a gut microbiota signature in psoriasis. *Exp Dermatol* 2018; **27**: 144-149 [PMID: 29130553 DOI: 10.1111/exd.13463]
- 86 **Batycka-Baran A**, Maj J, Wolf R, Szepietowski JC. The new insight into the role of antimicrobial proteins-alarmins in the immunopathogenesis of psoriasis. *J Immunol Res* 2014; **2014**: 628289 [PMID: 24901012 DOI: 10.1155/2014/628289]
- 87 **Yermekbayeva B**. Riloncept to improve artery function in patients with atherosclerosis. [accessed 2020 Feb 25]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine. Available from: <http://clinicaltrials.gov/show/NCT03594877> ClinicalTrials.gov Identifier: NCT03594877
- 88 **ProgenaBiome**. Riloncept to improve artery function in patients with atherosclerosis. [accessed 2020 Feb 25]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine. Available from: <http://clinicaltrials.gov/show/NCT04099979> ClinicalTrials.gov Identifier: NCT04099979
- 89 **Flint HJ**, Scott KP, Louis P, Duncan SH. The role of the gut microbiota in nutrition and health. *Nat Rev Gastroenterol Hepatol* 2012; **9**: 577-589 [PMID: 22945443 DOI: 10.1038/nrgastro.2012.156]
- 90 **Kragsnaes MS**, Kjeldsen J, Horn HC, Munk HL, Pedersen FM, Holt HM, Pedersen JK, Holm DK, Glerup H, Andersen V, Fredberg U, Kristiansen K, Christensen R, Ellingsen T. Efficacy and safety of faecal microbiota transplantation in patients with psoriatic arthritis: protocol for a 6-month, double-blind, randomised, placebo-controlled trial. *BMJ Open* 2018; **8**: e019231 [PMID: 29703851 DOI: 10.1136/bmjopen-2017-019231]
- 91 **Langan EA**, Griffiths CEM, Solbach W, Knobloch JK, Zillikens D, Taçi D. The role of the microbiome in psoriasis: moving from disease description to treatment selection? *Br J Dermatol* 2018; **178**: 1020-1027 [PMID: 29071712 DOI: 10.1111/bjd.16081]



Published By Baishideng Publishing Group Inc
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

