# Altered Gut Microbiota Contributes to the Onset of Psoriasis and Autoimmune Diseases

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## INTRODUCTION

- Psoriasis is an autoimmune disease that leads to scaly, itchy areas of the body.
- The underlying pathomechanism of psoriasis remains indefinite
- WBCs interact with dendritic cells, macrophages, and keratinocytes, resulting in the overproduction of secreted cytokines affecting hyperproliferation of skin cells
- Psoriasis affects patients beyond the skin's barrier, as they are at increased risk of developing numerous autoinflammatory/autoimmune diseases
- Dysbiosis can be injurious to the homeostasis and longevity of the gut lumen
- To understand the relation of dysbiosis in the microbiota, this review found that it is important to consider the immune response of the body.
- Healthy skin and psoriatic skin vary in their bacterial composition.
- Psoriatic lesions have an abundance of "bacterial load," compared to controls.
- Knowing there is connection lies in autoimmune diseases and the gut microbiota is immense, as therapies, such as FMTs and probiotic administration which can restore the bacteria in the gut.

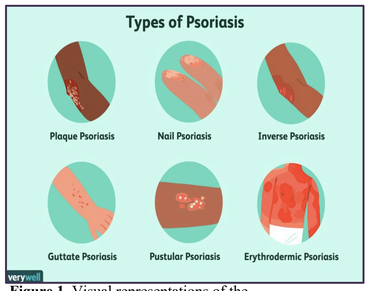


**Figure 1.** Visual representations of the various types of psoriasis

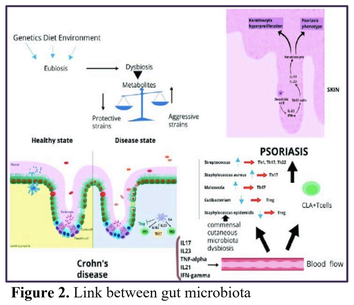


**Figure 2.** Link between gut microbiota dysbiosis, immune response dysregulation, Crohn's disease and psoriasis.

## THE DEVELOPMENT OF DISEASES SURPASSING THE GI TRACT

- Psoriasis affects more than just the skin
- Patients are often susceptible to joint inflammation, which is associated with many diseases affecting different organ systems
- Hyperlipidemia, hypertension, coronary artery disease, type 2 diabetes, and increased body mass index were observed in a study of psoriasis patients
- Coronary plaques are more likely to develop in individuals with psoriasis compared to control patients

| | Twin Pairs[b] | | | | | |
|---|---|---|---|---|---|---|
| | All (N = 449) | | Monozygotic (n = 179) | | Dizygotic (n = 270) | |
| Risk Factor | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Model 1[c] | | | | | | |
| BMI | 1.52 (0.92-2.53) | .10 | 1.26 (0.48-3.34) | .69 | 1.64 (0.90-2.99) | .11 |
| Type 2 diabetes mellitus | 1.04 (0.54-2.03) | .90 | 1.72 (0.55-5.34) | .35 | 0.70 (0.28-1.75) | .45 |
| Model 2[d] | | | | | | |
| Obesity | 1.92 (1.06-3.46) | .03 | 1.43 (0.50-4.07) | .50 | 2.13 (1.03-4.39) | .04 |
| Type 2 diabetes mellitus | 1.01 (0.52-1.97) | .97 | 1.66 (0.53-5.19) | .38 | 0.70 (0.28-1.75) | .45 |

**Table 1.** This population-based twin study found that psoriasis is strongly associated with type 2 diabetes, body mass index, and obesity.

## THE GUT-SKIN AXIS

- The relationship between the cutaneous and intestinal microbiome
- The gut microbiome describes the collection of all microbes, such as fungi, bacteria, and viruses and their genes
- Includes commensal, symbiotic and pathological bacteria, archaea, and eukaryote population in the body
- Makeup of the microbiome starts to establish after birth and stabilizes around age 2
- Diet, lifestyle, medical conditions, and other factors contribute to microbial makeup
- Dysbiosis is associated to the immune response of the body

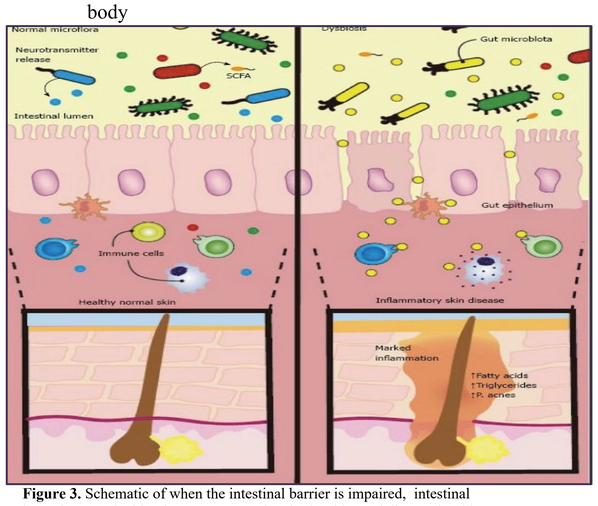


**Figure 3.** Schematic of when the intestinal barrier is impaired, intestinal bacteria enter the bloodstream, accumulate in the skin, and disrupt the skin microbiome.

## DYSBIOSIS IN THE GUT

- Skin, joint, and gastrointestinal inflammation relationship exists as demonstrated by psoriasis, psoriatic arthritis, and IBS co-occuring together
- Studies concerning the gut microbiota composition and its' role in disease pathogenesis demonstrate significant modifications in psoriatic patients
- Microorganism levels differ in psoriasis lesions

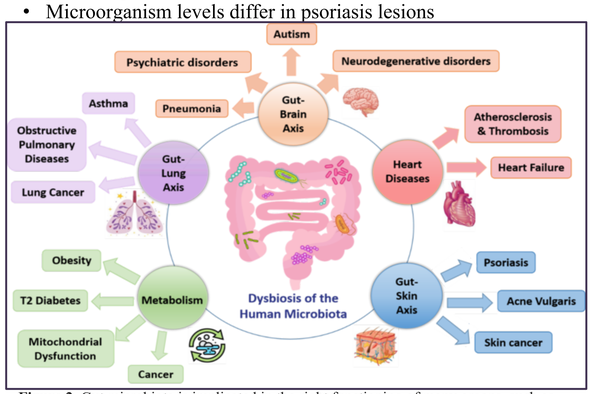


**Figure 2.** Gut microbiota is implicated in the right functioning of many organs, such as lungs, kidneys, liver, heart and brain. Any disruption of the homeostasis results in the malfunctioning of these affected organs, and the progression of many related diseases

## MICROBIAL COMMUNITIES

- Intestinal microbiome are Gram-negative and Gram-positive anaerobic bacteria
- Bacteroidetes and Firmicutes secrete (SCFAs), the end products of anaerobic fermentation
- Alterations in the "normal" cause the exacerbation of many diseases

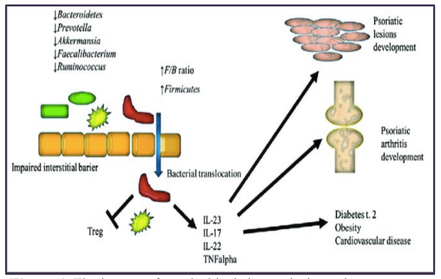


**Figure 4.** The impact of gut dysbiosis in psoriasis on the development of psoriatic lesions, psoriatic arthritis, and psoriasis comorbidities (F/B ratio -Firmicutes-to-Bacteroidetes ratio; Treg - T regulatory cells; TNFalpha -tumor necrosis factor alpha).

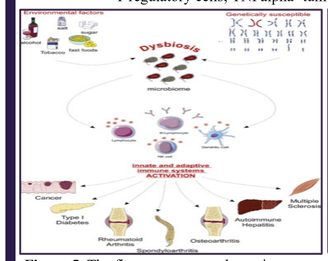


**Figure 5.** The figure represents the main factors involved in dysbiosis of the gut microbiome.

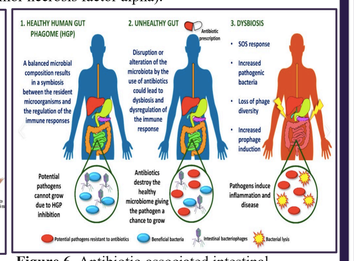


**Figure 6.** Antibiotic-associated intestinal dysbiosis.

## THERAPIES

- Reshaping the composition of the gut microbiome may be a promising approach as it has been supported by numerous experimental data
- Methods include diet alterations, specifically, mannose
- Herbal products such as polyphenols, berberine and metformin
- The administration of probiotics
- Drugs targeting IL-23 and IL-17 block immune signaling pathways, resulting in cytokine imbalance
- Fecal Microbiota Transplants (FMTs)

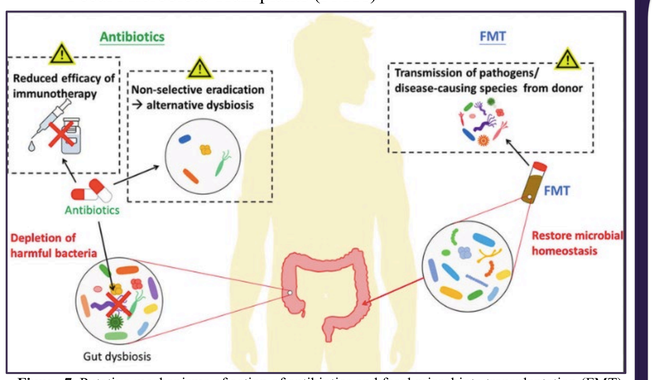


**Figure 7.** Putative mechanisms of action of antibiotics and fecal microbiota transplantation (FMT) and their associated safety concerns. Gut dysbiosis often leads to the development of various diseases, therefore antibiotics and fecal microbiota transplantation are viable approaches to reverse dysbiosis and restore homeostasis. Antibiotics are effective in eradicating the pathogenic or harmful bacteria, but its non-selective antimicrobial actions may lead to another state of dysbiosis by killing the commensal microflora.

## CONCLUSIONS & FUTURE DIRECTIONS

- Autoimmune diseases are a consequence of gut dysbiosis. This information can provide future therapies for improving treatment
- Modulation of the intestinal microbiota is essential for treating autoimmune diseases, including psoriasis
- Probiotics may be a promising therapeutic but are limited. Not all microbial organisms are available as probiotics
- Little information about interactions, dosage amounts, and duration of treatment
- FMTs are efficient and a direct solution for the gastrointestinal tract to change the microbial bacteria composition
- Further research on FMTs should include a fast and effective way of identifying fecal donors

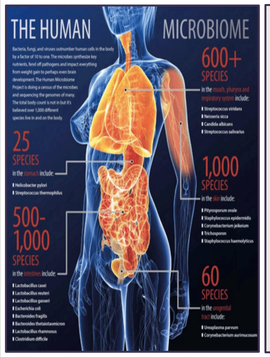


**Figure 8.** The microbiome is the assemblage of microorganisms living on and within our body, such as our gut.

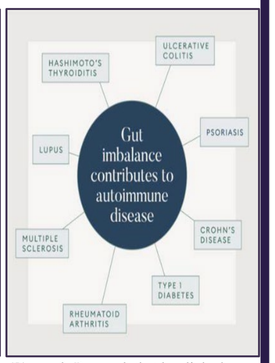


**Figure 9.** Research that has linked autoimmune issues to the health of the gut microbiome

## REFERENCES

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