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Gut Microbiome and Psoriasis - A Possible Link to be explored

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Letter to Editor

Dear editor. Just over 30 years ago, the US National Center for Human Genome Research, today known as the National Human Genome Research Institute, was established in the United States, with the ambitious goal of sequencing all 3 million nitrogenous bases in the human genome. In simple terms, it represented the determination of the exact order of DNA bases, determining the segments of human genetic material from blood samples from healthy individuals [1]. More than 2000 researchers from many countries participated in the project in a global joint effort (Universities and Research Centers, mostly from the USA, United Kingdom, France, Germany, Japan, and China, which represented the International Human Genome Sequencing Consortium). After just over 3 years from the date of the first publication of the Human Genome Project, ahead of the initial schedule, in October 2003 its final version was published, allowing the mapping of more than 20 thousand genes, representing more than 90% of human genetic material (technological ceiling at the time) [1-3]. The Human Genome project is one of the greatest scientific achievements in history and allowed the study of human DNA and its various implications. Furthermore, it boosted science and technology in different aspects, contributing to the evolution of knowledge in large areas [1,2,4] However, following its publication, some important aspects were highlighted. 99% of human genetic material is identical between people. Would only the remaining 1% be responsible for all the diversity and individuality of human beings? [5].

In parallel, we human beings share our body (organism) with trillions of microorganisms. For every human cell in our body, there are at least 10x more bacteria that cohabit with us, sharing space and contributing to our balance and functioning. With these microorganisms, we evolve, creating a complex, adaptive, dynamic ecosystem in constant physiological interaction [6]. Perhaps the totality of human genes mapped did not represent the complexity of our organism and its functioning. As noted above, humans are a holobiont, whose definition would be a grouping of a host and many other species that live in it and together they form a distinct ecological unit. We have 100 to 150 times more bacterial genes than human genes and it is estimated that around 99% of all genetic material transcribed in our organism comes from bacteria. Julian Davies, in 2001, suggested that, despite the sequencing of the human genome being a memorable advance, it would be essential to identify and understand the synergism between humans and microorganisms living together.6 In this way, a complete Understanding would require the most complete inventory possible of the genome of the microorganisms we harbor. As a result, the Human Microbiome project began in 2007, aiming to access information from our hologenome (human genome plus the genome of microorganisms) [7-9]. The microbiome can be defined as a commensal, symbiotic, and pathogenic ecological community of microorganisms that share space with their human hosts (Lederberg and McCray 2001) [7].

In 2010, the Metagenomes of Human Intestinal Tract (MetaHIT) published its findings about the intestinal microbiome of 124 healthy European individuals. Two years later, the Human Microbiome Project (HMP) added findings from 242 healthy American adults. Together, these were the studies that sequenced the "healthy" human microbiome and still constitute important databases and controls today, currently with samples from

around 2000 individuals from different continents [10-12]. There are three main sites: intestine, oral cavity, and skin; The human gastrointestinal tract accounts for around 95% of the entire microbiome, therefore being the most representative site [7]. There is a continuous interaction between the intestinal microbiome and the immune system. The term intestinal dysbiosis is dynamic and its understanding has evolved with a better understanding of the microbiome, however, simply, it can be defined as a change in the "architecture" of the complex network of microorganisms that inhabit the gastrointestinal tract. This change determines an "imbalance", with a reduction in so-called tolerogenic strains and an expansion of pro-inflammatory bacteria and yeasts. It is therefore postulated that intestinal dysbiosis may determine an alteration in immunological reactivity, contributing to the establishment of inflammatory diseases [8,9].

Certain patterns of intestinal dysbiosis determine a decrease in the mucus layer, dysregulation of tight junctions, qualitative and quantitative defects in Paneth cells, and increased permeability of the intestinal mucosa, promoting greater exposure of the host by exposing it to a series of antigens, especially bacterial (predominantly liposaccharides, components of the outer membrane of Gram-negative bacteria – LPS). There is a decrease in the population of regulatory T lymphocytes and an increase in the differentiation and expansion of T Helper 1 (TH1) and TH17 lymphocytes through the synthesis and secretion of interleukin-17 (IL17) and IL 23, in addition to a decrease in the production of immunoglobulin A (IgA) secretory and short-chain fatty acids. In parallel, this increase in intestinal permeability allows greater bacterial translocation, with the dissemination of this hypothetical antigenic trigger, inducing inflammation in different sites, including the skin and joints, the reason for the study [13].

Psoriasis is a chronic, inflammatory, immune-mediated, systemic disease that primarily affects the skin and joints [14-17]. It is relatively common, occurring in around 2 to 3% of the world's population, and may vary according to ethnicity and geographic location. In Brazil, a prevalence of 1.3% in the general population is estimated. Psoriatic disease, on the skin, manifests itself as erythematous and scaly lesions, which can affect the joints, in a heterogeneous way, but with erosive potential, including pain and permanent damage [17-21] The etiology of psoriasis is complex and not completely understood to this day. It appears to be determined primarily by an aberrant immune response, influenced by genetic factors involved with a pre-disposition for the development of the disease phenotype, associated with various environmental stimuli described as possible triggering and/or aggravating mechanisms of the disease [22] This immunological hyperactivation determines a persistent inflammatory state, not restricted to the skin. On the contrary, it is responsible for a growing number of comorbidities associated with psoriatic diseases, such as metabolic syndrome (obesity, hypertension, dyslipidemia, and diabetes), hepatic steatosis, and non-alcoholic steatohepatitis; cardio and cerebrovascular disease; inflammatory bowel disease, mood disorders, and cancer [23-25].

Thereby, the innate and adaptive immune systems are activated in a disorderly and persistent manner in psoriasis [14-17] Different stimuli determine the activation of antigen-presenting dendritic cells present in the epidermis and/or in the tissue and synovial space. These activated cells migrate through the lymphatic system to the regional lymph node, presenting the antigen to the naïve T lymphocyte. Once this antigen is recognized, the lymphocyte can be activated, triggering a sequence of reactions that allow the release of several cytokines, especially interleukins (IL) 12 and 23, already secreted by the presenting cells. Such interleukins are decisive for the differentiation of naïve T lymphocytes into T Helper (TH) 1 and TH 17 lymphocytes, which become the effector lymphocyte lineages after migrating to the target tissues (skin and joints). In the target tissue, TH1 mainly produces tumor necrosis factor-alpha, from English tumor necrosis factor (TNF) alpha and TH17 IL-17. Both determine dermal and synovial inflammation; epidermal differentiation and proliferation, polymorphonuclear chemotaxis, induction of apoptosis, neo angiogenesis, cartilage destruction, and bone erosion. The presence of TNF-alpha and IL-17, produced not only by cells of the adaptive immune system but also innate (naive T lymphocytes, mast cells, neutrophils) also contributes to the synthesis and exaggerated secretion of other pro-inflammatory cytokines (IL-1, IL-2, IL-6, IL-8, IL12, IL-23, interferon-gamma, transforming growth factor alpha and beta, macrophage and granulocyte colony-stimulating factor contribute, in addition to inflammation, to perpetuating the inflammatory process, justifying the chronic course of the disease [14,17,22,26]. The fact is that despite the elucidation of the inflammatory immunological pathways that determine the disease, it has not yet been possible to accurately determine the initiating factor of this immunological hyperactivation. What is the trigger for the activation of antigen-presenting dendritic cells? What determines antigen recognition? What plays the role of antigen? Which environmental antigen? If it is a self-antigen, at what point does it start to be recognized and activated with a non-selfie or non-self-antigen, triggering activation?

In brief research in different scientific databases and even in the so-called "lay media" (widely circulated), it is clear that there is a growing interest in the microbiome, its different sites, and its influence on inflammatory, immune-mediated, and autoimmune diseases [27-30] Recent studies relate, in the context of dysbiosis, greater production of microbial metabolites, such as short-chain fatty acids, which are capable of inducing epigenetic modifications through changes in DNA methylation, histone variations, and the expression of micro-RNAs., with potential implications regarding immunological homeostasis and greater susceptibility to autoimmune or immune-mediated phenomena, including psoriatic disease [31-33]. This data adds to the concept that autoimmunity is linked to increased gut permeability. Proof-of-concept studies, involving experimental models of spondyloarthritis, with arthritis, enthesitis, dactylitis, and psoriasiform skin lesions, showed that rats raised in a sterile environment did not develop the disease. Likewise, the use of broad-spectrum antibiotics

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showed a protective effect. On the other hand, the use of prebiotics and probiotics contributed to the immunological inflammatory process, worsening the disease phenotype [34-38] In this context, evidence also showed, in animal models, intestinal dysbiosis inducing activation of the IL23, TH17, and IL17 pathways [9].

The first evidence linking gastrointestinal inflammation, microbiota alteration, and spondyloarthritis was published around 2010. With the advancement of high-throughput genetic sequencing techniques, we watched a real boost in the field of microbiomes and their influence on human homeostasis, inflammation, and autoimmunity [39,49]. Scher and collaborators, in 2015, using high-throughput sequencing of the 16S ribosomal gene (the most widely used technique in this field of study, also used in our laboratory and line of research), studied 31 patients with psoriatic disease, of which 16 had psoriatic arthritis em 15 with plaque psoriasis; comparing them with 17 healthy controls [41,42] In concept, the more diverse a microbiome is, the more resilient and healthy the microbiome will be [8]. They demonstrated a decrease in gut microbiome diversity e among patients with psoriasis. In parallel, they identified decreased expression of the genera Akkermansia, Ruminococcus, Pseudobutyrivibrio, Parabacteroides, Alistipes, and Coprococcus in patients with psoriatic disease. When comparing patients with and without arthritis, a reduction in Firmicutes, Clostridiales, and Verrucomicrobiales was noted at the phylum level, in addition to an increase in Bacteroidetes in patients with established joint disease. The authors also showed, at the gender level, a marked decrease in Akkermansia, Ruminoccocus, and Pseudobutyvibrio among patients with psoriatic arthritis, with a pattern of intestinal dysbiosis resembling that found in inflammatory bowel disease [41,42].

Microbiome deserves our attention, as there is an established link between dysbiosis and autoimmunity, including psoriasis. The field of study must advance, seeking to understand whether the dysbiosis patterns found are cause or effect. If effect, what would be the magnitude of this effect? But one thing is clear and exciting: microbiome offers different opportunities for intervention through diet, prebiotics and probiotics, pre-treatment analysis, prognosis, and even microbiome modulation and transplantation. Again, there are still some key points to be confirmed with prospective studies. We established a project to better understand the intestinal microbiome of patients with severe psoriatic disease, within a national perspective (Brazil), trying to assess: Is there a difference in the intestinal microbiome of patients with moderate to severe psoriatic disease, followed by a state reference outpatient clinic, when compared to patients without psoriatic disease? With this objective, we carried out a case-control study, with 60 individuals, 30 patients, and 30 controls without psoriatic disease. Collection has been completed and the data is being analyzed for future publication.

References

1. Green D, Watson JD, Collins FS (2015) Twenty-five years of big biology. Nature 526(7571): 29-31.
2. (2022) National Human Genome Research Institute. The Human Genome Project.
3. Lander ES, Linton LM, Nusbaum C, Zodi MC, Baldwin J, et al. (2001) Initial sequencing and analysis of the human genome. NaturE 409(6822): 860-921.
4. Gibbs RA (2020) The Human Genome Project changed everything. Nat Rev Genet 21(10): 575-576.
5. Abecasis GR, Altshuler D, Auton A, Brooks LD, Durbin RM, et al. (2010) A map of human genome variation from population-scale sequencing. Nature 467(7319): 1061-1073.
6. Davies J (2001) In a map of human life, count the microbes, too. Science 291(5512): 2316.
7. Peterson J, Garges S, Giovanni M, Mcinnes P, Wang L, et al. (2009) The NIH Human Microbiome Project. Genome Res 19(12): 2317-2323.
8. Tlaskalova-Hogenova H, Stepankova R, Kozakova H, Hudcovic T, Vannucci L, et al. (2011) The role of gut microbiota (commensal bacteria) and the mucosal barrier in the pathogenesis of inflammatory and autoimmune diseases and cancer: contribution of germ-free and gnotobiotic animal models of human diseases. Cell Mol Immunol 8(2):110-120.
9. Zákostelská Z, Málková J, Klimesová K, Rossmann P, Hornová M, et al. (2016) Intestinal microbiota promotes psoriasis-like skin inflammation by enhancing TH17 response. PLoS One 11(7): e0159539.
10. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, et al. (2010) A human gut microbial gene catalogue was established by metagenomic sequencing. Nature 46(7285): 59-65.
11. Human Microbiome Project Consortium (2012) Structure, function, and diversity of the healthy human microbiome. Nature 486(7402): 207-214.
12. Lloyd-Price J, Abu-Ali G, Huttenhower C (2016) The healthy human microbiome. Genome Med 8(1): 51.
13. Chang JT (2020) Pathophysiology of Inflammatory Bowel Diseases. New Eng J Med 383(27): 2652-2664.
14. Carneiro, Sueli Coelho da Silva. Psoríase: mecanismos de doença e implicações terapêuticas / Sueli Coelho da Silva Carneiro. - São Paulo, 2007. Tese (livre-docência) - Faculdade de Medicina da Universidade de São Paulo. Departamento de Dermatologia.
15. Carneiro S, Ramos-e-Silva M Carneiro S, Ramos-e-Silva M Introdução; Loureiro MCAC, Carneiro S (2018) Epidemiologia; Accioly-Filho JW. Fatores etiológicos, de risco, desencadantes e agravantes da Psoríase. In: Fundamentos em Psoríase. Rio de Janeiro: Atheneu.
16. Nestle FO, Kaplan DH, Baker J (2009) Psoriasis. N Engl J Med 361(5): 469-509.
17. Boehncke WH, Schön MP (2015) Psoriasis. Lancet 386(9997): 983-994.
18. Christophers E (2001) Psoriasis: epidemiology and clinical spectrum. Clin Exp Dermatol 26(4): 314-320.
19. Rachakonda TD, Schupp CW, Armstrong AW (2014) Psoriasis prevalence among adults in the United States. J Am Acad Dermatol 70(3): 512-516.

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20. Michalek IM, Loring B, John SM (2017) A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol 31(2): 205-212.

21. Romiti R, Arnone M, Menter A, Miot HA (2017) Prevalence of psoriasis in Brazil - a geographical survey. Int J Dermatol 56(8): e167-e168.

22. Hawkes JE, Chan TC, Krueger JG (2017) Psoriasis pathogenesis and the development of novel target immune therapies. J Allergy Clin Immunol 140(3): 645-653.

23. Arnone M, Takahashi MDF, Carvalho AVE, Bernardo WM, Bressan AL, et al. (2019) Plaque psoriasis diagnostic and treatment guidelines. An Bras Dermatol 94(2 Suppl 1): S76-S107.

24. Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, et al. (2017) Psoriasis and comorbid diseases: epidemiology. J Am Acad Dermatol 76(3): 377-390.

25. Gelfand JM, Troxel AB, Lewis JD, Kurd SK, Shin DB, et al. (2007) The risk of mortality in patients with psoriasis: results from a population-based study. Arch Dermatol 143(12): 1493-1499.

26. Hugh JM, Weinberg JM (2018) Update on the pathophysiology of psoriasis. Cutis 102(5S): 6-12.

27. Eppinga H, Konstantinov SR, Peppelenbosch MP, Thio HB (2014) The microbiome and psoriatic arthritis. Curr Rheumatol Rep 16(3): 407.

28. Van Praet L, Van Den Bosch F, Mielants H, Elewaut D (2011) Mucosal inflammation in spondylarthritides: past, present, and future. Curr Rheumatol Rep 13(5): 409-415.

29. Sherlock JP, Joyce-Shaikh B, Turner SP, Chao CC, Sathe M, Grein J, et al. (2012) IL-23 induces spondyloarthropathy by acting on ROR-gammat+ CD3+CD4-CD8- entheseal resident T cells. Nat Med 18(7): 1069-1076.

30. Van Praet L, Van Den Bosch FE, Jacques P, Carron P, Jans L, et al. (2013) Microscopic gut inflammation in axial spondyloarthritis: a multiparametric predictive model. Ann Rheum Dis 72(3): 414-417.

31. Cuevas-Sierra A, Ramos-Lopez O, Riezu-Boj J, Milagro FI, Martinez JA (2019) Diet, gut microbiota, and obesity: links with host genetics and epigenetics and potential applications. Adv Nutr 10(Suppl 1): S17-S30.

32. Murdaca G, Greco M, Negrini S, Marco Casciaro, Gangemi S (2021) The role of skin and gut microbiome and epigenetic modifications in skin-autoimmune disorders. Curr Mol Med 21(4): 283-290.

33. Roszkiewickz M, Dopytalska K, Szymanska E, Jakimiuk A, Walecka I (2020) Environmental risk factors and epigenetic alternations in psoriasis. Ann Agric Environ Med 27(3): 335-342.

34. Hammer RE, Maika SD, Richardson JA, Tang JP, Taurog JD (1990) Spontaneous inflammatory disease in transgenic rats expressing HLA-B27 and human beta 2m: an animal model of HLA-B27-associated human disorders. Cell 63(5): 1099-1112.

35. Taurog JD, Richardson JA, Croft JT, Simmons WA, Zhou M, et al. (1994) The germ-free state prevents the development of gut and joint inflammatory disease in HLA-B27 transgenic rats. J Experiment Med 180(6): 2359-2364.

36. Rath HC, Herfarth HH, Ikeda JS, Hamm TE, Balish E, et al. (1996) Normal luminal bactéria, especially Bacteroides species, mediate chronic colitis, gastritis, and arthritis in HLA-B27/human beta2 microglobulin transgenic rats. J Clin Invest 98(4): 945-953.

37. Ruutu M, Thomas G, Steck R, Mariapia AD, Martin SZ, et al. (2012) Beta-glucan triggers spondyloarthritis and Crohn's disease-like ileitis in SKG mice. Arthritis and Rheumatism 64(7): 2211-22.

38. Rehaume LM, Mondot S, Aguirre de Carcer D, Jared V, Helen B, et al. (2014) ZAP-70 genotype disrupts the relationship between microbiota and host, leading to spondyloarthritis and ileitis in SKG mice. Arthritis Rheumatol 66(10): 2780-2792.

39. Stoll ML (2015) Gut microbes, immunity, and spondyloarthritis. Clin Immunol 159(2): 134-142.

40. Stebbings S, Munro K, Simon MA, Tannock G, Harmsen H, et al. (2002) Comparison of the fecal microflora of patients with ankylosing spondylitis and controls using molecular methods of analysis. Rheumatology (Oxford) 41(12):1395-401.

41. Scher JU, Ubeda C, Artacho A, Attur M, Isaac M, et al. (2015) Decreased bacterial diversity characterizes the altered gut microbiota in patients with psoriatic arthritis, resembling dysbiosis in inflammatory bowel disease. Arthritis Rheumatol 67(1): 128-139.

42. Eppinga H, Sperna Weiland CJ, Thio HB, Van Der Woude CJ, Nijsten TE, et al. (2016) Similar depletion of protective faecalibacterium prausnitzii in psoriasis and inflammatory bowel disease, but not in hidradenitis suppurativa. J Crohns Colitis 10(9): 1067-1075.

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