Review

Microbiome, Autoimmune Diseases and HIV Infection: Friends or Foes?

Chiara Pellicano 1, Giorgia Leodori 1, Giuseppe Pietro Innocenti 2, Antonietta Gigante 1 and Edoardo Rosato 1,*

1 Department of Translational and Precision Medicine-Scleroderma Unit, Sapienza University of Rome, 00185 Rome, Italy; chiara.pellicano@uniroma1.it (C.P.); giorgia.leodori@uniroma1.it (G.L.); antonietta.gigante@uniroma1.it (A.G.)
2 Department of Public Health and Infectious Diseases, Sapienza University of Rome, 00185 Rome Italy; giuseppe.innocenti@uniroma1.it

* Correspondence: edoardo.rosato@uniroma1.it; Tel.: +39-06-4997-2040

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Abstract: Several studies highlighted the importance of the interaction between microbiota and the immune system in the development and maintenance of the homeostasis of the human organism. Dysbiosis is associated with proinflammatory and pathological state-like metabolic diseases, autoimmune diseases and HIV infection. In this review, we discuss the current understanding of the possible role of dysbiosis in triggering and/or exacerbating symptoms of autoimmune diseases and HIV infection. There are no data about the influence of the microbiome on the development of autoimmune diseases during HIV infection. We can hypothesize that untreated patients may be more susceptible to the development of autoimmune diseases, due to the presence of dysbiosis. Eubiosis, re-established by probiotic administration, can be used to reduce triggers for autoimmune diseases in untreated HIV patients, although clinical studies are needed to evaluate the role of the microbiome in autoimmune diseases in HIV patients.

Keywords: microbiota; autoimmune diseases; HIV; eubiosis; dysbiosis

1. Introduction

The human microbiome is the aggregate of all microbiota, encompassing bacteria, archaea, fungi, protists and symbionts, that reside on or within human tissues and biofluids [1]. The species of bacteria that are most characterized in the microbiome, conversely, are the viruses and fungi. The characterization of the microbiome was primarily made by cell culture. Recently the microbiome was evaluated by DNA recombinant techniques [1]. Several studies highlighted the importance of the interaction between microbiota and the immune system in the development and maintenance of the homeostasis of the human organism [2–4]. The microbiome is influenced by diet [5,6], aging [6–8] and lifestyle and changes during human life in the type and number of bacteria [7]. The greatest conditioning factor for gut microbiota composition, diversity and richness seems to be the diet [5]. Over time, eating habits have changed—the diet is poor in carbohydrates and fibers and rich in fat and sugar and this has altered the balance of the bacterial population [5,9]. It has been seen that a diet rich in animal fats allows the development of Bacteroides, while a diet rich in carbohydrates or plant-based foods and low in animal fats favors the growth of Prevotella [5]. However, high Prevotella has also been described in inflammatory states such as rheumatoid arthritis (RA) [10] and has been linked with obesity [11] and insulin resistance [12]. During eubiosis, a healthy and balanced state marked by high diversity and the abundance of microbial populations, gut microbiota is mainly composed of Actinobacteria, Bacteroidetes, Proteobacteria and Firmicutes. Most of these are crucial for the synthesis...
of vitamins, the degradation of xenobiotics and sterols and the deconjugation of biliary acids [13]. Furthermore, microbiota can inhibit pathogens’ epithelial adhesion, colonization and translocation, competing for adhesion sites and nutrients, releasing bacteriocins and stimulating neutrophil migration and functions, IgA secretion and T cells maturation and differentiation [13–18]. Short-chain fatty acids (SCFAs), mainly butyrate, acetate and propionate, are produced by gut microbiota through the fermentation of fibers. They represent a source of energy for colonocytes and promote cellular reparation and differentiation, protecting the integrity of the intestinal barrier [19–21]. Moreover, SCFAs promote the differentiation of T cells into T regulatory (Treg) cells and inhibit inflammasome activation, leading to a tolerogenic phenotype, through the modifications of histone deacetylation and by the activation of metabolite-sensing G proteins-coupled receptors [22–25].

Recent studies have shown that SCFAs can promote the development of some autoimmune diseases, favoring the release of interleukins (i.e., IL10) and reducing the inflammatory response [26–28], metabolic diseases and neurological diseases [29]. In particular, SCFAs are able to modulate immune cell chemotaxis, reactive oxygen species (ROS) release as well as cytokine release. Zhang et al. showed an improvement of gastrointestinal symptoms in a mice model of colitis after the administration of butyrate by increasing Treg cells [30]. Treg cells are abundant in the lamina propria of the gut and microbiota might modulate their functions through IL10 and TGFbeta production, reducing inappropriate inflammatory responses [31,32]. It has been demonstrated that tryptophan-derived metabolites, produced by gut microbiota and the active aryl hydrocarbon receptor (AHR) on innate lymphoid cells (ILCs), induce the production of IL22 that provides colonization resistance to *Candida albicans* [33,34]. It has been hypothesized that there is a possible association between any alteration of the human microbiome (dysbiosis) and several diseases. Dysbiosis is associated with proinflammatory and pathological state-like obesity [11], HIV infection and such autoimmune diseases as Type 1 diabetes (T1D) [35–60], RA [61–69], systemic lupus erythematosus (SLE) [70–74], Sjögren’s syndrome (SS) [75–78], systemic sclerosis (SSc) [79,80], inflammatory bowel disease (IBD) [81–91], coeliac disease [92], autoimmune liver diseases [93–103], Behcet’s disease (BD) [104–107] and psoriasis vulgaris [108–113]. Dysbiosis, induced by several environmental factors (i.e., virus infections, drugs, diet), alters the fragile balance between microbiota and host, so there may be the development of autoimmune disease [2,114]. Table 1 summarizes the main alterations of the gut microbiota, found in the course of autoimmune diseases and HIV infection, and the main underlying pathogenetic mechanisms.

| Disease                        | Microbiota Alteration | Mechanism                      | References                              |
|-------------------------------|-----------------------|--------------------------------|-----------------------------------------|
| Type 1 Diabetes Mellitus      | ↑ *Bacteroidetes*/Firmicutes ratio, D. inersis, G. sanguinis, B. longum ↓ B. adolescentis, Lactobacillus | ↑ intestinal permeability, ↓ Treg differentiation due to ↓ SCFA | Maifeis et al. [115], Huang et al. [57], Mejia-Leon et al. [50] |
| Rheumatoid Arthritis          | ↑ *P. copri*, P. gingivalis, Bacilli and Lactobacillales ↓ Faecalibacterium | Molecular mimicry (FLNA, GNS), ↑ citrullinated proteins and Th17 pathway | Zhang et al. [63], Pianta et al. [65], Scher et al. [113], Montgomery et al. [116], Wu et al. [117] |
| Systemic Lupus Erythematosus  | ↑ *Bacteroidetes*/Firmicutes ratio ↓ Lactobacillaceae | ↑ Th17 | Hevia et al. [72], Zhang et al. [118], Johnson et al. [119] |
| Sjögren’s Syndrome            | ↑ *B. intestinalis*, B. fragilis | ↑ activation of R60-reactive T cells, molecular mimicry | Szymula et al. [75], De Paiva et al. [77] |
| Systemic Sclerosis            | ↑ *Bacteroidetes*/Firmicutes ratio | ↑ esophageal dysfunction, PPI use | Volkmann et al. [79], Andreasson et al. [80], Clooney et al. [120] |
Table 1. Cont.

| Disease                        | Microbiota Alteration | Mechanism                                      | References                                      |
|--------------------------------|-----------------------|------------------------------------------------|------------------------------------------------|
| Inflammatory Bowel Diseases    | ↑ Proteobacteria,     | ↑ intestinal permeability,                      | Manichanh et al. [83], Wang et al. [87],        |
|                                | ↓ Firmicutes, Bacteroides, Eubacterium, Faecalibacterium, Ruminococcus | ↓ Treg differentiation due to ↓ SCFA and AHR agonists | Takahashi et al. [89], Geremia et al. [121] |
| Coeliac Disease                | ↑ S. mutans, S. anginosus, S. epidermidis, S. pasteuri, K. oxytoca | ↑ dysbiosis                                    | Nagao-Kitamoto et al. [92]                      |
| Autoimmune Liver Diseases      | ↑ Veillonella, Enterobacteriaceae, Enterococcus, Lactobacillus | Molecular mimicry, ↑ ursodeoxycholic acid      | Tang et al. [93], Hov et al. [95], Kumnmen et al. [102], Ma et al. [122] |
| Behcet’s Disease               | ↑ Bilophila, Parabacteroides, Paraprevotella | ↓ Treg differentiation due to ↓ SCFA           | Ye et al. [107], Tanabe et al. [123]            |
| Psoriasis                      | ↓ Akkermansia, Ruminococcus, Pseudobutyrivibrio | ↑ Th17                                         | Chang et al. [112], Scher et al. [113]          |
| HIV Infection                  | ↓ Lactobacillales, Bacteroidetes, Bifidobacteria, Pseudomonas, Streptococcus, Candida, Proteobacteria, Prevotella, Enterobacteriales | Sexual habits, GI barrier dysfunction, viral load, CD4+ count | Dillon et al. [124], Mutlu et al. [125], Lozupone CA [126,127] |

SCFAs: Short-chain fatty acids, FLNA: Filamin A, GNS: N-acetylglucosamine-6-sulfatase, PPI: Proton pump inhibitors, AHR: Active aryl hydrocarbon receptor, GI: Gastrointestinal, HIV: Human immunodeficiency virus. ↑ = increase, ↓ = decrease.

2. Type 1 Diabetes

T1D is a systemic and chronic disease due to the marked and progressive inability of the pancreas to secrete insulin because of the autoimmune destruction of the beta cells, which results in an alteration of carbohydrate, fat and protein metabolism [128]. Currently, autoimmunity is considered the major factor in the pathophysiology of T1D. In a genetically susceptible individual, viral infection may stimulate the production of antibodies against a viral protein that trigger an autoimmune response against antigenically similar beta cell molecules. Several studies on animal models [36–40,44,51] and humans [42,43,45,46,48,49,53] have hypothesized a critical role of gut dysbiosis in T1D onset [47], as well as diet [50]. The possible role of molecular mimicry by the microbiome in immune tolerance breakdown is supported by the evidence of a microbial peptide mimic of the islet-specific glucose-6-phosphatase catalytic subunit-related protein (IGRP), an islet-specific auto-antigen, in accelerated T1D MyD88-/mice with an altered intestinal microbiome [129]. The Old Friends Hypothesis sustains that dysbiosis, which results in a loss of commensal microbes evolved together with their host, might have a role in the host’s immune response regulation and homeostasis [130]. Probably, a combination of dysbiosis, increased gut permeability and an impaired intestinal immune responsiveness intrude together, leading to anti-islet autoimmunity, as the Perfect Storm Hypothesis postulates [131]. Maffeis et al. observed in Italian T1D-affected children an increased intestinal permeability that correlates with alterations in the microbiota composition with an increase in Dialister invisus, Glocibactella sanguinis and Bifidobacterium longum in T1D patients as compared to healthy controls [115]. Huang et al. found a prevalence of Bacteroidetes in gut microbiota of 12 T1D Han Chinese children. Conversely, Firmicutes were prevalent in healthy controls [57], according to a previous study conducted on Caucasian patients [50]. These data support the hypothesis of reduced epithelial barrier activity due to alterations of epithelial tight junctions caused by products of Bacteroidetes anaerobic respiration (i.e., acetate and succinate) [50].
3. Rheumatoid Arthritis

RA is a chronic systemic inflammatory disease. In genetically susceptible individuals, an autoimmune reaction, triggered by environmental factors, leads to synovial hypertrophy and chronic joint inflammation, along with the potential for extra-articular manifestations [132]. The microbiome may have a pivotal role in the development of autoimmunity as suggested by the observation that germ-free mice were protected against experimental arthritis [117,133]. It has been hypothesized an important contribution of segmented filamentous bacteria (SFB) is in the development of autoimmune arthritis, influencing adaptive and innate immunity through enhanced Th17 infiltration in the intestinal lamina propria [117,133–137]. Moreover, SFB might selectively expand Th17 cells expressing dual TCRs, which recognize both SFB antigens and self-antigens. These cells are recruited to the lung by CCL20-CCR6 axis and trigger RA-related lung autoimmunity [138]. An alteration of the gut microbiome in RA patients is described—new-onset RA patients have a higher abundance of *Prevotella copri* than patients with established RA [63,139]. The theory of molecular mimicry in RA is supported by the evidence of two auto-antigens (N-acetylglucosamine-6-sulfatase (GNS) and filamin A (FLNA)) with sequence homology to epitopes of *Prevotella* spp. [65]. These self-antigens are expressed in inflamed synovial tissues and GNS antibody values correlate with anti-citrullinated protein antibodies (ACPAs) [65]. High levels of ACPAs are associated with periodontitis, suggesting a role of infection by *Porphyromonas gingivalis* and RA onset [140]. It has been proposed that the citrullination of peptides by peptidylarginine deiminase (PAD), an enzyme expressed by *P. gingivalis*, might break immune tolerance [116]. Furthermore, RA patients present a greater alteration in gut microbial diversity than controls, with a reduction of *Faecalibacterium* and an increase of *Lactobacillaceae* and *Bacilli* [65,68,69].

4. Systemic Lupus Erythematosus

SLE is a chronic inflammatory disease with a highly variable clinical presentation and course [141]. Although a correlation between SLE development and dysbiosis has not been demonstrated, several studies observed an alteration of the microbiome composition with an increase of the *Bacteroides* phyla and *Lachnospiraceae* and a decrease in the *Firmicutes* and *Lactobacillaceae* [72,118]. According to Johnson et al., dysbiosis is associated with local inflammatory responses (specifically the Th17 response) and high circulating levels of antibodies against ds-DNA and histone [117]. In addition, the possible role of periodontal disease in the SLE condition has been investigated [70,71,73], as has been demonstrated by the alteration of subgingival microbiota, with a more elevated subgingival bacterial load and a reduced microbial diversity at the diseased sites than in controls [74]. In the literature, there are no exhaustive data on the possible influence of the microbiome and its alterations in the development of the antiphospholipid antibody syndrome, both primary and secondary to LES.

5. Sjögren’s Syndrome

SS is a systemic chronic inflammatory disorder characterized by lymphocytic infiltrates in exocrine organs and the presence of specific antibodies against Ro (SS-A) and La (SS-B) antigens [142]. A possible role in the pathogenesis of SS has been hypothesized for the microbiome since peptides derived from oral, gut and skin commensal bacteria (*P. disiens*, *Capnocytophaga* spp., *B. finegoldii*, *B. intestinalis*, *B. fragilis*, *Alistipes finegoldii*, *Corynebacterium amycolatum* and *Acinetobacter johnsonii*) may induce an immune response by the activation of Ro60-reactive T cells [75–78]. Furthermore, Mandl et al. found higher disease activity (evaluated by Sjögren’s Syndrome Disease Activity Index), lower levels of complement component and higher levels of fecal calprotectin in patients with decreased levels of *Bifidobacterium* and *Alistipes* [78].

6. Systemic Sclerosis

SSc is a systemic connective tissue disease, characterized by the aberrant activation of the immune system, functional and structural vascular damage and the progressive fibrosis of skin and
visceral organs [143]. Most patients have dysfunction of the gastrointestinal tract and alteration of the composition of the gut microbiota with low levels of *Faecalibacterium* and *Clostridium* and high levels of *Fusobacterium*, *γ-Proteobacteria*, *Bifidobacterium* and *Lactobacillus* [79,80]. Moreover, a reduction of *Faecalibacterium praunitzii* and *Clostridiaceae* and an increase of *Lactobacillus* were more pronounced among patients with esophageal dysfunction and malnutrition [80]. It has been shown that gut microbiota alterations, due to proton pump inhibitors (PPI) use favors *C. difficile* infection [144]. In particular, the chronic use of PPI causes dysbiosis with an increase in *Bacteroidetes* compared to *Firmicutes*, which favors the development of enteric infections [120].

7. Inflammatory Bowel Diseases

Ulcerative colitis (UC) is a diffuse, nonspecific inflammatory disease whose etiology is unknown [145]. A variety of immunologic changes have been documented in UC Subsets of T cells accumulate in the lamina propria of the diseased colonic segment and these T cells are cytotoxic to the colonic epithelium. This change is accompanied by an increase in the population of B cells and plasma cells, with an increased production of immunoglobulin G (IgG) and immunoglobulin E (IgE) [146]. A small proportion of patients with UC have antismooth muscle (ASMA) and anticytoskeletal antibodies. Serum and mucosal autoantibodies against intestinal epithelial cells may be involved in the alteration of the intestinal epithelial barrier. The presence of antineutrophil cytoplasmic antibodies (ANCA) and anti–Saccharomyces cerevisiae antibodies (ASCA) is a feature of inflammatory bowel disease [147]. Sulfate-reducing bacteria, which produce sulfides, are found in large numbers in patients with UC, and sulfide production is higher in patients with UC than in other people. Sulfide production is even higher in patients with active UC than in patients in remission and a decrease in Klebsiella species is seen in the ileum of patients relative to control subjects. This difference disappears after proctocolectomy [148]. Crohn disease (CD) is an idiopathic, chronic regional enteritis that most commonly affects the terminal ileum but has the potential to affect any part of the gastrointestinal tract from mouth to anus. A combination of factors, including aberrant mucosal immune responses, intestinal epithelial dysfunction and defects of host interactions with intestinal microbes, likely contribute to CD [149]. The alteration of innate and adaptive immune responses directed towards pathogen-associated molecular patterns (PAMPs) derived from intestinal microbiota in genetically susceptible patients contributes to the pathogenesis of these diseases. This hypothesis is supported by the observation of impaired epithelial barriers and increased intestinal permeability in UC and CD patients [121]. Several studies reported a correlation between dysbiosis and IBD and it could be present before the onset of the disease [81,83,84,90]. An increase in the Proteobacteria has been observed in patients with UC or CD, whereas Firmicutes was reduced in the fecal samples of CD patients with respect to healthy individuals [82,83,86]. Furthermore, there is a reduction in butyrate-producing bacteria (i.e., *Bacteroides*, *Eubacterium*, *Faecalibacterium* and *Ruminococcus*) [87,89].

8. Coeliac Disease

Coeliac disease is an inflammatory disease of the small intestine, triggered by wheat gliadin (gluten) [150]. A reduction of *Streptococcus mutans* and *Streptococcus anginosus* has been seen in patients with coeliac disease, compared to healthy people. Moreover, there is an increase of *Staphylococcus epidermidis*, *Staphylococcus pasteuri* and *Klebsiella oxytoca* in duodenal biopsies of coeliac patients [92]. Dysbiosis may have a role in the onset and/or progression of coeliac disease, though further studies are needed to elucidate this assumption.

9. Autoimmune Liver Diseases

Primary sclerosing cholangitis (PSC) is a chronic liver disease characterized by a progressive course of cholestasis with inflammation and fibrosis of the intrahepatic and extrahepatic bile ducts [151]. The condition may lead to cirrhosis of the liver with portal hypertension and end-stage liver disease [151]. An autoimmune mechanism is suggested because approximately 75%–90% of patients with PSC have
IBD, however, only approximately 4% of patients with IBD have or develop PSC [152]. A marked increase in serum autoantibody levels occurs in patients with PSC as well, with ANCA in 87%, anticardiolipin (aCL) antibodies in 66% and antinuclear antibodies (ANA) in 53%. It has been reported that PSC and IBD have overlapping yet distinct genetic architectures [153]. Furthermore, in the biliary ducts, an inflammatory response to chronic or recurrent bacterial infection in the portal circulation and from exposure to toxic bile acids has been postulated [154]. Primary biliary cholangitis (PBC) is a chronic disease of the liver, possibly autoimmune in nature, which leads to progressive cholestasis and often end-stage liver disease [155]. It is characterized by abnormalities of the humoral and cellular immune systems (i.e., elevated serum levels of immunoglobulins), circulating autoantibodies (i.e., antimitochondrial antibodies, AMAs), granulomas in the liver and regional lymph nodes, the impaired regulation of both B and T lymphocytes and the association with a variety of autoimmune-mediated diseases (i.e., autoimmune thyroiditis, SSc, SS) [155]. Subsequent to the loss of the intrahepatic bile ducts, mediated by activated CD4 and CD8 lymphocytes, a disruption of the normal bile flow occurs with the retention and deposition of toxic substances, with a further secondary destruction of the bile ducts and the hepatocytes. In addition, increased expression of the HLA class II antigens in the liver occurs, rendering the hepatocytes and bile duct epithelial cells more susceptible to activated T lymphocytes and perhaps exacerbating immunologically mediated cytotoxicity [122]. Moreover, infection with organisms of the family Enterobacteriaceae may play a role in the pathogenesis of this disease. It has been postulated that a cross-reactivity between antigens on the bacterial wall and the mitochondria, as bacterial lipoteichoic acid is detected around the damaged bile ducts in PBC and chronic bacterial exposure in normal mice, leads to autoantigen production and subsequent cholangitis that mimics PBC [156]. Intestinal dysbiosis has been associated with these diseases and several studies have reported an altered gut microbial community in PSC and PBC, although there are discrepancies at species levels [93–103].

10. Behcet’s Disease

BD is a rare vasculitic disorder characterized by a triple-symptom complex of recurrent oral aphthous ulcers, genital ulcers and uveitis, though systemic manifestations can be heterogeneous [157]. The specific etiology of BD remains elusive but the interplay between genetic factors and infectious-agent exposure may have a role in eliciting a cross-reactive immune response responsible for the vascular damage [157]. Several studies highlighted the atypical composition of the gut microbiome in BD patients [104–107]. Ye et al. showed an increase of Bilophila spp. and several opportunistic pathogens (i.e., Parabacteroides spp. and Paraprevotella spp.) and a reduction in butyrate-producing bacteria, Clostridium spp. and methanogens (Methanoculleus spp. and Methanomethylophilus spp.) in fecal samples from active BD patients [107]. Moreover, the fecal microbiota transplant from active BD patients in B10RIII mice exacerbated experimental autoimmune uveitis activity, with strong inflammatory cell infiltration within the retina, the choroid and the vitreous cavity [107]. The possible association between BD and specific gut microbiome alterations is supported by the demonstration that BD patients show defects in Th1, Th17 and Treg cells, whose functions are regulated by gut microbiota [123,158,159].

11. Psoriasis

Psoriasis is a chronic, multifactorial, inflammatory disease that involves the hyperproliferation of the keratinocytes in the epidermis, with an increase in the epidermal cell turnover rate. The epidermis is infiltrated by a large number of activated T cells, which appear to be capable of inducing keratinocyte proliferation. T cell hyperactivity and the resulting proinflammatory mediators (IL17/23) play a major role in the pathogenesis of psoriasis [160]. Chang et al. confirmed a marked upregulation of the Th17 response, which could have a role in IL17-driven inflammation in psoriasis [112]. A statistically significant association between psoriasis and IBD and another important comorbidity of psoriasis is psoriatic arthritis has been demonstrated [161,162]. The gut microbiota profile of patients with psoriatic arthritis and patients with psoriasis showed decreased bacterial diversity and a reduced abundance of
Akkermansia, Ruminococcus and Pseudobutyricibrio compared to healthy controls, and the microbiota profile of psoriatic arthritis resembled that published for patients with IBD [113].

12. HIV Infection

The human immunodeficiency virus (HIV) is a retrovirus. HIV binds to receptors of CD4 and to the coreceptor CCR5. This link favors the entry of the virus into T-helper lymphocyte and viral replication. The course of the disease is divided into phases based on clinical changes and CD4 cell count. The last phase is the acquired immunodeficiency syndrome (AIDS), characterized by opportunistic infections and tumors. The introduction of highly active antiretroviral therapy (HAART) has allowed an improvement in the life expectancy of HIV-positive patients [163–165]. However, HAART treatment does not protect against an increased risk of infectious diseases and non-infectious chronic comorbidities, typical of HIV-positive individuals [165,166]. Several studies have characterized the microbiome of subjects with HIV. There are no unique results in the literature about the microbiome in HIV patients. Most of the studies reported a change in bacterial gut composition [124–127,167,168]. Current data indicate increases in commensal bacteria that may be pathogenic in HIV patients, and decreases in beneficial commensals [125,169,170]. The proportion of the families of bacteria change in HIV patients, but not the diversity of these [169]. The proportion of Firmicutes/Bacteroidetes seems to increase significantly in HIV-1-infected patients because the concentration of Bacteroidetes decreases and that of Prevotella increases [124,169,171]. A significant difference in concentration and in the types of SCFAs was highlighted in HIV-positive patients compared to HIV-negative subjects. In HIV-positive patients, propionic acid increased and acetic and butyric acid had a significantly lower concentration [125,169,171]. The relationship with the use of HAART and the microbiota of HIV patients is unclear [172]. A possible hypothesis is that HIV therapy promotes the restoration of normal microbial flora [173]. Other studies show a minimal role of HAART [126,127,173] or even its negative impact [168]. Synthesizing these data, both HIV and antiviral therapy seem to play a different role in the type of microbiome. These studies show a strong correlation between HIV and dysbiosis. The presence of one (HIV) favors the development of the other (dysbiosis) and vice versa [170].

13. Autoimmune Disease and HIV Infection

The immune alteration (depending on the CD4 and CD8 count) may lead to the development of autoimmune diseases, although this is not a frequent event [8]. Rheumatological diseases such as reactive arthritis, psoriatic arthritis and various forms of connective tissue diseases are less frequent after the introduction of HAART among HIV-infected individuals [11,12]. Some authors have hypothesized that autoimmune diseases may develop in the first stage of infection, when the symptoms of HIV are few and CD4 count is still high [166].

In the HAART era, the thrombocytopenia (ITP) is the main autoimmune disease associated to HIV [174]. It is an autoimmune coagulation disorder characterized by isolated thrombocytopenia (platelets < 100,000/microL) and causes severe visceral bleeding (hematuria, gastrointestinal or cerebro-meningal haemorrhage). In the early stage of HIV infection, HIV-related ITP depends on immune-mediated peripheral platelet destruction (anti-GpIIa antibodies and immune complexes). In the late phase of HIV infection, there is a defect of platelet production [175,176]. Sarcoidosis is a multisystemic disease, the causes of which are not known, which is characterized by the formation of immune granulomas in the organs. In granulomas, CD4 lymphocytes accumulate and for this reason, sarcoidosis is rare in patients with AIDS [177]. Polymyositis (PM) is associated with HIV through an unknown mechanism. While dermatomyositis (DM) is rarer, PM can occur in all stages of HIV infection regardless of the state of immunodeficiency. It presents with classical proximal weakness, myalgia, mechanic’s hands, dactylitis and possible interstitial lung disease, and it is important to distinguish this form from the toxic effect of drugs (i.e., zidovudine, stavudine), which improves with the end of HAART treatment [178]. In the literature, there are conflicting data regarding the association
between autoimmune thyroid diseases and HIV infection [179,180]. The association with HIV infection and other autoimmune diseases such as RA, autoimmune liver diseases and SLE is quite rare [8].

14. Role of Probiotics and Fecal Microbiota Transplantation

Eubiosis can be re-established by probiotic (mainly *Bifidobacterium* spp. and *Lactobacillus* spp.) administration or by fecal microbiota transplantation (FMT) [181–183]. Several studies showed a reduction of proinflammatory cytokines (IL1, IL6, TNFalfa, IL12, IL17) and an increase in IL10 production in RA patients after the administration of *Lactobacillus casei*, *L. acidophilus* and *Bifidobacterium bifidum*, associated with improvement in the disease activity score [184]. In the literature, there are less data about the possible benefit of FMT in patients with autoimmune diseases, although it is considered a rescue therapy in patients with IBD [185].

15. Conclusions

In the literature, there are no data about the influence of the microbiome on the development of autoimmune diseases during HIV infection. However, we can hypothesize that untreated patients may be more susceptible to the development of autoimmune diseases, due to the presence of dysbiosis. We can suppose that CD4+ T lymphocytes depletion in HIV-infected and untreated patients results in CD8 T lymphocyte and B lymphocyte hyperfunction or expansion. CD40-activated B cells are potent antigen-presenting cells that induce specific T cell responses in vitro and in vivo. The CD40-activated B cell was able to induce an autoimmune response by the activation of CD8+ T lymphocytes. We can therefore hypothesize that the activation of APC with CD8+ T lymphocytes recruitment (i.e., IBD, psoriasis and ankylosing spondylitis) can facilitate the development of autoimmune diseases. Eubiosis, re-established by probiotic administration, can be used to reduce triggers for autoimmune diseases in untreated HIV patients. Clinical studies are needed to evaluate the role of the microbiome in autoimmune diseases in HIV patients.

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References

1. Marchesi, J.R.; Ravel, J. The vocabulary of microbiome research: A proposal. *Microbiome* 2015, 3, 31. [CrossRef] [PubMed]
2. Belkaid, Y.; Hand, T.W. Role of the microbiota in immunity and inflammation. *Cell* 2014, 157, 121–141. [CrossRef] [PubMed]
3. PrabhuDas, M.; Adkins, B.; Gans, H.; King, C.; Levy, O.; Ramilo, O.; Siegrist, C.A. Challenges in infant immunity: Implications for responses to infections and vaccines. *Nat. Immunol.* 2011, 12, 189–194. [CrossRef] [PubMed]
4. Siegrist, C.A. Neonatal and early life vaccinology. *Vaccine* 2001, 19, 3331–3346. [CrossRef]
5. Wu, G.D.; Chen, J.; Hoffmann, C.; Bittinger, K.; Chen, Y.-Y.; Keilbaugh, S.A.; Bewtra, M.; Knights, D.; Walters, W.A.; Knight, R.; et al. Linking long-term dietary patterns with gut microbial enterotypes. *Science* 2011, 334, 105–108. [CrossRef] [PubMed]
6. Albenberg, L.G.; Wu, G.D. Diet and the Intestinal Microbiome: Associations, Functions, and Implications for Health and Disease. *Gastroenterology* 2014, 146, 1564–1572.
7. Jones, L.; Kumar, J.; Mistry, A.; Sankar Chittoor Mana, T.; Perry, G.; Reddy, V.P.; Obrenovich, M. The Transformative Possibilities of the Microbiota and Mycobiota for Health, Disease, Aging, and Technological Innovation. *Biomedicines* 2019, 7, 24. [CrossRef]
8. Ward, T.L.; Dominguez-Bello, M.G.; Heisel, T.; Al-Ghalith, G.; Knights, D.; Gale, C.A. Development of the Human Mycobiome over the First Month of Life and across Body Sites. *mSystems* 2018, 3, e00140-17. [CrossRef]
9. Makki, K.; Deehan, E.C.; Walter, J.; Backhed, F. The Impact of Dietary Fiber on Gut Microbiota in Host Health and Disease. *Cell Host Microbe* 2018, 23, 705–715. [CrossRef]

10. Scher, J.U.; Szczeszak, A.; Longman, R.S.; Segata, N.; Ubeda, C.; Bielski, C.; Rostron, T.; Cerundolo, V.; Pamer, E.G.; Abramson, S.B.; et al. Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis. *eLife* 2013, 2, e01022. [CrossRef]

11. Berer, K.; Mues, M.; Koutrolos, M.; Rasbi, Z.A.; Boziki, M.; Johner, C.; Wekerle, H.; Krishnamoorthy, G. Commensal microbiota and myelin autoantigen cooperate to trigger autoimmune demyelination. *Nature* 2011, 479, 538–541. [CrossRef] [PubMed]

12. Cani, P.D.; Amar, J.; Iglesias, M.A.; Poggi, M.; Knauf, C.; Bastelica, D.; Neyrinck, A.M.; Fava, F.; Tuohy, K.M.; Chabo, C.; et al. Metabolic Endotoxemia Initiates Obesity and Insulin Resistance. *Diabetes* 2007, 56, 1761–1772. [CrossRef] [PubMed]

13. Castaner, O.; Goday, A.; Park, Y.-M.; Lee, S.H.; Magkos, F.; Shiow, S.-A.T.E.; Schröder, H. The Gut Microbiome Profile in Obesity: A Systematic Review. *Hindawi Int. J. Endocrinol.* 2018, 2018, 4095789. [CrossRef] [PubMed]

14. Wang, Y.; Begum-Haque, S.; Telesford, K.M.; Ochoa-Reparaz, J.; Christy, M.; Kasper, E.J.; Robson, S.C.; Scheppach, W. E

15. Kosiewicz, M.M.; Zirnheld, A.L.; Alard, P. Gut Microbiota, Immunity, and Disease: A Complex Relationship. *Gut Microbes* 2014, 5, 552–561. [CrossRef]

16. Rolhion, N.; Chassaing, B. When pathogenic bacteria meet the intestinal microbiota. *Philos. Trans. R. Soc. B Biol. Sci.* 2016, 371, 20150504. [CrossRef]

17. Elsen, L.W.V.D.; Poyntz, H.C.; Weyrich, L.S.; Young, W.; E Forbes-Blom, E. Embracing the gut microbiota: The new frontier for inflammatory and infectious diseases. *Clin. Transl. Immunol.* 2017, 6, e125. [CrossRef]

18. Francino, M.P. Early Development of the Gut Microbiota and Immune Health. *Pathogens* 2014, 3, 769–790. [CrossRef]

19. Scheppach, W. Effects of short chain fatty acids on gut morphology and function. *Gut* 1994, 35, S35–S38. [CrossRef]

20. Heerdt, B.G.; A Houston, M.; Augenlicht, L.H. Short-chain fatty acid-initiated cell cycle arrest and apoptosis of colonic epithelial cells is linked to mitochondrial function. *Cell Growth Differ. Mol. Biol. J. Am. Assoc. Cancer Res.* 1997, 8, 523–532.

21. Willemesen, L.E.M.; A Koetsier, M.; Van Deventer, S.J.H.; Tol, E.A.F.V. Short chain fatty acids stimulate epothilidal mucin 2 expression through differential effects on prostaglandin E1 and E2 production by intestinal myofibroblasts. *Gut* 2003, 52, 1442–1447. [CrossRef] [PubMed]

22. Tao, R.; De Zoeten, E.F.; Ozkaynak, E.; Chen, C.; Wang, L.; Porrett, P.M.; Li, B.; A Turka, L.; Olson, E.N.; I Greene, M.; et al. Deacetylase inhibition promotes the generation and function of regulatory T cells. *Nat. Med.* 2007, 13, 1299–1307. [CrossRef] [PubMed]

23. Furusawa, Y.; Obata, Y.; Fukuda, S.; Endo, T.A.; Nakato, G.; Takahashi, D.; Nakanishi, Y.; Uetake, C.; Kato, K.; Kato, T.; et al. Commensal microbe-derived butyrate induces the differentiation of colonic regulatory T cells. *Nature* 2013, 504, 446–450. [CrossRef] [PubMed]

24. Smith, P.M.; Howitt, M.R.; Panikov, N.; Michaud, M.; Gallini, C.A.; Bohlooly-Y, M.; Glickman, J.N.; Garrett, W.S. The microbial metabolites, short-chain fatty acids, regulate colonic Treg cell homeostasis. *Science* 2013, 341, 569–573. [CrossRef]

25. Macia, L.; Tan, J.; Vieira, A.T.; Leach, K.; Stanley, D.; Luong, S.; Maruyu, M.; McKenzie, C.I.; Hijikata, A.; Wong, C.; et al. Metabolite-sensing receptors GPR43 and GPR109A facilitate dietary fibre-induced gut homeostasis through regulation of the inflammasome. *Nat. Commun.* 2015, 6, 6734. [CrossRef]

26. Greer, J.B.; O’Keefe, S.J. Microbial Induction of Immunity, Inflammation, and Cancer. *Front. Physiol.* 2011, 1, 168. [CrossRef]

27. Encarnação, J.C.; Abrantes, A.M.; Pires, A.S.; Botelho, M.F.; Pires, S. Revisit dietary fiber on colorectal cancer: Butyrate and its role on prevention and treatment. *Cancer Metastasis Rev.* 2015, 34, 465–478. [CrossRef]

28. Dalle, B.; Van Oudenhove, L.; Vervliet, B.; Verbeke, K. The role of short-chain fatty acids in microbiota–gut–brain communication. *Nat. Rev. Gastroenterol. Hepatol.* 2019, 21, 461–478. [CrossRef]

29. Tan, J.; McKenzie, C.; Potamitis, M.; Thorburn, A.N.; Mackay, C.R.; Macia, L. The Role of Short-Chain Fatty Acids in Health and Disease. *Adv. Immunol.* 2014, 121, 91–119.
30. Zhang, M.; Zhou, Q.; Dorfman, R.G.; Huang, X.; Fan, T.; Zhang, H.; Zhang, J.; Yu, C. Butyrate inhibits interleukin-17 and generates Tregs to ameliorate colorectal colitis in rats. *BMC Gastroenterol.* 2016, 16, 84. [CrossRef]

31. Collins, C.B.; Aherne, C.M.; Kominsky, D.; McNamee, E.N.; Lebsack, M.D.; Eltzschig, H.; Jedlicka, P.; Rivera–Nieves, J. Retinoic acid attenuates ileitis by restoring the balance between T-helper 17 and T regulatory cells. *Gastroenterology* 2011, 141, 1821–1831. [CrossRef] [PubMed]

32. Wu, H.; Wu, E. The role of gut microbiota in immune homeostasis and autoimmunity. *Gut Microbes* 2012, 3, 4–14. [CrossRef] [PubMed]

33. Rooks, M.G.; Garrett, W.S. Gut microbiota, metabolites and host immunity. *Nat. Rev. Immunol.* 2016, 16, 341–352. [CrossRef] [PubMed]

34. Zelante, T.; Iannitti, R.G.; Cunha, C.; De Luca, A.; Giovannini, G.; Pieraccini, G.; Zecchi, R.; D’Angelo, C.; Massi-Benedetti, C.; Fallarino, F.; et al. Tryptophan Catabolites from Microbiota Engage Aryl Hydrocarbon Receptor and Balance Mucosal Reactivity via Interleukin-22. *Immunity* 2013, 39, 372–385. [CrossRef]

35. Gianchecchi, E.; Fiorabracci, A. On the pathogenesis of insulin-dependent diabetes mellitus: The role of microbiota. *Immunol. Res.* 2017, 65, 242–256. [CrossRef]

36. Graham, S.; Courtois, P.; Malaisse, W.J.; Rozing, J.; Scott, F.W.; Mc I Mowat, A. Enteropathy precedes type 1 diabetes in the BB rat. *Gut* 2004, 53, 1437–1444. [CrossRef]

37. Neu, J.; Reverte, C.M.; Mackey, A.D.; Libon, K.; Tuhacec-Tenace, L.M.; Hatch, M.; Li, N.; A Caicedo, R.; A Schatz, D.; Atkinson, M. Changes in intestinal morphology and permeability in the biobreeding rat before the onset of type 1 diabetes. *J. Pediatr. Gastroenterol. Nutr.* 2005, 40, 589–595. [CrossRef]

38. Brugman, S.; Klatter, F.A.; Visser, J.T.; Wildeboer-Veloo, A.C.; Harmsen, H.J.; Rozing, J.; Bos, N.A. Antibiotic treatment partially protects against type 1 diabetes in the Bio-Breeding diabetes-prone rat. Is the gut florainvolved in the development of type 1 diabetes? *Diabetologia* 2006, 49, 2105–2108. [CrossRef]

39. Wen, L.; Ley, R.E.; Volchkov, P.Y.; Stranges, P.B.; Avanesyan, L.; Stonebraker, A.C.; Hu, C.; Wong, F.S.; Szot, G.L.; Bluestone, J.A.; et al. Innate immunity and intestinal microbiota in the development of Type 1 diabetes. *Nature* 2008, 455, 1109–1113. [CrossRef]

40. Valladares, R.; Sankar, D.; Li, N.; Williams, E.; Lai, K.-K.; Abdelgeliel, A.S.; Gonzalez, C.F.; Wasserfall, C.H.; Larkin, J.; Schatz, D.; et al. Lactobacillus johnsonii N6.2 Mitigates the Development of Type 1 Diabetes in BB-DP Rats. *PLoS ONE* 2010, 5, 10507. [CrossRef]

41. Giongo, A.; Gano, K.A.; Crabb, D.B.; Mukherjee, N.; Novelo, L.L.; Casella, G.; Drew, J.C.; Ilnonen, J.; Knip, M.; Hyöty, H.; et al. Toward defining the autoimmune microbiome for type 1 diabetes. *ISME J.* 2011, 5, 82–91. [CrossRef] [PubMed]

42. De Goffau, M.C.; Luopajärvi, K.; Knip, M.; Ilnonen, J.; Ruohotula, T.; Härkönen, T.; Orivuori, L.; Hakala, S.; Wellin, G.W.; Harmsen, H.J.; et al. Fecal Microbiota Composition Differs Between Children With β-Cell Autoimmunity and Those Without. *Diabetes* 2013, 62, 1238–1244. [CrossRef] [PubMed]

43. Murri, M.; Leiva, I.; Gómez-Zumaquero, J.M.; Tjahanes, F.J.; Cardona, F.; Soriguer, F.; Queipo-Ortuño, M.I. Gut microbiota in children with type 1 diabetes differs from that in healthy children: A case-control study. *BMJ Med.* 2013, 11, 46. [CrossRef] [PubMed]

44. Patrick, C.; Wang, G.-S.; Lefebvre, D.E.; Crookshank, J.A.; Sonier, B.; Eberhard, C.; Mojibian, M.; Kennedy, C.R.; Brooks, S.P.; Kalmokoff, M.L.; et al. Promotion of Autoimmune Diabetes by Cereal Diet in the Presence or Absence of Microbes Associated with Gut Immune Activation, Regulatory Imbalance, and Altered Cathelicidin Antimicrobial Peptides. *Diabetes* 2013, 62, 2036–2047. [CrossRef] [PubMed]

45. Davis-Richardson, A.G.; Ardissone, A.N.; Dias, R.; Simell, V.; Leonard, M.T.; Kemppainen, K.M.; Drew, J.C.; Schatz, D.; Atkinson, M.A.; Kolaczkowski, B.; et al. Bacteroides dorei dominates gut microbiome prior to autoimmunity in Finnish children at high risk for type 1 diabetes. *Front. Microbiol.* 2014, 5, 678. [CrossRef] [PubMed]

46. Mejia-León, M.E.; Petrosino, J.F.; Ajami, N.J.; Dominguez-Bello, M.G.; De La Barca, A.M.C. Fecal microbiota imbalance in Mexican children with type 1 diabetes. *Sci. Rep.* 2014, 4, 3814. [CrossRef]

47. Soyucen, E.; Gucan, A.; Aktuglu-Zeybek, A.C.; Onal, H.; Kiykim, E.; Aydin, A. Differences in the gutmicrobiota of healthy children and those with type 1 diabetes. *Pediatr. Int.* 2014, 56, 336–343. [CrossRef]

48. Alkanani, A.K.; Hara, N.; Gottlieb, P.A.; Ir, D.; Robertson, C.E.; Wagner, B.D.; Frank, D.N.; Zipris, D. Alterations in intestinal microbiota correlate with susceptibility to type 1 diabetes. *Diabetes* 2015, 64, 3510–3520. [CrossRef]
49. Kostic, A.D.; Gevers, D.; Siljander, H.; Vatanen, T.; Hyötyläinen, T.; Hämäläinen, A.M.; Peet, A.; Tillmann, V.; Pööhö, P.; Mattila, I.; et al. The dynamics of the human infant gut microbiome in development and in progression toward type 1 diabetes. *Cell Host Microbe* 2015, 17, 260–273. [CrossRef]

50. Mejía-León, M.E.; Barca, A.; De La Barca, A.M.C. Diet, Microbiota and Immune System in Type 1 Diabetes Development and Evolution. *Nutrients* 2015, 7, 9171–9184. [CrossRef]

51. Sun, J.; Furio, L.; Mecheri, R.; van der Does, A.M.; Lundeborg, E.; Saveanu, L.; Chen, Y.; van Endert, P.; Agerberth, B.; Diana, J. Pancreatic β-Cells Limit Autoimmune Diabetes via an Immunoregulatory Antimicrobial Peptide Expressed under the Influence of the Gut Microbiota. *Immunity* 2015, 43, 304–317. [CrossRef][PubMed]

52. Uusitalo, U.; Liu, X.; Yang, J.; Aronsson, C.A.; Hummel, S.; Butterworth, M.; Lernmark, Å.; Rewers, M.; Hagopian, W.; She, J.-X.; et al. Association of Early Exposure of Probiotics and Islet Autoimmunity in the TEDDY Study. *JAMA Pediatr.* 2016, 170, 20–28. [CrossRef][PubMed]

53. Pinto, E.; Anselmo, M.; Calha, M.; Bottrill, A.; Duarte, I.; Andrew, P.W.; Faleiro, M.L. The intestinal proteome of diabetic and control children is enriched with different microbial and host proteins. *Microbiology* 2017, 163, 161–174. [CrossRef][PubMed]

54. Gavin, P.G.; Mullaney, J.A.; Loo, D.; Cao, K.-A.L.; Gottlieb, P.A.; Hill, M.M.; Zipris, D.; Hamilton-Williams, E.E. Intestinal Metaproteomics Reveals Host-Microbiota Interactions in Subjects at Risk for Type 1 Diabetes. *Diabetes Care* 2018, 41, 2178–2186. [CrossRef][PubMed]

55. Gürsoy, S.; Koçkar, T.; Atik, S.U.; Önal, Z.; Önal, H.; Adal, E. Autoimmunity and intestinal colonization by Candida albicans in patients with type 1 diabetes at the time of the diagnosis. *Korean J. Pediatr.* 2018, 61, 217–220. [CrossRef]

56. Henschel, A.M.; Cabrera, S.M.; Kaldunski, M.L.; Jia, S.; Geoffrey, R.; Roethle, M.F.; Lam, V.; Chen, Y.G.; Wang, X.; Salzman, N.H.; et al. Modulation of the diet and gastrointestinal microbiota normalizes systemic inflammation and β-cell chemokine expression associated with autoimmunity in diabetes susceptibility. *PLoS ONE* 2018, 13, e0190351. [CrossRef]

57. Huang, Y.; Li, S.C.; Hu, J.; Ruan, H.B.; Guo, H.M.; Zhang, H.H.; Wang, X.; Pei, Y.F.; Pan, Y.; Fang, C. Gut microbiota profiling in Han Chinese with type 1 diabetes. *Diabetes Res. Clin. Pract.* 2018, 141, 256–263. [CrossRef]

58. Mullaney, J.A.; Stephens, J.E.; Costello, M.E.; Fong, C.; Geeling, B.E.; Gavin, P.G.; Wright, C.M.; Spector, T.D.; Brown, M.A.; Hamilton-Williams, E.E. Correction to: Type 1 diabetes susceptibility alleles are associated with distinct alterations in the gut microbiota. *Microbiome* 2018, 6, 51. [CrossRef]

59. Arpaia, N.; Campbell, C.; Fan, X.; Dikiy, S.; van der Veeken, J.; deRoos, P.; Liu, H.; Cross, J.R.; Pfeffer, K.; Coffey, P.J.; et al. Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. *Nature* 2013, 504, 451–455. [CrossRef]

60. De Groot, P.F.; Belzer, C.; Aydin, O.; Levin, E.; Levels, J.H.; Aalvink, S.; Boot, F.; Holleman, F.; van Raalte, D.H.; Scheithauer, T.P.; et al. Distinct fecal and oral microbiota composition in human type 1 diabetes, an observational study. *PLoS ONE* 2017, 12, e0188475. [CrossRef]

61. Liao, F.; Li, Z.; Wang, Y.; Shi, B.; Gong, Z.; Cheng, X. Porphyromonas gingivalis may play an important role in the pathogenesis of periodontitis-associated rheumatoid arthritis. *Med. Hypotheses* 2009, 72, 732–735. [CrossRef][PubMed]

62. De Aquino, S.G.; Abdollahi-Roodsaz, S.; Koenders, M.I.; Van De Loo, F.A.J.; Pruinj, G.J.M.; Marijnissen, R.J.; Walgreen, B.; Helsen, M.M.; Bersetlaar, L.A.V.D.; De Molon, R.S.; et al. Periodontal Pathogens Directly Promote Autoimmune Experimental Arthritis by Inducing a TLR2- and IL-1–Driven Th17 Response. *J. Immunol.* 2014, 192, 4103–4111. [CrossRef][PubMed]

63. Zhang, X.; Zhang, D.; Jia, H.; Feng, Q.; Wang, D.; Liang, D.; Wu, X.; Li, J.; Tang, L.; Li, Y.; et al. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. *Nat. Med.* 2015, 21, 895–905. [CrossRef][PubMed]

64. Chen, J.; Wright, K.; Davis, J.M.; Jeraldo, P.; Marietta, E.V.; Murray, J.; Nelson, H.; Matteson, E.L.; Taneja, V. An expansion of rare lineage intestinal microbes characterizes rheumatoid arthritis. *Genome Med.* 2016, 8, 43. [CrossRef][PubMed]

65. Pianta, A.; Arvika, S.L.; Strle, K.; Drouin, E.E.; Wang, Q.; Costello, C.E.; Steere, A.C. Two rheumatoid arthritis–specific autoantigens correlate microbial immunity with autoimmune responses in joints. *J. Clin. Investig.* 2017, 127, 2946–2956. [CrossRef][PubMed]
66. Sato, K.; Takahashi, N.; Kato, T.; Matsuda, Y.; Yokoji, M.; Yamada, M.; Nakajima, T.; Kondo, N.; Endo, N.; Yamamoto, R.; et al. Aggravation of collagen-induced arthritis by orally administered Porphyromonas gingivalis through modulation of the gut microbiota and gut immune system. *Sci. Rep.* 2017, 7, 6955. [CrossRef]

67. Teng, F.; Felix, K.M.; Bradley, C.P.; Naskar, D.; Ma, H.; Raslan, W.A.; Wu, H.-J.J. The impact of age and gut microbiota on Th17 and Tfh cells in K/BxN autoimmune arthritis. *Arthritis Res. Ther.* 2017, 19, 188. [CrossRef]

68. Jubair, W.K.; Hendrickson, J.D.; Severs, E.L.; Schulz, H.M.; Adhikari, S.; Ir, D.; Pagan, J.D.; Anthony, R.M.; Robertson, C.E.; Frank, D.N.; et al. Modulation of Inflammatory Arthritis in Mice by Gut Microbiota Through Mucosal Inflammation and Autoantibody Generation. *Arthritis Rheumatol.* 2018, 70, 1220–1233. [CrossRef]

69. Picchianti-Diamanti, A.; Panebianco, C.; Salemì, S.; Sorgi, M.L.; Di Rosa, R.; Tropea, A.; Sgrulletti, M.; Salerno, G.; Terracciano, F.; D’Amelio, R.; et al. Analysis of Gut Microbiota in Rheumatoid Arthritis Patients: Disease-Related Dysbiosis and Modifications Induced by Etanercept. *Int. J. Mol. Sci.* 2018, 19, 2938. [CrossRef]

70. Mutlu, S.; Richards, A.; Maddison, P.; Scully, C. Gingival and periodontal health in systemic lupus erythematosus. *Commun. Dent. Oral Epidemiol.* 1993, 21, 158–161. [CrossRef]

71. Navas, E.D.A.; Sato, E.; Pereira, D.; Back-Brito, G.; Ishikawa, J.; Jorge, A.; Brighenti, F.L.; Koga-Ito, C.Y. Oral microbial colonization in patients with systemic lupus erythematosus: Correlation with treatment and disease activity. *Lupus* 2012, 21, 969–977. [CrossRef] [PubMed]

72. Hevia, A.; Milani, C.; Lópe, P.; Cuervo, A.; Arboley, S.; Duranti, S.; Turroni, F.; González, S.; Suárez, A.; Gueimonde, M.; et al. Intestinal Dysbiosis Associated with Systemic Lupus Erythematosus. *mBio* 2014, 5, 1–10. [CrossRef] [PubMed]

73. Calderaro, D.C.; Ferreira, G.A.; de Mendonça, S.M.S.; Correia, J.D.; Santos, F.X.; Sançao, J.G.C.; da Silva, T.A.; Teixeira, A.L. Hássociação entre o lúpus eritematoso sistêmico e doença periodontal? *Rev. Bras. Reumatol.* 2016, 56, 280–284. [CrossRef]

74. Correia, J.D.; Calderaro, D.C.; Ferreira, G.A.; Mendonça, S.M.S.; Fernandes, G.R.; Xiao, E.; Teixeira, A.L.; Leys, E.J.; Graves, D.T.; Silva, T.A. Subgingival microbiota dysbiosis in systemic lupus erythematosus: Association with periodontal status. *Microbiome* 2017, 5, 34. [CrossRef]

75. Szymula, A.; Rosenthal, J.; Szczepańska, B.M.; Bagavant, H.; Fu, S.M.; Deshmukh, U.S. T cell epitope mimicry between Sjögren’s syndrome antigen A (SSA)/Ro60 and oral, gut, skin and vaginal bacteria. *Clin. Immunol.* 2014, 152, 1–9. [CrossRef]

76. Siddiqui, H.; Chen, T.; Aliko, A.; Mydel, P.M.; Jonsson, R.; Olsen, I. Microbiological and bioinformatics analysis of primary Sjögren’s syndrome patients with normal salivation. *J. Oral Microbiol.* 2016, 8, 3119. [CrossRef]

77. De Paiva, C.S.; Jones, D.B.; Stern, M.E.; Bion, F.; Moore, Q.L.; Corbiere, S.; Streckfus, C.E.; Hutchinson, D.S.; Ajami, N.J.; Petrosino, J.F.; et al. Altered Mucosal Microbiome Diversity and Disease Severity in Sjögren Syndrome. *Sci. Rep.* 2016, 6, 23561. [CrossRef]

78. Mandl, T.; Marsal, J.; Olsson, P.; Olsén, B.; Andréasson, K. Severe intestinal dysbiosis is prevalent in primary Sjögren’s syndrome and is associated with systemic disease activity. *Arthritis Res. Ther.* 2017, 19, 237. [CrossRef]

79. Volkman, E.R.; Chang, Y.-L.; Barroso, N.; Furst, D.E.; Clements, P.J.; Gorn, A.H.; Roth, B.E.; Conklin, J.L.; Getzug, T.; Borneman, J.; et al. Association of Systemic sclerosis with a Unique Colonic Microbial Consortium. *Arthritis Rheumatol.* 2016, 68, 1483–1492. [CrossRef]

80. Andréasson, K.; Alrawi, Z.; Persson, A.; Jönsson, G.; Marsal, J. Intestinal dysbiosis is common in systemic sclerosis and associated with gastrointestinal and extraintestinal features of disease. *Arthritis Res. Ther.* 2016, 18, 278. [CrossRef]

81. Ott, S.J.; Musfeldt, M.; Wenderoth, D.F.; Hampe, J.; Brant, O.; Fölsch, U.R.; Timmis, K.N.; Schreiber, S. Reduction in diversity of the colonic mucosa associated bacterial microflora in patients with active inflammatory bowel disease. *Gut* 2004, 53, 685–693. [CrossRef] [PubMed]

82. Gophna, U.; Sommerfeld, K.; Gophna, S.; Doolittle, W.F.; Veldhuyzen van Zanten, S.J. Differences between tissue-associated intestinal microfloras of patients with Crohn’s disease and ulcerative colitis. *J. Clin. Microbiol.* 2006, 44, 4136–4141. [CrossRef] [PubMed]
83. Manichanh, C.; Rigottier-Gois, L.; Bonnaud, E.; Gloux, K.; Pelletier, E.; Frangeul, L.; Nalin, R.; Jarrin, C.; Chardon, P.; Marteau, P.; et al. Reduced diversity of faecal microbiota in Crohn’s disease revealed by a metagenomic approach. *Gut* 2006, 55, 205–211. [CrossRef] [PubMed]
84. Frank, D.N.; Amand, A.L.S.; Feldman, R.A.; Boedecker, E.C.; Harpaz, N.; Pace, N.R. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc. Natl. Acad. Sci. USA* 2007, 104, 13780–13785. [CrossRef] [PubMed]
85. Sokol, H.; Pigneur, B.; Watterlot, L.; Lakhadi, O.; Bermúdez-Humárán, L.G.; Gratadoux, J.-J.; Blugeon, S.; Bridonneau, C.; Furet, J.-P.; Corthier, G.; et al. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc. Natl. Acad. Sci. USA* 2008, 105, 16731–16736. [CrossRef]
86. Walker, A.W.; Sanderson, J.D.; Churcher, C.; Parkes, G.C.; Hudspith, B.N.; Raymond, N.; Brostoff, J.; Parkhill, J.; Dougan, G.; Petrovska, L. High-throughput clone library analysis of the mucosa-associated microbiota reveals dysbiosis and differences between inflamed and non-inflamed regions of the intestine in inflammatory bowel disease. *BMC Microbiol.* 2011, 11, 7. [CrossRef]
87. Wang, W.; Chen, L.; Zhou, R.; Wang, X.; Song, L.; Huang, S.; Wang, G.; Xia, B. Increased proportions of *Bifidobacterium* and the *Lactobacillus* group and loss of butyrate-producing bacteria in inflammatory bowel disease. *J. Clin. Microbiol.* 2014, 52, 398–406. [CrossRef]
88. Norman, J.M.; Handley, S.A.; Baldridge, M.T.; Droit, L.; Liu, C.Y.; Keller, B.C.; Kambal, A.; Monaco, C.L.; Zhao, G.; Fleshner, P.; et al. Disease-Specific Alterations in the Enteric Virome in Inflammatory Bowel Disease. *Cell 2015*, 160, 447–460. [CrossRef]
89. Tang, R.; Wei, Y.; Li, Y.; Chen, W.; Chen, H.; Wang, Q.; Yang, F.; Miao, Q.; Xiao, X.; Zhang, H.; et al. Reduced Abundance of Butyrate-Producing Bacteria Species in the Fecal Microbial Community in Crohn’s Disease. *Digestion 2016*, 93, 59–65. [CrossRef]
90. Ni, J.; Wu, G.D.; Albenberg, L.; Tomov, V.T. Gut microbiota and IBD: Causation or correlation? *Nat. Rev. Gastroenterol. Hepatol.* 2017, 14, 573–584. [CrossRef]
91. Lv, L.X.; Fang, D.Q.; Shi, D.; Chen, D.Y.; Yan, R.; Zhu, Y.X.; Chen, Y.F.; Shao, L.; Guo, F.F.; Wu, W.R.; et al. Alterations and correlations of the gut microbiome, metabolism and immunity in patients with primary biliary cirrhosis. *Environ. Microbiol.* 2016, 18, 2272–2286. [CrossRef]
92. Hov, J.R.; Kummen, M. Intestinal microbiota in primary sclerosing cholangitis. *Curr. Opin. Gastroenterol.* 2017, 33, 85–92. [CrossRef] [PubMed]
93. Torres, J.; Bao, X.; Goel, A.; Colombel, J.F.; Pekow, J.; Jabri, B.; Williams, K.M.; Castillo, A.; Odin, J.A.; Meckel, K.; et al. The features of mucosa-associated microbiota in primary sclerosing cholangitis. *Aliment Pharmacol. Ther.* 2016, 43, 790–801. [CrossRef]
94. Quraishi, M.N.; Sergeant, M.; Kay, G.; Iqbal, T.; Chan, J.; Constantinidou, C.; Trivedi, P.; Ferguson, J.; Adams, D.H.; Palen, M.; et al. The gut-adherent microbiota of PSC-IBD is distinct to that of IBD. *Gut* 2017, 66, 386–388. [CrossRef]
95. Rossen, N.G.; Fuentes, S.; Boonstra, K.; D’Haens, G.R.; Heilig, H.G.; Zoetendal, E.G.; de Vos, W.M.; Ponsioen, C.Y. The mucosa-associated microbiota of PSC patients is characterized by low diversity and low abundance of uncultured Clostridiales II. *J. Crohns Colitis* 2015, 9, 342–348. [CrossRef]
96. Kevens, D.; Tyle, A.D.; Holm, K.; Jorgensen, K.K.; Vatn, M.H.; Karlsen, T.H.; Kaplan, G.G.; Eksteen, B.; Gevers, D.; Hov, J.R.; et al. Characterization of intestinal microbiota in ulcerative colitis patients with and without primary sclerosing cholangitis. *J. Crohns Colitis* 2016, 10, 330–337. [CrossRef]
97. Ruhlemann, M.C.; Heinsen, F.A.; Zenouzi, R.; Lieb, W.; Franke, A.; Schramm, C. Faecal microbiota profiles as diagnostic biomarkers in primary sclerosing cholangitis. *Gut* 2017, 66, 753–754. [CrossRef]
119. Johnson, B.M.; Gaudreau, M.-C.; Al-Gadban, M.M.; Gudi, R.; Vasu, C. Impact of dietary deviation on disease progression and gut microbiome composition in lupus-prone SNF1 mice. *Clin. Exp. Immunol.* 2015, 181, 323–337. [CrossRef]
120. Clooney, A.G.; Bernstein, C.N.; Leslie, W.D.; Vagianos, K.; Sargent, M.; Laserna-Mendieta, E.J.; Claesson, M.J.; Targownik, L.E.; Claesson, M. A comparison of the gut microbiome between long-term users and non-users of proton pump inhibitors. *Aliment. Pharmacol. Ther.* 2016, 43, 974–984. [CrossRef]
121. Geremia, A.; Biancheri, P.; Allan, P.; Corazza, G.R.; Di Sabatino, A. Innate and adaptive immunity in inflammatory bowel disease. *Autoimmun. Rev.* 2014, 13, 3–10. [CrossRef] [PubMed]
122. Ma, W.-T.; Chen, D.-K. Immunological abnormalities in patients with primary biliary cholangitis. *Clin. Sci.* 2019, 133, 741–760. [CrossRef] [PubMed]
123. Tanabe, S. The Effect of Probiotics and Gut Microbiota on Th17 Cells. *Int. Rev. Immunol.* 2013, 32, 511–525. [CrossRef] [PubMed]
124. Dillon, S.M.; Lee, E.J.; Kotter, C.V.; Austin, G.L.; Dong, Z.; Hecht, D.K.; Gianella, S.; Siewe, B.; Smith, D.M.; Landay, A.L.; et al. An altered intestinal mucosal microbiome in HIV-1 infection is associated with mucosal and systemic immune activation and endotoxemia. *Mucosal Immunol.* 2014, 7, 983–994. [CrossRef] [PubMed]
125. Mutlu, E.A.; Keshavarzian, A.; Losurdo, J.; Swanson, G.; Forsyth, C.; French, A.; DeMarais, P.; Sun, Y.; Koenig, L.; et al. A Compositional Look at the Human Gastrointestinal Microbiome and Immune Activation Parameters in HIV Infected Subjects. *PLoS Pathog.* 2014, 10, 2. [CrossRef]
126. Lozupone, C.A.; Li, M.; Campbell, T.B.; Flores, S.C.; Linderman, D.; Gebert, M.J.; Knight, R.; Fontenot, A.P.; Palmer, B.E. Alterations in the Gut Microbiota Associated with HIV-1 Infection. *Cell Host Microbe* 2013, 14, 329–339. [CrossRef]
127. Lozupone, C.A.; Rhodes, M.E.; Neff, C.P.; Fontenot, A.P.; Campbell, T.B.; Palmer, B.E. HIV-induced alteration in gut microbiota: Driving factors, consequences, and effects of antiretroviral therapy. *Gut Microbes* 2014, 5, 562–570. [CrossRef]
128. Sinclair, A.J.; Dunning, T.; Dhatteriya, K.; An International Group of Experts. Clinical guidelines for type 1 diabetes mellitus with an emphasis on older adults: An executive summary. *Diabet. Med.* 2019. [CrossRef]
129. Tai, N.; Peng, J.; Liu, F.; Gulden, E.; Hu, Y.; Zhang, X.; Chen, L.; Wong, E.S.; Wen, L. Microbial antigen mimics activate diabetogenic CD8 T cells in NOD mice. *J. Exp. Med.* 2016, 213, 2129–2146. [CrossRef]
130. Rook, G.A.W.; Brunet, L.R. Microbes, immunoregulation, and the gut. *Gut* 2005, 54, 317–320. [CrossRef]
131. Vaarala, O.; Atkinson, M.A. The “perfect storm” for type 1 diabetes: The complex interplay between intestinal microbiota, gut permeability, and mucosal immunity. *Diabetes* 2008, 57, 2555–2562. [CrossRef] [PubMed]
132. Abdollahi-Roodsaz, S.; Joosten, L.A.; Koenders, M.I.; Devesa, I.; Roelofs, M.F.; Radstake, T.R.; Heuvelmans-Jacobs, M.; Akira, S.; Nicklin, M.J.; Ribeiro-Dias, F.; et al. Stimulation of TLR2 and TLR4 differentially skews the balance of T cells in a mouse model of arthritis. *J. Clin. Investig.* 2008, 118, 205–216. [CrossRef] [PubMed]
133. Aletaha, D.; Neogi, T.; Silman, A.J.; Funovits, J.; Felson, D.T.; Bingham, C.O., 3rd; Birnbaum, N.S.; Burmester, G.R.; Bykerk, V.P.; Cohen, M.D.; et al. Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum.* 2010, 62, 2569–2581. [CrossRef] [PubMed]
134. Ericsson, A.C.; Hagan, C.E.; Davis, D.J.; Franklin, C.L. Segmented filamentous bacteria: Commensal microbes with potential effects on the immune. *Comp. Med.* 2014, 64, 90–98.
135. Ivanov, I.I.; Atarashi, K.; Manel, N.; Brodie, E.L.; Shima, T.; Karaoz, U.; Wei, D.; Goldfarb, K.C.; Santee, C.A.; Lynch, S.V.; et al. Induction of intestinal Th17 cells by segmented filamentous bacteria. *Cell* 2009, 139, 485–498. [CrossRef]
136. Rogier, R.; Evans-Martin, H.; Manasson, J.; van der Kraan, P.M.; Waligren, B.; Helsen, M.M.; van den Berselaar, L.A.; van de Loo, F.A.; van Lent, P.L.; Abramson, S.B.; et al. Alteration of the intestinal microbiome characterizes preclinical inflammatory arthritis in mice and its modulation attenuates established arthritis. *Sci. Rep.* 2017, 7, 15613. [CrossRef]
137. Teng, F.; Klinger, C.N.; Felix, K.M.; Bradley, C.P.; Wu, E.; Tran, N.L.; Umesaki, Y.; Wu, H.J. Gut microbiota drive autoimmune arthritis by promoting differentiation and migration of Peyer’s patch T follicular helper cells. *Immunity* 2016, 44, 875–888. [CrossRef]
157. Esatoglu, S.N.; Kutlubay, Z.; Hatemi, G. Highlights of the 18th International Conference on Behçet’s syndrome. Clin. Exp. Rheumatol. 2018, 36 (Suppl. 115), 3–12.
158. Takeuchi, M.; Kastner, D.L.; Remmers, E.F. The immunogenetics of Behcet’s disease: A comprehensive review. J. Autoimmun. 2015, 64, 137–148. [CrossRef]
159. Zeidan, M.J.; Saadoun, D.; Garrido, M.; Klatzmann, D.; Six, A.; Cacoub, P. Behcet’s disease physiopathology: A contemporary review. Auto. Immun. Highlights 2016, 7, 4. [CrossRef]
160. Hugh, J.M.; Weinberg, J.M. Update on the pathophysiology of psoriasis. Cutis 2018, 102, 6–12.
161. Fu, Y.; Lee, C.-H.; Chi, C.-C. Association of Psoriasis with Inflammatory Bowel Disease: A Systematic Review and Meta-analysis. JAMA Dermatol. 2018, 154, 1417–1423. [CrossRef] [PubMed]
162. Shaw, C.A.; Kole, L.C.S.; Elewski, B.E. Association of psoriasis/psoriatic arthritis with inflammatory bowel disease influences management strategy. J. Eur. Acad. Dermatol. Venereol. 2019. [CrossRef] [PubMed]
163. Fukui, Y.; Aoki, K.; Ishii, Y.; Tateda, K. The palatine tonsil bacteriome, but not the mycobiome, is altered in HIV infection. BMC Microbiol. 2018, 18, 127. [CrossRef] [PubMed]
164. Fanales-Belasio, E.; Raimondo, M.; Suligoi, B.; Buttò, S. HIV virology and pathogenetic mechanisms of infection: A brief overview. Ann. Ist. Super Sanità 2010, 46, 5–14.
165. Guaraldi, G.; Orlando, G.; Zona, S.; Menozzi, M.; Carli, F.; Garlassi, E.; Berti, A.; Rossi, E.; Roverato, A.; Palella, F. Premature Age-Related Comorbidities among HIV-Infected Persons Compared with the General Population. Clin. Infect. Dis. 2011, 53, 1120–1126. [CrossRef]
166. Gebo, K.A.; Justice, A. HIV Infection in the Elderly. Curr. Infect. Dis. Rep. 2009, 11, 246–254. [CrossRef]
167. Vazquez-Castellanos, J.F.; Serrano-Villar, S.; Latorre, A.; Artacho, A.; Ferrús, M.L.; Madrid, N.; Vallejo, A.; Sainz, T.; Martínez-Botas, J.; Ferrando-Martínez, S.; et al. Altered metabolism of gut microbiota contributes to chronic immune activation in HIV-infected individuals. Mucosal Immunol. 2015, 8, 760–772. [CrossRef]
168. Gili, Z.-S.; Niv, Z.; Shlomik, I.; Stavros, B.; Hila, E.; Eran, E. The gut microbiome in human immunodeficiency virus infection. BMC Med. 2016, 14, 83.
169. Liu, J.; Johnson, R.; Dillon, S.; Kroehl, M.; Frank, D.N.; Tuncil, Y.E.; Zhang, X.; Ir, D.; Robertson, C.E.; Seifert, S.; et al. Among older adults, age-related changes in the stool microbiome differ by HIV-1 serostatus. EBioMedicine 2019, 40, 583–594. [CrossRef]
170. Mudd, J.C.; Brenchley, J.M. Gut Mucosal Barrier Dysfunction, Microbial Dysbiosis, and Their Role in HIV-1 Disease Progression. J. Infect. Dis. 2016, 214, 558–566. [CrossRef]
171. González-Hernández, L.A.; Ruiz-Briseño, M.d.R.; Sánchez-Reyes, K.; Alvarez-Zavala, M.; Vega-Magaña, N.; López-Íñiguez, A.; Díaz-Ramos, J.A.; Martínez-Ayala, P.; Soria-Rodriguez, R.A.; Ramos-Solano, M.; et al. Alterations in bacterial communities, SCFA and biomarkers in an elderly HIV-positive and HIV-negative population in western Mexico. BMC Infect. Dis. 2019, 19, 234. [CrossRef] [PubMed]
172. Nowak, R.G.; Bentzen, S.M.; Ravel, J.; Crowell, T.A.; Dauda, W.; Ma, B.; Liu, H.; Blattner, W.A.; Baral, S.D.; Charurat, M.E.; et al. Rectal microbiota among HIV-uninfected, untreated HIV, and treated HIV-infected men who have sex with men (MSM) in Nigeria. AIDS 2017, 31, 857–862. [CrossRef] [PubMed]
173. Nowak, P.; Troseid, M.; Avershina, E.; Barqasho, B.; Neogi, U.; Holm, K.; Hov, J.R.; Noyan, K.; Vesterbacka, J.; Svärd, J.; et al. Gut microbiota diversity predicts immune status in HIV-1 infection. AIDS 2015, 29, 2409–2418. [CrossRef] [PubMed]
174. Wondimeneh, Y.; Aki, Y.; Ishii, Y.; Tateda, K. The palatine tonsil bacteriome, but not the mycobiome, is altered in HIV infection. BMC Microbiol. 2018, 18, 127. [CrossRef] [PubMed]
175. Johnsen, J. Pathogenesis in immune thrombocytopenia: New insights. Hematology 2012, 2012, 306–312. [CrossRef] [PubMed]
176. Passos, A.M.; Treitinger, A.; Spada, C. An overview of the mechanisms of HIV-related thrombocytopenia. Acta Haematol. 2010, 124, 13–18. [CrossRef] [PubMed]
177. Gomez, V.; Smith, P.R.; Burack, J.; Daley, R.; Rosa, U. Sarcoidosis after antiretroviral therapy in a patient with acquired immunodeficiency syndrome. Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am. 2000, 31, 1278–1280. [CrossRef]
178. Cupler, E.J.; Jay, C.; Dalakas, M.C.; Danon, M.J.; Ropka, M.; Hench, K. Early features of zidovudine-associated myopathy: Histopathological findings and clinical correlations. Acta Neuropathol. 1995, 90, 1–6. [CrossRef]
179. Parsa, A.A.; Bhangoo, A. HIV and thyroid dysfunction. Rev. Endocr. Metab. Disord. 2013, 14, 127–131. [CrossRef]
180. Jubault, V.; Penfornis, A.; Schillo, F.; Hoen, B.; Izembart, M.; Timsit, J.; Kazatchkine, M.D.; Gilquin, J.; Viard, J.-P. Sequential Occurrence of Thyroid Autoantibodies and Graves’ Disease after Immune Restoration in Severely Immunocompromised Human Immunodeficiency Virus-1-Infected Patients. *J. Clin. Endocrinol. Metab.* **2000**, *85*, 4254–4257.

181. Solis, B.; Samartín, S.; Gómez, S.; Nova, E.; de la Rosa, B.; Marcos, A. Probiotics as a help in children suffering from malnutrition and diarrhea. *Eur. J. Clin. Nutr.* **2002**, *56*, S57–S59. [CrossRef] [PubMed]

182. Gough, E.; Shaikh, H.; Manges, A.R. Systematic review of intestinal microbiota transplantation (fecal bacteriotherapy) for recurrent *Clostridium difficile* infection. *Clin. Infect. Dis.* **2011**, *53*, 994–1002. [CrossRef] [PubMed]

183. De Oliveira, G.L.V.; Leite, A.Z.; Higuchi, B.S.; Gonzaga, M.I.; Mariano, V.S. Intestinal dysbiosis and probiotic applications in autoimmune diseases. *Immunology* **2017**, *152*, 1–12. [CrossRef] [PubMed]

184. Vaghef-Mehrabany, E.; Alipour, B.; Homayouni-Rad, A.; Sharif, S.-K.; Asghari-Jafarabadi, M.; Zavvari, S. Probiotic supplementation improves inflammatory status in patients with rheumatoid arthritis. *Nutrition* **2014**, *30*, 430–435. [CrossRef]

185. Zhou, Y.; Xu, H.; Huang, H.; Li, Y.; Chen, H.; He, J.; Du, Y.; Chen, Y.; Zhou, Y.; Nie, Y. Are There Potential Applications of Fecal Microbiota Transplantation beyond Intestinal Disorders? *BioMed Res. Int.* **2019**, 2019, 3469754. [CrossRef]

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