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Review

The Role of Gut Microbiota in Food Allergies and the Potential Role of Probiotics for Their Treatment

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Abstract

The number of food allergies (FAs) is growing, particularly in industrialized countries, resulting in discomfort and a reduction in the quality of life of those who suffer from these allergies. Despite numerous epidemiological studies on FAs worldwide, the different approaches used constitute a limitation for an accurate prevalence of these disorders. The onset of FAs is multifactorial, since it depends on lifestyle, habitat, diet, and particularly on the diversity of gut microbiota. In fact, they occur in conditions of gut dysbiosis, an increase of the inflammatory state, an alteration of gut permeability, and an impairment of the resident immune cells, thus leading to a disruption and/or lack of tolerance towards food allergens. It is important to emphasize that the reduction of some bacteria leads to a decrease in their metabolite production, which, in turn, is crucial for the correct performance of immune responses and to ensure tolerance against allergens. Therefore, various strategies such as pre- and probiotic administration must be employed to avoid or prevent the onset of FAs.

Keywords: diet; food allergies; gut microbiota; immune cell system; immunoglobulins; interleukins; probiotics; short-chain fatty acids; tolerance

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Academic Editor: Małgorzata Ziarno

Received: 17 May 2025
Revised: 24 August 2025
Accepted: 29 August 2025
Published: 31 August 2025

Citation: Magrone, T.; Magrone, M.; Notaristefano, R.; Gaxhja, E.; Rezaeinezhad, N.; Topi, S.; Santacroce, L.; Colella, M. The Role of Gut Microbiota in Food Allergies and the Potential Role of Probiotics for Their Treatment. *Appl. Sci.* **2025**, *15*, 9590. https://doi.org/10.3390/app15179590

1. Introduction

The prevalence of food allergies (FAs) is influenced by several factors, such as geographic region, food intake, exposure to environmental factors, and the healthcare and diagnostic methods used [1]. Higher percentages of FAs are observed in urban areas of Western countries [2], whereas the prevalence of FAs tends to decrease in rural areas. These events could be determined by early-life microbial exposure, air pollution, and individuals' habitats. Despite epidemiological studies performed worldwide, the prevalence of FAs is not easily determined, since different approaches to defining these disorders are used. Moreover, only in a few cases, specific tests to understand the individual's pathological condition (e.g., determination of specific IgE) [3] are used. For this reason, the results reported in the literature are extremely heterogeneous, and the monitoring system related to FAs should be optimized.

The gut microbiota plays a significant role in the development of FAs, as discussed below, as well as in other disorders. Gut microbiota is represented by a wide variety of microorganisms, including bacteria, archaea, fungi, and viruses. Among bacteria, they are distinguished in six main phyla: Bacillota, Bacteroidota, Actinomycetota, Pseudomonadota, Verrucomicrobiota, and Methanobacterota [4]. These microorganisms establish complicated relationships, not only with each other but also with the host, varying from symbiotic to parasitic interactions; thus, they have an important impact on the host's immune system [5]. The gut barrier, which is constantly exposed to several foreign antigens, is composed of the epithelium, the mucous layer, and mucosal immune cells. The mucosal layer is an outer layer formed by intestinal epithelial cells (IECs), which constitute the first barrier against the access of antigens into the host. In fact, IECs allow the interaction between the gut environment and host, since they can sense signals from outside through pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) and nucleotide-binding and oligomerization domain-like receptors, which can recognize microbe-associated molecular patterns such as lipopolysaccharides (LPS), peptidoglycan, lipoteichoic acid, and flagellin [6]. IECs are distinguished in enterocytes, Paneth cells involved in the production of antimicrobial peptides such as defensins and cathelicidins [7], and Goblet cells. The latest are involved in mucus production, with the secretion of mucin resulting in the formation of a mucous layer that has a protective function; indeed, it reduces the interaction between epithelium and gut microbiota [8,9]. Another important group of cells is the so-called microfold (M) cells, which permit antigen transit from the gut lumen to immune cells placed in the lamina propria [10]. M cells cover Peyer's patches, which represent the secondary lymphoreticular tissue associated with the gut. Each component of the gut barrier is fundamental to defending the host from harmful antigens introduced via ingestion. The gut microbiota has important and well-known roles, e.g., the prevention of bacterial translocation and the protection of the gut mucosa from pathogen invasion, respectively. Both the gut barrier and gut microbiota provide for host wellbeing via the absorption and metabolism of nutrients and protect immune cells via a targeted protective response initiated by the host itself. It is important to highlight that gut microbiota have a variable age-related composition, and in infants, Pseudomonadota are mainly represented, followed by Actinomycetota, whereas in adulthood, gut microbiota are mainly characterized by Bacillota and Bacteroidota [11]. An alteration of both the gut barrier and the composition of gut microbiota, respectively, leads to a state of dysbiosis accompanied by an immune response of different intensities due to a well-known gut–immune system axis. FAs are immunological reactions caused by food allergens (i.e., proteins) that usually do not lead to any damage. When the host is exposed to a specific allergen, a series of immune responses is triggered to counteract the adverse effects of the allergen. There are distinct types of allergies depending on the type of allergen, including FAs. Food-derived allergens undergo biochemical reactions that subvert their initial composition, triggering an immune response of different severity. Moreover, FAs are distinguished from food intolerances, since in the latter, the immune system is not involved [12]. Therefore, FAs are classified according to the type of immune response into three distinct groups, as follows: IgE-mediated FAs, in which food allergens cause a type I hypersensitivity reaction, where IgE production occurs, and mast cells (MCs) and basophils are ultimately activated [13]. Non-IgE-mediated FAs, on the other hand, are distinguished by the presence of allergen-specific helper T (Th)2 cells and characterized by delayed symptoms [14]. Finally, in combined FAs, IgE-dependent and IgE-independent, the above-described reactions coexist, and individuals with these allergies are more susceptible to eosinophilic gastrointestinal disorders, such as eosinophilic esophagitis [15].

In this review, we will report some results obtained from several studies performed on FAs. In addition, at the same time, we will examine the intricate relationship between the gut microbiota and the immune response that, under unbalanced circumstances, allows the development of FAs, and the important role of probiotics in mitigating FAs.

2. Search Strategy

Both original articles and reviews, meta-analyses, and clinical and randomized trials were searched on Medline (PubMed), Scopus, and Web of Science. The main keywords were "Gut microbiota", "Gut microbiota and food allergies", "Gut microbiota and immune cells", "Short Fatty Acids" or "SCFAs", "Prebiotics", and "Probiotics". Only articles written in English were included, without limitation on the years of publication.

2.1. Mechanisms of Action of Resident Gut Immune Cells

A well-functioning immune system requires specific regulatory mechanisms to achieve a balance between tolerant and immunogenic responses directed towards foreign antigens and self-antigens. Hypersensitivity type I reactions are triggered by the introduction of an allergen, which is then presented in association with major histocompatibility complex-II (MHC-II) by dendritic cells (DCs) to Th2 lymphocytes, which, in turn, secrete interleukin (IL)-4 and IL-5, thus activating B lymphocytes, which undergo an isotype switching (under the regulation of IL-4) and, after their differentiation into plasma cells, begin to secrete IgE. Meanwhile, IL-5 promotes the numerical increase of both eosinophils and basophils, where the latter expresses a specific receptor for IL-5 on their plasma membrane. Allergen-specific IgEs produced by plasma cells bind a specific receptor of the crystallizable fragment exposed to MCs, and during a subsequent exposure to the same allergen, IgEs bind via their antigen-binding fragment to a specific allergen, and MCs degranulate with the release of several mediators, the first of all being histamine [16]. Therefore, FAs arise when cells of the immune system have been sensitized to specific allergens. In particular, at the gut level, allergens travel across the gut barrier, then they are picked up via M cells, and at the end, they are recognized by DCs [17,18]. However, when the gut epithelial barrier is compromised, due for example to an increase of inflammatory status, allergens can easily pass through it and stimulate the secretion of ILs such as IL-25, IL-33, and thymic stromal lymphopoietin, which, in turn, promote the differentiation of naive T lymphocytes into Th2 lymphocytes, and MC tissue accumulation [19,20] (see Figure 1).

The gut microbiota represents an important component of this complex mechanism of allergic sensitization [21]. Therefore, FAs occur upon prior sensitization, which is determined by food-specific IgE [22]. It is important to keep in mind that in eubiosis conditions, antigens that reach the gut barrier are unable to cross it without the intervention of both Goblet cells and CX3CR1 macrophages, which transfer antigens to DCs cells and to draining lymph nodes, thus contributing to the differentiation of T naive cells into food allergen-specific regulatory T cells (Treg) [23]. With regard to DCs, they are mainly represented by three subsets, specifically two types of conventional DCs (cDCs) and plasmacytoid DCs (pDCs) [24]. The cDCs activate naive T cells, and they express CD11c and MHC-II molecules. Depending on their stage of differentiation, they are classified into immature, mature, and regulatory DCs, respectively. DCs serve as sentinel cells distributed throughout the body [25]. In this regard, it has been hypothesized that, in the absence of inflammatory signals, the sensing in the environment by DCs increases peripheral T-cell tolerance, thus contributing to the maintenance of immune homeostasis [26]. When PRRs detect pathogen- or damage-associated molecular patterns, DCs are activated [27] via upregulation of chemokine C-C receptor 7, which promotes DC-mediated antigenic presentation to T lymphocytes [28]. From an immunological point of view, DCs ensure a balanced Th2 response and contribute to humoral immunity, protecting the host from extracellular pathogens. From an immunological point of view, FAs are characterized by an exaggerated Th2-dependent response [29], caused by an altered homeostasis of the gut microbiota. Intestinal DCs, distributed in the lamina propria and mesenteric lymph nodes, pick up allergens and activate Th2 lymphocytes by secreting IL-4, IL-5, and IL-13, which in turn stimulate B lymphocytes to differentiate into plasma cells producing allergen-specific IgE (see Figure 2) [30].

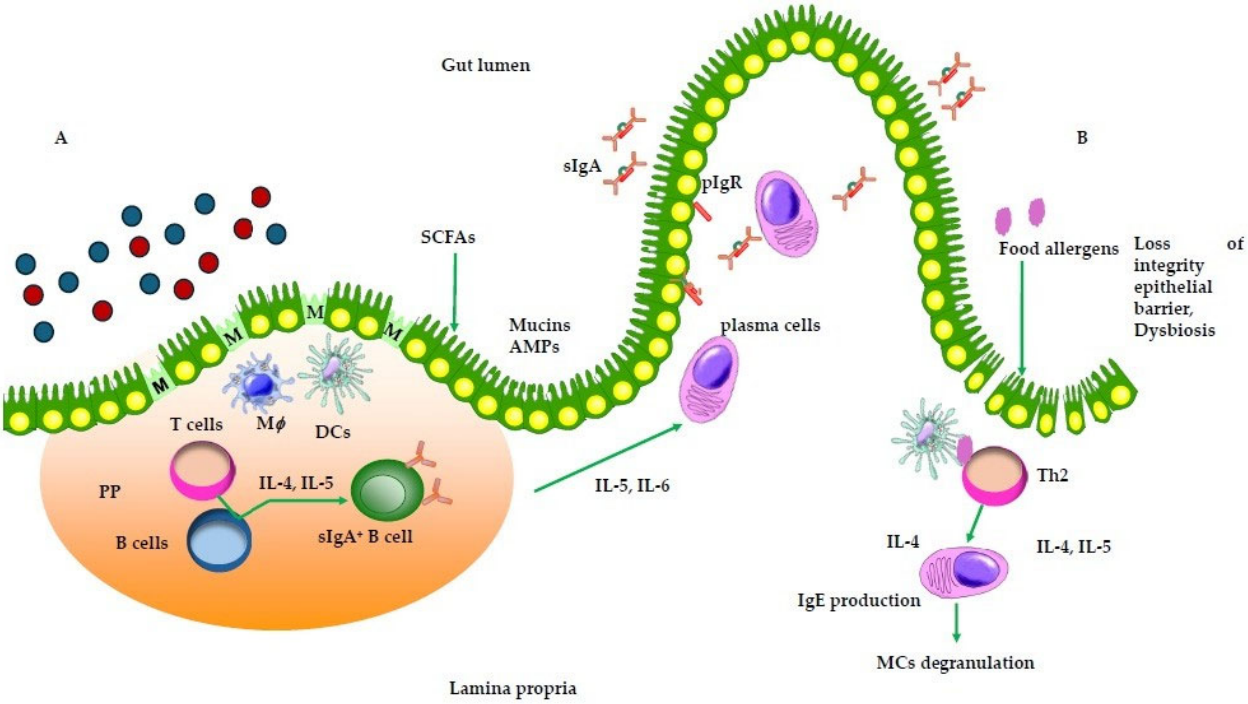

Figure 1. Gut microbiota and the interaction with the resident immune cells. (**A**). In the gut lumen, a diversified and balanced content of Gram-positive (in blue) and Gram-negative (in red) bacteria ensures a proper function of Peyer Patches (PPs) beneath the gut barrier, containing DCs, macrophages, Th cells, and B cells. Under homeostatic conditions, sIgA production confers an efficient immune response as well as oral tolerance. In addition, SCFA, mucins, and AMPs also contribute to the maintenance of gut barrier integrity. (**B**). Food allergens lead to an alteration of the gut epithelial barrier, thus increasing and activating Th2 cells, which in turn trigger MC degranulation. Abbreviations: Antimicrobial peptides, AMPS; Dendritic cells, DCs; Mast cells, MCs; Peyer patches, PPs; secretory IgA, sIgA; SCFAs, Short-chain fatty acids; helper T cells, Th. (Figure credits: Thea Magrone).

Regarding Treg cells, they represent a subset of CD3+CD4+CD25+ T lymphocytes characterized by the presence of the nuclear transcription factor FoxP3 [31]. Tregs are involved in immune tolerance processes, and their numerical reduction or functional deficiency leads to inappropriate immune responses to harmless food antigens, commensal bacteria, and self-antigens [32], leading to allergic and autoimmune reactions. Diet is one of the most crucial factors in regulating Treg cells [33], and it also affects the gut microbiota [34]. Treg cells differentiate in the thymus and are divided into thymic-derived cells (tTregs) and peripheral-derived cells (pTregs) [35], and each of them expresses different functions. The differences lie in the expression of biomarkers such as Cytotoxic T-Lymphocyte Antigen 4 (CTLA-4) and Programmed Cell Death protein 1 (PDL-1), and also in their ability to produce ILs. Self-antigens are presented by medullary thymic epithelial cells (mTECs) and their recognition by T-cell receptors (TCRs) causes clonal deletion for apoptosis of tTregs, so a low percentage of T cells survive and differentiate into Treg cells. The binding of the co-stimulatory molecule CD28 with the CD80/CD86 ligand, expressed by antigen-presenting cells, promotes tTreg differentiation [36]. The mTECs represent a cellular subset mainly involved in antigenic presentation in the thymus; this mechanism is governed by the autoimmune regulatory transcription factor in collaboration with the Fez family zinc finger protein 2 [36]. After thymic regression, the development of tTreg cells is impaired, since thymic progenitors are unable to drive the differentiation of tTreg cells [37]. Thymic regression is a developmental mechanism targeted to preserve a tolerogenic microenvironment during pregnancy and the early exposure to environmental antigens. The newly formed tTreg pool is characterized by a broad heterogeneity of TCR repertoire and a marked expression of FoxP3 and CTLA-4, in comparison to adult tTreg cells [38]. By contrast, pTregs derive from naive CD4+ T lymphocytes or peripheral DCs and, unlike tTreg, pTreg differentiation is dependent on tumor growth factor-β (TGF-β), which upregulates FoxP3 expression [39]. In summary, oral tolerance has been defined as an unresponsive systemic state, where the gut secondary lymphoid tissue immune cells recognize food allergens [40], which are then endocytosed by tolerogenic CD103+ DCs [41] and degraded into peptides into vesicles in association with MHC-II. Thus, CD 103+ DCs begin to secrete TGF-β and retinoic acid. In this way, CD103+ DCs contribute to the differentiation of naive T lymphocytes into Treg cells [42], which secrete IL-10 and TGF-β [43], and it has been shown that anergy, such as non-responsiveness and T-cell depletion via apoptosis, are part of the tolerance mechanisms. The main features of the gut immune cells and their interactions with the gut microbiota are summarized in Table 1.

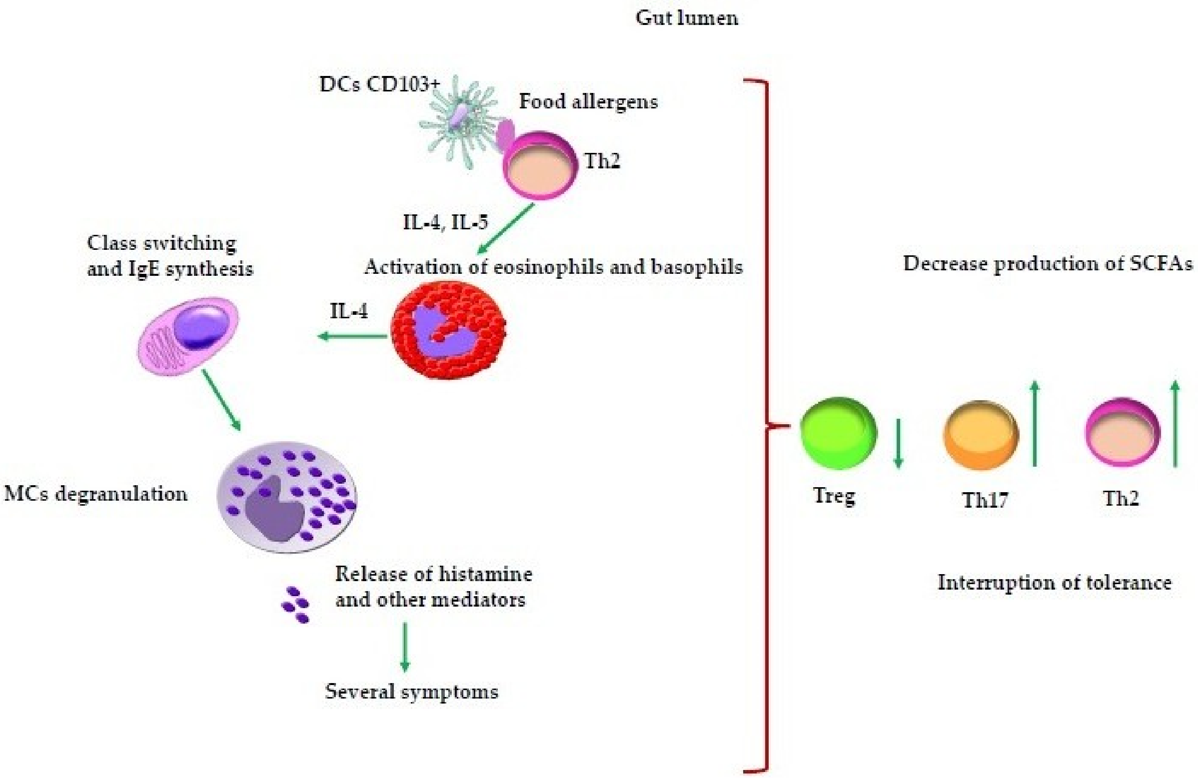

Figure 2. Interaction, in the gut lumen, between food allergens and immune cells. DCs present dietary allergens to Th2 cells, which, in turn, via the release of IL-4 and IL-5, trigger activation of eosinophils and basophils, respectively. IL-4 enhances isotype switching production of IgE via plasma cells, which binds to the specific receptor on MCs, causing their degranulation with the release of several mediators, which contribute to several symptoms. Therefore, an increase in Th2 and Th17 cells, respectively, secreting pro-inflammatory ILs, and a decrease in Treg cells, leads to a failure of oral tolerance. Abbreviations: Dendritic cells, DCs; Interleukins, ILs; Mast cells, MCs; helper T cells, Th; regulatory T cells, Treg. (Figure credits: Thea Magrone).

Table 1. Main features and mechanisms of action of resident gut immune cells. The table offers an overview of the key functions of immune cells and of the intestinal microbiota, focusing on allergic sensitization and immune tolerance.

Cell Type/Subset	Phenotypic Markers	Main Functions	Role in FAs	Role in Immune Tolerance
DCs	cDCs: CD11c$^+$, MHC-II, pDC subsets;	Antigen capture, processing, and presentation; PRR sensing; IL secretion	Present allergens to naive CD3$^+$CD4$^+$ T cells; Th2 polarization via IL-4, IL-5, IL-13; Promote IgE class switching in B cells	-----
Tolerogenic DCs	CD103$^+$ PDL-1, MHC-II	Antigen capture, processing, TGF-β and IL-10 secretion	Induce Treg differentiation	In the absence of inflammation, promote peripheral tolerance
Naïve CD4$^+$ T lymphocytes	CD3$^+$, CD4$^+$	Differentiate into several subsets depending on IL milieu	IL-4/IL-13 influence, differentiation into Th2 amplifying allergic inflammation	Under TGF-β/retinoic acid, differentiate into pTreg, maintaining tolerance
Th2 lymphocytes	CD3$^+$CD4$^+$, GATA-3$^+$	Secrete IL-4, IL-5, IL-13	IL-4: IgE class switching; IL-5: Eosinophil/basophil recruitment; IL-13: Mucus production, barrier alteration	-----
B lymphocytes/ Plasma cells	CD3$^-$CD19, CD3$^-$CD20$^+$/CD138$^+$	Antibody production	Production of allergen-specific IgE that binds FcεRI on MCs/basophils	Under IL-10/TGF-β influence, produce IgG4 (blocking antibodies)
MCs	FcεRI$^+$, c-kit$^+$	Degranulation: histamine, Leukotrienes, Prostaglandins release	Type I hypersensitivity reaction: vasodilation, smooth muscle contraction, mucus secretion	Regulated activation prevents inappropriate inflammation
Basophils	FcεRI$^+$, IL-5Rα$^+$	Circulating effector cells, IL producers	Amplify Th2 inflammation; release mediators on IgE crosslinking	Minimal or null role in immune tolerance
Eosinophils	CCR3$^+$, IL-5Rα$^+$	Cytotoxic granule release, IL secretion	Tissue damage and amplification of inflammation in FAs	-----
Treg cells	CD3$^+$CD4$^+$ CD25$^+$FoxP3$^+$	Immunosuppression via IL-10, TGF-β, CTLA-4	Deficiency/dysfunction: Loss of tolerance; FA development	Maintain tolerance to food antigens, commensals, and self-antigens
Goblet cells and CX3CR1$^+$ macrophages	MUC2$^+$/CX3CR1$^+$	Antigen sampling and transfer to DCs	When the barrier is impaired, increased allergen translocation can occur	Facilitate tolerogenic Ag presentation to DCs
Gut microbiota	-----	Modulate immune development and barrier function	Dysbiosis leads to Th2 skewing and FA risk	Eubiosis supports Treg induction and mucosal barrier integrity

Abbreviations: Conventional DCs, cDCs; Cytotoxic T lymphocyte antigen 4 (CTLA-4); Dendritic cells, DCs; Interleukin, IL; Mast cells, MCs; MHC, Major histocompatibility complex; plasmacytoid DCs, pDCs; Programmed death ligand 1, PDL-1; Peripheral Treg, pTreg; Transforming growth factor, TGF-β; helper T cell, Th; regulatory T cells, Tregs.

2.2. Role of Short-Chain Fatty Acids in Gut Immune Regulation

Several studies have revealed that FAs were associated with alterations in gut microbiota metabolism [44,45]. In fact, in the intestines, a large number of molecules are produced, all crucial for the gut microbiota and host immune system, and these interactions inhibit pathogen proliferation [46]. Fermentation of dietary fibers, mediated by bacteria, leads to the synthesis of short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate, which have exhibited beneficial effects in autoimmune and inflammatory disorders [47], in maintaining the integrity of gut epithelium, and in promoting immune tolerance. SCFAs, in particular butyrate and propionate, are mainly produced by Bacillota [48] and exert an anti-inflammatory action aiming to improve the integrity of the epithelial barrier and to reduce sensitization to food allergens [49]. By contrast, dysbiosis and low intestinal SCFA levels have been associated with the onset of FAs [50]. The main producers of butyrate are Bacillota, especially *Clostridiaceae*, *Faecalibacterium prausnitzii,* and *Agathobacter rectalis* (formerly *Eubacterium rectale*) [51,52]. Furthermore, in case of a low-fiber diet, the gut microbiota starts to absorb and metabolize glycoproteins, which are part of the muco-epithelial barrier, resulting in its impairment and consequently increasing gut permeability [53]. Lastly, it is important to highlight that decreased expression of the vitamin D receptor downregulates the claudin-2 protein, which is part of the multiprotein tight junction complex, thereby increasing intestinal permeability [54]. In fact, according to the "epithelial barrier" hypothesis, dysfunction of the gut barrier, due to increased sensitivity to environmental factors, leads to the development of FAs [55,56]. It has been established that SCFAs are required for the modulation of the mucosal immune system [57]. For example, butyrate acts on IECs and on DCs, and it is involved in mucosal Tregs development [57]. In this regard, butyrate stimulates the activation of hypoxia-inducible factor, preserving the integrity of the gut barrier [58] and, in combination with the other SCFAs, stimulates mucin production [59]. In addition, SCFAs are responsible for the production of antimicrobial peptides and IL-18, implicated in tolerance and the promotion of gut homeostasis [60,61]. In fact, butyrate interacts with intestinal CD103+ DCs via the stimulation of their surface receptor GPR109a, promoting the proliferation of Treg cells [62]. Several studies show that Treg cells in the small intestine, after the recognition of food allergens, can inhibit the onset of adverse reactions via immunosuppressive feedback [63], sustained by butyrate and retinoic acid [63]. In addition, butyrate is an activator of peroxisome proliferator-activated receptor gamma (PPARγ), mitochondrial respiration, and oxidative phosphorylation. In this way, an anaerobic environment is established, and both epithelium proliferation and Th2-dependent responses are reduced [64]. On the other hand, acetate promotes vitamin A metabolism in IECs and DCs via GPR43, which, in turn, increases IgA production [65]. Therefore, SCFAs promote the differentiation of B lymphocytes into IgG or IgA-secreting plasma cells [66].

2.3. Relationship Between the Development of Food Allergies and Changes in Gut Microbiota in Early Life

Multiple factors influence the development of FAs, such as genetic predisposition, the period of life when the host encounters an allergen, maternal or artificial breast-feeding, weaning, the pregnant women's dietary behavior, abuse of antibiotics, type of childbirth (see Figure 3) [67,68], and, last but not least, alterations of gut barrier and gut microbiota. A newborn's gut microbiota is influenced by the SCFAs produced by the maternal gut microbiota since prenatal life [69,70]. In the first two weeks after birth, the gut microbiota of breastfed infants mainly contains *Bifidobacteriaceae*, and in two years, their gut microbiota becomes really similar to that of adults, with a greater presence of Bacteroidota. Instead, the gut microbiota of infants with caesarean sections (CSs) is associated with reduced microbial diversity and colonization dominated by *Staphylococcaceae*, *Propionibacteriaceae*, and *Corynebacteriaceae*, which is similar to the microbial composition of maternal skin [71]. In contrast, in vaginal delivery, *Lactobacillaceae* are predominant in a newborn's oral cavity, skin, and gut, in combination with *Sneathia* and *Prevotellaceae*, thus showing a microbiota profile typical of the vaginal microbiota [72]. In CS newborns, a reduced amount of *Es-*

cherichia coli and *Bacteroides fragilis* and an increase of *Clostridioides difficile* are found on the first day after delivery [73]. In addition, Jakobsson et al. [74] in their study have observed that CS newborns have a reduced microbiota biodiversity, with limited colonization of Bacteroidota up to 24 months after birth in comparison to vaginal delivery newborns. Furthermore, CS delivery is one of the risk factors for the development of FAs [75]. In another study, Khodayar-Pardo et al. [76] observed that in breast milk of women with CS delivery, the *Bifidobacteriaceae* content is reduced in comparison to breast milk of mothers who vaginally delivered [76]. The PASTURE study has demonstrated that poor dietary variation during the first year of life is associated with a higher risk of developing FAs around 4–6 years of age [77]. The gut microbiota of newborns is composed of commensals from both the maternal gut microbiota and milk. Human milk plays a pivotal role in the prevention or promotion of FAs due to the presence of human milk oligosaccharides (HMOs), glyco-macropeptides, lactoferrin, defensins [78], and other molecules [79]. HMOs act as prebiotics, as they inhibit bacterial adhesion to the gut mucosa and, therefore, prevent the colonization of pathogens [80]. Casein glyco-macropeptides, defensins, and tryptophan metabolites possess antimicrobial properties [81]. Lactoferrin, an iron-binding protein, has antiviral and antibacterial activities and hampers the binding of LPS to TLR-4, thus preventing the release of pro-inflammatory ILs [78,82]. *Bifidobacterium* spp. are present in breastfed neonates from their second day of life and represent the predominant bacteria until weaning [83], whereas after the introduction of a varied diet, an increase in Bacteroidota and Bacillota is observed. After 2–3 years, the gut microbiota of a child becomes similar to that of an adult and is characterized by an increased number of Bacteroidota [84]. Concerning HMOs, only *Bifidobacterium (B.) breve*, *B. longum subspecies infantis,* and *B. bifidum* can utilize them. Breast milk also contains probiotic *Lactobacillaceae* species; for example, *L. salivarius* is predominant along with *B. breve* [85]. Finally, *Streptococcaceae* and *Staphylococcaceae* are also found in breast milk. *Bifidobacteriaceae* can ferment HMOs and convert some amino acids, such as tryptophan, into lactic acid derivatives. Tryptophan-derived indoleacetic acid has proven to activate the aryl hydrocarbon receptor (AhR), which, in turn, activates Treg cells via a reduction of Th2 and Th17 cells [86,87] with a consequent reduction of proinflammatory ILs. Other bacteria, such as *Escherichia coli*, can metabolize food-derived L-tryptophan to promote the production of indole [88], whereas *Lactobacillaceae* form indole derivatives [89]. These indole derivatives act on the immune response via the AhR receptors [90], thereby triggering Th cells differentiation and synthesis of anti-inflammatory ILs [91]. Furthermore, AhR activation constrains the increase of permeability of the gut epithelium, stabilizing the tight junctions [91]. The gut microbiota of term vaginal delivery of newborns with maternal breastfeeding provides the basis for the development of immune tolerance. Indeed, in CS delivery and formula-fed newborns, the gut microbiota is characterized by the expansion of Th2 lymphocytes [92], which promotes allergic responses. Kalliomaki et al. [93] have demonstrated that in 3-week-old neonates, the reduction of *Bifidobacteriaceae* and the increase of *Clostridiaceae* led to an increased risk of developing atopic dermatitis (AD). Abrahamsson et al. [94] have conducted a clinical trial where they demonstrated that newborns with AD have higher IgE concentrations and a reduced presence of Bacteroidota in comparison to newborns without allergic manifestations. Other authors [95] have identified the fecal bacterial species liable for FAs in children with AD. Their results revealed a reduction of *B. breve,* which is normally present in children's gut microbiota and breast milk. However, during the fetal period, the immune system develops the Th2-dependent profile [96], so in infants, the gut barrier is impaired due to the absence of secretory IgA (sIgA) and mucus [97]. *B. breve* M-16V has been shown to prevent allergies via the production of sIgA [98]. In addition, the IgAs contained in breast milk seem to retain good bacteria in the gut mucous layer, thus promoting their colonization in the neonate's gut [99]. A study performed on premature neonates has verified that the administration of *B. breve* M-16V for four weeks increases the amount of SCFAs in neonates' feces due to the abundance of *Bifidobacteriaceae*, resulting in the reinforcement of gut epithelial barrier [100] and thus conferring protection from pathogens. Finally, the feces of subjects with FAs had a reduced amount of SCFAs in comparison to healthy controls. In particular, *Prevoltella copri* was more abundant in subjects without allergies in comparison to subjects with FAs [101,102]. Later, the introduction of solid foods leads to delayed microbial maturation, thus increasing a child's susceptibility to allergies [103]. On the other hand, the premature introduction of solid foods could expose children to pathogens and allergens. Therefore, the time for the introduction of solid foods for children should be reconsidered due to the latest evidence about FAs [104,105]. In one study regarding infant feeding, egg introduction was recommended around 4–6 months of age and peanut between 4 and 11 months, since this approach was correlated with a reduced risk of egg and peanut allergy, respectively [106]. These recommendations are in contrast to prior ones about the introduction of allergenic foods into the child's diet to delay the sensitization process [107]. However, early introduction of allergenic foods was associated with a reduction in IgE-mediated allergy, in line with the results obtained from the PreventADALL study [108]. Maternal breastfeeding and a varied diet promote healthy gut microbiota both during weaning and in early life [109]. Indeed, during weaning, a heterogeneous diet leads to greater diversity of gut microbiota, thus increasing immune tolerance in neonates. Du Toit et al. [110] have observed that low-dose allergen introduction promotes the development of immune tolerance. A heterogeneous microbiota promotes the tolerance of the immune system for innocuous antigens (derived from gut bacterial communities) and food allergens via IgA-mediated response, together with an appropriate function of Treg cells [111]. IgAs secreted across mucosal barriers and in breast milk act as immunomodulators, whereas IgG antibodies are present in high amounts in the lymph and blood, supporting systemic immunity [112]. Evidence has shown that IgAs participate in the maintenance of the composition of the gut microbiota, so their reduction has been associated with a decrease in bacterial diversity [113]. Furthermore, high concentrations of IgA in the gut have been associated with a lower risk of IgE-mediated allergy [114]. In patients with FAs, a reduced concentration of IgA-coated bacteria and an increased level of IgE-coated bacteria were observed. Children with IgE-mediated and non-IgE-mediated cow milk allergy (CMA) were recruited, and different IgA-coating bacterial profiles were identified in the two groups. The results identified different microbial signatures in children with CMA. The reduced alpha diversity (diversity within a community) and dysbiosis observed in children with CMA were attributed to altered IgA and IgG concentrations [115]. Finally, an increase in IgG-binding bacteria was observed in the AD group, perhaps due to the increased amount of *Staphylococcaceae* and *Corynebacteriaceae* [116,117]. Furthermore, it was observed that AD precedes FA development [118], and an abundant skin colonization by *Staphylococcus aureus* increases the risk of FAs [119].

Going back to SCFAs, they exert a protective role in FAs, stimulating immune tolerance and IgA production in the gut lumen [120,121]. In fact, patients with FAs show a reduction in both gut commensals and SCFAs. Acetate has been found to stimulate IgA production via GPR43 on IECs and DCs [122]. Furthermore, SCFAs promote the differentiation of B lymphocytes into IgG- or IgA-secreting plasma cells [123]. There are four subgroups of IgG: IgG1, IgG2, IgG3, and IgG4. The first one is more abundant than the others [124]. While IgG1 and IgG3 react against protein antigens, IgG2 acts against the polysaccharides of encapsulated bacteria [125]. In addition, the spontaneous disappearance of CMA in children is associated with a higher concentration of IgG4 [126]. Of note, IgG4 promotes peanut tolerance in allergic patients [127].

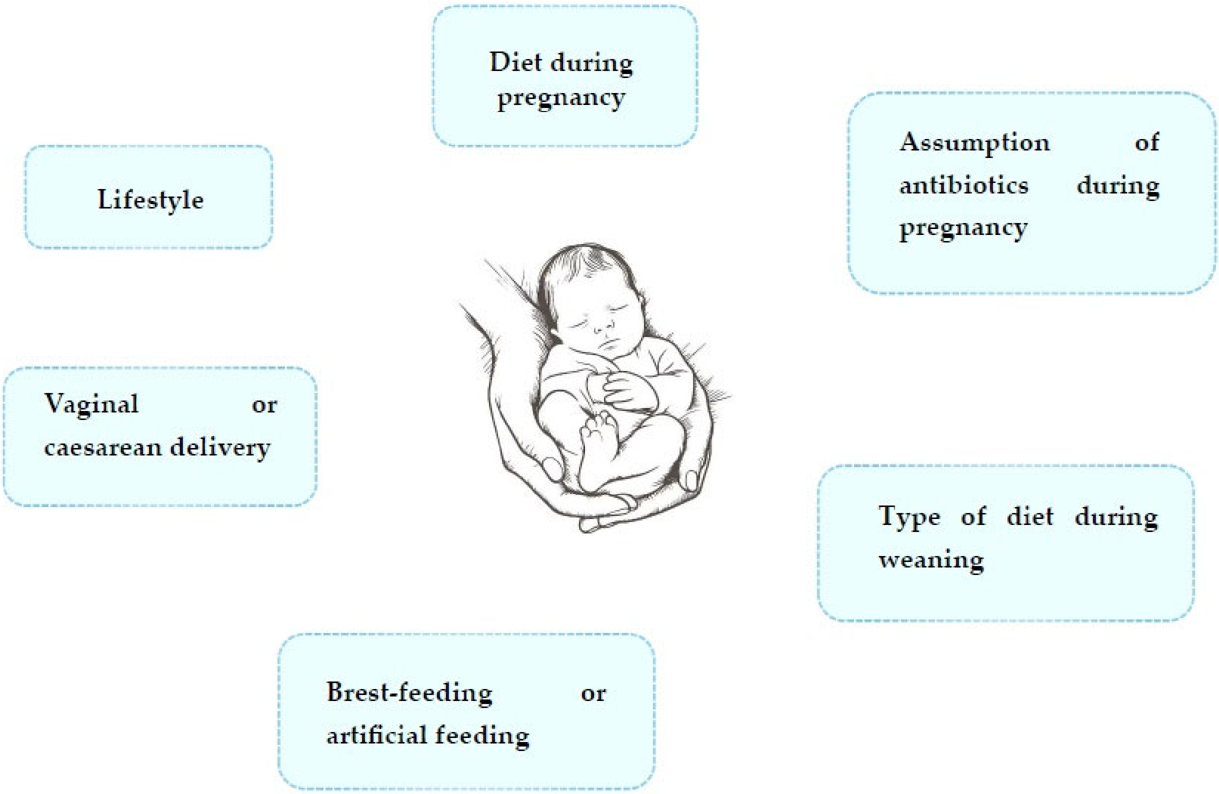

Figure 3. Factors involved in the development of food allergies.

Ultra-processed foods (UPFs) were first introduced to avoid contamination of food by bacteria [128]. UPFs have elevated levels of advanced glycation end products (AGEs) due to their higher sugar content [129]. AGE receptors [130] are capable of binding high molecular weight group box 1 and acting as inducers of FAs [131]. Several studies have shown that UPFs alter the composition of gut microbiota, resulting in impaired immune tolerance [132–134]. Reduction of UPF use was associated with fewer Bacteroidota, *Faecalibacterium prausnitzii,* and *Ruminococcaceae*, whilst promoting an increased number of *Prevotellaceae*. In addition, exposure to AGEs causes alterations in the gut barrier, and consequently, the reduction of SCFAs, thus increasing the migration of food allergens [135]. Thanks to metagenomic sequencing, it has been observed that a neonate developed allergic sensitization in early infancy due to the lack of essential genes for butyrate production [136]. Therefore, SCFA production in early infancy has a protective effect against the onset of FAs [137]. This study documented that feces collected from children aged one year contain high amounts of butyrate and propionate, which are associated with reduced development of FAs. Thus, a diet containing fiber promotes immune tolerance and reduces the risk of FAs. Moreover, in another study [138], it was observed that the intake of UPFs during pregnancy had a negative effect on the subsequent milk composition.

Finally, other studies have demonstrated that the persistence of FAs, particularly towards eggs, milk, and peanuts, is associated with high concentrations of allergen-specific IgE, despite low allergen doses [139,140]. For all these reasons, the early addition of supplementary food allergens in infants at high risk of FAs has reduced the development of FAs [141].

2.4. Interventional Effects of Probiotics and Prebiotics

Subjects sensitized to multiple allergens had an imbalanced gut microbiota, with a reduced number of “good bacteria”. In fact, in these individuals, low amounts of *Clostridiales* were found, whereas they had high levels of *Bacteroidales* [142]. Therefore, supplementation with probiotics would contribute to correcting the low gut diversity even in subjects with FAs. Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host [143]. The most common probiotics belong to the families of *Lactobacillaceae* and *Bifidobacteriaceae* and are used for their ability to change the composition of the gut microbiota, aiming to restore homeostasis. In addition, probiotics promote a balance between Th1 and Th2 cells, controlling AD symptoms [144]. Several studies have been conducted on CMA neonates [145] who received probiotics formulas containing a mixture of bacteria (e.g., *Lacticaseibacillus* (L.) *rhamnosus GG*, *Lacticaseibacillus casei*, *B. lactis*, *B. bifidum*, and *B. breve*) [146,147]. In some cases, only *L. rhamnosus* GG was used [148], whereas in other cases both *L. rhamnosus GG* and *B. lactis* were used [149]. The results confirmed that probiotics have reduced CMA-related symptoms. The action of probiotics in allergic conditions consists, on the one hand, of the ability to improve immune responses by enhancing Treg cell numbers and, on the other hand, the restoration of the permeability of the gut barrier [150]. In general terms, the beneficial effects of probiotics on allergies have been associated with an increase in Treg cells and with suppression of Th2 and Th17 responses [151–153]. Instead, prebiotics are non-digestible ingredients aiming to promote the growth and activity of certain bacteria, including the probiotic ones, thus modifying the composition of gut microbiota [154]. The most consumed prebiotics are non-digestible carbohydrates, such as fructo-oligosaccharides (FOSs) and galacto-oligosaccharides (GOSs) [155]. Furthermore, probiotic administration in CMA subjects has been shown to lead to an early immune tolerance towards cow's milk proteins [156]. Immune tolerance to the above-mentioned proteins in CMA children was increased when they received extensively hydrolyzed casein formula (EHCF) plus *L. rhamnosus GG* (LGG) in comparison to children who received EHCF alone [157,158]. Therefore, supplementation of LGG with EHCF has increased the number of bacteria producing butyrate. In a study conducted on CMA children, the administration of a probiotic containing *L. rhamnosus* and *L. casei* had reduced the severity of symptoms [159]. Regarding the administration of both prebiotics and probiotics, Sorensen et al. [160] have proved that the administration of amino acid mixtures supplemented with *Bifidobacterium breve* M16-V, inulin, and oligofructose in CMA patients has reduced the symptoms and infections in comparison to the administration of the amino acid preparations alone. Chatchatee et al. [161] have confirmed the results obtained by [160]. Nowak-Węgrzyn et al. [162] have reported that the supplementation of probiotics rectified gut microbiota alterations in allergic children and, therefore, probiotics could be used in prophylaxis and prevention of FAs. In some studies, probiotics containing LGG or *L. casei* have been shown to reduce the presence of pathogens and increase the number of *Bifidobacteriaceae* in allergic neonates [163]. Therefore, probiotics decreased the prolonged presence of pathogens in the gut lumen, thus promoting their elimination via their immune system [164]. Among the functional mechanisms of probiotics, a mention goes to their ability to restore the gut epithelial barrier and improve the expression of both tight junction proteins and proteins associated with mucus secretion [165]. Finally, probiotics also regulate DC maturation by stimulating the secretion of IL-10, but also, *B. longum* and *B. animals* have been shown to enhance the secretion of Interferon-γ and Tumor Necrosis Factor-α, whereas *B. bifidum* stimulates Th17 cells [166].

3. Conclusions and Perspectives

In general terms, the current literature records the efficacy of some probiotics in both the prevention and treatment of FAs. However, the use of different probiotic strains, dosage, and time of administration accounts for a limit on the sustainability of probiotics' effects. In conclusion, further studies on the complex interplay between the gut microbiota and resident immune cells are needed to identify preventive strategies against FAs. The use of metabolomics and metagenomics technologies, together with interdisciplinary research work, would play a fundamental role in favoring the growth and clinical application of personalized medicine, thus improving both the results obtained as well as the quality of life of individuals at risk of developing FAs and of those already suffering from FAs.

Several factors are related to the development of food allergies leading to oral tolerance failure, starting from intra-uterine life to old age. Lifestyle—i.e., geographical and environmental factors, diet, diseases, and therapies—mainly influence the composition and function of our intestinal microbiota.

Author Contributions: Conceptualization, T.M. and L.S.; investigation, R.N., E.G. and M.C.; resources, L.S.; data curation, N.R.; writing—original draft preparation, T.M.; writing—review and editing, M.M. and S.T.; supervision, M.C.; project administration, L.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors thank Giuseppe Divittorio and Michelangelo Ferri for their help in data retrieval.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

AD	Atopic dermatitis
AGE	Advanced glycation end product
AhR	Aryl hydrocarbon receptor
AMPs	Antimicrobial peptides
cDCs	Conventional DCs
CMA	Cow milk allergy
CS	Caesarean section
CTLA-4	Cytotoxic T-Lymphocyte Antigen 4
DCs	Dendritic cells
EHCF	Extensively hydrolyzed casein formula
FAs	Food allergies
HMO	Human milk oligosaccharide
IECs	Intestinal epithelial cells
IL	Interleukin
LGG	*L. rhamnosus GG*
LPS	Lipopolysaccharides
M cells	Microfold cells
MCs	Mast cells
MHC	Major histocompatibility complex
mTECs	Medullary thymic epithelial cells
pDCs	Plasmacytoid DCs
PDL-1	Programmed cell death protein 1
PPs	Peyer Patches
PRR	Pattern recognition receptor

pTreg	Peripheral T regulatory
SCFAs	Short-chain fatty acids
sIgA	Secretory IgA
TCR	T cell receptor
TGF-β	Tumor growth factor-β
Th	T helper cells
TLR	Toll-like receptor
Treg	Regulatory T cell
tTreg	Thymic-derived Treg cell
UPF	Ultra-processed food

References

1. Warren, C.M.; Jiang, J.; Gupta, R.S. Epidemiology and Burden of Food Allergy. *Curr. Allergy Asthma Rep.* **2020**, *20*, 6. [CrossRef]
2. Gupta, R.; Warren, C.M.; Smith, B.M.; Jiang, J.; Blumenstock, J.A.; Davis, M.M.; Schleimer, R.P.; Nadeau, K.C. Prevalence and Severity of Food Allergies Among US Adults. *JAMA Netw. Open* **2019**, *2*, e185630. [CrossRef] [PubMed]
3. Wong, G.W. Food allergies around the world. *Front. Nutr.* **2024**, *11*, 1373110. [CrossRef]
4. Kılıç, M.; Beyazıt, E.; Önalan, E.E.; Kaymaz, T.; Taşkın, E. Evaluation of toll-like receptors 2 and 4 polymorphism and intestinal microbiota in children with food allergies. *Turk. J. Pediatr.* **2023**, *65*, 758–768. [CrossRef] [PubMed]
5. Santacroce, L.; Man, A.; Charitos, I.A.; Haxhirexha, K.; Topi, S. Current knowledge about the connection between health status and gut microbiota from birth to elderly. A narrative review. *Front. Biosci.* **2021**, *26*, 135–148. [CrossRef]
6. Magrone, T.; Jirillo, E. The interplay between the gut immune system and microbiota in health and disease: Nutraceutical intervention for restoring intestinal homeostasis. *Curr. Pharm. Des.* **2013**, *19*, 1329–1342. [CrossRef]
7. Magrone, T.; Russo, M.A.; Jirillo, E. Antimicrobial Peptides: Phylogenic Sources and Biological Activities. First of Two Parts. *Curr. Pharm. Des.* **2018**, *24*, 1043–1053. [CrossRef]
8. Paone, P.; Cani, P.D. Mucus barrier, mucins and gut microbiota: The expected slimy partners? *Gut* **2020**, *69*, 2232–2243. [CrossRef]
9. Charitos, I.A.; Scacco, S.; Cotoia, A.; Castellaneta, F.; Castellana, G.; Pasqualotto, F.; Venneri, M.; Ferrulli, A.; Aliani, M.; Santacroce, L.; et al. Intestinal Microbiota Dysbiosis Role and Bacterial Translocation as a Factor for Septic Risk. *Int. J. Mol. Sci.* **2025**, *26*, 2028. [CrossRef]
10. Takiishi, T.; Fenero, C.I.M.; Câmara, N.O.S. Intestinal barrier and gut microbiota: Shaping our immune responses throughout life. *Tissue Barriers* **2017**, *5*, e1373208. [CrossRef] [PubMed]
11. Santacroce, L.; Bottalico, L.; Charitos, I.A.; Castellaneta, F.; Gaxhja, E.; Topi, S.; Palmirotta, R.; Jirillo, E. Exploitation of Natural By-Products for the Promotion of Healthy Outcomes in Humans: Special Focus on Antioxidant and Anti-Inflammatory Mechanisms and Modulation of the Gut Microbiota. *Antioxidants* **2024**, *13*, 796. [CrossRef]
12. Costa, J.; Villa, C.; Verhoeckx, K.; Cirkovic-Velickovic, T.; Schrama, D.; Roncada, P.; Rodrigues, P.M.; Piras, C.; Martín-Pedraza, L.; Monaci, L.; et al. Are Physicochemical Properties Shaping the Allergenic Potency of Animal Allergens? *Clin. Rev. Allergy Immunol.* **2022**, *62*, 1–36. [CrossRef]
13. Anvari, S.; Miller, J.; Yeh, C.Y.; Davis, C.M. IgE-Mediated Food Allergy. *Clin. Rev. Allergy Immunol.* **2019**, *57*, 244–260. [CrossRef]
14. Leonard, S.A. Non-IgE-mediated Adverse Food Reactions. *Curr. Allergy Asthma Rep.* **2017**, *17*, 84. [CrossRef]
15. Niess, J.H.; Kaymak, T. Eosinophilic Esophagitis Pathogenesis: All Clear? *Inflamm. Intest. Dis.* **2025**, *10*, 135–150. [CrossRef]
16. Charitos, I.A.; Castellaneta, F.; Santacroce, L.; Bottalico, L. Historical Anecdotes and Breakthroughs of Histamine: From Discovery to Date. *Endocr. Metab. Immune Disord. Drug Targets* **2021**, *21*, 801–814. [CrossRef]
17. León, B. Understanding the development of Th2 cell-driven allergic airway disease in early life. *Front. Allergy* **2023**, *3*, 1080153. [CrossRef] [PubMed]
18. Worbs, T.; Hammerschmidt, S.I.; Förster, R. Dendritic cell migration in health and disease. *Nat. Rev. Immunol.* **2017**, *17*, 30–48. [CrossRef] [PubMed]
19. Valizadeh, A.; Khosravi, A.; Zadeh, L.J.; Parizad, E.G. Role of IL-25 in Immunity. *J. Clin. Diagn. Res.* **2015**, *9*, OE01-4. [CrossRef]
20. Berni Canani, R.; Caminati, M.; Carucci, L.; Eguiluz-Gracia, I. Skin, gut, and lung barrier: Physiological interface and target of intervention for preventing and treating allergic diseases. *Allergy* **2024**, *79*, 1485–1500. [CrossRef] [PubMed]
21. De Martinis, M.; Sirufo, M.M.; Suppa, M.; Ginaldi, L. New Perspectives in Food Allergy. *Int. J. Mol. Sci.* **2020**, *21*, 1474. [CrossRef]
22. Magrone, T.; Magrone, M.; Jirillo, E. Mast Cells as a Double-Edged Sword in Immunity: Their Function in Health and Disease. First of Two Parts. *Endocr. Metab. Immune Disord. Drug Targets* **2020**, *20*, 654–669. [CrossRef] [PubMed]

23. Wiechers, C.; Zou, M.; Galvez, E.; Beckstette, M.; Ebel, M.; Strowig, T.; Huehn, J.; Pezoldt, J. The microbiota is dispensable for the early stages of peripheral regulatory T cell induction within mesenteric lymph nodes. *Cell. Mol. Immunol.* **2021**, *18*, 1211–1221. [CrossRef] [PubMed]
24. Cabeza-Cabrerizo, M.; Cardoso, A.; Minutti, C.M.; Pereira da Costa, M.; Reis e Sousa, C. Dendritic Cells Revisited. *Annu. Rev. Immunol.* **2021**, *39*, 131–166. [CrossRef]
25. Tai, J.; Kwak, J.; Han, M.; Kim, T.H. Different Roles of Dendritic Cells for Chronic Rhinosinusitis Treatment According to Phenotype. *Int. J. Mol. Sci.* **2022**, *23*, 8032. [CrossRef] [PubMed]
26. Sasaki, I.; Kato, T.; Hemmi, H.; Fukuda-Ohta, Y.; Wakaki-Nishiyama, N.; Yamamoto, A.; Kaisho, T. Conventional Type 1 Dendritic Cells in Intestinal Immune Homeostasis. *Front. Immunol.* **2022**, *13*, 857954. [CrossRef]
27. Carroll, S.L.; Pasare, C.; Barton, G.M. Control of adaptive immunity by pattern recognition receptors. *Immunity* **2024**, *57*, 632–648. [CrossRef]
28. Rawat, K.; Tewari, A.; Li, X.; Mara, A.B.; King, W.T.; Gibbings, S.L.; Nnam, C.F.; Kolling, F.W.; Lambrecht, B.N.; Jakubzick, C.V. CCL5-producing migratory dendritic cells guide CCR5+ monocytes into the draining lymph nodes. *J. Exp. Med.* **2023**, *220*, e20222129. [CrossRef]
29. Ellenbogen, Y.; Jiménez-Saiz, R.; Spill, P.; Chu, D.K.; Waserman, S.; Jordana, M. The Initiation of Th2 Immunity Towards Food Allergens. *Int. J. Mol. Sci.* **2018**, *19*, 1447. [CrossRef]
30. Nowak-Wegrzyn, A.; Szajewska, H.; Lack, G. Food allergy and the gut. *Nat. Rev. Gastroenterol. Hepatol.* **2017**, *14*, 241–257. [CrossRef]
31. Georgiev, P.; Charbonnier, L.M.; Chatila, T.A. Regulatory T Cells: The Many Faces of Foxp3. *J. Clin. Immunol.* **2019**, *39*, 623–640. [CrossRef]
32. Topi, S.; Bottalico, L.; Charitos, I.A.; Colella, M.; Di Domenico, M.; Palmirotta, R.; Santacroce, L. Biomolecular Mechanisms of Autoimmune Diseases and Their Relationship with the Resident Microbiota: Friend or Foe? *Pathophysiology* **2022**, *29*, 507–536. [CrossRef]
33. Arroyo Hornero, R.; Hamad, I.; Côrte-Real, B.; Kleinewietfeld, M. The Impact of Dietary Components on Regulatory T Cells and Disease. *Front. Immunol.* **2020**, *11*, 253. [CrossRef]
34. Zmora, N.; Suez, J.; Elinav, E. You are what you eat: Diet, health and the gut microbiota. *Nat. Rev. Gastroenterol. Hepatol.* **2019**, *16*, 35–56. [CrossRef]
35. Kondo, K.; Takada, K.; Takahama, Y. Antigen processing and presentation in the thymus: Implications for T cell repertoire selection. *Curr. Opin. Immunol.* **2017**, *46*, 53–57. [CrossRef] [PubMed]
36. Magrone, T.; Jirillo, E. The Tolerant Immune System: Biological Significance and Clinical Implications of T Cell Tolerance. *Endocr. Metab. Immune Disord. Drug Targets* **2019**, *19*, 580–593. [CrossRef] [PubMed]
37. Tao, Z.; Jiang, Y.; Xia, S. Regulation of thymic T regulatory cell differentiation by TECs in health and disease. *Scand. J. Immunol.* **2021**, *94*, e13094. [CrossRef] [PubMed]
38. Santosh Nirmala, S.; Kayani, K.; Gliwiński, M.; Hu, Y.; Iwaszkiewicz-Grześ, D.; Piotrowska-Mieczkowska, M.; Sakowska, J.; Tomaszewicz, M.; Marín Morales, J.M.; Lakshmi, K.; et al. Beyond FOXP3: A 20-year journey unravelling human regulatory T-cell heterogeneity. *Front. Immunol.* **2024**, *14*, 1321228. [CrossRef]
39. Wang, J.; Zhao, X.; Wan, Y.Y. Intricacies of TGF-beta signaling in Treg and Th17 cell biology. *Cell. Mol. Immunol.* **2023**, *20*, 1002–1022. [CrossRef]
40. Tordesillas, L.; Berin, M.C. Mechanisms of Oral Tolerance. *Clin. Rev. Allergy Immunol.* **2018**, *55*, 107–117. [CrossRef]
41. Allen, F.; Tong, A.A.; Huang, A.Y. Unique Transcompartmental Bridge: Antigen-Presenting Cells Sampling across Endothelial and Mucosal Barriers. *Front. Immunol.* **2016**, *7*, 231. [CrossRef] [PubMed]
42. Harada, Y.; Miyamoto, K.; Chida, A.; Okuzawa, A.T.; Yoshimatsu, Y.; Kudo, Y.; Sujino, T. Localization and movement of Tregs in gastrointestinal tract: A systematic review. *Inflamm. Regen.* **2022**, *42*, 47. [CrossRef] [PubMed]
43. Du, Y.; He, C.; An, Y.; Huang, Y.; Zhang, H.; Fu, W.; Wang, M.; Shan, Z.; Xie, J.; Yang, Y.; et al. The Role of Short Chain Fatty Acids in Inflammation and Body Health. *Int. J. Mol. Sci.* **2024**, *25*, 7379. [CrossRef] [PubMed]
44. Losol, P.; Wolska, M.; Wypych, T.P.; Yao, L.; O'Mahony, L.; Sokolowska, M. A cross talk between microbial metabolites and host immunity: Its relevance for allergic diseases. *Clin. Transl. Allergy* **2024**, *14*, e12339. [CrossRef]
45. Belkaid, Y.; Harrison, O.J. Homeostatic Immunity and the Microbiota. *Immunity* **2017**, *46*, 562–576. [CrossRef]
46. Zheng, D.; Liwinski, T.; Elinav, E. Interaction between microbiota and immunity in health and disease. *Cell. Res.* **2020**, *30*, 492–506. [CrossRef]
47. Luu, M.; Visekruna, A. Short-chain fatty acids: Bacterial messengers modulating the immunometabolism of T cells. *Eur. J. Immunol.* **2019**, *49*, 842–848. [CrossRef]

48. Fusco, W.; Lorenzo, M.B.; Cintoni, M.; Porcari, S.; Rinninella, E.; Kaitsas, F.; Lener, E.; Mele, M.C.; Gasbarrini, A.; Collado, M.C.; et al. Short-Chain Fatty-Acid-Producing Bacteria: Key Components of the Human Gut Microbiota. *Nutrients* **2023**, *15*, 2211. [CrossRef]
49. Tan, J.K.; Macia, L.; Mackay, C.R. Dietary fiber and SCFAs in the regulation of mucosal immunity. *J. Allergy Clin. Immunol.* **2023**, *151*, 361–370. [CrossRef] [PubMed]
50. Bunyavanich, S.; Berin, M.C. Food allergy and the microbiome: Current understandings and future directions. *J. Allergy Clin. Immunol.* **2019**, *144*, 1468–1477. [CrossRef]
51. Narushima, S.; Sugiura, Y.; Oshima, K.; Atarashi, K.; Hattori, M.; Suematsu, M.; Honda, K. Characterization of the 17 strains of regulatory T cell-inducing human-derived Clostridia. *Gut Microbes* **2014**, *5*, 333–339. [CrossRef]
52. Vinelli, V.; Biscotti, P.; Martini, D.; Del Bo', C.; Marino, M.; Meroño, T.; Nikoloudaki, O.; Calabrese, F.M.; Turroni, S.; Taverniti, V.; et al. Effects of Dietary Fibers on Short-Chain Fatty Acids and Gut Microbiota Composition in Healthy Adults: A Systematic Review. *Nutrients* **2022**, *14*, 2559. [CrossRef]
53. Desai, M.S.; Seekatz, A.M.; Koropatkin, N.M.; Kamada, N.; Hickey, C.A.; Wolter, M.; Pudlo, N.A.; Kitamoto, S.; Terrapon, N.; Muller, A.; et al. A Dietary Fiber-Deprived Gut Microbiota Degrades the Colonic Mucus Barrier and Enhances Pathogen Susceptibility. *Cell* **2016**, *167*, 1339–1353.e21. [CrossRef]
54. Kellermann, L.; Jensen, K.B.; Bergenheim, F.; Gubatan, J.; Chou, N.D.; Moss, A.; Nielsen, O.H. Mucosal vitamin D signaling in inflammatory bowel disease. *Autoimmun. Rev.* **2020**, *19*, 102672. [CrossRef]
55. Akdis, C.A. Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions? *Nat. Rev. Immunol.* **2021**, *21*, 739–751. [CrossRef] [PubMed]
56. Celebi Sozener, Z.; Ozdel Ozturk, B.; Cerci, P.; Turk, M.; Gorgulu Akin, B.; Akdis, M.; Altiner, S.; Ozbey, U.; Ogulur, I.; Mitamura, Y.; et al. Epithelial barrier hypothesis: Effect of the external exposome on the microbiome and epithelial barriers in allergic disease. *Allergy* **2022**, *77*, 1418–1449. [CrossRef]
57. Koh, A.; De Vadder, F.; Kovatcheva-Datchary, P.; Bäckhed, F. From Dietary Fiber to Host Physiology: Short-Chain Fatty Acids as Key Bacterial Metabolites. *Cell* **2016**, *165*, 1332–1345. [CrossRef]
58. Wang, T.M.; Wang, R.X.; Colgan, S.P. Physiologic hypoxia in the intestinal mucosa: A central role for short-chain fatty acids. *Am. J. Physiol. Cell. Physiol.* **2024**, *327*, C1087–C1093. [CrossRef]
59. Lange, O.; Proczko-Stepaniak, M.; Mika, A. Short-Chain Fatty Acids-A Product of the Microbiome and Its Participation in Two-Way Communication on the Microbiome-Host Mammal Line. *Curr. Obes. Rep.* **2023**, *12*, 108–126. [CrossRef] [PubMed]
60. Feng, Y.; Wang, Y.; Wang, P.; Huang, Y.; Wang, F. Short-Chain Fatty Acids Manifest Stimulative and Protective Effects on Intestinal Barrier Function Through the Inhibition of NLRP3 Inflammasome and Autophagy. *Cell. Physiol. Biochem.* **2018**, *49*, 190–205. [CrossRef] [PubMed]
61. Seo, K.; Seo, J.; Yeun, J.; Choi, H.; Kim, Y.I.; Chang, S.Y. The role of mucosal barriers in human gut health. *Arch. Pharm. Res.* **2021**, *44*, 325–341. [CrossRef]
62. Singh, N.; Gurav, A.; Sivaprakasam, S.; Brady, E.; Padia, R.; Shi, H.; Thangaraju, M.; Prasad, P.D.; Manicassamy, S.; Munn, D.H.; et al. Activation of Gpr109a, receptor for niacin and the commensal metabolite butyrate, suppresses colonic inflammation and carcinogenesis. *Immunity* **2014**, *40*, 128–139. [CrossRef]
63. Kim, K.S.; Hong, S.W.; Han, D.; Yi, J.; Jung, J.; Yang, B.G.; Lee, J.Y.; Lee, M.; Surh, C.D. Dietary antigens limit mucosal immunity by inducing regulatory T cells in the small intestine. *Science* **2016**, *351*, 858–863. [CrossRef] [PubMed]
64. Lee, M.J.; Park, Y.M.; Kim, B.; Tae, I.H.; Kim, N.E.; Pranata, M.; Kim, T.; Won, S.; Kang, N.J.; Lee, Y.K.; et al. Disordered development of gut microbiome interferes with the establishment of the gut ecosystem during early childhood with atopic dermatitis. *Gut Microbes* **2022**, *14*, 2068366. [CrossRef] [PubMed]
65. Licciardi, P.V.; Ververis, K.; Karagiannis, T.C. Histone deacetylase inhibition and dietary short-chain Fatty acids. *ISRN Allergy* **2011**, *2011*, 869647. [CrossRef]
66. Rajput, M.; Momin, T.; Singh, A.; Banerjee, S.; Villasenor, A.; Sheldon, J.; Paudel, P.; Rajput, R. Determining the association between gut microbiota and its metabolites with higher intestinal Immunoglobulin A response. *Vet. Anim. Sci.* **2022**, *19*, 100279. [CrossRef] [PubMed]
67. Tan, T.H.; Ellis, J.A.; Saffery, R.; Allen, K.J. The role of genetics and environment in the rise of childhood food allergy. *Clin. Exp. Allergy* **2012**, *42*, 20–29. [CrossRef]
68. Renz, H.; Holt, P.G.; Inouye, M.; Logan, A.C.; Prescott, S.L.; Sly, P.D. An exposome perspective: Early-life events and immune development in a changing world. *J. Allergy Clin. Immunol.* **2017**, *140*, 24–40. [CrossRef]
69. Younes, J.A.; Lievens, E.; Hummelen, R.; van der Westen, R.; Reid, G.; Petrova, M.I. Women and Their Microbes: The Unexpected Friendship. *Trends Microbiol.* **2018**, *26*, 16–32. [CrossRef]
70. Vandenplas, Y.; Carnielli, V.P.; Ksiazyk, J.; Luna, M.S.; Migacheva, N.; Mosselmans, J.M.; Picaud, J.C.; Possner, M.; Singhal, A.; Wabitsch, M. Factors affecting early-life intestinal microbiota development. *Nutrition* **2020**, *78*, 110812. [CrossRef]

71. Montoya-Williams, D.; Lemas, D.J.; Spiryda, L.; Patel, K.; Carney, O.O.; Neu, J.; Carson, T.L. The neonatal microbiome and its partial role in mediating the association between birth by cesarean section and adverse pediatric outcomes. *Neonatology* **2018**, *114*, 103–111. [CrossRef]
72. Yao, Y.; Cai, X.; Ye, Y.; Wang, F.; Chen, F.; Zheng, C. The Role of Microbiota in Infant Health: From Early Life to Adulthood. *Front. Immunol.* **2021**, *12*, 708472. [CrossRef]
73. Pan, K.; Zhang, C.; Tian, J. The Effects of Different Modes of Delivery on the Structure and Predicted Function of Intestinal Microbiota in Neonates and Early Infants. *Pol. J. Microbiol.* **2021**, *70*, 45–55. [CrossRef]
74. Jakobsson, H.E.; Abrahamsson, T.R.; Jenmalm, M.C.; Harris, K.; Quince, C.; Jernberg, C.; Björkstén, B.; Engstrand, L.; Andersson, A.F. Decreased gut microbiota diversity, delayed Bacteroidetes colonisation and reduced Th1 responses in infants delivered by caesarean section. *Gut* **2014**, *63*, 559–566. [CrossRef]
75. Papathoma, E.; Triga, M.; Fouzas, S.; Dimitriou, G. Cesarean Section Delivery and Development of Food Allergy and Atopic Dermatitis in Early Childhood. *Pediatr. Allergy Immunol.* **2016**, *27*, 419–424. [CrossRef]
76. Khodayar-Pardo, P.; Mira-Pascual, L.; Collado, M.C.; Martínez-Costa, C. Impact of lactation stage, gestational age and mode of delivery on breast milk microbiota. *J. Perinatol.* **2014**, *34*, 599–605. [CrossRef]
77. Roduit, C.; Frei, R.; Depner, M.; Schaub, B.; Loss, G.; Genuneit, J.; Pfefferle, P.; Hyvärinen, A.; Karvonen, A.M.; Riedler, J.; et al. Increased food diversity in the first year of life is inversely associated with allergic diseases. *J. Allergy Clin. Immunol.* **2014**, *133*, 1056–1064. [CrossRef] [PubMed]
78. Magrone, T.; Russo, M.A.; Jirillo, E. Antimicrobial Peptides in Human Disease: Therapeutic Approaches. Second of Two Parts. *Curr. Pharm. Des.* **2018**, *24*, 1148–1156. [CrossRef] [PubMed]
79. van den Elsen, L.W.J.; Garssen, J.; Burcelin, R.; Verhasselt, V. Shaping the gut microbiota by breastfeeding: The gateway to allergy prevention? *Front. Pediatr.* **2019**, *7*, 47. [CrossRef]
80. Lyons, K.E.; Ryan, C.A.; Dempsey, E.M.; Ross, R.P.; Stanton, C. Breast Milk, a Source of Beneficial Microbes and Associated Benefits for Infant Health. *Nutrients* **2020**, *12*, 1039. [CrossRef] [PubMed]
81. Agus, A.; Planchais, J.; Sokol, H. Gut Microbiota Regulation of Tryptophan Metabolism in Health and Disease. *Cell Host Microbe* **2018**, *23*, 716–724. [CrossRef]
82. Ongena, R.; Dierick, M.; Vanrompay, D.; Cox, E.; Devriendt, B. Lactoferrin impairs pathogen virulence through its proteolytic activity. *Front. Vet. Sci.* **2024**, *11*, 1428156. [CrossRef] [PubMed]
83. Dominguez-Bello, M.G.; Costello, E.K.; Contreras, M.; Magris, M.; Hidalgo, G.; Fierer, N.; Knight, R. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 11971–11975. [CrossRef]
84. Thompson, A.L.; Monteagudo-Mera, A.; Cadenas, M.B.; Lampl, M.L.; Azcarate-Peril, M.A. Milk- and solid-feeding practices and daycare attendance are associated with differences in bacterial diversity, predominant communities, and metabolic and immune function of the infant gut microbiome. *Front. Cell. Infect. Microbiol.* **2015**, *5*, 3. [CrossRef] [PubMed]
85. McGuire, M.K.; McGuire, M.A. Got bacteria? The astounding, yet not-so-surprising, microbiome of human milk. *Curr. Opin. Biotechnol.* **2017**, *44*, 63–68. [CrossRef]
86. Henrick, B.M.; Rodriguez, L.; Lakshmikanth, T.; Pou, C.; Henckel, E.; Arzoomand, A.; Olin, A.; Wang, J.; Mikes, J.; Tan, Z.; et al. Bifidobacteria-mediated immune system imprinting early in life. *Cell* **2021**, *184*, 3884–3898.e11. [CrossRef]
87. Laursen, M.F.; Sakanaka, M.; von Burg, N.; Mörbe, U.; Andersen, D.; Moll, J.M.; Pekmez, C.T.; Rivollier, A.; Michaelsen, K.F.; Mølgaard, C.; et al. Bifidobacterium species associated with breastfeeding produce aromatic lactic acids in the infant gut. *Nat. Microbiol.* **2021**, *6*, 1367–1382. [CrossRef] [PubMed]
88. Li, X.; Zhang, B.; Hu, Y.; Zhao, Y. New insights into gut-bacteria-derived indole and its derivatives in intestinal and liver diseases. *Front. Pharmacol.* **2021**, *12*, 769501. [CrossRef]
89. Scott, S.A.; Fu, J.; Chang, P.V. Microbial tryptophan metabolites regulate gut barrier function via the aryl hydrocarbon receptor. *Proc. Natl. Acad. Sci. USA* **2020**, *117*, 19376–19387. [CrossRef] [PubMed]
90. Kim, K.; Kim, H.; Sung, G.Y. Effects of indole-3-lactic acid, a metabolite of tryptophan, on IL-4 and IL-13-induced human skin-equivalent atopic dermatitis models. *Int. J. Mol. Sci.* **2022**, *23*, 13520. [CrossRef]
91. Yu, M.; Wang, Q.; Ma, Y.; Li, L.; Yu, K.; Zhang, Z.; Chen, G.; Li, X.; Xiao, W.; Xu, P.; et al. Aryl hydrocarbon receptor activation modulates intestinal epithelial barrier function by maintaining tight junction integrity. *Int. J. Biol. Sci.* **2018**, *14*, 69–77. [CrossRef]
92. Pascal, M.; Perez-Gordo, M.; Caballero, T.; Escribese, M.M.; Lopez Longo, M.N.; Luengo, O.; Manso, L.; Matheu, V.; Seoane, E.; Zamorano, M.; et al. Microbiome and Allergic Diseases. *Front. Immunol.* **2018**, *9*, 1584. [CrossRef]
93. Kalliomäki, M.; Kirjavainen, P.; Eerola, E.; Kero, P.; Salminen, S.; Isolauri, E. Distinct patterns of neonatal gut microflora in infants in whom atopy was not developing. *J. Allergy Clin. Immunol.* **2001**, *107*, 129–134. [CrossRef] [PubMed]

94. Abrahamsson, T.R.; Jakobsson, H.E.; Andersson, A.F.; Björkstén, B.; Engstrand, L.; Jenmalm, M.C. Low diversity of the gut microbiota in infants with atopic eczema. *J. Allergy Clin. Immunol.* **2012**, *129*, 434–440. [CrossRef]
95. Fieten, K.B.; Totté, J.E.E.; Levin, E.; Reyman, M.; Meijer, Y.; Knulst, A.; Schuren, F.; Pasmans, S.G.M.A. Fecal Microbiome and Food Allergy in Pediatric Atopic Dermatitis: A Cross-Sectional Pilot Study. *Int. Arch. Allergy Immunol.* **2018**, *175*, 77–84. [CrossRef] [PubMed]
96. Brugman, S.; Perdijk, O.; van Neerven, R.J.; Savelkoul, H.F. Mucosal immune development in early life: Setting the stage. *Arch. Immunol. Ther. Exp.* **2015**, *63*, 251–268. [CrossRef]
97. Olin, A.; Henckel, E.; Chen, Y.; Lakshmikanth, T.; Pou, C.; Mikes, J.; Gustafsson, A.; Bernhardsson, A.K.; Zhang, C.; Bohlin, K.; et al. Stereotypic immune system development in newborn children. *Cell* **2018**, *174*, 1277–1292. [CrossRef] [PubMed]
98. Rigo-Adrover, M.D.M.; Franch, À.; Castell, M.; Pérez-Cano, F.J. Preclinical immunomodulation by the probiotic Bifidobacterium breve M-16V in early life. *PLoS ONE* **2016**, *11*, e0166082. [CrossRef] [PubMed]
99. Donaldson, G.P.; Ladinsky, M.S.; Yu, K.B.; Sanders, J.G.; Yoo, B.B.; Chou, W.C.; Conner, M.E.; Earl, A.M.; Knight, R.; Bjorkman, P.J.; et al. Gut microbiota utilize immunoglobulin A for mucosal colonization. *Science* **2018**, *360*, 795–800. [CrossRef]
100. Saturio, S.; Nogacka, A.M.; Alvarado-Jasso, G.M.; Salazar, N.; de Los Reyes-Gavilán, C.G.; Gueimonde, M.; Arboleya, S. Role of Bifidobacteria on Infant Health. *Microorganisms* **2021**, *9*, 2415. [CrossRef]
101. Goldberg, M.R.; Mor, H.; Magid Neriya, D.; Magzal, F.; Muller, E.; Appel, M.Y.; Nachshon, L.; Borenstein, E.; Tamir, S.; Louzoun, Y.; et al. Microbial signature in IgE-mediated food allergies. *Genome Med.* **2020**, *12*, 92. [CrossRef]
102. Morrison, D.J.; Preston, T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes* **2016**, *7*, 189–200. [CrossRef]
103. Bäckhed, F.; Roswall, J.; Peng, Y.; Feng, Q.; Jia, H.; Kovatcheva-Datchary, P.; Li, Y.; Xia, Y.; Xie, H.; Zhong, H.; et al. Dynamics and stabilization of the human gut microbiome during the first year of life. *Cell Host Microbe* **2015**, *17*, 690–703. [CrossRef] [PubMed]
104. Caffarelli, C.; Di Mauro, D.; Mastrorilli, C.; Bottau, P.; Cipriani, F.; Ricci, G. Solid food introduction and the development of food allergies. *Nutrients* **2018**, *10*, 1790. [CrossRef] [PubMed]
105. Koukou, Z.; Papadopoulou, E.; Panteris, E.; Papadopoulou, S.; Skordou, A.; Karamaliki, M.; Diamanti, E. The effect of breastfeeding on food allergies in newborns and infants. *Children* **2023**, *10*, 1046. [CrossRef]
106. Scarpone, R.; Kimkool, P.; Ierodiakonou, D.; Leonardi-Bee, J.; Garcia-Larsen, V.; Perkin, M.R.; Boyle, R.J. Timing of allergenic food introduction and risk of immunoglobulin E-mediated food allergy: A systematic review and meta-analysis. *JAMA Pediatr.* **2023**, *177*, 489–497. [CrossRef]
107. Halken, S.; Muraro, A.; de Silva, D.; Khaleva, E.; Angier, E.; Arasi, S.; Arshad, H.; Bahnson, H.T.; Beyer, K.; Boyle, R.; et al. EAACI guideline: Preventing the development of food allergy in infants and young children (2020 update). *Pediatr. Allergy Immunol.* **2021**, *32*, 843–858. [CrossRef] [PubMed]
108. Skjerven, H.O.; Lie, A.; Vettukattil, R.; Rehbinder, E.M.; LeBlanc, M.; Asarnoj, A.; Carlsen, K.H.; Despriee, Å.W.; Färdig, M.; Gerdin, S.W.; et al. Early food intervention and skin emollients to prevent food allergy in young children (PreventADALL): A factorial, multicentre, cluster-randomised trial. *Lancet.* **2022**, *399*, 2398–23411. [CrossRef]
109. Tsuang, A.J.; Nowak-Węgrzyn, A.H. Increased food diversity in the first year of life is inversely associated with allergic diseases. *Pediatrics* **2014**, *134*, S139–S140. [CrossRef]
110. Du Toit, G.; Foong, R.X.; Lack, G. Corrigendum to "Prevention of food allergy-Early dietary interventions" [Allergol Int 65 (2016) 370-377]. *Allergol. Int.* **2017**, *66*, 159. [CrossRef]
111. Augustine, T.; Kumar, M.; Al Khodor, S.; van Panhuys, N. Microbial dysbiosis tunes the immune response towards allergic disease outcomes. *Clin. Rev. Allergy Immunol.* **2023**, *65*, 43–71. [CrossRef] [PubMed]
112. Shamji, M.H.; Valenta, R.; Jardetzky, T.; Verhasselt, V.; Durham, S.R.; Würtzen, P.A.; van Neerven, R.J.J. The role of allergen-specific IgE, IgG and IgA in allergic disease. *Allergy* **2021**, *76*, 36273641. [CrossRef]
113. Catanzaro, J.R.; Strauss, J.D.; Bielecka, A.; Porto, A.F.; Lobo, F.M.; Urban, A.; Schofield, W.B.; Palm, N.W. IgA-deficient humans exhibit gut microbiota dysbiosis despite secretion of compensatory IgM. *Sci. Rep.* **2019**, *9*, 13574. [CrossRef]
114. Kukkonen, K.; Kuitunen, M.; Haahtela, T.; Korpela, R.; Poussa, T.; Savilahti, E. High intestinal IgA associates with reduced risk of IgE-associated allergic diseases. *Pediatr. Allergy Immunol.* **2010**, *21*, 67–73. [CrossRef]
115. Abdel-Gadir, A.; Stephen-Victor, E.; Gerber, G.K.; Noval Rivas, M.; Wang, S.; Harb, H.; Wang, L.; Li, N.; Crestani, E.; Spielman, S.; et al. Microbiota therapy acts via a regulatory T cell MyD88/RORγt pathway to suppress food allergy. *Nat. Med.* **2019**, *25*, 1164–1174. [CrossRef] [PubMed]
116. Di Domenico, M.; Ballini, A.; Boccellino, M.; Scacco, S.; Lovero, R.; Charitos, I.A.; Santacroce, L. The Intestinal Microbiota May Be a Potential Theranostic Tool for Personalized Medicine. *J. Pers. Med.* **2022**, *12*, 523. [CrossRef]

117. Jones, A.L.; Curran-Everett, D.; Leung, D.Y.M. Food allergy is associated with *Staphylococcus aureus* colonization in children with atopic dermatitis. *J. Allergy Clin. Immunol.* **2016**, *137*, 1247–1248.e3. [CrossRef] [PubMed]
118. Leung, D.Y.; Guttman-Yassky, E. Deciphering the complexities of atopic dermatitis: Shifting paradigms in treatment approaches. *J. Allergy Clin. Immunol.* **2014**, *134*, 769–779. [CrossRef]
119. Tham, E.; Chia, M.; Riggioni, C.; Nagarajan, N.; Common, J.E.A.; Kong, H.H. The skin microbiome in pediatric atopic dermatitis and food allergy. *Allergy.* **2024**, *79*, 1470–1484. [CrossRef]
120. Zhu, Z.; Zhu, B.; Hu, C.; Liu, Y.; Wang, X.; Zhang, J.; Wang, F.; Zhu, M. Short-chain fatty acids as a target for prevention against food allergy by regulatory T cells. *JGH Open* **2019**, *3*, 190–195. [CrossRef]
121. Goverse, G.; Molenaar, R.; Macia, L.; Tan, J.; Erkelens, M.N.; Konijn, T.; Knippenberg, M.; Cook, E.C.; Hanekamp, D.; Veldhoen, M.; et al. Diet-derived short chain fatty acids stimulate intestinal epithelial cells to induce mucosal tolerogenic dendritic cells. *J. Immunol.* **2017**, *198*, 2172–2181. [CrossRef]
122. Wu, W.; Sun, M.; Chen, F.; Cao, A.T.; Liu, H.; Zhao, Y.; Huang, X.; Xiao, Y.; Yao, S.; Zhao, Q.; et al. Microbiota metabolite short-chain fatty acid acetate promotes intestinal IgA response to microbiota which is mediated by GPR43. *Mucosal Immunol.* **2017**, *10*, 946–956. [CrossRef]
123. Kim, M.; Qie, Y.; Park, J.; Kim, C.H. Gut microbial metabolites fuel host antibody responses. *Cell Host Microbe* **2016**, *20*, 202–214. [CrossRef]
124. Vidarsson, G.; Dekkers, G.; Rispens, T. IgG subclasses and allotypes: From structure to effector functions. *Front. Immunol.* **2014**, *5*, 520. [CrossRef]
125. de Taeye, S.W.; Rispens, T.; Vidarsson, G. The ligands for human IgG and their effector functions. *Antibodies* **2019**, *8*, 30. [CrossRef] [PubMed]
126. Savilahti, E.M.; Rantanen, V.; Lin, J.S.; Karinen, S.; Saarinen, K.M.; Goldis, M.; Mäkelä, M.J.; Hautaniemi, S.; Savilahti, E.; Sampson, H.A. Early recovery from cow's milk allergy is associated with decreasing IgE and increasing IgG4 binding to cow's milk epitopes. *J. Allergy Clin. Immunol.* **2010**, *125*, 1315–1321.e9. [CrossRef] [PubMed]
127. Santos, A.F.; James, L.K.; Bahnson, H.T.; Shamji, M.H.; Couto-Francisco, N.C.; Islam, S.; Houghton, S.; Clark, A.T.; Stephens, A.; Turcanu, V.; et al. IgG4 inhibits peanut-induced basophil and mast cell activation in peanut-tolerant children sensitized to peanut major allergens. *J. Allergy Clin. Immunol.* **2015**, *135*, 1249–1256. [CrossRef] [PubMed]
128. Brichacek, A.L.; Florkowski, M.; Abiona, E.; Frank, K.M. Ultra-Processed Foods: A Narrative Review of the Impact on the Human Gut Microbiome and Variations in Classification Methods. *Nutrients* **2024**, *16*, 1738. [CrossRef]
129. Davis, K.E.; Prasad, C.; Vijayagopal, P.; Juma, S.; Adams-Huet, B.; Imrhan, V. Contribution of dietary advanced glycation end products (AGE) to circulating AGE: Role of dietary fat. *Br. J. Nutr.* **2015**, *114*, 1797–1806. [CrossRef]
130. Sterenczak, K.A.; Nolte, I.; Murua, E.H. RAGE splicing variants in mammals. *Methods Mol. Biol.* **2013**, *963*, 265–276. [CrossRef]
131. Forde, B.; Yao, L.; Shaha, R.; Murphy, S.; Lunjani, N.; O'Mahony, L. Immunomodulation by foods and microbes: Unravelling the molecular tango. *Allergy* **2022**, *77*, 3513–3526. [CrossRef] [PubMed]
132. Atzeni, A.; Martínez, M.; Babio, N.; Konstanti, P.; Tinahones, F.J.; Vioque, J.; Corella, D.; Fitó, M.; Vidal, J.; Moreno-Indias, I.; et al. Association between ultra-processed food consumption and gut microbiota in senior subjects with overweight/obesity and metabolic syndrome. *Front. Nutr.* **2022**, *9*, 976547. [CrossRef] [PubMed]
133. Cuevas-Sierra, A.; Milagro, F.I.; Aranaz, P.; Martinez, J.A.; Riezu-Boj, J.I. Gut microbiota differences according to ultra-processed food consumption in a Spanish population. *Nutrients* **2021**, *13*, 2710. [CrossRef] [PubMed]
134. Noh, H.; Jang, H.H.; Kim, G.; Zouiouich, S.; Cho, S.Y.; Kim, H.J.; Kim, J.; Choe, J.S.; Gunter, M.J.; Ferrari, P.; et al. Taxonomic composition and diversity of the gut microbiota in relation to habitual dietary intake in Korean adults. *Nutrients* **2021**, *13*, 366. [CrossRef]
135. Akagawa, S.; Kaneko, K. Gut microbiota and allergic diseases in children. *Allergol. Int.* **2022**, *71*, 301–309. [CrossRef] [PubMed]
136. Cait, A.; Cardenas, E.; Dimitriu, P.A.; Amenyogbe, N.; Dai, D.; Cait, J.; Sbihi, H.; Stiemsma, L.; Subbarao, P.; Mandhane, P.J.; et al. Reduced Genetic Potential for Butyrate Fermentation in the Gut Microbiome of Infants Who Develop Allergic Sensitization. *J. Allergy Clin. Immunol.* **2019**, *44*, 1638–1647.e3. [CrossRef]
137. Roduit, C.; Frei, R.; Ferstl, R.; Loeliger, S.; Westermann, P.; Rhyner, C.; Schiavi, E.; Barcik, W.; Rodriguez-Perez, N.; Wawrzyniak, M.; et al. High Levels of Butyrate and Propionate in Early Life Are Associated with Protection Against Atopy. *Allergy* **2019**, *74*, 799–809. [CrossRef]
138. Berdi, M.; de Lauzon-Guillain, B.; Forhan, A.; Castelli, F.A.; Fenaille, F.; Charles, M.A.; Heude, B.; Junot, C.; Adel-Patient, K.; EDEN Mother-Child Cohort Study Group. Immune Components of Early Breastmilk: Association with Maternal Factors and with Reported Food Allergy in Childhood. *Pediatr. Allergy Immunol.* **2019**, *30*, 107–116. [CrossRef]
139. Savage, J.; Sicherer, S.; Wood, R. The Natural History of Food Allergy. *J. Allergy Clin. Immunol. Pract.* **2016**, *4*, 196–203, quiz 204. [CrossRef]

140. Leonard, S.A.; Sampson, H.A.; Sicherer, S.H.; Noone, S.; Moshier, E.L.; Godbold, J.; Nowak-Wegrzyn, A. Dietary baked egg accelerates resolution of egg allergy in children. *J. Allergy Clin. Immunol.* **2012**, *130*, 473–480.e471. [CrossRef]
141. Adam, T.; Divaret-Chauveau, A.; Roduit, C.; Adel-Patient, K.; Deschildre, A.; Raherison, C.; Charles, M.A.; Nicklaus, S.; de Lauzon-Guillain, B. Complementary feeding practices are related to the risk of food allergy in the ELFE cohort. *Allergy* **2023**, *78*, 2456–2466. [CrossRef]
142. Hua, X.; Song, L.; Yu, G.; Vogtmann, E.; Goedert, J.J.; Abnet, C.C.; Landi, M.T.; Shi, J. MicrobiomeGWAS: A Tool for identi-fying Host Genetic Variants Associated with Microbiome Composition. *Genes* **2022**, *13*, 1224. [CrossRef]
143. Hill, C.; Guarner, F.; Reid, G.; Gibson, G.R.; Merenstein, D.J.; Pot, B.; Morelli, L.; Canani, R.B.; Flint, H.J.; Salminen, S.; et al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat. Rev. Gastroenterol. Hepatol.* **2014**, *11*, 506–514. [CrossRef]
144. Matsumoto, M.; Aranami, A.; Ishige, A.; Watanabe, K.; Benno, Y. LKM512 yogurt consumption improves the intestinal environment and induces the T-helper type 1 cytokine in adult patients with intractable atopic dermatitis. *Clin. Exp. Allergy* **2007**, *37*, 358–370. [CrossRef] [PubMed]
145. Cela, L.; Brindisi, G.; Gravina, A.; Pastore, F.; Semeraro, A.; Bringheli, I.; Marchetti, L.; Morelli, R.; Cinicola, B.; Capponi, M.; et al. Molecular Mechanism and Clinical Effects of Probiotics in the Management of Cow's Milk Protein Allergy. *Int. J. Mol. Sci.* **2023**, *24*, 9781. [CrossRef]
146. Ahanchian, H.; Nouri, Z.; Jafari, S.A.; Moghiman, T.; Amirian, M.H.; Ezzati, A.; Kianifar, H.R. Synbiotics in Children with Cow's Milk Allergy: A Randomized Controlled Trial. *Iran. J. Pediatr.* **2014**, *24*, 29–34.
147. Berni Canani, R.; Di Costanzo, M.; Bedogni, G.; Amoroso, A.; Cosenza, L.; Di Scala, C.; Granata, V.; Nocerino, R. Extensively hydrolyzed casein formula containing *Lactobacillus rhamnosus* GG reduces the occurrence of other allergic manifestations in children with cow's milk allergy: 3-year randomized controlled trial. *J. Allergy Clin. Immunol.* **2017**, *139*, 1906–1913.e4. [CrossRef]
148. Berni Canani, R.; Nocerino, R.; Terrin, G.; Coruzzo, A.; Cosenza, L.; Leone, L.; Troncone, R. Effect of Lactobacillus GG on tolerance acquisition in infants with cow's milk allergy: A randomized trial. *J. Allergy Clin. Immunol.* **2012**, *129*, 580–582.e5. [CrossRef] [PubMed]
149. Vandenplas, Y.; Steenhout, P.; Planoudis, Y.; Grathwohl, D.; Althera Study Group. Treating cow's milk protein allergy: A double-blind randomized trial comparing two extensively hydrolysed formulas with probiotics. *Acta Paediatr.* **2013**, *102*, 990–998. [CrossRef] [PubMed]
150. 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]
151. Sharma, G.; Im, S.H. Probiotics as a Potential Immunomodulating Pharmabiotics in Allergic Diseases: Current Status and Future Prospects. *Allergy Asthma Immunol. Res.* **2018**, *10*, 575–590. [CrossRef] [PubMed]
152. Plaza-Diaz, J.; Ruiz-Ojeda, F.J.; Gil-Campos, M.; Gil, A. Mechanisms of Action of Probiotics. *Adv. Nutr.* **2019**, *10*, S49–S66. [CrossRef]
153. Gholizadeh, P.; Mahallei, M.; Pormohammad, A.; Varshochi, M.; Ganbarov, K.; Zeinalzadeh, E.; Yousefi, B.; Bastami, M.; Tanomand, A.; Mahmood, S.S.; et al. Microbial balance in the intestinal microbiota and its association with diabetes, obesity and allergic disease. *Microb. Pathog.* **2019**, *127*, 48–55. [CrossRef] [PubMed]
154. Gibson, G.R.; Probert, H.M.; Van Loo, J.; Rastall, R.A.; Roberfroid, M.B. Dietary modulation of the human colonic microbiota: Updating the concept of prebiotics. *Nutr. Res. Rev.* **2004**, *17*, 259–275. [CrossRef] [PubMed]
155. Cuello-Garcia, C.A.; Fiocchi, A.; Pawankar, R.; Yepes-Nuñez, J.J.; Morgano, G.P.; Zhang, Y.; Ahn, K.; Al-Hammadi, S.; Agarwal, A.; Gandhi, S.; et al. World Allergy Organization-McMaster University guidelines for allergic disease prevention (GLAD-P): Prebiotics. *World Allergy Organ J.* **2016**, *9*, 10. [CrossRef]
156. Santos, S.C.D.; Konstantyner, T.; Cocco, R.R. Effects of probiotics in the treatment of food hypersensitivity in children: A systematic review. *Allergol. Immunopathol.* **2020**, *48*, 95–104. [CrossRef]
157. Qamer, S.; Deshmukh, M.; Patole, S. Probiotics for cow's milk protein allergy: A systematic review of randomized controlled trials. *Eur. J. Pediatr.* **2019**, *178*, 1139–1149. [CrossRef]
158. Canani, R.B.; Nocerino, R.; Terrin, G.; Frediani, T.; Lucarelli, S.; Cosenza, L.; Passariello, A.; Leone, L.; Granata, V.; Di Costanzo, M.; et al. Formula selection for management of children with cow's milk allergy influences the rate of acquisition of tolerance: A prospective multicenter study. *J. Pediatr.* **2013**, *163*, 771–777.e1. [CrossRef]
159. Cukrowska, B.; Ceregra, A.; Maciorkowska, E.; Surowska, B.; Zegadło-Mylik, M.A.; Konopka, E.; Trojanowska, I.; Zakrzewska, M.; Bierła, J.B.; Zakrzewski, M.; et al. The Effectiveness of Probiotic Lactobacillus rhamnosus and Lactobacillus casei Strains in Children with Atopic Dermatitis and Cow's Milk Protein Allergy: A Multicenter, Randomized, Double Blind, Placebo Controlled Study. *Nutrients* **2021**, *13*, 1169. [CrossRef]

160. Sorensen, K.; Cawood, A.L.; Cooke, L.H.; Acosta-Mena, D.; Stratton, R.J. The Use of an Amino Acid Formula Containing Synbiotics in Infants with Cow's Milk Protein Allergy-Effect on Clinical Outcomes. *Nutrients* **2021**, *13*, 2205. [CrossRef]
161. Chatchatee, P.; Nowak-Wegrzyn, A.; Lange, L.; Benjaponpitak, S.; Chong, K.W.; Sangsupawanich, P.; van Ampting, M.T.J.; Oude Nijhuis, M.M.; Harthoorn, L.F.; Langford, J.E.; et al. Tolerance development in cow's milk-allergic infants receiving amino acid-based formula: A randomized controlled trial. *J. Allergy Clin. Immunol.* **2022**, *149*, 650–658.e5. [CrossRef] [PubMed]
162. Nowak-Węgrzyn, A.; Chatchatee, P. Mechanisms of Tolerance Induction. *Ann. Nutr. Metab.* **2017**, *70*, 7–24. [CrossRef] [PubMed]
163. Aureli, P.; Capurso, L.; Castellazzi, A.M.; Clerici, M.; Giovannini, M.; Morelli, L.; Poli, A.; Pregliasco, F.; Salvini, F.; Zuccotti, G.V. Probiotics and health: An evidence-based review. *Pharmacol. Res.* **2011**, *63*, 366–376. [CrossRef] [PubMed]
164. Reid, G. Probiotics and prebiotics-Progress and challenges. *Int. Dairy J.* **2008**, *18*, 969–975. [CrossRef]
165. MacDonald, T.T.; Monteleone, G. Immunity, inflammation, and allergy in the gut. *Science* **2005**, *307*, 1920–1925. [CrossRef]
166. Baba, N.; Samson, S.; Bourdet-Sicard, R.; Rubio, M.; Sarfati, M. Commensal bacteria trigger a full dendritic cell maturation program that promotes the expansion of non-Tr1 suppressor T cells. *J. Leukoc. Biol.* **2008**, *84*, 468–476. [CrossRef]