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The impact of gut microbiota on the pathogenesis of type 1 diabetes in children: Current evidence and potential interventions

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ABSTRACT

Type 1 diabetes (T1D) is a chronic autoimmune disease characterized by selective destruction of pancreatic β-cells, resulting in an absolute insulin deficiency and the need for lifelong replacement therapy from the time of diagnosis. At the same time, the role of the gut microbiota has been increasingly emphasized; under conditions of eubiosis, it participates in digestion, production of key metabolites, maturation of the immune system, and maintenance of intestinal barrier integrity.

The aim of this paper is to present the role of the gut microbiota–immune system axis in the pathogenesis of T1D in children. We discuss evidence showing that children with T1D exhibit a characteristic dysbiosis: reduced microbial diversity, decreased abundance of short-chain fatty acid (SCFA)-producing bacteria, and a predominance of Gram-negative bacteria. The consequences include weakening of the intestinal barrier ("leaky gut"), chronic low-grade inflammation, and enhancement of autoimmunity against β-cells. We present findings from cross-sectional and prospective studies, as well as animal models, indicating that alterations in the microbiota and increased intestinal permeability may precede the clinical manifestation of T1D. Potential microbiota-targeted interventions are also outlined, including dietary strategies, prebiotics, probiotics, and modulation of SCFA.

KEYWORDS: type 1 diabetes, gut microbiota, leaky gut, short-chain fatty acids, children

BACKGROUND

T1D

Diabetes is currently ranked as the third most common chronic disease of childhood. Type 1 diabetes is a metabolic disease, but fundamentally an autoimmune disorder. The immune system mistakenly recognizes self-tissues as foreign, in this case targeting the pancreatic β-cells. This leads to a gradual decline and eventual cessation of insulin production. A clinical marker of the ongoing autoimmune process is the presence of islet autoantibodies, which may appear in the serum years before the overt clinical onset of the disease. Suspicion of diabetes in a child

is an indication for testing antibodies against pancreatic antigens. Their presence is crucial for confirming the autoimmune basis of T1D and for classifying the early stages of the disease [1,2].

The most important autoantibodies include:

- Glutamic acid decarboxylase antibodies (anti-GAD)
- Insulin autoantibodies (IAA)
- Tyrosine phosphatase–related islet antigen 2 antibodies (IA-2A)
- Zinc transporter 8 antibodies (ZnT8A)
- Islet cell antibodies (ICA)

The presence of one or more of these markers indicates an active immune attack leading to progressive loss of β-cell mass. The disease is characterized by hyperglycemia, resulting in disturbances in carbohydrate, fat, and protein metabolism. Although several types of diabetes exist, type 1 diabetes is by far the most common form in children and adolescents.

The burden of T1D in the pediatric population is substantial worldwide. Globally, it is among the most prevalent chronic diseases of childhood. It is estimated that in 2021 alone more than 108,000 children under the age of 15 developed T1D, while the total number of children and adolescents living with the disease exceeded 650,000. This underscores the importance of seeking new preventive and therapeutic strategies [3,4]. Epidemiological observations from different regions consistently indicate that the peak age of onset is in late childhood and early adolescence, typically between 10 and 14 years of age—a critical period of rapid growth and major hormonal changes [5].

T1D is caused by an autoimmune process leading to destruction of the pancreatic β-cells. Diagnosis is based primarily on the blood glucose levels as the main diagnostic criteria.

Status	Laboratory parameter	Diagnostic criteria
Normal Glucose tolerance	Fasting plasma glucose	<100mg/dL (<5,6 mmol/L)
IFG – Impaired Fasting Glucose	Fasting plasma glucose	100-125 mg/dL (5,6-6,9 mmol/L)
IGT – Impaired Glucose Tolerance	2-hour plasma glucose during OGTT	140-199 mg/dL (7,8-11,0mmol/L)
Diabetes	Random plasma glucose	≥200 mg/dL (≥11,1 mmol/L) + classic symptoms
Diabetes	Fasting plasma glucose	≥126 mg/dL (7,0 mmol/L)
Diabetes	2-hour plasma glucose during OGTT	≥ 200 mg/dL (11,1 mmol/L)
Diabetes	Glycated Hemoglobin (HbA1c)	≥6,5%

Table 1. Diagnostic criteria for diabetes. [1]

Prospective studies have made it possible to structure the pathogenesis of type 1 diabetes (T1D) into three distinct stages based on the presence of islet autoantibodies and dysglycaemia [6]:

1. **Stage 1:** Multiple islet autoantibodies with normoglycemia (asymptomatic increased risk).
2. **Stage 2:** Multiple islet autoantibodies with dysglycemia (prediabetic state, still asymptomatic).
3. **Stage 3:** Clinical manifestation of diabetes with fulfilment of biochemical criteria for hyperglycemia.

This long preclinical course (from stages 1 and 2 to stage 3) highlights the urgent need to identify modifiable environmental factors to enable primary prevention at the earliest phases of T1D development.

Gut microbiota

The human gastrointestinal tract is an elaborate ecosystem of microorganisms known as the gut microbiota. This massive community of bacteria, fungi, viruses - whose collective genetic material overrun that of the host - is crucial for maintaining homeostasis. The microbiota consists predominantly of anaerobic bacteria, with Firmicutes and Bacteroidetes as the dominants.

Adequate balance and high species diversity (eubiosis) are essential not only for metabolic functions (e.g. fermentation of non-digestible dietary components, production of short-chain fatty acids [SCFAs], synthesis of certain vitamins), but above all for the proper functioning of the immune system [7]. A key role of the microbiota is its reciprocal interaction with gut-associated lymphoid tissue (GALT), which represents the largest mass of immune tissue in the body. This constant, bidirectional communication is often referred to as the gut–immune axis. Through this axis, the microbiota shapes the development and differentiation of immune cells early in life and promotes immunological tolerance.

Disruption of this delicate balance, known as dysbiosis, involves quantitative and qualitative changes in the composition of the microbiota. Dysbiosis has become an intensive area of research across many fields of medicine and is recognized as a major environmental factor promoting autoimmune diseases, including T1D. It contributes to two principal pathogenic mechanisms that directly link the gut to autoimmune destruction of pancreatic β-cells:

- **Disruption of the intestinal barrier ("leaky gut"):** Increased intestinal permeability allows dietary antigens, toxins, and bacterial components to cross the mucosal barrier and enter the systemic circulation and lymphoid tissues. This leads to chronic activation of GALT and breakdown of immunological tolerance.

- **Aberrant modulation of immune cells:** Alterations in the profile of bacterial metabolites—particularly a reduction in SCFA production—directly affect key immune cell populations responsible for maintaining tolerance. As a result, the microbiota loses its ability to restrain autoimmune responses [8,9].

AIM

The aim of this paper is to provide a critical overview of the current scientific evidence on the complex role of the gut microbiota in the pathogenesis of type 1 diabetes (T1D) in children and adolescents. The paper seeks to analyze in detail the immunological mechanisms underlying the interaction along the gut–immune axis that may lead to autoimmune destruction of pancreatic β-cells.

In particular, the objectives are to:

- identify characteristic patterns of dysbiosis and functional alterations of the gut microbiota observed in children with a genetic predisposition to T1D, in those with islet autoimmunity, and in patients with newly diagnosed T1D,

- discuss the role of key microbiota-derived metabolites, especially short-chain fatty acids (SCFAs), in regulating intestinal barrier integrity and immunological tolerance,
- assess the therapeutic potential of microbiota-modulating interventions in the context of primary prevention and slowing the progression of the autoimmune process in children and adolescents.

MATERIALS AND METHODS

This paper is a narrative, critical review of the literature on the role of the gut microbiota in the pathogenesis of type 1 diabetes in children and adolescents. The aim was not to perform a formal systematic review with meta-analysis, but rather to conduct an in-depth, qualitative analysis of available experimental, clinical, and epidemiological data in the context of immunological mechanisms, dysbiosis patterns, and microbiota-modulating interventions.

The literature search was conducted in the electronic databases PubMed/MEDLINE, Embase, and Web of Science. In addition, selected secondary sources were screened, including textbook chapters and scientific society guidelines (e.g. ISPAD Clinical Practice Consensus Guidelines), as well as the reference lists of review articles to identify further relevant publications.

The search strategy used combinations of keywords including:

- "Type 1 diabetes", "T1D", "children", "adolescents", "pediatric",
- "Gut microbiota", "gut microbiome", "intestinal microbiota",
- "Dysbiosis", "short-chain fatty acids", "SCFA",
- "Intestinal permeability", "leaky gut", "gut barrier".

RESULTS

In recent years, it has become increasingly clear that, in the pathogenesis of type 1 diabetes, not only islet autoimmunity itself but also disbalance along the axis gut microbiota-bacterial metabolites-intestinal barrier-immune system plays a key role. Studies clearly demonstrate a strong association between intestinal dysbiosis and type 1 diabetes (T1D) in children, although the question of causality remains under debate. In children with T1D, the gut microbiota is less diverse, the pool of beneficial bacteria is reduced, and pro-inflammatory taxa are more frequent [10,11]. Patients with T1D exhibit a characteristic dysbiosis combined with profound functional alterations: reduced capacity to produce short-chain fatty acids (SCFAs), disturbances in bile

acid metabolism, and an increased potential for lipopolysaccharide (LPS) biosynthesis. These features differentiate children with T1D from healthy peers.

One line of evidence supporting this hypothesis comes from microbiota transplantation experiments: transfer of gut microbiota from children with T1D into mice led to exacerbation of hyperglycemia and reduced insulin sensitivity [11]. Additional, very strong support for the involvement of the microbiota in T1D pathogenesis comes from comparative studies of children with type 1 diabetes, MODY2 diabetes, and healthy controls. One study showed that the microbiome of children with T1D is not only less diverse, but also qualitatively distinct from that of both healthy children and patients with MODY2, in whom hyperglycemia has a monogenic basis and is not associated with autoimmunity [12]. In T1D, there is a clear shift towards a predominance of Gram-negative bacteria, an increased wealth of taxa associated with inflammation, and a reduction in SCFA-producing bacteria (including members of the families Lachnospiraceae and Ruminococcaceae).

Importantly, functional (metagenomic) analysis revealed enrichment of pathways related to LPS biosynthesis and lipid and sphingolipid metabolism, accompanied by a reduced potential for butyrate and secondary bile acid production. This pattern distinguishes T1D from MODY2 and indicates that microbiome alterations in T1D are not a simple consequence of hyperglycemia but are linked to the underlying autoimmune process [12,13]. An increased wealth of Bacteroides and a decrease in Firmicutes have been observed. The latter are major producers of butyrate, a key molecule regulating the immune system at the level of the gut. At the same time, bacteria with beneficial effects on the host, including Bifidobacterium, are reduced [10,11].

Long-term follow-up studies of children at high risk of T1D suggest that certain microbiome features emerge even before clinical disease onset: microbial diversity declines, the relative wealth of Bacteroides increases, and the functional profile shifts towards heightened activity of pro-inflammatory pathways. As a result of this dysregulation, newly diagnosed with T1D display a microbiome with decreased capacity to produce butyrate and other SCFAs, as well as disturbed bile acid metabolism, together with an increased potential for LPS biosynthesis.

SCFAs are crucial energy substrates for enterocytes and are key regulators of intestinal barrier function. They promote epithelial cell proliferation and upregulate the expression of tight junction proteins, thereby strengthening barriers. From an immunological perspective, SCFAs, via G-protein-coupled receptors (GPR41, GPR43, GPR109A) and inhibition of histone deacetylases, support the development and function of regulatory T cells (Tregs), weaken excessive inflammatory responses, and foster immunological tolerance.

Larger attention is being paid to the role of local mucosal immunity, particularly IgA responses, in regulating host–microbiota interactions. Bacterial metabolites, including SCFAs, significantly modulate the IgA response profile in the gut, influencing which bacteria are selectively coated with IgA and thus kept under immunological control. In individuals with T1D, some potentially pro-inflammatory bacteria are less effectively coated with IgA. This disrupts the delicate balance between tolerance and elimination of microbes in the intestinal lumen and may preserve a pro-inflammatory mucosal environment that favors persistent "leaky gut" and chronic inflammation [14,15].

Reviews on autoimmunity indicate that disturbances in SCFA production and profiles are a common pathophysiological pattern across many autoimmune diseases, including T1D [16]. The consequences of reduced SCFA production and dysbiosis include increased intestinal permeability, which has been demonstrated prospectively in children with multiple islet autoantibodies as well as in those with newly diagnosed T1D. These children show a higher lactulose/rhamnose ratio, lower microbial diversity, and reduced wealth of SCFA-producing bacteria [17]. The data suggest that decreased SCFA production may serve as an early biomarker of disease development. In animal models, these changes are associated with the development of intestinal inflammation and disruption of the epithelial barrier [18]. A complementary component of this axis is lipopolysaccharide (LPS), a constituent of the outer membrane of Gram-negative bacteria. Under eubiotic conditions, small amounts of LPS are locally neutralized, dysbiosis however combined with an overrepresentation of Gram-negative bacteria and increased intestinal permeability ("leaky gut"), promotes the translocation of LPS into the circulation and the development of so-called metabolic endotoxemia. In individuals with type 1 diabetes, a predominance of Gram-negative bacteria in the stool has been observed, as well as a correlation between their wealth, poorer glycemic control (higher HbA1c) and elevated levels of the pro-inflammatory cytokine interleukin-6 (IL-6). In animal models, administration of LPS exacerbates pancreatic inflammation and damage to the islets, whereas butyrate exerts a protective effect by activating Ins1/Ins2 gene expression and improving islet structure and function [19].

Increased intestinal permeability is a key link between these phenomena. In both T1D and other autoimmune diseases, disruption of epithelial tight junctions, thinning of the mucus layer and an altered composition of the gut microbiota lead to a disruption of the barrier and facilitate the translocation of bacterial and dietary antigens into the lamina propria and systemic circulation. The "partners in leaky gut" concept posits that dysbiosis and barrier dysfunction act synergistically: the altered microbiome generates a pro-inflammatory milieu while

simultaneously damaging the physical barrier, which further enhances immune system exposure to antigens and fuels autoimmunity [20].

Clinical data from microbiota studies in diabetes indicate that these disturbances are observed not only in T1D, but also in type 2 diabetes (T2D), suggesting shared immuno-metabolic mechanisms. In patients with diabetes, irrespective of type, reduced levels of short-chain fatty acids (SCFA), impaired integrity of the intestinal barrier, increased circulating bacterial toxins and a state of chronic low-grade inflammation are more frequently reported. Reviews emphasize a "shift in balance" between protective microbiota-derived metabolites (SCFA) and pro-inflammatory bacterial cell wall components (LPS), which is reflected in both immunological and metabolic parameters.

Actual state of knowledge allows viewing T1D as a disease in which impaired production and signaling of SCFA, together with excessive exposure to LPS-resulting from dysbiosis and a "leaky gut"-jointly create an environment that favors persistent inflammation, loss of intestinal barrier integrity and destabilization of the balance between immune tolerance and autoimmunity. Understanding these interrelationships provides a rationale for incorporating the analysis of gut microbiota and its metabolites into research on early diagnosis, risk stratification and the design of novel preventative and therapeutic interventions in T1D.

Axis element	Main phenomenon in T1D	Potential consequences	References
Gut microbiota	Dysbiosis, predominance of Gram-negative bacteria, decreased abundance of SCFA-producing bacteria.	Chronic inflammation, poorer glycemic control.	[11,19]
SCFA (acetate, propionate, butyrate)	Decreased production and reduced concentrations in plasma and stool.	Impaired intestinal barrier infunction, reduced numbers of regulatory T cells (Treg), increased inflammation.	[19,21]
LPS (lipopolysaccharide)	Increased biosynthesis and enhanced translocation across a "leaky gut".	Metabolic endotoxemia, activation of Toll-like receptors (TLR), damage to pancreatic islets.	[11,19,20]
Intestinal barrier	Increased permeability	Increased exposure of the immune system to	[20]

Immune system	Chronic low-grade inflammation.	environmental and bacterial antigens. Initiation of autoimmunity, progression of pancreatic β-cell destruction.	[11,16]

Table 2. Connections between the microbiota, SCFA, LPS and the intestinal barrier in T1D

Microbiota-targeted interventions in type 1 diabetes in children

The role of the gut microbiota-immune system axis in the pathogenesis of T1D has prompted the search for therapeutic and preventive interventions aimed at modifying the microbiota in individuals at high risk of developing the disease. The most physiological strategy is dietary modification-particularly increasing fiber intake, which provides substrate to produce SCFA by commensal bacteria. In animal models, diets rich in soluble fiber (e.g. inulin, resistant starch) lead to an increased wealth of bacteria from the genera Bifidobacterium and Faecalibacterium, higher butyrate concentrations, strengthening of the intestinal barrier, reduced severity of inflammatory infiltrates and delayed onset of hyperglycemia [15,18]. Reviews emphasize that in autoimmune diseases, including T1D, a diet that promotes SCFA production may improve intestinal barrier integrity, increase Treg numbers and attenuate chronic inflammation [15,16]. Initial observational studies in children with T1D suggest that higher fiber intake is associated with a more favorable microbiota profile and lower inflammatory markers [17].

A second group of interventions comprises prebiotics and probiotics used as supplements. Prebiotics selectively stimulate the growth of SCFA-producing bacteria, which may help restore intestinal barrier integrity [15,17]. Probiotics-most commonly strains from the genera Lactobacillus and Bifidobacteriu-have been studied in the context of their effects on glucose metabolism, inflammatory markers and microbiota composition. Some studies report modest improvements in glycemic control, reductions in pro-inflammatory cytokine levels and beneficial changes in the microbiome profile however, the findings are inconsistent, and the studies differ in terms of probiotic composition, dose, patient age and duration of the intervention. As of this moment there is insufficient evidence to recommend routine use of any specific probiotic in pediatric T1D, but reviews underscore that this remains a promising area of research.

Another, more “targeted” strategy is the direct administration of short-chain fatty acids or their precursors. In animal models of T1D, supplementation with butyrate, propionate or SCFA

mixtures increases the number of regulatory T cells in the gut and lymphoid organs, enhances the expression of tight junction proteins, reduces LPS translocation and lowers the incidence or delays the onset of diabetes [15,18]. These effects are linked to activation of the receptors GPR41, GPR43 and GPR109A, as well as inhibition of histone deacetylases, resulting in altered expression of pro- and anti-inflammatory genes. In humans, data on SCFA supplementation are currently very limited, and long-term studies in children at risk of T1D are lacking.

The most far-reaching intervention in the microbiome is fecal microbiota transplantation (FMT). In animal models of T1D, transplantation of microbiota from healthy donors to susceptible animals reduced disease incidence or delayed onset, whereas transfer of microbiota from animals with T1D exacerbated hyperglycemia and insulin resistance [11,18]. In humans, experience with FMT in T1D is very limited, and the procedure is currently used primarily for other conditions (e.g. Clostridioides difficile infection) [17,19].

In the context of T1D prevention, attention has also been drawn to early environmental factors that modulate microbiota development: mode of delivery, breastfeeding, antibiotic exposure and dietary composition in the first years of life [17,20]. Cohort and review studies indicate that the "developmental window" of the microbiota in early childhood is particularly sensitive to these factors and that alterations during this period may have long-term consequences for the immune system [13,17,20]. The "partners in leaky gut" concept further strengthen the importance of such interventions: any measure that supports eubiosis, adequate SCFA production and intestinal barrier integrity may potentially counteract the synergistic effects of dysbiosis and a leaky gut [20]. As of this moment microbiota-targeted interventions are recommended to be considered as an adjunct to standard diabetological care, with careful evaluation of the efficacy and safety of each specific approach [15–17,19,20].

CONCLUSIONS

On this basis, type 1 diabetes in children should be viewed not only as an isolated autoimmune disease of the pancreas, but as a condition in which the gut microbiota–immune system axis plays a pathogenic role. Children with T1D exhibit a characteristic gut dysbiosis: reduced microbial diversity, decreased wealth of SCFA-producing bacteria and a predominance of Gram-negative bacteria with an increased capacity for LPS biosynthesis. These disturbances lead to limited SCFA production, disruption of the intestinal barrier ("leaky gut"), increased translocation of LPS and other bacterial antigens, and the development of metabolic endotoxemia, thereby promoting chronic inflammation and loss of immune tolerance to pancreatic β cells.

Data from prospective studies and animal models indicate that alterations in the microbiota, metabolite profile and intestinal permeability may precede the clinical onset of T1D, making them potential early biomarkers of risk and targets for future preventive interventions.

Microbiota-targeted interventions, dietary modification, prebiotics, probiotics and modulation of SCFA show promising effects in animal models and preliminary clinical studies but require further investigation in children.

The integration of assessments of microbiota composition and function, concentrations of key microbial metabolites and markers of intestinal barrier integrity should become an essential component of future research on early diagnosis, risk stratification and the design of personalized preventive and therapeutic strategies in pediatric T1D.

Disclosure

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REFERENCES

1. Libman I, Haynes A, Lyons S, et al. Chapter 01: Definition, epidemiology, and classification of diabetes in children and adolescents. In: Craig ME, et al. (eds.) *ISPAD Clinical Practice Consensus Guidelines 2022*. Springer; 2022.
2. Lucier J, Mathias PM. Type 1 Diabetes. 2024 Oct 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29939535.
3. Shah AS, Nadeau KJ. The changing face of paediatric diabetes. Diabetologia. 2020;63(4):683-691.
4. Ogle GD, James S, Dabelea D, et al. Global estimates of incidence of type 1 diabetes in children and adolescents: results from the Interna- tional Diabetes Federation Atlas, 10(th) Edition. Diabetes Res Clin Pract. 2021;183:109083.
5. Tuomilehto J, Ogle GD, Lund-Blix NA, Stene LC. Update on world- wide trends in occurrence of childhood type 1 diabetes in 2020. Pediatr Endocrinol Rev. 2020;17(suppl 1):198-209.
6. Besser REJ, Bell KJ, Couper JJ, Ziegler AG, Wherrett DK, Knip M, Speake C, Casteels K, Driscoll KA, Jacobsen L, Craig ME, Haller MJ. ISPAD Clinical Practice Consensus Guidelines 2022: Stages of type 1 diabetes in children and adolescents. Pediatr Diabetes. 2022 Dec;23(8):1175-1187. doi: 10.1111/pedi.13410. Epub 2022 Sep 30. PMID: 36177823.
7. Kuziel GA, Rakoff-Nahoum S. The gut microbiome. Curr Biol. 2022 Mar 28;32(6):R257-R264. doi: 10.1016/j.cub.2022.02.023. PMID: 35349808.
8. Yoo, J.Y.; Groer, M.; Dutra, S.V.O.; Sarkar, A.; McSkimming, D.I. Gut Microbiota and Immune System Interactions. *Microorganisms* **2020**, *8*, 1587. https://doi.org/10.3390/microorganisms8101587
9. Maynard, C., Elson, C., Hatton, R. *et al.* Reciprocal interactions of the intestinal microbiota and immune system. *Nature* **489**, 231–241 (2012). https://doi.org/10.1038/nature11551
10. Dedrick, S., Sundaresh, B., Huang, Q., Brady, C., Yoo, T., Cronin, C., Rudnicki, C., Flood, M., Momeni, B., Ludvigsson, J., & Altindis, E. (2020). The Role of Gut Microbiota and Environmental Factors in Type 1 Diabetes Pathogenesis. Frontiers in Endocrinology, 11. https://doi.org/10.3389/fendo.2020.00078.
11. Yuan, X., Wang, R., Han, B., Sun, C., Chen, R., Wei, H., Chen, L., Du, H., Li, G., Yang, Y., Chen, X., Cui, L., Xu, Z., Fu, J., Wu, J., Gu, W., Chen, Z., Fang, X., Yang, H., Su, Z., Wu, J., Li, Q., Zhang, M., Zhou, Y., Zhang, L., Ji, G., & Luo, F. (2022). Functional and metabolic

alterations of gut microbiota in children with new-onset type 1 diabetes. *Nature Communications*, 13. https://doi.org/10.1038/s41467-022-33656-4.

12. Leiva-Gea, I., Sánchez-Alcoholado, L., Martín-Tejedor, B., Castellano-Castillo, D., Moreno-Indias, I., Urda-Cardona, A., Tinahones, F., Fernández-García, J., & Queipo-Ortuño, M. (2018). Gut Microbiota Differs in Composition and Functionality Between Children With Type 1 Diabetes and MODY2 and Healthy Control Subjects: A Case-Control Study. Diabetes Care, 41, 2385 - 2395. https://doi.org/10.2337/dc18-0253.
13. Vatanen, T., Franzosa, E., Schwager, R., Tripathi, S., Arthur, T., Vehik, K., Lernmark, Å., Hagopian, W., Rewers, M., She, J., Toppari, J., Ziegler, A., Akolkar, B., Krischer, J., Stewart, C., Ajami, N., Petrosino, J., Gevers, D., Lähdesmäki, H., Vlamakis, H., Huttenhower, C., & Xavier, R. (2018). The human gut microbiome in early-onset type 1 diabetes from the TEDDY study. Nature, 562, 589 - 594. https://doi.org/10.1038/s41586-018-0620-2.
14. Huang, J., Pearson, J., Peng, J., Hu, Y., Sha, S., Xing, Y., Huang, G., Li, X., Hu, F., Xie, Z., Xiao, Y., Luo, S., Chao, C., Wong, F., Zhou, Z., & Wen, L. (2020). Gut microbial metabolites alter IgA immunity in type 1 diabetes. JCI insight. https://doi.org/10.1172/jci.insight.135718.
15. Liu, W., Luo, X., Tang, J., Mo, Q., Zhong, H., Zhang, H., & Feng, F. (2020). A bridge for short-chain fatty acids to affect inflammatory bowel disease, type 1 diabetes, and non-alcoholic fatty liver disease positively: by changing gut barrier. European Journal of Nutrition, 60, 2317 - 2330. https://doi.org/10.1007/s00394-020-02431-w.
16. Rasouli-Saravani, A., Jahankhani, K., Moradi, S., Gorgani, M., Shafaghat, Z., Mirsanei, Z., Mehmandar, A., & Mirzaei, R. (2023). Role of microbiota short-chain fatty acid chains in the pathogenesis of autoimmune diseases. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie, 162, 114620. https://doi.org/10.1016/j.biopha.2023.114620.
17. Mokhtari, P., Metos, J., & Babu, P. (2021). Impact of type 1 diabetes on the composition and functional potential of gut microbiome in children and adolescents: possible mechanisms, current knowledge, and challenges. Gut Microbes, 13. https://doi.org/10.1080/19490976.2021.1926841.
18. , Q., Li, Y., Wang, J., Li, P., Duan, Y., Dai, H., An, Y., Cheng, L., Wang, T., Wang, C., Wang, T., & Zhao, B. (2020). Investigation of gut microbiome changes in type 1 diabetic mellitus rats based on high-throughput sequencing. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie, 124, 109873. https://doi.org/10.1016/j.biopha.2020.109873.
19. Lau, W., Tran, T., Rhee, C., Kalantar-Zadeh, K., & Vaziri, N. (2021). Diabetes and the Gut Microbiome.. Seminars in nephrology, 41 2, 104-113 . https://doi.org/10.1016/j.semnephrol.2021.03.005.
20. Kinashi, Y., & Hase, K. (2021). Partners in Leaky Gut Syndrome: Intestinal Dysbiosis and Autoimmunity. Frontiers in Immunology, 12. https://doi.org/10.3389/fimmu.2021.673708.

21. Harbison, J., Roth-Schulze, A., Giles, L., Tran, C., Ngui, K., Penno, M., Thomson, R., Wentworth, J., Colman, P., Craig, M., Morahan, G., Papenfuss, A., Barry, S., Harrison, L., & Couper, J. (2019). Gut microbiome dysbiosis and increased intestinal permeability in children with islet autoimmunity and type 1 diabetes: A prospective cohort study. Pediatric Diabetes, 20, 574 - 583. https://doi.org/10.1111/pedi.12865.