



Clinical outcomes of metabolomics and gut microbiota in the treatment of inflammatory bowel diseases: a systematic review

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Abstract

Introduction: Inflammatory bowel diseases (IBDs) are multifactorial diseases characterized by chronic inflammation of the gastrointestinal tract. Nutrients, gut microbiota, exosomes, and microRNAs play crucial roles in the pathophysiology of IBD. **Objective:** It was to conduct a systematic review of the main clinical studies on the nutritional management of inflammatory bowel diseases, focusing on the gut microbiota and metabolomics. **Methods:** The PRISMA Platform systematic review rules were followed. The search was carried out from September to October 2025 in the Web of Science, Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 177 articles were found, and 58 articles were evaluated in full, and 30 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 06 studies with a high risk of bias and 25 studies that did not meet GRADE and AMSTAR-2. Most studies showed homogeneity in their results, with Chi-Square $X^2=84.7\%>50\%$. It was concluded that inflammatory bowel diseases are associated with

various gastrointestinal symptoms and, therefore, affect patients' quality of life. Although intestinal bacteria and the host's immune response are considered important factors in its pathogenesis, a sufficient explanation of their role in its pathophysiological mechanism has not been presented. Exosomes and microRNAs, together with nutrients and gut microbiota, participate in the molecular interactions of inflammatory bowel diseases. Recent studies have confirmed the important role of miRNAs in targeting certain molecules in signaling pathways that regulate intestinal barrier homeostasis, inflammatory reactions, and autophagy of the intestinal epithelium. Several studies have identified specific miRNAs associated with inflammatory bowel diseases in colon tissues. The correlation between the gut microbiota and cytokines suggests that exosomes and microRNAs can modulate intestinal immunity by influencing the gut microbiota.

Keywords: Inflammatory bowel diseases. Nutrients. Gut microbiota. Exosomes/microRNAs.

Introduction

Inflammatory bowel diseases (IBDs) are multifactorial conditions characterized by chronic

inflammation of the gastrointestinal tract, specifically comprising Crohn's disease (CD) and ulcerative colitis (UC). CD and UC primarily affect young people, causing bloody diarrhea, abdominal pain, malabsorption, fatigue, and impaired quality of life. Long-standing inflammation also increases the risk of colorectal cancer in IBD patients, a condition associated with a mortality rate of 10–15% [1,2].

In this context, microRNAs (miRNAs or miR-) play important roles in the pathophysiology of IBDs [1]. miRNAs are evolutionarily conserved, endogenous, single-stranded, non-coding RNAs that bind to the 3' untranslated region (UTR), 5' UTR, or a partially translated region of a target mRNA, thereby inhibiting mRNA translation and blocking its expression. miRNAs are key regulators of cellular function and homeostasis, and their abnormal activity has been demonstrated in various diseases, including IBDs. Consequently, novel treatment options could be developed to address imbalances in miRNA expression. miRNAs influence the intestinal barrier and inflammatory responses through various pathological mechanisms [3].

In this regard, metabolism encompasses the interactions between diet, the microbiome, and cellular enzymatic processes that generate the chemical pathways necessary to sustain life and regulate the balance of the gut microbiota, particularly in the context of IBD treatment. Both endogenous metabolites and dietary nutrients can directly influence epigenetic enzymes [3–6]. Epigenetic modifications to DNA and histone proteins alter cell fate by controlling chromatin accessibility and downstream gene expression patterns [7–10].

Beyond the link between metabolism and epigenetic pathways, nutrients can influence cellular status by modulating signaling pathway activity. A clear example is the mechanistic target of rapamycin (mTOR) signaling pathway—specifically the mTOR complex 1 (mTORC1)—which regulates cell growth only when nutrients and growth factors are present [3,10]. Nutrients also influence cellular status via AMP-activated protein kinase (AMPK); when cellular ATP levels are low, AMPK phosphorylates substrates to restore the cell's energy balance [3,4].

These epigenetic and nutritional mechanisms are of paramount importance, given that approximately 70–80% of patients lose weight during the course of IBDs, leading to some degree of nutritional impairment; malnutrition affects around 23% of outpatients and 85% of hospitalized patients [11,12]. The Western diet is characterized by excessive consumption of refined sugars, salt, and saturated fat, along with low dietary fiber intake and

limited overall dietary diversity. New elements of human nutrition in modern society include artificial sweeteners, gluten, and genetically modified foods [9].

Consequently, deficiencies in micro- and macronutrients, as well as an overabundance of calories and macronutrients, trigger inflammatory processes and increase susceptibility to infections [13]. Several micronutrients are particularly important for immunonutrition, including vitamins (such as A, C, D, and E, folic acid, and beta-carotene) and trace elements (such as zinc, selenium, manganese, and iron). Deficiencies in zinc and vitamins A, C, and D can impair natural killer cell function [14–17].

Therefore, the present study aimed to conduct a systematic review of key clinical studies on the nutritional management of inflammatory bowel diseases, focusing on gut microbiota and metabolomics.

Methods

Study Design

This study followed an international systematic review model, adhering to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Available at: <http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1>. Accessed on: September 10, 2025. Methodological quality standards from AMSTAR-2 (Assessing the Methodological Quality of Systematic Reviews) were also followed. Available at: <https://amstar.ca/>. Accessed on: September 10, 2025.

Data Sources and Search Strategy

The literature search process was conducted from September to October 2025 using Web of Science, Scopus, PubMed, LILACS, EBSCO, SciELO, and Google Scholar, covering scientific articles from various periods up to the present. The following descriptors (DeCS/MeSH terms) were used: "Inflammatory bowel diseases," "Nutrients," "Gut microbiota," and "Exosomes/microRNAs," employing the Boolean operator "AND" between MeSH terms and "OR" between related concepts.

Study Quality and Risk of Bias

Quality regarding risk of bias, clarity of comparisons, precision, and consistency of analyses was classified as high, moderate, low, or very low. Priority was given to systematic reviews or meta-analyses of randomized clinical trials, followed by

randomized clinical trials themselves. Evidence quality was rated as low for case reports, editorials, and brief communications, in accordance with the GRADE instrument. Risk of bias was assessed using the Cochrane tool via funnel plot analysis (sample size versus effect size) and Cohen's d test.

Results and Discussion

Summary of Findings

A total of 177 articles were identified and subjected to an eligibility assessment, with 30 studies ultimately selected for inclusion in the results of this systematic review. The selected studies demonstrated moderate to high quality (Figure 1), based on the level of scientific evidence—ranging from meta-analyses and consensus statements to randomized clinical, prospective, and observational studies. Bias did not compromise the scientific foundation of the studies. According to the GRADE instrument, the majority of studies showed homogeneity in their results (Chi-square $[X^2] = 84.7\% > 50\%$). Based on the Cochrane risk-of-bias tool, the overall assessment identified six studies with a high risk of bias, while 25 studies failed to meet the criteria for GRADE and AMSTAR-2.

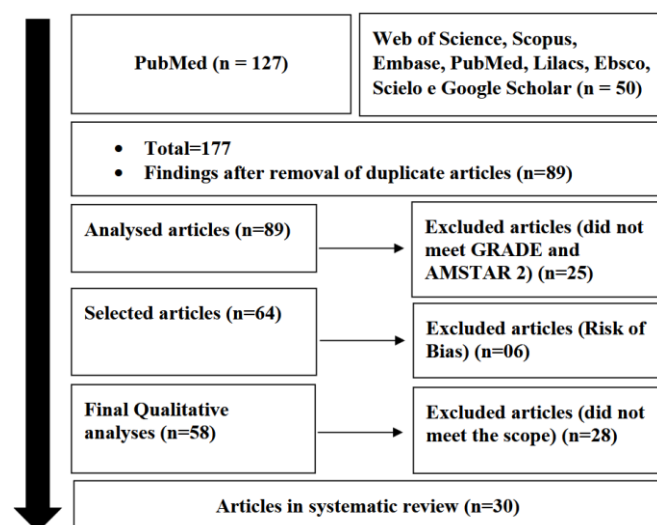


Figure 1. Flowchart showing the article selection process. Source: Own Authorship.

Figure 2 presents the results regarding the risk of bias across the studies using a funnel plot, showing the calculation of effect size (magnitude of difference) via Cohen's d. Precision (sample size) was determined indirectly by the inverse of the standard error (1/standard error). The plot exhibited a symmetrical pattern, suggesting no significant risk of bias among either studies with small sample sizes (lower precision), shown at the base of the plot, or studies with large sample sizes, shown at the top.

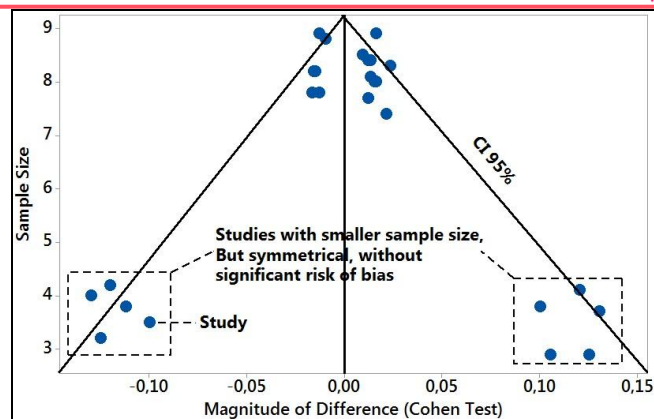


Figure 2. The symmetrical funnel plot suggests no risk of bias among studies with small sample sizes, which are shown at the bottom of the plot. Studies with high confidence and high recommendation levels are shown at the top of the plot (n=30 studies). Source: Own Authorship.

Major Clinical Outcomes

Compromised intestinal barriers are a significant factor in the pathogenesis of IBD. TNF- α is known to be a key pro-inflammatory cytokine in the pathogenesis of IBD [18]. Certain miRNAs, such as miR-191a and miR-212, are known to damage intestinal barriers, while others strengthen them. c-Jun and myosin light-chain kinase (MLCK) have been shown to be targets of miR-200b [19]. Silencing protein tyrosine kinase 6 (PTK6) expression via miR-93 in the intestinal epithelium increases resistance to TNF- α -induced injury [20].

Furthermore, miRNAs are known to contribute to the immune responses leading to IBD. The nucleotide-binding oligomerization domain-containing protein 2 (NOD2) gene is clearly associated with Crohn's disease (CD) [21]. Some studies have found abnormally elevated miRNA levels in the mucosal tissues of patients with ulcerative colitis (UC) compared to healthy controls. Researchers found that miR-16, miR-21, miR-23a, miR-24, miR-29a, miR-126, miR-195, and let-7f were upregulated in patients with active UC compared to healthy controls [22]. In a comparison of colonic mucosa between UC patients and healthy controls, researchers demonstrated that miR-7, miR-26a, miR-29a, miR-29b, miR-31, miR-126, miR-127-3p, miR-135b, and miR-324-3p were elevated in the inflamed mucosa of UC patients [23].

Elevated levels of miR-21, miR-155, miR-923, let-7a, let-7c, let-7d, and let-7g were found in colon biopsy samples from patients with active UC compared to healthy controls [24]. Frozen distal colectomy biopsy samples from UC patients were found to exhibit significant increases in miR-31, miR-146a, miR-206, and miR-424 levels [25], and increased levels of miR-20b, miR-26b, miR-98, miR-99a, and miR-203 were observed in colon biopsy samples from patients with

active UC compared to healthy controls [26]. These and other findings are summarized in Table 1.

Table 1. Key insights regarding microRNAs in IBD [18-26].

microRNAs – Weaken the intestinal barrier		
miR-874	Aquaporin 3	Decreases the expression of aquaporin 3
miR-675	Cadherin E, ZO-1	Destabilizes the mRNA of cadherin E and ZO-1
miR-122a	EGFR	Enhances the expression of zonulin and increases epithelial permeability
miR-191a, -212	ZO-1	Reduce the expression of ZO-1
miR-21	PTEN/PI3K/Akt pathway	Increases the paracellular permeability of the intestinal epithelium
microRNAs – Strengthen the intestinal barrier		
miR-93 (downregulation)	PTK6	Reduces the expression of PTK6 and attenuates epithelial injury
miR-200b	c-Jun, MLCK	Decreases epithelial damage induced by TNF- α
microRNAs – Reduction of inflammation		
miR-10a	IL-12/23p40	Downregulates the expression of IL-12/23p40 and Th1/Th17 cell responses
miR-141	CXCL12 β	Inhibits CXCL12 β -mediated leukocyte migration
miR-320	NOD2	Decreases the expression of NOD2

In this regard, a study conducted by Tong et al. (2021) [27] explored the therapeutic effects of exosomes and microRNAs (mEVs) derived from cow's milk on IBD. The microRNA and protein content of mEVs were analyzed via RNA sequencing and proteomics, respectively, followed by functional annotation. Proteins and microRNAs abundant in mEVs were involved in regulating immune and inflammatory pathways; furthermore, oral administration of mEVs prevented colon shortening, reduced intestinal epithelial disruption, and inhibited inflammatory cell infiltration and tissue fibrosis. The mEVs attenuated the inflammatory response by inhibiting the TLR4-NF- κ B signaling pathway and NLRP3 inflammasome activation. Additionally, mEVs were able to correct cytokine production imbalances and restore the equilibrium between T-helper 17 (Th17) cells and interleukin-10+Foxp3+ regulatory T cells (Tregs) in the inflamed colon. The gut microbiota, disrupted in UC, was also partially restored following mEV treatment.

Within the context of dietary microRNA manipulation, prebiotic and probiotic therapies can selectively modulate the gut microbiota [3,4]. In this sense, prebiotics are non-digestible carbohydrates that promote the growth of beneficial gut bacteria, thereby increasing short-chain fatty acid production and modulating cytokine production in the intestinal mucosa [5]. Probiotics, in turn, contain live bacteria that appear to exert positive health effects on the human gut by modulating mucosal permeability and strengthening immune system maintenance to keep pathogens away from the intestinal mucosal surface [1].

In this context, the gut microbiota is fundamental to immune system activation— notably involving *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*, and *Lactobacillus casei*, which increase IgA levels for non-inflammatory antigen removal and boost T and B lymphocyte counts—while *Faecalibacterium prausnitzii* stands out as one of the most prevalent intestinal bacterial species in healthy adults, acting as a beneficial, butyrate-producing bacterium [7]. *Lactobacillus* and *Bifidobacterium* species inhibit the growth of exogenous and/or harmful bacteria, stimulate immune functions, aid in the digestion and/or absorption of food nutrients and minerals, and contribute to vitamin synthesis [1,3,6].

In this regard, short-chain fatty acids—such as butyrate, propionate, and acetate— serve as an energy source for intestinal epithelial cells and induce protective regulatory immune responses [15]. The intestinal adaptive immune system is also rapidly activated following exposure to commensal bacteria, characterized by increased expression of major histocompatibility complex (MHC) class II molecules and an increase in T cells [3]. T cells can give rise to subpopulations with either pro-inflammatory or anti-inflammatory immune responses. Th1 and Th17 cells (T helper cells) are pro-inflammatory, whereas Treg cells (CD4+ CD25+ phenotype) and Th2 cells are anti-inflammatory [10].

In this context, the Gram-negative bacterium *Bacteroides fragilis* induces the differentiation of CD4+ T cells into Treg cells, leading to the production of anti-inflammatory cytokines such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF- β), thereby counteracting the pro-inflammatory Th17 response. Treg cell differentiation depends on the recognition by CD4+ T cells of the polysaccharide presented by dendritic cells (DCs) [10].

Many studies have evaluated the capacity of diet to modulate the gut microbiota and microRNAs, thereby influencing epithelial barrier function. Low-fiber diets have been associated with IBD, with a postulated mechanism involving reduced production of short-chain fatty acids by commensal bacteria that rely on fiber as their preferred energy source. Butyrate, a short-chain fatty acid, is essential for colonic health and serves as the primary energy source for colonocytes. Furthermore, short-chain fatty acids promote immune tolerance by fostering the development of regulatory T cells [28-30].

Conclusion

It is concluded that inflammatory bowel diseases are associated with various gastrointestinal symptoms

and, consequently, affect patients' quality of life. Although gut bacteria and the host immune response are considered key factors in their pathogenesis, a comprehensive explanation of their specific roles in the pathophysiological mechanism has not yet been established. Exosomes and microRNAs, alongside nutrients and the gut microbiota, participate in the molecular interactions underlying inflammatory bowel diseases. Recent studies have confirmed the significant role of miRNAs in targeting specific molecules within signaling pathways that regulate intestinal barrier homeostasis, inflammatory reactions, and intestinal epithelial autophagy. Several studies have identified specific miRNAs associated with inflammatory bowel diseases in colon tissues. The correlation between gut microbiota and cytokines suggests that exosomes and microRNAs can modulate intestinal immunity by influencing the gut microbiota.

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References

1. Alfaifi J, Germain A, Heba AC, Arnone D, Gailly L, Ndiaye NC, Viennois E, Caron B, Peyrin-Biroulet L, Dreumont N. Deep Dive Into MicroRNAs in Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2023 Jun 1;29(6):986-999. doi: 10.1093/ibd/izac250.
2. So D, Quigley EMM, Whelan K. Probiotics in irritable bowel syndrome and inflammatory bowel disease: review of mechanisms and effectiveness. *Curr Opin Gastroenterol*. 2023 Mar 1;39(2):103-109. doi: 10.1097/MOG.0000000000000902.
3. Jung H, Kim JS, Lee KH, Tizaoui K, Terrazzino S, Cargnin S, Smith L, Koyanagi A, Jacob L, Li H, Hong SH, Yon DK, Lee SW, Kim MS, Wasuwanich P, Karnsakul W, Shin JI, Kronbichler A. Roles of microRNAs in inflammatory bowel disease. *Int J Biol Sci*. 2021 May 17;17(8):2112-2123. doi: 10.7150/ijbs.59904.
4. Mah C, Jayawardana T, Leong G, Koentgen S, Lemberg D, Connor SJ, Rokkas T, Grimm MC, Leach ST, Hold GL. Assessing the Relationship between the Gut Microbiota and Inflammatory Bowel Disease Therapeutics: A Systematic Review. *Pathogens*. 2023 Feb 6;12(2):262. doi: 10.3390/pathogens12020262.
5. Zhang Y, Si X, Yang L, Wang H, Sun Y, Liu N. Association between intestinal microbiota and inflammatory bowel disease. *Animal Model Exp Med*. 2022 Dec;5(4):311-322. doi: 10.1002/ame2.12255.
6. Adolph TE, Zhang J. Diet fuelling inflammatory bowel diseases: preclinical and clinical concepts. *Gut*. 2022 Dec;71(12):2574-2586. doi: 10.1136/gutjnl-2021-326575.
7. Danilova NA, Abdulkhakov SR, Grigoryeva TV, Markelova MI, Vasilyev IY, Boulygina EA, Ardatskaya MD, Pavlenko AV, Tyakht AV, Odintsova AK, Abdulkhakov RA. Markers of dysbiosis in patients with ulcerative colitis and

- Crohn's disease. *Ter Arkh.* 2019 May 15;91(4):17-24. doi: 10.26442/00403660.2019.04.000211.
8. He Q, Gao Y, Jie Z, Yu X, Laursen JM, Xiao L, Li Y, Li L, Zhang F, Feng Q, Li X, Yu J, Liu C, Lan P, Yan T, Liu X, Xu X, Yang H, Wang J, Madsen L, Brix S, Wang J, Kristiansen K, Jia H. Two distinct metacommunities characterize the gut microbiota in Crohn's disease patients. *Gigascience.* 2017 Jul 1;6(7):1-11. doi: 10.1093/gigascience/gix050.
 9. Green N, Miller T, Suskind D, Lee D. A Review of Dietary Therapy for IBD and a Vision for the Future. *Nutrients.* 2019 Apr 26;11(5). pii: E947. doi: 10.3390/nu11050947.
 10. Shapira SN, Christofk HR. Metabolic Regulation of Tissue Stem Cells. *Trends Cell Biol.* 2020 Jul;30(7):566-576. doi: 10.1016/j.tcb.2020.04.004.
 11. Basson A. Vitamin D. Crohn's disease in the adult patient: a review. *J Parenter Enteral Nutr.* 2014;38:438-58.
 12. Roth MP, Petersen GM, McElree C, Vadheim CM, Panish JF, Rotter JJ. Familial empiric risk estimates of inflammatory bowel disease in Ashkenazi Jews. *Gastroenterology.* 1989;96(4):1016-20.
 13. Lee YK, Menezes JS, Umesaki Y, Mazmanian SK. Proinflammatory T-cell responses to gut microbiota promote experimental autoimmune encephalomyelitis. *Proc Natl Acad Sci USA.* 2011;108(suppl 1):4615-4622.
 14. Teng F, Klinger CN, Felix KM, et al. Gut microbiota drive autoimmune arthritis by promoting differentiation and migration of Peyer's patch T follicular helper cells. *Immunity.* 2016;44(4):875-888.
 15. Donohoe DR, Garge N, Zhang X, et al. The microbiome and butyrate regulate energy metabolism and autophagy in the mammalian colon. *Cell Metab.* 2011;13(5):517-526.
 16. Smith PM, Howitt MR, Panikov N, et al. The microbial metabolites, short-chain fatty acids, regulate colonic Treg cell homeostasis. *Science.* 2013;341(6145):569-573.
 17. Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, et al. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2011;60:571-607.
 18. Ma TY, Boivin MA, Ye D, Pedram A, Said HM. Mechanism of TNF- α modulation of Caco-2 intestinal epithelial tight junction barrier: role of myosin light-chain kinase protein expression. *Am J Physiol Gastrointest Liver Physiol.* 2005;288:G422-30.
 19. Shen Y, Zhou M, Yan J, Gong Z, Xiao Y, Zhang C. et al. miR-200b inhibits TNF- α -induced IL-8 secretion and tight junction disruption of intestinal epithelial cells in vitro. *Am J Physiol Gastrointest Liver Physiol.* 2017;312:G123-G32.
 20. Haines RJ, Beard RS Jr, Eitner RA, Chen L, Wu MH. TNF α /IFN γ Mediated Intestinal Epithelial Barrier Dysfunction Is Attenuated by MicroRNA-93 Downregulation of PTK6 in Mouse Colonic Epithelial Cells. *PLoS One.* 2016;11:e0154351.
 21. Corridoni D, Arseneau KO, Cominelli F. Functional defects in NOD2 signaling in experimental and human Crohn disease. *Gut Microbes.* 2014;5:340-4.
 22. Wu F, Zikusoka M, Trindade A, Dassopoulos T, Harris ML, Bayless TM. et al. MicroRNAs are differentially expressed in ulcerative colitis and alter expression of macrophage inflammatory peptide-2 α . *Gastroenterology.* 2008;135:1624-35. e24.
 23. Fasseu M, Treton X, Guichard C, Pedruzzi E, Cazals-Hatem D, Richard C, Identification of restricted subsets of mature microRNA abnormally expressed in inactive colonic mucosa of patients with inflammatory bowel disease. *PLoS One.* 2010. 5.
 24. Takagi T, Naito Y, Mizushima K, Hirata I, Yagi N, Tomatsuri N. et al. Increased expression of microRNA in the inflamed colonic mucosa of patients with active ulcerative colitis. *J Gastroenterol Hepatol.* 2010;25(Suppl 1):S129-33.
 25. Lin J, Welker NC, Zhao Z, Li Y, Zhang J, Reuss SA. et al. Novel specific microRNA biomarkers in idiopathic inflammatory bowel disease unrelated to disease activity. *Mod Pathol.* 2014;27:602-8.
 26. Coskun M, Bjerrum JT, Seidelin JB, Troelsen JT, Olsen J, Nielsen OH. miR-20b, miR-98, miR-125b-1*, and let-7e* as new potential diagnostic biomarkers in ulcerative colitis. *World J Gastroenterol.* 2013;19:4289-99.
 27. Tong L, Hao H, Zhang Z, Lv Y, Liang X, Liu Q, Liu T, Gong P, Zhang L, Cao F, Pastorin G, Lee CN, Chen X, Wang JW, Yi H. Milk-derived extracellular vesicles alleviate ulcerative colitis by regulating the gut immunity and reshaping the gut microbiota. *Theranostics.* 2021 Jul 25;11(17):8570-8586. doi: 10.7150/thno.62046.
 28. Dong Y, Xu T, Xiao G, Hu Z, Chen J. Opportunities and challenges for synthetic biology in the therapy of inflammatory bowel disease. *Front Bioeng Biotechnol.* 2022 Aug

- 10;10:909591. doi: 10.3389/fbioe.2022.909591.
- 29.** Li G, Lin J, Zhang C, Gao H, Lu H, Gao X, Zhu R, Li Z, Li M, Liu Z. Microbiota metabolite butyrate constrains neutrophil functions and ameliorates mucosal inflammation in inflammatory bowel disease. *Gut Microbes.* 2021 JanDec;13(1):1968257. doi: 10.1080/19490976.2021.1968257.
- 30.** Parada Venegas D, De la Fuente MK, Landskron G, González MJ, Quera R, Dijkstra G, Harmsen HJM, Faber KN, Hermoso MA. Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. *Front Immunol.* 2019 Mar 11;10:277. doi: 10.3389/fimmu.2019.00277. Erratum in: *Front Immunol.* 2019 Jun 28;10:1486.