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Gut Microbiome and Breast Cancer: A Concise Review

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Abstract

The Gut Microbiome influences Breast Cancer risk through Estrogen Metabolism, inflammation throughout the body, and Immune System Regulation. A decrease in the diversity of microbes will result in an imbalance of the gut microbiome (dysbiosis), which will support the increase of pro-inflammatory microbes, leading to elevated Circulating Estrogens and ultimately supporting greater Tumor Growth; conversely, some beneficial microbes (such as *Lactobacillus*) will help maintain hormonal equilibrium, reducing the likelihood of developing breast cancer. The combination of what we eat and how we eat (diet) has a significant impact on the types of bacteria that grow and multiply within our gut microbiome. Studies show that a diet rich in Fiber and Plant-Based foods supports the growth of short-chain fatty acids. SCFAs(bacteria, while diets that are high in Fat and Sugar contribute to an increased incidence of dysbiosis and systemic inflammation. Intervening to restore a healthy balance of gut bacteria has been proven to reduce Inflammation and improve health and wellness. Personalized Interventions based on the Gut Microbiome will have tremendous potential as an additional method for Breast Cancer Prevention and Treatment.

Keywords: Breast cancer, Gut Microbiome, estrogen metabolism, inflammation, immune modulation, and nutritional factors.

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Introduction

Breast cancer is one of the most common cancers globally, and it has recently been shown that the diversity of our gut bacteria has a large impact on how our body processes hormones and fights against inflammation, both of which can lead to the development and progression of breast cancer. Women with breast cancer tend to have a lower diversity of gut bacteria, as well as an increase in the number of proinflammatory bacteria (Clostridium species), indicating these bacteria may lead to a systemic inflammatory response in the body that promotes tumor formation [1] .

The gut microbiome is also involved in how the body breaks down and metabolizes estrogen. Because estrogen is a significant contributor to hormone-positive breast cancer, the ability of certain gut bacteria, specifically Bacteroides and Clostridium species, to produce β-glucuronidase means that these bacteria can break down estrogen, allowing for a greater amount of estrogen to be reabsorbed back into the blood. Increased levels of estrogen in the blood can stimulate the growth of estrogen-sensitive tumors [2]. Conversely, the beneficial bacteria *Lactobacillus* help to eliminate some of the estrogen being reabsorbed back into the blood, thereby reducing a woman's risk for developing breast cancer.

Another mechanism that connects breast cancer and the gut microbiome is through the action of the inflammatory response, which is caused by dysbiosis (the imbalance of gut bacteria). Dysbiosis leads to increased permeability of the intestinal wall, allowing products from the gut (for example, lipopolysaccharide (LPS)) to enter the bloodstream and create a chronic inflammatory response, which then increases the likelihood of developing tumors [3]. Because of these two mechanisms, women with breast cancer tend to have elevated levels of proinflammatory cytokines, specifically Interleukin-6 and Tumor Necrosis Factor-alpha(IL-6 , TNF-α) , which could be due to their microbiome-induced immune response**.**

Impact of Dietary Choices on the Gut Microbiome and Breast Cancer Risk

Dietary choices play a strong role in influencing our gut microbes/gut microbiome as well as affecting our susceptibility to breast cancer. Diets high in sugars and saturated fats promote pro-inflammatory microbes and increase systemic inflammation, which may make individuals more susceptible to disease [4]. On the other hand, a diet rich in fiber enhances the growth

of short-chain fatty acid (SCFA) producing gut microbes (e.g., Roseburia), which have anti-inflammatory properties and may protect individuals from developing breast cancer. A plant-based diet, rich in fiber and antioxidants, has been associated with decreased incidence of breast cancer and supports the use of diet as a potential modulator.

The therapeutic modulation of the gut microbiome has been proposed to be a preventive and/or therapeutic approach for breast cancer. Probiotic administration with *Lactobacillus* or *Bifidobacterium longum* has been associated with improved estrogen metabolism and reduced inflammation, whereas prebiotic treatment enhances short-chain fatty acids (SCFAs) production and may have the ability to inhibit tumor formation [5]. Although fecal microbiota transplantation (FMT) is currently less studied, data from pre-clinical studies suggest that FMT may aid in restoring the microbial balance of the gut [6]. Although these approaches offer promising adjunctive treatment options, additional, well-designed clinical trials are needed to confirm their efficacy.

In future research, there should be a focus on producing educational material for healthcare practitioners regarding the function of the microbiome in the development of breast cancer, as well as tailoring treatment options to fit the client. It is expected that the advancement of metabolomic technology and improvements in microbiome sequencing will enable us to develop systems allowing for accurate identification of specific microorganisms for custom preventative measures and development of microbial-based therapies. To establish causal relationships or form effective prevention/treatment strategies for different types of diseases associated with the microbiome, the conduct of long-term studies is required [7].

Estrogen Metabolism and the Gut Microbiome

Estrogen metabolism is significantly affected by the trillions of microorganisms that make up the gut microbiome; these microorganisms are found in the gastrointestinal (GI) tract and comprise a substantial part of the overall microbe population of humans. The relationships between estrogen metabolism and the development/progression of breast cancer and other hormone-related cancers depend at least in part on the presence of certain bacteria in the GI tract. Certain species of bacteria found in the gut are responsible for either reducing the amount of estrogen in the

body or preventing the reabsorption of estrogen into the bloodstream. Any disruption of the normal ratio of beneficial to pathogenic bacteria, termed dysbiosis, disrupts the balance of circulating estrogen and increases a woman's risk of developing breast cancer. This section will summarize the various ways that the gut microbiome affects the pathways of estrogen metabolism and how this relates to ER+ breast cancer.

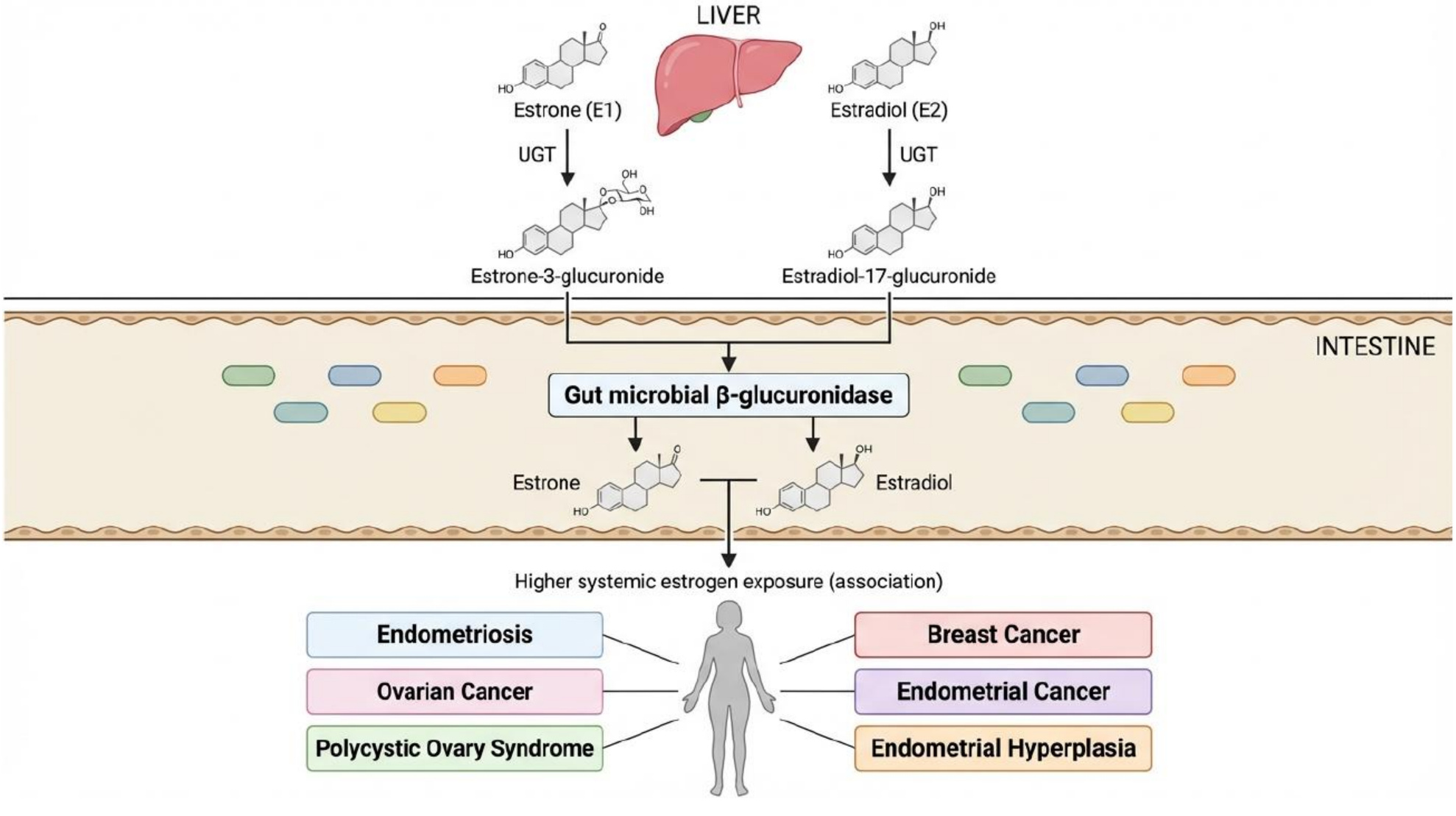

Figure 1. Bidirectional relationship between gut microbes and estrogent hormones.

Mechanisms of Microbiome-Mediated Estrogen Metabolism

Estrogens are metabolized by conjugation in the liver before they are moved from the liver to the intestines. Once in the intestines, estrogens can continue to be processed via gut bacteria (i.e., the intestinal microbiome). The way that estrogens are metabolized by the gut microbiome is primarily using microbial enzymes that facilitate the deconjugation of estrogens (and conjugated estrogen) ability to be absorbed back into the blood (i.e., into systemic circulation). Disruption in the composition of gut microbiota can result in the accumulation of too much estrogen in the blood, thus increasing the likelihood of developing breast cancer [8] . Regulation of estrogen

metabolism by the gut microbiome involves microbial enzyme actions' involvement in the intestinal barrier, and an interaction between the liver production of the hormone and systems that regulate its transport back into circulation.

β-Glucuronidase Activity and Estrogen Recirculation

β-glucuronidase is an important enzyme produced by many gut microbes, including *Escherichia coli,* Clostridium, and other intestinal bacteria, that helps to metabolize the hormone estrogen. Estrogen–glucuronides (estrogens attached to the sugar molecule glucuronic acid) are deconjugated (broken down) in the gut by the action of this enzyme, enabling the return of free estrogens to the bloodstream [9]. Dysbiosis (an imbalance in gut bacteria), characterized by an abundance of β-glucuronidase-producing bacteria, can therefore lead to increased availability of estrogen and may also facilitate the development of estrogen-related cancers (such as breast cancer) [2]. Estrogen levels also promote the activation of estrogen receptor (ER) signaling in ER-positive breast cancer cells, which contributes to their growth and survival.

Estrogen–Microbiome–Immune Interactions in Breast Cancer

The gut microbiome affects how the liver breaks down estrogens, which can affect the immune system and inflammation and increase the risk of breast cancer. When there is an increase in the level of circulating estrogens, estrogen receptors are activated within the breast, leading to an increase in the growth of tumors and changes in the local immune environment. Disruption of the normal gut microbiome causes an increase in the amount of pro-inflammatory cytokines produced, which supports the development and spread of tumors [8]. Thus, these findings demonstrate how the composition of the gut microbiome, the way that hormones are regulated by the body, and how the immune system communicates wit

h the body are all interrelated in the pathogenesis of breast cancer.

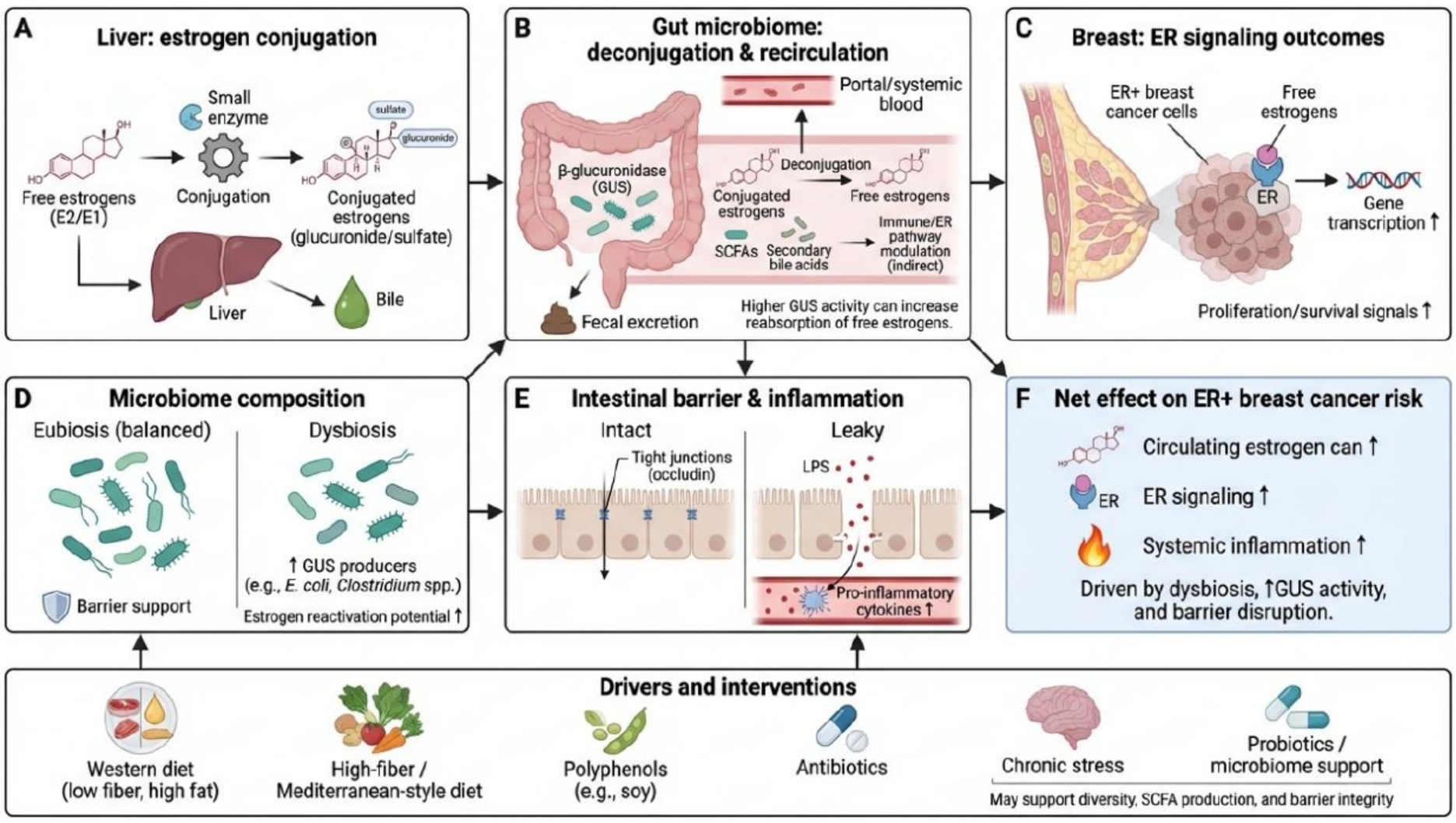

Figure 2: Dysbiosis, Estrogen Reactivation, and Inflammation: Integrated Pathways Linking the Gut Microbiome to ER+ Breast Cancer.

Microbial Composition and Estrogen Regulation

The gut microbiome is composed of many species of bacteria that contribute to the regulation of estrogen levels. The species of bacteria in the genera Bacteroides, Clostridium, and Ruminococcus produce the enzymes that break down the conjugated form of estrogen and convert it back into the unmodified (or metabolically active) form. Having more β-glucuronidase-producing bacteria and less diversity in your gut is associated with greater amounts of circulating estrogen and higher risk for developing breast cancer [9]. On the other hand, *Lactobacillus*, one type of beneficial gut bacterium, also assists with regulating estrogen levels and reducing the amount of estrogen that is reabsorbed into circulation and therefore may act as a protective factor against the development of hormone-dependent cancers.

2.3 Role of Microbial Metabolites in Estrogen-Driven Breast Cancer

In addition to the enzymatic activity of microbial metabolites influence via assumed best guess (ABC) through the estrogen signaling pathway (e.g., Indirect Influence), the short-chain fatty acids (SCFA) and secondary bile acids (SBA) produced by gut bacteria both mediate the activity of the estrogen receptor and all inflammatory

pathways through disruption via dysbiosis, which changes the types and amounts being produced. Because dysbiosis is associated with the Metabolically Imbalanced state, there is excessive estrogen signaling and inflammation. Certain SBAs produced by members of the genus Clostridium are known to interact with the estrogen receptor(s) and are associated with the progression of various estrogen-dependent cancers, including breast cancer [10]. Thus, the development of metabolites contained in the gut microbiome(s) is another means to increase the relative risk factor associated with certain types of cancer(s) based upon the relationship to estrogens.

Gut Permeability and Estrogen-Driven Inflammation

The gut microbiome has an important role in both modulating how estrogen is metabolized and preserving the function of the intestinal barrier. When dysbiosis occurs, there is a breakdown in the intestinal barrier, resulting in an increase in intestinal permeability and a pathway for estrogens and microbial components to pass from the gut into the bloodstream, which is thought to be involved in linking the changes in gut microbiota with cancer development as it relates to inflammatory responses to estrogen.

Decreased expression of tight junction proteins (e.g., occludin) associated with dysbiosis disrupts the integrity of the epithelial barrier and increases intestinal permeability, which allows estrogens (conjugated forms) and microbial-derived products, such as lipopolysaccharides (LPS), to enter the systemic circulation[11] . Reentry of estrogens into circulation stimulates estrogen receptor activation in breast tissue, thereby promoting growth and survival of estrogen receptor-positive breast cancer cells [2] ; additionally, LPS in circulation stimulates inflammatory signals in the body, which facilitate cancer progression.

The continuous inflammation caused by both the gut-derived estrogen and the essential metabolite byproducts of the gut microbiota has an additive effect on the estrogen-mediated signaling pathway, resulting in a more accelerated growth of human breast cancer. Thus, preserving the integrity of the gut epithelial barrier will be critical to assessing the relationship between the microbiota and gut-derived estrogens during breast cancer progression. A few types of microbiome-targeting therapeutic interventions (e.g., probiotics, dietary modification that restores the intestinal barrier) may provide additional benefit in decreasing inflammation caused by estrogen

and thus may result in decreased breast cancer progression [10].

Environmental and Lifestyle Influences

While there are many environmental and lifestyle factors that contribute to how our (gut) microflora metabolizes estrogen, these same factors also affect the composition of the gut microbiome. The presence of certain beneficial bacteria in the gut can decrease estrogen production and, therefore, decrease the likelihood of developing breast cancer. Diet is one of the largest contributors to changes in the composition of our gut microbiome. A diet high in saturated fat and low in dietary fibres causes a shift in the composition of the gut microbiome. This shift creates dysbiosis, which is characterized by an excess of β-glucuronidase (β-gluc) producing bacteria. These bacteria have been shown to increase the level of β-gluc produced by bacteria, resulting in larger amounts of estrogen being released into our bloodstream, therefore increasing the risk for developing ER+ breast cancer [12]. Beverages rich in polyphenols (e.g., soy products) are also beneficial for the development of short-chain fatty acids), SCFAs (acids needed to maintain proper estrogen levels and may help to reduce the risk of developing breast cancer. The Mediterranean Diet is rich in fibres and therefore promotes the diversity and abundance of bacteria capable of producing SCFA, which have been shown to exhibit an anti-inflammatory response and may suppress the proliferation of ER-positive breast cancer cells [13].

In addition to the impact of diet on the gut microbiome, there are environmental factors such as antibiotics and psychological stress that can also impact the stability of the gut microbiome. Usage of antibiotics reduces the number of beneficial bacteria present in the gut and increases the activity of €-glucuronidase, which allows for more estrogens to be recycled into the bloodstream; thus, increasing a person's risk for developing breast cancer [14]. Chronic stress through interactions between the gut and brain influences the composition of the microbiota in the intestines as well as increases the permeability of the intestinal walls and allows estrogens to be recycled back into the bloodstream; thus, contributing to ongoing estrogen-driven inflammatory processes and breast cancer progression [15]. All these negative impacts can be addressed through proper use of antibiotics, management of stress, and other lifestyle interventions designed to promote the health of the gut's microbiota [2].

Therapeutic Strategies Targeting the Gut Microbiome in Estrogen Receptor–Positive (ER+) Breast Cancer

The gut microbiome plays an important role in regulating estrogen-related pathways and systemic inflammation, both of which are closely associated with the development and progression of estrogen receptor–positive (ER+) breast cancer. Alterations in microbial composition (dysbiosis) can influence estrogen metabolism, inflammatory signaling, and gut barrier integrity, thereby contributing to conditions that may precede or promote ER+ tumor development. For this reason, increasing attention has been directed toward therapeutic strategies that target gut microbial balance in the prevention and treatment of breast cancer.

Probiotics and Prebiotics

Research indicates that probiotics, particularly members of the *Lactobacillus* genus, can reduce β-glucuronidase activity. Because β-glucuronidase is involved in the deconjugation of estrogens in the intestine, lowering its activity may decrease circulating estrogen levels and potentially reduce the risk of ER+ breast cancer development [5].

Prebiotics such as inulin promote the production of short-chain fatty acids (SCFAs). SCFAs enhance gut barrier integrity and contribute to reduced inflammatory responses, thereby supporting mechanisms associated with cancer prevention [16]. The combination of probiotics and prebiotics in synbiotic formulations has demonstrated enhanced effectiveness in preclinical models of estrogen-dependent cancers, suggesting a synergistic effect through microbiome modulation [17] .

Dietary Interventions

Dietary composition strongly influences the diversity and metabolic activity of intestinal bacteria. High-fiber dietary patterns, such as the Mediterranean diet, promote the growth of bacteria that produce SCFAs, including butyrate and propionate. These metabolites are associated with reduced levels of proinflammatory cytokines and decreased estrogen-driven tumor growth [13].

In contrast, high-fat and low-fiber diets promote the proliferation of β-glucuronidase-producing bacteria, which may increase circulating estrogen levels and potentially elevate breast cancer risk [12]. Additionally, polyphenol-rich foods such as soy have been shown to support balanced estrogen metabolism and may reduce the risk of estrogen-related diseases[18].

Table 1. Biological Pathways Connecting Dysbiosis, Estrogen Metabolism, and ER+ Breast Cancer.

Pathway	microbiome factor	Biological effect	Breast cancer relevance (ER+)	Ref
Estrogen deconjugation ("estrobolome")	β-glucuronidase (GUS) producing bacteria	Converts conjugated estrogens → free estrogens → reabsorption	↑ circulating estrogen → ↑ ER signaling → tumor growth	[8] [5]
Dysbiosis and inflammation	Reduced diversity; pro-inflammatory taxa	↑ inflammatory mediators, altered immune tone	Chronic inflammation supports initiation/progression	[3][19]
Gut barrier disruption ("leaky gut")	Tight junction impairment; endotoxin translocation	LPS enters blood → TLR4/NF-κB → IL-6/TNF-α	Inflammation, invasion, metastasis potential	[11, 20]
SCFA production	Fiber-fermenting bacteria (butyrate producers)	SCFAs strengthen barrier; anti-inflammatory signaling	Potential protective role via reduced inflammation	[21, 22]
Diet-driven microbiome changes	Western diet vs Mediterranean diet	Western: dysbiosis; Mediterranean: diversity & SCFAs	Diet modifies estrogen/inflammation axis	[4, 12].
Microbiome manipulation	Probiotics / prebiotics / synbiotics	↓ inflammation; modulate estrogen metabolism; ↑ SCFAs	Adjunct prevention/therapy potential	[10, 17, 23] .
Immunotherapy interaction (broader cancer)	Beneficial commensals	Enhanced anti-tumor immune response	Relevance to breast cancer immuno-approaches	[6, 24]
Stress and neuroimmune signaling	Gut–brain axis effects	Stress alters microbiome and permeability	Indirect risk via inflammation and barrier	[2, 15].

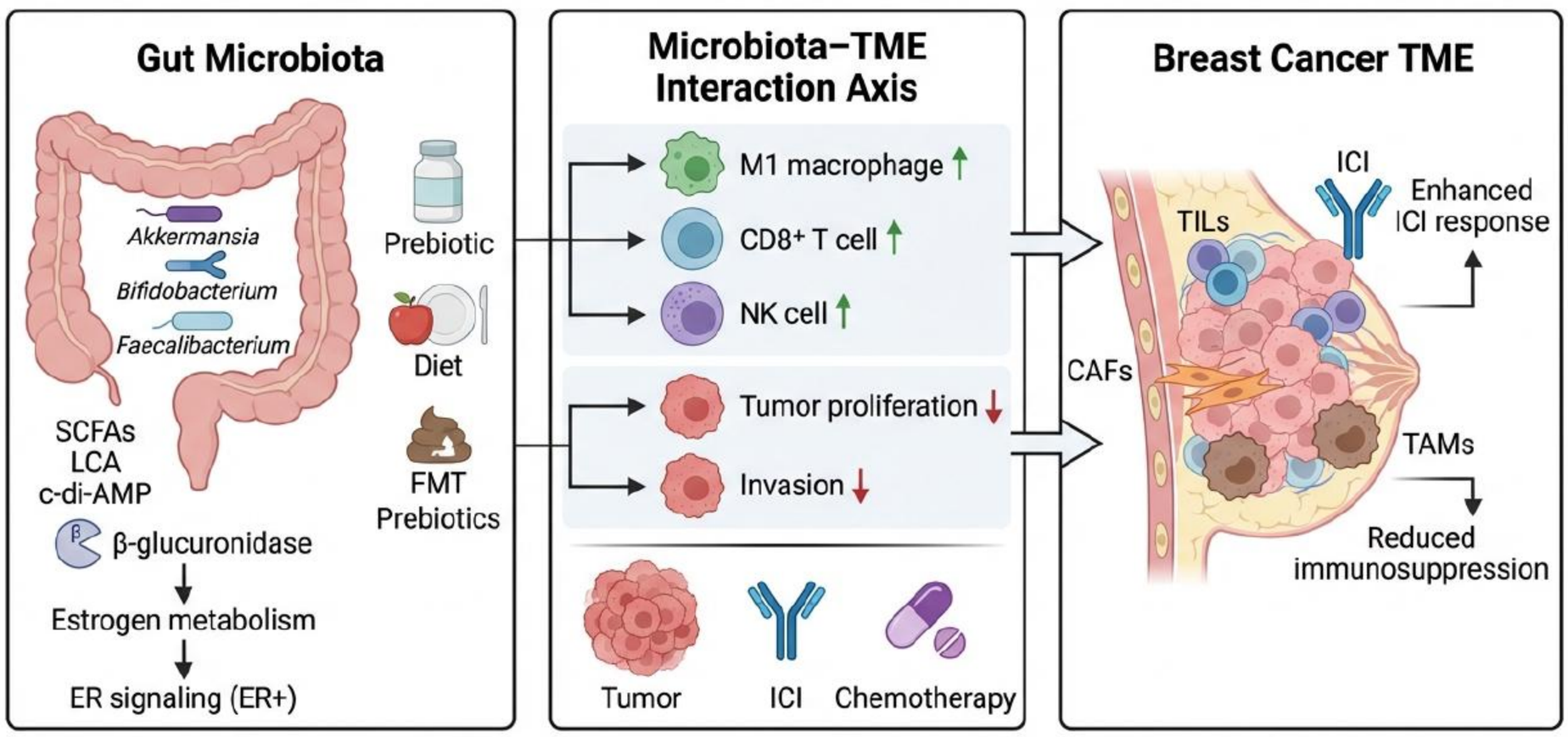

Figure 3. Modulation of Gut microbiota Enhancement BC Immunotherapy via Tumor Microenvironment Remodeling.

Modulation of Systemic Inflammation

The gut microbiome contributes to systemic inflammatory responses that may influence breast cancer progression and metastasis. Dysbiosis can lead to increased production of microbial-derived components such as lipopolysaccharide (LPS). LPS activates Toll-like receptor 4 (TLR4), triggering downstream signaling pathways including NF-κB activation and cytokine production (IL-17, IL-6, TNF-α), which are associated with increased tumor cell invasiveness [20]. Restoration of microbial homeostasis through probiotics, prebiotics, or dietary modification may reduce inflammatory signaling and potentially limit metastatic progression.

Emerging Therapies

Recent studies have examined postbiotic therapies in preclinical models of breast cancer. Postbiotics include microbial-derived metabolites such as SCFAs that influence estrogen metabolism and inflammatory pathways [23]. These compounds may provide opportunities for personalized therapeutic approaches by targeting the estrobolome, the microbial component responsible for estrogen metabolism. Such strategies may enhance breast cancer treatment outcomes and contribute to personalized medicine approaches [25] .

Integration

Combining multiple gut health strategies including probiotics, prebiotics, and dietary interventions may support the development of a balanced microbiome. The integration of these approaches offers potential therapeutic applications in the prevention and management of ER+ breast cancer.

Systemic Inflammation in Breast Cancer: Therapeutic Strategies

Systemic inflammation associated with gut microbiome dysbiosis appears to play a significant role in disease development and metastasis. Microbiome-targeted interventions, including probiotics, prebiotics, dietary modification, and fecal microbiota transplantation, represent potential strategies for reducing inflammation and modulating disease risk.

Probiotics and Prebiotics

Probiotics, particularly *Lactobacillus* species, can inhibit NF-κB activation, promote regulatory T-cell activity, and reduce pro-inflammatory cytokine production [9]. Prebiotic fibers such as inulin promote SCFA production, which supports gut barrier integrity and suppresses inflammatory signaling. Synbiotic formulations combining both components have shown promising results in preclinical models [17] .

Fecal Microbiota Transplantation and Diet

Fecal microbiota transplantation (FMT) is a strategy used to restore microbial balance in the gut. FMT may reduce inflammation associated with TLR activation [26] . In addition, high-fiber diets promote the growth of SCFA-producing bacteria and reduce systemic inflammation mediated by NF-κB, contributing to decreased breast cancer tumor progression [13].

Integrating with Pharmaceutical Interventions

Microbiome-targeted therapies may complement anti-inflammatory medications, potentially enhancing reductions in systemic inflammation and slowing tumor progression [27]. Combining microbiome-based and pharmacological approaches may therefore strengthen therapeutic outcomes.

Dietary Influences on the Gut Microbiome and Breast Cancer

The composition of the gut microbiome is strongly influenced by diet and affects systemic inflammation, estrogen metabolism, and breast cancer progression. Dietary intake determines microbial diversity, metabolite production, and intestinal barrier strength, collectively influencing disease risk and progression.

Impact of Diet on Mechanisms of Action

Dietary fiber provides substrates for beneficial bacteria that produce SCFAs. SCFAs enhance gut barrier function, reduce systemic inflammation, and regulate immune responses [21, 22]. High-fat, low-fiber diets promote dysbiosis and increase pro-inflammatory bacteria such as *Bacteroides*, leading to increased production of secondary bile acids that may promote breast cancer growth and metastasis [12, 28]

Specific Dietary Patterns

The Mediterranean diet, characterized by high fiber, polyphenols, and omega-3 fatty acids, promotes SCFA-producing bacteria, maintains intestinal barrier integrity, and reduces inflammatory cytokines. These mechanisms may reduce systemic inflammation and potentially slow breast cancer progression [5, 13, 29]. In contrast, Western-style diets high in saturated fats and sugars disrupt microbial equilibrium, impair barrier function, and increase inflammation, thereby increasing cancer risk [12].

Nutrient-Specific Effects

Dietary fiber supports SCFA production, gut barrier integrity, and suppression of inflammatory signaling [30, 31]. Omega-3 fatty acids and polyphenols enhance beneficial microorganisms such as *Lactobacilli* and *Akkermansia*, improving barrier function and reducing inflammation associated with breast cancer [5, 13].

Diet, Gut Barrier, and Systemic Inflammation

Insufficient nutrient and fiber intake impairs intestinal barrier function, permitting translocation of microbial endotoxins into circulation. Activation of Toll-like receptor pathways stimulates inflammatory signaling that may promote breast cancer growth and metastasis [19, 20] . In contrast, nutrient-rich, high-fiber diets support barrier restoration and reduce systemic inflammation.

Lifestyle Interactions

Antibiotic use and chronic stress contribute to dysbiosis and reduce SCFA-producing bacteria, increasing systemic inflammation through impaired gut barrier integrity. Dietary strategies emphasizing fiber and antioxidants may help counteract these effects and reduce inflammation-associated cancer risk [2].

Therapeutic Dietary Strategies

Targeted dietary approaches may modify gut microbial ecology and reduce breast cancer risk. Diets rich in fiber, polyphenols, and omega-3 fatty acids demonstrate consistent anti-inflammatory properties and support healthier microbial composition.

Personalized dietary regimens based on metagenomic profiling of individual gut microbiota may offer future opportunities for tailored cancer prevention and treatment strategies [25, 32]

Conclusion

Breast cancer is influenced by gut microbiota, which may play a role in the development, progression, and possible prevention of breast cancer. Dysbiosis is an imbalance of microbiota within the gut, which decreases Microbial Diversity while increasing Pro-Inflammatory bacteria such as Clostridia and Escherichia coli, and causes systemic inflammation and hormone dysregulation, especially the metabolism of estrogen. The other good bacteria, such as *Lactobacillus*, are considered good because they provide balance within the body and reduce the risk of developing breast cancer [18, 33]. Also, Dysbiosis will prolong or worsen the chronic inflammatory response and may promote the development of Tumors. In addition, Dysbiosis will continue to increase the permeability of the intestines, which leads to the translocation of microbial products such as lipopolysaccharides into the bloodstream, whereas these products act on and activate immune pathways such as Toll-Like Receptors (TLR) and NF-κB, leading to increased production of Pro-Inflammatory cytokines, thereby causing greater Tumor growth and/or Metastasis [3, 20] . Diet plays an important role in modulating Gut Microbiota and Breast Cancer risk. High Fat and High Sugar diets promote the growth of Pro-Inflammatory Bacteria and Systemic Inflammation; however, High Fiber Diets or Polyphenol-Rich Diets enhance the growth of Short-Chain Fatty Acid-producing Bacteria, provide a stronger gut barrier, and reduce inflammation and, therefore, should have protective effects against Breast Cancer [4, 13]. The Mediterranean Diet and other dietary patterns provide preventive benefits through increasing Microbial Diversity, Short Chain Fatty acids (SCFA) generation, and supporting anti-inflammatory pathways. The use of Microbiome-focused treatments (Probiotics, Prebiotics, Postbiotics, and Dietary guidelines) in animal studies, has shown these therapies to be promising in restoring microbial balance, improving Estrogen metabolism, and lowering systemic inflammation [23, 29]. Although the potential uses of Fecal Microbiota Transplantation (FMT) in Breast Cancer are limited, some early studies have shown that FMT has the capability of positively modulating the Microbiome [6]. Therefore, future studies should emphasize personalized Microbiome-

guided treatment approaches based upon Metagenomic profiling and Longitudinal study designs to determine causation and improve upon current prevention and treatment strategies [7, 25]. In summary, the Gut Microbiome is a critical point of interaction between Diet, Immunity, and Hormonal Regulation in Breast Cancer, and its complex interactions with systemic inflammation and Estrogen Metabolism offer opportunities for the development of new preventive and therapeutic approaches through Personalized Modulation of the Microbiome for Complementary Intervention in the Treatment of Breast Cancer.

References

1. Goedert, J.J., et al., *Investigation of the association between the fecal microbiota and breast cancer in postmenopausal women: a population-based case-control pilot study.* Journal of the National Cancer Institute, 2015. **107**(8): p. djv147.
2. Foster, J.A., L. Rinaman, and J.F. Cryan, *Stress & the gut-brain axis: regulation by the microbiome.* Neurobiology of stress, 2017. **7**: p. 124-136.
3. Cani, P.D., et al., *Selective increases of bifidobacteria in gut microflora improve high-fat-diet-induced diabetes in mice through a mechanism associated with endotoxaemia.* Diabetologia, 2007. **50**(11): p. 2374-2383.
4. Shapira, I., et al., *Evolving concepts: how diet and the intestinal microbiome act as modulators of breast malignancy.* International Scholarly Research Notices, 2013. **2013**(1): p. 693920.
5. Lakritz, J.R., et al., *Beneficial bacteria stimulate host immune cells to counteract dietary and genetic predisposition to mammary cancer in mice.* International journal of cancer, 2014. **135**(3): p. 529-540.
6. Sivan, A., et al., *Commensal Bifidobacterium promotes antitumor immunity and facilitates anti–PD-L1 efficacy.* Science, 2015. **350**(6264): p. 1084-1089.
7. Goedert, J.J., et al., *Postmenopausal breast cancer and oestrogen associations with the IgA-coated and IgA-noncoated faecal microbiota.* British journal of cancer, 2018. **118**(4): p. 471-479.
8. Plottel, C.S. and M.J. Blaser, *Microbiome and malignancy.* Cell host & microbe, 2011. **10**(4): p. 324-335.
9. Kwon, H.-K., et al., *Amelioration of experimental autoimmune encephalomyelitis by probiotic mixture is mediated by a shift in T helper cell immune response.* Clinical immunology, 2013. **146**(3): p. 217-227.
10. Bron, P.A., et al., *Can probiotics modulate human disease by impacting intestinal barrier function?* British Journal of Nutrition, 2017. **117**(1): p. 93-107.
11. Mu, Q., et al., *Leaky gut as a danger signal for autoimmune diseases.* Frontiers in immunology, 2017. **8**: p. 598.
12. De Filippis, F., et al., *High-level adherence to a Mediterranean diet beneficially impacts the gut microbiota*

and associated metabolome. Gut, 2016. **65**(11): p. 1812-1821.
13. Nagpal, R., et al., *Modified Mediterranean-ketogenic diet modulates gut microbiome and short-chain fatty acids in association with Alzheimer's disease markers in subjects with mild cognitive impairment.* EBioMedicine, 2019. **47**: p. 529-542.
14. Vangay, P., et al., *Antibiotics, pediatric dysbiosis, and disease.* Cell host & microbe, 2015. **17**(5): p. 553-564.
15. Lyte, M., L. Vulchanova, and D.R. Brown, *Stress at the intestinal surface: catecholamines and mucosa–bacteria interactions.* Cell and tissue research, 2011. **343**(1): p. 23-32.
16. Haghikia, A., et al., *Dietary fatty acids directly impact central nervous system autoimmunity via the small intestine.* Immunity, 2015. **43**(4): p. 817-829.
17. Zamani, B., et al., *Synbiotic supplementation and the effects on clinical and metabolic responses in patients with rheumatoid arthritis: a randomised, double-blind, placebo-controlled trial.* British Journal of Nutrition, 2017. **117**(8): p. 1095-1102.
18. Luo, X.M., et al., *Gut microbiota in human systemic lupus erythematosus and a mouse model of lupus.* Applied and environmental microbiology, 2018. **84**(4): p. e02288-17.
19. Radstake, T.R., et al., *Expression of toll-like receptors 2 and 4 in rheumatoid synovial tissue and regulation by proinflammatory cytokines interleukin-12 and interleukin-18 via interferon-gamma.* Arthritis Rheum, 2004. **50**(12): p. 3856-65.
20. Li, J., et al., *TLR4 Promotes Breast Cancer Metastasis via Akt/GSK3β/β-Catenin Pathway upon LPS Stimulation.* Anat Rec (Hoboken), 2017. **300**(7): p. 1219-1229.
21. Sonnenburg, E.D. and J.L. Sonnenburg, *Starving our microbial self: the deleterious consequences of a diet deficient in microbiota-accessible carbohydrates.* Cell metabolism, 2014. **20**(5): p. 779-786.
22. Arpaia, N., et al., *Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation.* Nature, 2013. **504**(7480): p. 451-455.
23. Suez, J., et al., *The pros, cons, and many unknowns of probiotics.* Nature medicine, 2019. **25**(5): p. 716-729.
24. Zitvogel, L., et al., *The microbiome in cancer immunotherapy: Diagnostic tools and therapeutic strategies.* Science, 2018. **359**(6382): p. 1366-1370.
25. Gupta, V.K., et al., *A predictive index for health status using species-level gut microbiome profiling.* Nature communications, 2020. **11**(1): p. 4635.
26. Sun, M.-F., et al., *Neuroprotective effects of fecal microbiota transplantation on MPTP-induced Parkinson's disease mice: Gut microbiota, glial reaction and TLR4/TNF-α signaling pathway.* Brain, behavior, and immunity, 2018. **70**: p. 48-60.
27. Loyala, J.V., et al., *Treatment of cachexia in gastric cancer: exploring the use of anti-inflammatory natural products and their derivatives.* Nutrients, 2024. **16**(8): p. 1246.
28. Yoshimoto, S., et al., *Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome.* Nature, 2013. **499**(7456): p. 97-101.
29. Bahr, L.S., et al., *Fasting, ketogenic, and anti-inflammatory diets in multiple sclerosis: a randomized controlled trial with 18-month follow-up.* BMC Nutr, 2025. **11**(1): p. 167.
30. Unger, M.M., et al., *Short chain fatty acids and gut microbiota differ between patients with Parkinson's disease and age-matched controls.* Parkinsonism & related disorders, 2016. **32**: p. 66-72.
31. Liu, T., et al., *Effect of dietary fiber on gut barrier function, gut microbiota, short-chain fatty acids, inflammation, and clinical outcomes in critically ill patients: a systematic review and meta-analysis.*

Journal of Parenteral and Enteral Nutrition, 2022. **46**(5): p. 997-1010.
32. Fava, F., L. Rizzetto, and K. Tuohy, *Gut microbiota and health: connecting actors across the metabolic system.* Proceedings of the Nutrition Society, 2019. **78**(2): p. 177-188.
33. Larnder, A.H., A.R. Manges, and R.A. Murphy, *The estrobolome: Estrogen-metabolizing pathways of the gut microbiome and their relation to breast cancer.* International Journal of Cancer, 2025. **157**(4): p. 599-613.

الميكروبيوم المعوي وسرطان الثدي: مراجعة

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الخلاصة

يؤثر ميكروبيوم الأمعاء في خطر الإصابة بسرطان الثدي من خلال ايض الإستروجين ، والالتهاب على مستوى الجسم، وتنظيم الجهاز المناعي. إن انخفاض تنوع الكائنات الدقيقة يؤدي إلى اختلال توازن ميكروبيوم الأمعاء (الديسبيوزيس)، مما يدعم زيادة الميكروبات المسببة للالتهاب، ويؤدي إلى ارتفاع مستويات الإستروجين المتداول في الدم، وبالتالي يعزز نمو الأورام. وعلى العكس من ذلك، فإن بعض الميكروبات النافعة (مثل Lactobacillus) تساعد في الحفاظ على التوازن الهرموني، مما يقلل من احتمالية الإصابة بسرطان الثدي.

كما أن مزيج ما نتناوله من طعام وطريقة تناولنا له (النظام الغذائي) يؤثر بشكل كبير في أنواع البكتيريا التي تنمو وتتضاعف داخل ميكروبيوم الأمعاء. وتشير الدراسات إلى أن النظام الغذائي الغني بالألياف والأطعمة النباتية يدعم نمو البكتيريا المنتجة للأحماض الدهنية قصيرة السلسلة (SCFAs) ، في حين أن الأنظمة الغذائية الغنية بالدهون والسكريات تسهم في زيادة حدوث اختلال توازن الميكروبيوم والالتهاب الجهازي.

وقد ثبت أن التدخلات التي تهدف إلى استعادة التوازن الصحي لبكتيريا الأمعاء تقلل من الالتهاب وتحسن الصحة العامة والرفاهية. كما أن التدخلات الشخصية المعتمدة على خصائص ميكروبيوم الأمعاء تمتلك إمكانات كبيرة كوسيلة إضافية للوقاية من سرطان الثدي وعلاجه.

وهدفت هذه الدراسة إلى استكشاف كيفية تأثير التغيرات في ميكروبيوم الأمعاء على خطر الإصابة بسرطان الثدي من خلال ايض الإستروجين، والالتهاب، وتعديل الاستجابة المناعية، والعوامل الغذائية.