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REVIEW ARTICLE

Gut Microbiota and Colon Cancer Prevention: Emerging Evidence for Protective Blautia wexlerae BwKU-11

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Despite the remarkable advances in epidemiology, diagnosis, treatment, and prevention over the last decade, CRC is undeniably one of the most important causes of cancer-related morbidity and mortality world-wide, and there is growing evidence that the gut microbiota plays a crucial role in carcinogenesis of CRC. Changes in the microbial composition (dysbiosis) are associated with the appearance of chronic inflammation, loss of the integrity of the epithelial barrier and the formation of carcinogenic metabolites, which play a role in the development of colorectal tumorigenesis. On the other hand, there are also commensal bacteria that are beneficial in the regulation of intestinal homeostasis and cancer prevention. Of these, the member Blautia wexlerae BwKU-11 is a strain that generates short-chain fatty acids, regulates immune responses, reinforces intestinal barrier function and suppresses inflammatory signaling pathways linked to colorectal cancer. Recent experimental studies show that this strain can increase the microbial diversity and decrease pro-inflammatory and pathogenic bacteria. This review aims to summarize the previous work done on the biological properties, mechanistic actions and therapeutic efficiency of B. wexlerae BwKU-11 as a next generation probiotic capable of the prevention from colorectal cancer and future microbiome-based interventions.

Keywords: Blautia Wexlerae Bwku-11; Gut Microbiota; Colorectal Cancer; Next-Generation Probiotics; Short-Chain Fatty Acids

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0.1 List of Abbreviations

Abbreviation	Full Form
APC	Adenomatous Polyposis Coli
CRC	Colorectal Cancer
DNA	Deoxyribonucleic Acid
GALT	Gut-Associated Lymphoid Tissue
IL	Interleukin
LPS	Lipopolysaccharide
NF-κB	Nuclear Factor Kappa B
NGP	Next-Generation Probiotic
ROS	Reactive Oxygen Species
SCFA	Short-Chain Fatty Acid
TGF-β	Transforming Growth Factor Beta
TLR	Toll-Like Receptor
TNF-α	Tumor Necrosis Factor Alpha
Treg	Regulatory T Cell

1 Introduction

Colorectal cancer (CRC) is one of the most common malignancies and causes of death from cancer all over the world (1, 2). Although there have been significant developments in both screening approaches and surgical, chemotherapy, targeted therapies and immunotherapy treatments, the burden of CRC is still on the rise internationally because of the aging population, social habits (diet, obesity, physical inactivity), and environmental factors (3, 4). CRC is polyetiologic and this has drawn more interest to the concept of CRC prevention based on modulation of biological determinants that are still useful to alter, such as the gut microbiota. **Figure 1**

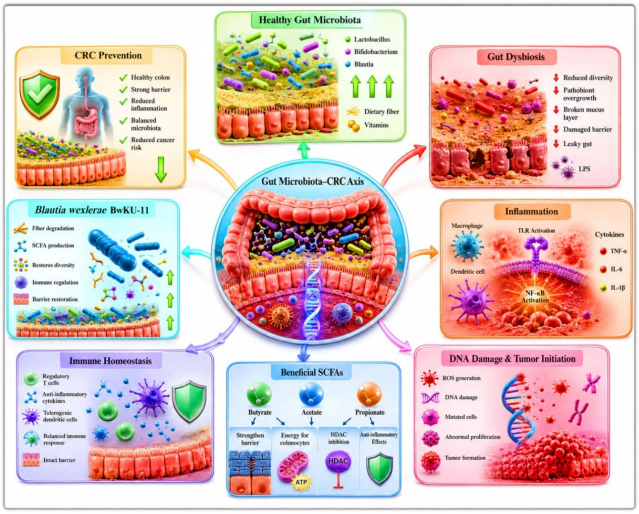

Fig. 1 Schematic representation of the gut microbiota–colorectal cancer axis illustrating dysbiosis-induced inflammation, DNA damage, and tumorigenesis, alongside the protective effects of Blautia wexlerae BwKU-11 through short-chain fatty acid production, immune homeostasis, and intestinal barrier restoration.

There are trillions of microorganisms (bacteria, archaea, fungi and viruses) in our gastrointestinal tract, which together form the gut microbiota (5, 6). These microbial communities are essential for nutrient metabolism, vitamin production, maturation of the immune system, maintenance of integrity of the intestinal barrier and protection against pathogenic microorganism (7, 8). A normal intestinal environment is characterized by a balance among microorganisms that colonize the intestine, when this is altered (dysbiosis), a strong correlation has been detected with inflammatory bowel disease, metabolic diseases, obesity, diabetes, and colorectal cancer (9, 10).

There is a growing amount of evidence in all pointing to multiple intertwined ways in which dysbiosis contributes to colorectal carcinogenesis (11, 12). Changes in microbial balance also leads to gut leakiness which results in the leakage of toxins and lipopolysaccharides, a condition that leads to chronic inflammation. Toll like receptor (TLR) and nuclear factor-kappa B (NF-κB) inflammatory signaling pathways are persistently activated, leading to the induction of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) and thus tumor promoting microenvironment (13, 14). Additionally, some pathogenic bacteria are even known to directly trigger uncontrolled populations of epithelial cells, genotoxic compounds and reactive oxygen species which cause DNA damage and genomic instability.

On the other hand, good gut microbes provide a protection mechanism through microbial diversity, production of health supporting metabolites and regulation of host immune response . Among these beneficial metabolites, the short-chain fatty acids (SCFAs) such as butyrate, acetate and propionate are getting a lot of attention for all their anti-inflammatory, antioxidant and anti-neoplastic effects. SCFAs promote the tightness of junctions between epithelial cells, help cells in the colon to generate energy, and facilitate the development of regulatory T cells, thereby supporting anti-inflammatory properties that inhibit the action of certain enzymes called histone deacetylases and the activation of inflammatory signaling pathways involved in the formation of colorectal tumors.

In the friend zone of the microorganisms derives from beneficial microorganisms, genus Blautia has been identified as a very important factor in the well-being of the intestines. The genus represents the family Lachnospiraceae and has been identified for their capability of degrading the dietary fibers into SCFAs and regulating the immune homeostasis. Bacterial studies of the microbiome have shown that the number of Blautia species are consistently decreased in patients with colorectal cancer, inflammatory bowel disease, obesity and metabolic syndrome, implying that the species plays a significant role in human health.

In this group, the newly discovered bacteria Blautia wexlerae BwKU-11 promises to be an excellent oncoming probiotic. Experimental data showed that this strain up regulates SCFA production, down regulates inflammatory cytokine expression, restores integrity of the intestine and alters gut microbial communities to a healthier composition. All of the above biological actions combine to a less favorable colorectal tumor initiation and progression environment. While clinical evidence is still in its infancy, the preclinical results are compelling for studying B. wexlerae BwKU-11 as a preventive strategy based on the microbiome against CRC.

This review outlines state-of-the-art understanding of the axis gut microbiota-colorectal cancer (CRC), biological properties of Blautia wexlerae BwKU-11, its mode of action, and its potential for being considered as a next-generation probiotic for preventing CRC. Elucidating these pathways could ease the way for new and improved approaches to treating CRC, which involve targeting the microbiome alongside more traditional forms of therapy and that help lower the worldwide burden of CRC. **Table 1**

Table 1 Summary of gut microbiota functions, dysbiosis-associated colorectal carcinogenesis, inflammatory mechanisms, microbial metabolites, and the therapeutic potential of Blautia wexlerae BwKU-11 as a next-generation probiotic for colorectal cancer prevention.

Aspect	Healthy Gut	Dysbiosis in CRC	Key Mechanisms	Protective Role of *Blautia wexlerae* BwKU-11	Clinical Significance
Gut microbiota	Diverse beneficial microbes	Reduced diversity; pathogenic overgrowth	Loss of microbial homeostasis	Restores microbial balance	Supports intestinal health
Intestinal barrier	Intact mucus and tight junctions	Increased permeability (leaky gut)	Barrier disruption	Enhances epithelial integrity	Reduces toxin translocation
Inflammation	Controlled immune response	Chronic inflammation	TLR/NF-κB activation; TNF-α, IL-6	Suppresses inflammatory cytokines	Lowers CRC-promoting inflammation
Microbial metabolites	High SCFA production	Reduced SCFAs; harmful metabolites	Energy metabolism and immune regulation	Increases butyrate, acetate, propionate	Promotes anti-tumor effects
Carcinogenesis	Genomic stability	DNA damage and tumor progression	ROS and genotoxic compounds	Reduces oxidative stress	Decreases CRC initiation risk
Therapeutic potential	Homeostasis maintained	Microbiome imbalance	Microbiome modulation	Next-generation probiotic candidate	Promising strategy for CRC prevention

2 Gut Microbiota and Colorectal Carcinogenesis

2.1 *Gut Microbial Dysbiosis in Colorectal cancer*

The healthy gut flora exists in a dynamic equilibrium that helps in digestion, nutrient metabolism, immune surveillance and epithelia integrity. But, microbial dysbiosis – disruption of the diversity of microbes – has been well linked with colorectal cancer (CRC) (15, 16). In cases of dysbiosis, not only the number of beneficial bacteria decreases, but the presence of opportunistic pathogens, which are able to release inflammatory mediators and carcinogenic metabolites, increases (17, 18). These microbial changes compromise the barrier integrity, lower the body's immune protection and provide a pathway for the ongoing onset of inflammation. It has been consistently shown in clinical studies that the microbial diversity in CRC patients is reduced, suggesting that dysbiosis is an important early player in the initiation, progression and recurrence of CRC**. Figure 2**

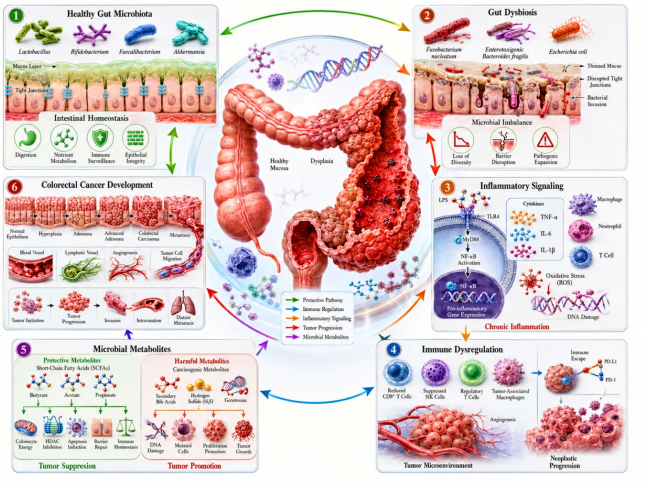

Fig. 2 Systems biology overview illustrating how gut microbial dysbiosis disrupts intestinal homeostasis, activates inflammatory and immune pathways, alters microbial metabolites, and promotes colorectal carcinogenesis through epithelial damage, tumor initiation, progression, and metastatic transformation.

2.2 *Inflammatory and Immune Mechanisms*

Persistent gut inflammation is known to be a big cause of colorectal cancer (19, 20). The harmful part of bacteria, such as lipopolysaccharide, and microbial toxin activates Toll-like receptor on intestinal epithelial cell and immune cell that stimulates NF-κB (nuclear factor-kappa B) signaling. This activation induces an excess production of pro-inflammatory cytokines like the tumour necrosis factor-alpha, interleukin 6 and interleukin 1 beta, which result in the formation of a tumour-supportive micro-environment. Chronic inflammation leads to higher levels of oxidative stress, DNA damage, epithelial proliferation and reduced programmed cell death. In parallel (21, 22), the weakened surveillance of the immune system accelerates the growth of transformed cells leading to the development of neoplastic lesions and their gradual development into invasive colorectal cancer.

2.3 *Microbial Metabolites and Tumor Suppression*

The gut microbiome produces many metabolites that have a major impact on the physiology of the host and on the risk of colorectal cancer (23, 24). Of these, the short-chain fatty acids, especially the butyrate, acetate & propionate acids have shown to have strong anti-inflammatory and anti-tumor properties. Butyrate is needed for the main source of energy for colonocytes, and it also plays a role as an energy source, to maintain the epithelium barrier function and to regulate the immune homeostasis (7, 25). It has also been shown to act as an inhibitor of histone deacetylases, leading to the apoptosis of malignant cells and curbing the uncontrolled proliferation of these cells. On the other hand, dysbiosis produces more harmful metabolites like Secondary bile acids and Genotoxins which help in the formation and subsequent progression of cancer (26). It is vital then to maintain a balanced metabolic profile on the basis of the bacteria overgrowth and to decrease the susceptibility to CRC. **Table 2**

Table 2 Summary of gut microbial dysbiosis, inflammatory signaling, immune alterations, and microbial metabolites highlighting their mechanisms, biological effects, and clinical significance in colorectal cancer initiation, progression, and potential therapeutic intervention.

Component	Key Factors	Mechanism	Effect on Colon	CRC Outcome	Clinical Significance
Healthy Microbiota	Lactobacillus, Bifidobacterium	Maintains homeostasis	Intact epithelial barrier	Protection	Supports gut health
Gut Dysbiosis	Pathogenic bacteria	Loss of microbial diversity	Barrier disruption	CRC initiation	Early diagnostic marker
Inflammatory Response	LPS, microbial toxins	TLR/NF-κB activation	Cytokine release	Chronic inflammation	Therapeutic target
Immune Dysfunction	TNF-α, IL-6, IL-1β	Oxidative stress, DNA damage	Reduced immune surveillance	Tumor progression	Disease progression marker
Beneficial Metabolites	Butyrate, acetate, propionate	HDAC inhibition, apoptosis	Barrier repair	Tumor suppression	Protective metabolites
Harmful Metabolites	Secondary bile acids, genotoxins	DNA injury, proliferation	Cellular transformation	CRC progression	Risk assessment biomarker

3 Protective Role of Blautia wexlerae BwKU-11

3.1 *Biological Characteristics of Blautia wexlerae BwKU-11*

One commensal anaerobic bacterium that is Gram-positive and included in the family Lachnospiraceae is Blautia wexlerae BwKU-11 (27, 28). It normally lives in the human body, inside the healthy colon where it helps to break down the complex carbohydrates and dietary fibers. This metabolic process yields so called short chain fatty acids that are used for intestinal homeostasis and support intestinal barrier integrity (29, 30). In contrast to the pathogenic type of bacteria, B. wexlerae fosters diversification of the micro-organisms and a stable intestinal environment (31, 32). In the past few years, several microbiome studies have indicated decreased levels of Blautia species observed in patients with CRC and inflammatory diseases, which suggests Blautia restoration might have protective effects against intestinal diseases. **Figure 3**

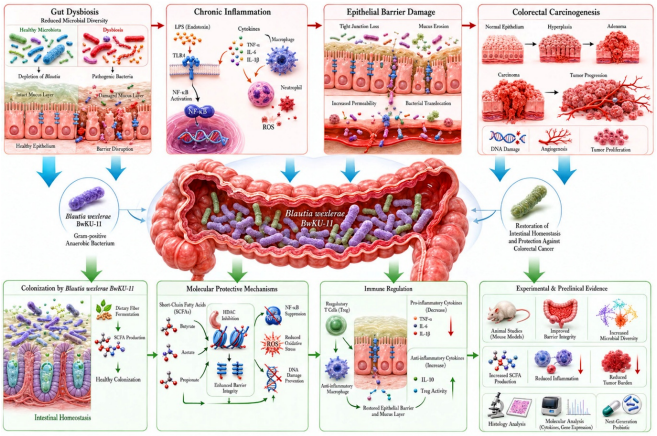

Fig. 3 Protective mechanisms of Blautia wexlerae BwKU-11 against colorectal carcinogenesis, highlighting restoration of microbial balance, enhanced short-chain fatty acid production, immune modulation, epithelial barrier protection, inflammation suppression, and supportive preclinical evidence.

3.2 *Molecular Mechanisms Underlying Its Protective Effects*

The protection mechanism of B. wexlerae BwKU-11 is a combination of several biological mechanisms (33, 34). It promotes the production of healthy delves and enhances levels of short chain fatty acids, especially butyrate, that is anti-inflammatory and strengthens epithelial barrier. It also down regulates pro-inflammatory cytokines and stimulates anti-inflammatory immune responses by activation of regulatory T-cells. Experimental data shows that B (35, 36). wexlerae acts to help diminish oxidative stress and prevent activation of the NF-κB signaling pathway, both of which would otherwise make it easier for tumors to form. Moreover, microbial exclusion of pathogenic microorganisms prevents microbial imbalance and bacterial colonization leading to colorectal carcinogenesis (37, 38).

3.3 *Experimental & Preclinical Evidence*

Preclinical studies have shown promising results on the positive effect of Blautia wexlerae BwKU-11 on managing intestinal health. Studies on animals have shown that the supplementation leads to increased microbial diversity, increased production of health promoting metabolites and a decrease in intestinal inflammation (13, 39). Experimental models have also revealed barrier integrity with epithelial barrier maintenance and reduced expression of inflammatory cytokines and oxidative stress(40). These biological changes lead to the establishment of a less favorable environment within the intestine for initiation and progression of colorectal tumors. While data from clinical trials involving BwKU-11 is still scarce, existing experimental data is highly favourable for the use of BwKU-11 as a potential next generation probiotic for the prevention of CRC. **Table 3**

Table 3 Summary of the biological characteristics, protective mechanisms, immune modulation, microbial regulation, preclinical findings, and therapeutic potential of Blautia wexlerae BwKU-11 in preventing colorectal cancer progression and maintaining intestinal homeostasis.

Aspect	Key Features	Mechanism	Biological Effect	CRC Relevance	Evidence
Biological Characteristics	Gram-positive anaerobe (Lachnospiraceae)	Ferments dietary fiber	Produces SCFAs	Maintains gut homeostasis	Microbiome studies
SCFA Production	Butyrate, acetate, propionate	Carbohydrate fermentation	Barrier maintenance	Reduces CRC risk	Experimental
Immune Regulation	Regulatory T-cell activation	Suppresses pro-inflammatory cytokines	Anti-inflammatory response	Limits tumor-promoting inflammation	Preclinical
Molecular Protection	NF-κB inhibition, reduced oxidative stress	Modulates signaling pathways	DNA protection	Prevents tumor initiation	Animal studies
Microbial Balance	Excludes pathogenic bacteria	Restores microbial diversity	Stable gut ecosystem	Reduces dysbiosis	Experimental models
Preclinical Evidence	Improved intestinal health	Enhanced barrier integrity	Lower inflammation	Delays CRC progression	Animal and laboratory studies

4 Clinical Translation and Therapeutic Potential

4.1 *Blautia wexlerae BwKU-11 is next generation probiotic*

Next generation probiotics (NGPs) are a new generation of beneficial microorganisms, which are not only based on traditional fermentation properties, but with their well-defined mechanisms of action as well (27, 41). Due to its capability of restoring microbial balance, boosting short-chain fatty acid production and regulating the immune response in the intestine, Blautia wexlerae BwKU-11 is a promising NGP (30, 42). This strain has been shown to have given specific biological activities different from those of conventional probiotics, which could directly affect pathways related to colorectal carcinogenesis (43, 44). Its ability to maintain epithelial barrier function and to down-regulate chronic inflammation suggests that it is a possible therapeutic agent as a preventive for CRC patients. **Figure 4**

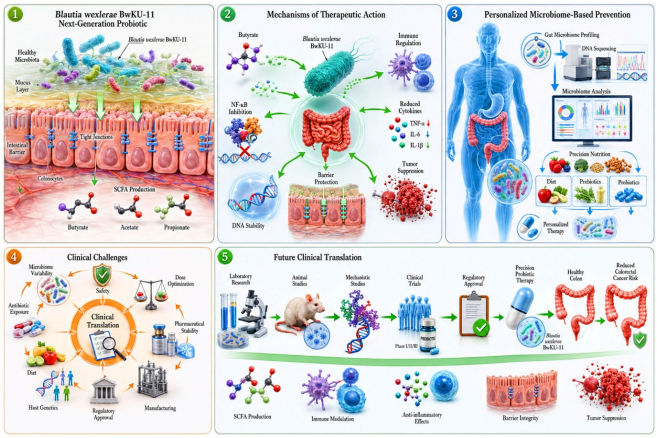

Fig. 4 Graphical overview highlighting the therapeutic potential of Blautia wexlerae BwKU-11 as a next-generation probiotic, illustrating its mechanisms of action, personalized microbiome-based prevention strategies, clinical translation pathway, and challenges for colorectal cancer prevention.

4.2 *Personalized Microbiome Based Prevention Strategies*

Precision medicine and improved sequencing technology in the field of microbiomes has provided options for the personalization of CRC prevention (33, 34). Application of Blautia wexlerae BwKU-11 in treatment would be particular to rescue specific microbes imbalance and therefore Arab individuals would be susceptible to specific conditions. Diet, prebiotics and probiotics, and microbiome profiling could additionally improve therapies (45, 46). Modulation of gut bacteria to achieve a personalized immune response to target chronic inflammatory pathways, optimal production of metabolites and better regulation of immune pathways could provide an alternative and preventative strategy to standard screening and lifestyle changes (38, 47).

4.3 Current challenges and limitations

In light of promising experimental data, there are numerous obstacles that need to be overcome prior to the adoption of Blautia wexlerae BwKU-11 in clinical applications. Safety, dose, formulation stability and consistent pharmaceutical manufacturing processes must be carefully researched and evaluated (48, 49). Potential host and environmental differences in microbiota composition, nutrition, antibiotic therapy and host genetics could affect the colonization and treatment effects. In addition, the bulk of the evidence available is from laboratory and animal work, with the number of well-designed RCTs limited (50). The hope is to develop standardized treatments using the microbiome that are capable of giving reproducible clinical benefits to prevent CRC, which will require addressing these scientific and regulatory challenges. **Table 4**

Table 4 Summary of the clinical translation, therapeutic mechanisms, personalized microbiome-based prevention strategies, benefits, current challenges, and future prospects of *Blautia wexlerae* BwKU-11 as a next-generation probiotic for colorectal cancer prevention.

Aspect	Key Feature	Mechanism	Clinical Benefit	Challenges	Future Direction
Next-generation probiotic	*Blautia wexlerae* BwKU-11	Restores microbial balance	CRC prevention potential	Clinical validation	Therapeutic development
SCFA production	Butyrate, acetate, propionate	Anti-inflammatory effects	Barrier protection	Variable colonization	Optimized formulations
Immune regulation	Reduced NF-κB activation	Decreased cytokine release	Lower chronic inflammation	Host variability	Precision immunomodulation
Personalized prevention	Microbiome profiling	Precision intervention	Individualized therapy	Population differences	Precision medicine integration
Adjunct strategies	Diet, prebiotics, probiotics	Microbiota modulation	Enhanced treatment efficacy	Compliance variability	Combined therapeutic approaches
Clinical translation	Standardized probiotic therapy	Safe pharmaceutical formulation	Improved CRC prevention	Safety, RCTs, manufacturing	Large-scale clinical trials

5 Discussion

The idea of modulating the gut microbiota is a fresh and promising approach to preventing colorectal cancer is gaining increasing support. Blautia wexlerae BwKU-11 is particularly promising among the beneficial intestinal microorganisms that play a role in regulating inflammation, strengthening the intestinal barrier function, boosting the production of short-chain fatty acids and maintaining the diversity of microorganisms. Each of these complementary mechanisms is something that decreases conditions that are beneficial for colorectal tumors to form. However, work on the mechanisms underlying these observations and on humans is still needed to translate these observations into clinical practice. Combination of microbiome-targeted therapy and dietary habits and routine cancer screening will significantly enhance cancer prevention strategies in the future.

6 Future Directions

Further studies need to focus more on clinical trials involving more than one center or institution to determine the efficacy and long-term safety of Blautia wexlerae BwKU-11 in different groups of individuals. Recent progress in the fields of metagenomics, metabolomics, transcriptomics and artificial intelligence will help to better understand host–microbiome interactions and identification of biomarkers to predict therapeutic responses. Colonisation efficiency and clinical outcomes may be further improved through the development of precision P formulation, synbiotics and targeted delivery of microbes. Co-ordinated work between microbiologists, oncologists, gastroenterologists and Pharmaceutical scientists will speed up the transformation of ideas and findings related to the microbiome into evidence-based preventive strategies for CRC and other chronic gastrointestinal diseases.

7 Conclusion

Recent evidence has placed the gut microbiota in the spotlight, showing its major role in the regulation of colorectal health, including the regulation of inflammatory, immune, epithelial and metabolic levels. Accumulating evidence shows that Blautia wexlerae BwKU-11 has a number of biological properties which could offer protection against colorectal carcinogenesis via re-establishing and/or maintaining microbial homeostasis and interfering with pathways promoting the growth of tumor cells. While most of the results so far come from preclinical research, there is high promise that the therapeutic applications of this next generation probiotic will provide. Further interdisciplinary research and well-designed trials will be used to define its future in precision medicine, potentially paving a new path in the future for the prevention and management of CRC via the microbiome.

7.1 CRediT Author Statement

Natarajan Kiruthiga, Balaji Pandiyan conceptualization of the study, drafted the manuscript, designed the figures, manuscript review and editing. All authors reviewed the manuscript.

7.2 Ethical Statement

This study did not involve human participants, animals, or biological materials, and therefore, ethics approval and consent to participate were not applicable.

7.3 Declaration Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Conflicts of Interest

All authors declare that there are no conflicts of interest associated with the publication of this manuscript.

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