Xuena Li[1,2], Ying Han[2], Aihua Zhang[2], Jianhua Miao[1], Hui Sun[2]*, Guangli Yan[2], Fangfang Wu[1,2] and Xijun Wang[1,2]*

[1]National Engineering Laboratory for the Development of Southwestern Endangered Medicinal Materials, Guangxi Botanical Garden of Medicinal Plant, Nanning Guangxi, China
[2]Sino-America Chinmedomics Technology Collaboration Center, National TCM Key Laboratory of Serum Pharmacochemistry, Chinmedomics Research Center of State Administration of TCM, Laboratory of Metabolomics, Department of Pharmaceutical Analysis, Heilongjiang University of Chinese Medicine, Heping Road 24, Harbin, China

*Corresponding author: Xi-jun Wang, Professor, Sino-America Chinmedomics Technology Collaboration Center, National TCM Key Laboratory of Serum Pharmacochemistry, Chinmedomics Research Center of State Administration of TCM, Laboratory of Metabolomics, Department of Pharmaceutical Analysis, Heilongjiang University of Chinese Medicine, Heping Road 24, Harbin, China. State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology, Avenida Wai Long, Taipa, Macau. National Engineering Laboratory for the Development of Southwestern Endangered Medicinal Materials, Guangxi Botanical Garden of Medicinal Plant, Nanning Guangxi, China. Tel/Fax +86-451-82110818; Email: xijunwangls@126.com

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Research Article

Mechanistic and Therapeutic Advances in Colon Cancer: A Systematic Review

Abstract

Colon cancer is a common gastrointestinal malignancy in daily life and is the third most common cancer. So far, the global incidence of colon cancer has risen every year. Colon cancer mortality accounts for half of the incidence, colon cancer mortality ranks fifth in malignant tumor mortality, which seriously threatens human survival and health. This article refers to the latest domestic and foreign related articles related to colon cancer. It summarizes common and emerging screening methods for colon cancer which can make early detection and early treatment of the disease for reducing the deterioration and metastasis of colon cancer. It discusses the diagnostic markers of colon cancer found out in recent years and its mechanism of action, to improve the level, accuracy and scientificity of diagnosis. This article points out that the metastasis of colon cancer is the main cause of death in patients with colon cancer and to discuss the mechanism of its metastasis. It also summarizes the therapy thereof and advantages and disadvantages of colon cancer from different aspects such as intestinal flora, targeted therapy, traditional Chinese medicine and western medicine. Finally, the article summaries some methods that can effectively prevent colon cancer, reduce the occurrence of colon cancer from the source and improve people's quality of life.

Introduction

Colon cancer is one of the most common gastrointestinal malignancy in the world, with high incidence rate and death rate [1,2], and the incidence of it is increasing year by year [3]. The region with the highest incidence is Europe and the United States [4]. Recently, it has been reported that the incidence and mortality of colon cancer in China are 28.08/100,000 and 13.41/100,000 respectively, and the incidence of colon cancer accounts for the third place in the incidence of malignant tumors [5], and the mortality rate is about half of the morbidity. According to statistics, one third of the deaths
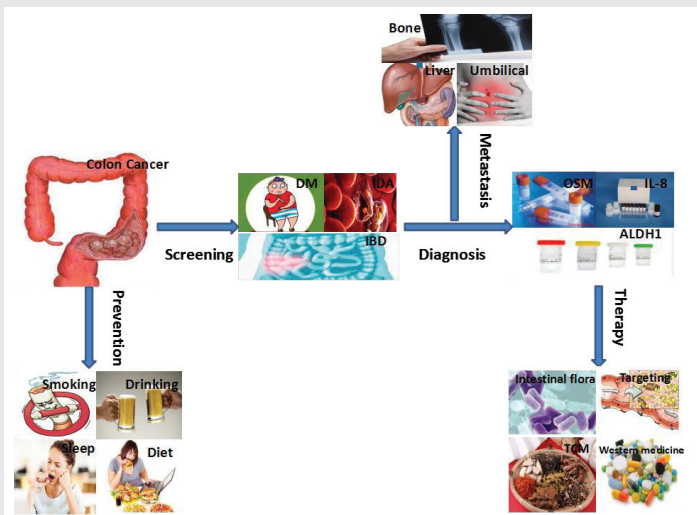
from colon cancer are mostly people over 80 years old [6,7]. The early clinical symptoms of colon cancer often manifest as abdominal pain, diarrhea, adenomatous polyps, blood in the stool, anemia, thrombosis, spleen cyst, intestinal obstruction, *etc.*, and intestinal obstruction is a complication of advanced cancer, which seriously affect people's life and health [8–11]. The procedure of screening, diagnosis, metastasis, therapy and prevention of colon cancer is shown in figure 1. Screening for colon cancer refers to the examination of related symptoms and sites by colonoscopy, occult blood test in feces, and computed tomography (CTC) [12-14]. The diagnosis of colon cancer is through continuous research and found that more diagnostic markers such as serum oncostatin M (OSM), interleukin-8 (IL-8), aldehyde dehydrogenase 1 (ALDH1), *etc.*, accurately determine the patient's the situation and determine whether cancer is metastatic [15,16]. Metastasis of colon cancer to vital organs such as the liver and lungs is a major cause of death in colon cancer patients [17,18]. The treatment of colon cancer can be studied from the intestinal flora, targeted therapy, traditional Chinese medicine, western medicine and other aspects [19,20].

Screening of colon cancer

The development of colon cancer is generally from the normal colonic mucosa to the staging of the adenoma. With the deepening of the research, this staged progression can be

Figure 1: Screening, diagnosis, metastasis, therapy and prevention of colon cancer. (Screening: In addition to routine screening, screening for diabetes, iron deficiency anemia and inflammatory bowel disease is also required; Diagnosis: Diagnostic markers such as serum oncostatin M (OSM), interleukin-8 (IL-8), and aldehyde dehydrogenase 1 (ALDH1) can be used for diagnosis; Metastasis: colon cancer will metastasize to bone, lung and umbilical organs and cause death of patients; Therapy: It can be treated with intestinal flora, targeted therapy, traditional Chinese medicine, western medicine and other methods.; Prevention: colon cancer can be prevented by smoking, alcohol, sleep and diet control).

screened and treated early. The classic screening method is divided into non-invasive and invasive. Including occult blood test in feces, fecal immunochemical test, flexible sigmoidoscopy and colonoscopy, early detection of early treatment can reduce the mortality of patients due to the deterioration of the disease [21,22]. CTC is a non-invasive and easy-to-use medical imaging technique for identifying colorectal polyps and colon cancer masses. It has become a routine diagnosis and treatment method in Western countries. I hope that CTC can be widely used for colon cancer screening in the future [23]. Colon cancer patients often have gastrointestinal bleeding, which can lead to iron deficiency anemia (IDA). Teng et al. had explored that IDA is closely related to colon cancer in adult male and postmenopausal women, and early colonoscopy can be diagnosed early and treatment to improve survival rate [24]. Intestinal flora imbalance is associated with the development of many gastrointestinal diseases, such as inflammatory bowel disease (IBD), however patients with IBD, including Crohn's disease (CD) and ulcerative colitis (UC), the risk of colon cancer is high and should be screened in time [25,26]. In addition to screening for patients with colon cancer-related symptoms, there are some special populations with high rates of cancer and should be examined accordingly. Bloom's syndrome (BS) is an example. BS is due to genetic diseases caused by mutations in the BLM gene, patients with BS have a higher risk of developing various malignancies, and therefore early screening for colon cancer should also be performed in patients with BS [27]. Diabetes mellitus (DM) affects the structure and function of the colon and increases the risk of colon cancer. Therefore, DM patients should also be properly screened [28]. Heo et al. had found that supportive liver abscess (PLA) is associated with colon cancer. Colonoscopy of cryptogenic PLA may detect hidden colon tumors, which can be transmitted to the liver

through the tumor, so screening for PLA patients should also be performed [29]. In addition to conventional screening methods, as technology advances, some new screening methods have been discovered, such as mean platelet volume (MPV), and Li et al. have known that patients with colon cancer have a higher level of MPV, the level of MPV after surgery is reduced, so perhaps MPV can be used as a new diagnostic screening tool for colon cancer [30].

Diagnosis

Prospective radial array echogenic endoscopy can be used to diagnose colon cancer, but it has been concluded that this method is not suitable for locally advanced colon cancer, nor is it suitable for assessing peripheral lesions of colon cancer, and its accuracy also needs to be expanded to continue research [31]. Further research has found many diagnostic markers. For example, aldehyde dehydrogenase (ALDH) is a group of is enzymes that protect cells from peroxide damage while oxidizing acetaldehyde to acetic acid. Hou et al. have explored that aldehyde dehydrogenase 1 (ALDH1) expression is associated with colon cancer invasion and metastasis. It can be used as a diagnostic marker for colon cancer and can reduce the growth and metastasis of colon cancer by inhibiting ALDH1 protein expression, thereby improving patient's survival rate [4]. Serum oncostatin M (OSM) is an amino acid peptides can act as pro-inflammatory cytokines. Gurluler et al. have found that OSM can be used as a diagnostic marker for colon cancer patients and can be transferred to lymph nodes and distal organs [21]. Interleukin-8 (IL-8) is involved in many pathophysiological processes, and IL-8 is also involved in the proliferation and metastasis of other cancers such as colon cancer, together with family members of TNF, so we can use IL-8 together with other biomarkers as markers for colon cancer diagnosis [32].

Metastasis

Although colon cancer mortality is high, patients do not die directly from colon cancer. Colon cancer metastasis to vital organs such as the liver and lungs is the main cause of death of the patient [33,34], although colon cancer can be diagnosed in the early stages through screening, still more than 25% of patients are diagnosed with metastatic colon cancer [35]. Sinagra et al. have evidence that the John Cunningham virus (JC virus) in the polyoma family can infect humans and is associated with several human tumors, which can be infected with the JC virus and produce liver metastasis [36]. Ying et al. have noticed that the intestinal flora can produce lipopolysaccharide, which can transfer colon cancer to the liver. The expression of Toll-like receptor 4 (TLR4) promotes metastasis of colon cancer, while aspirin can inhibit its expression and inhibit colon cancer metastasis [37]. Colon cancer rarely occurs when it is transferred to bones. There was some data through previous research reports suggested that colon cancer also has cases of bone metastasis, and the probability of metastasis is 2%-24% [38]. Colon cancer rarely metastasizes to the spermatic cord or the scrotum, but there are cases where colon cancer can be transferred to the spermatic cord, but the mechanism of metastasis remains unclear and remains to be studied [39].

Colon cancer also metastasizes to the umbilicus, and Mary Joseph's nodule (SMJN) is a rare umbilical nodule secondary to colon cancer [40]. Since colon cancer metastasis is a main factor of death in patients, we should study the mechanism of metastasis to prevent colon cancer metastasis. Hirai et al. have found that CCR1 and its metalloproteinase MMP9 and MMP2 produced in the microenvironment of colon cancer cells can promote cancer cell metastasis, but the results of this study are based on a single model that can be further studied. It can find effective measures to prevent cancer metastasis [41]. Thioredoxin-like protein 2 (Tx-2) is the target of colon cancer monoclonal antibody MC3. Lu et al. explored that Txl-2 expression is elevated in colon cancer, and Txl-2 subtype Txl-2b can interact with Ran and PI3K signaling pathways to promote cells transfer [42], we can use this study to adjust the relationship between the three to achieve the purpose of controlling colon cancer metastasis.

Therapy

There are many methods for the treatment of colon cancer. This paper introduces the advantages and disadvantages of methods and methods for treating colon cancer from intestinal flora, targeting, traditional Chinese medicine, western medicine and other aspects. Intestinal flora, targeting, traditional Chinese medicine, western medicine and other treatment methods for colon cancer are shown in figure 2.
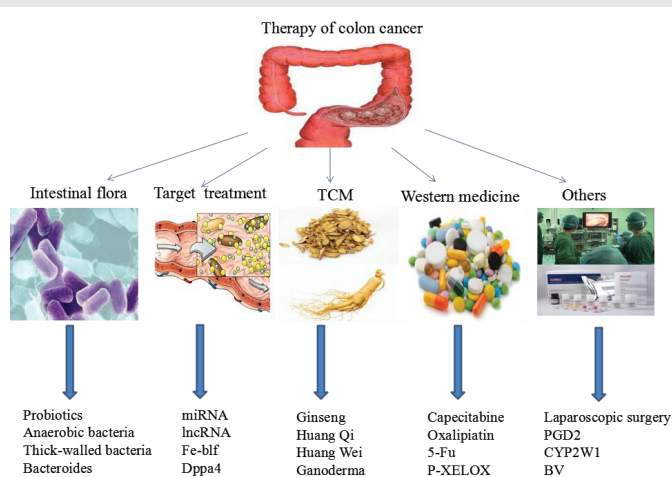
Figure 2: Therapy methods of colon cancer.
Colon cancer can pass through the intestinal flora (Probiotics, Anaerobic bacteria, Thick-walled bacteria, Bacteroides), targeted therapy (miRNA, lncRNA, Fe-blf, Dppa4), Chinese medicine (Ginseng, Huang Qi, Huang Wei, Ganoderma), Western medicine (Capecitabine, Oxalipiatin, 5-Fu, P-XELOX) and other treatments (Laparoscopic surgery, PGD2, CYP2W1, BV) for effective therapy.

Intestinal flora

The gut microbiota, commonly referred to as the "intestinal flora", is a complex, large microbial ecosystem. The intestinal flora can regulate some metabolic and physiological functions, including regulation of lumen pH, metabolism of undigested food, regulation of intestinal movement and stimulation of immune function, *etc.* It is regarded as a unique organ with metabolic, immune and inflammatory central functions in the human body, and the pathogenesis of colon cancer is related to the intestinal flora [43-47]. Under normal circumstances, in the human intestinal tract, the intestinal flora maintains a steady state, and the disorder of the intestinal flora triggers abnormal intestinal signaling pathways and epigenetic modifications, through the 16S rRNA gene or whole genome micro genomic sequencing analysis found that intestinal flora is associated with IBD, colon cancer and other diseases. Researchers also through the study of human patients and rodent cancer models, found that the intestinal flora changes will increase the risk of cancer such as colon cancer [48-52]. Similarly, the 16S rDNA sequencing platform was used to find differences in colony characteristics between colon cancer and adjacent normal mucosa tissues, and by genomic analysis of colon cancer flora and histological analysis of tumor tissues, it was found that Fusobacterium is a key factor in colon cancer [53-56]. The advantage of these studies is the use of the molecular pathology epidemiology database, but there are certain limitations. For example, depending on the number of tissue Fusobacterium nucleatum DNA, the distribution of chemotherapy use may not be significantly different, we need to continue to study [57,58]. Zhu et al. have noticed that probiotics include Bifid bacterium strains as beneficial bacteria that regulate intestinal flora and its metabolism, and tungstate treatment selectively inhibits molybdenum-cofactor-dependent microbial respiratory pathways that are only operable during the onset of inflammation to prevent probiotic expansion and thus beneficial for the treatment of colon cancer [59]. In addition, vitamin D receptor (VDR) and leptin receptor (LPR) can induce probiotics to produce anti-inflammatory effects, although there are still obstacles to the widespread use of probiotics in the clinic, it has been of great help in the treatment of colon cancer [60-62]. The anaerobic fungus *Faecalibacterium prausnitzii* is one of the main components of the intestinal flora and has been considered as a biological indicator of human health. The increase in the amount of *Faecalibacterium prausnitzii* can reduce the risk of colon cancer. The use of Faecalibacterium prausnitzii as a potential active ingredient in probiotic preparations is expected to be used to treat colon cancer [63]. Gao et al. have explored that histamine has a potential anti-tumor effect, and the intestinal flora can mediate inhibition of inflammation-related colon cancer through luminalamine histamine production [64]. Intestinal flora is also affected by many factors, such as genetic factors, intestinal inflammation, diet and environmental factors [65]. Bultman et al. have evidence that dietary fiber can produce butyrate under the action of intestinal flora, it can inhibit the survival and growth of colon cancer cell lines, so we can prevent and treat colon cancer in this way [66,67]. Dietary fiber can also increase the abundance of Prevo bacteria to improve glucose metabolism, and sugar metabolism can affect drug resistance. Therefore, controlling intestinal flora may be an effective strategy to reduce drug resistance [68]. By studying the dietary components of specific pathogen-free (SPF) and sterile (GF) mice, it has been found that complex nutrient mixtures such as proteins and fibers affect intestinal permeability and have a great influence on the development of colitis [69]. It has been found that adding walnuts to the diet can increase the

number of thick-walled bacteria in the intestine and reduce the number of bacteria such as Bacteroides, which indicates that eating walnuts can change the intestinal flora and provide us with a new mechanism for health [70]. However, Wang et al. have noticed that inadequate characterization of the intestinal flora may contribute to the onset of colon cancer, as symbiotic infected macrophages activate Wnt/β-catenin signaling and dedifferentiation through the bystander effect (MIBE) caused by the flora. Reprogramming and pluripotency transcription factors associated with the development of colorectal cancer stem cells (CSCs), on the other hand, also provide a mechanism for colony-induced colon cancer, providing a new potential target for the prevention of colon cancer [71]. Metabolomics uses high-resolution mass spectrometry to provide chemical maps of metabolites in cells, tissues, or body fluids, and can study various disease states [72]. Metabolomics can be used to demonstrate the role of gut microbiota and to demonstrate that the relevant metabolites of the gut flora can serve as new preventive and chemical targets [73,74].

Targeted therapy

MicroRNAs (miRNAs) are non-coding small RNA molecules that are present in prokaryotes and eukaryotes that regulate translation and transcription to regulate gene expression, while microRNA21 (miR21) is involved in chronic inflammatory processes and colitis-associated colon cancer in the development of the disease, Yang et al. found that miR21 is a downstream target of F.nucleatum in the colon, so miRNA can be used as a new target for anticancer therapy, and miRNA-based therapies may be an effective method for individuals to treat colon cancer [75-77]. Luo et al. have explored that the expression of long-chain non-coding RNA (lncRNA) HOTAIR is closely related to tumor metastasis, and plays an important role in cancers such as colon cancer, gastric cancer, pancreatic cancer, esophageal cancer, especially in the occurrence and metastasis of colon cancer, can be used as a new target for the treatment of colon cancer [78-80]. TPX2 is a microtubule-associated protein encoded by a gene located on a human chromosome that promotes proliferation and metastasis of colon cancer cells and serves as a novel prognostic biomarker and therapeutic target for colon cancer [81]. Iron-saturated bovine lactoferrin (Fe-bLf) nanocarriers have anti-cancer effects and can be used to target colon cancer and other cancer stem cells [82]. The p38γ-activated ternary complex of Hsp90 and K-Ras can be used as a novel target for the treatment of K-Ras-dependent colon cancer [83]. The developmental pluripotency-related 4 (Dppa4) gene plays an important role in the self-renewal of embryonic stem cells. This gene can be re-expressed in many malignant tumors and has been shown to play a large role in the development of colon cancer. So it can be used as a new target for the treatment of colon cancer [84]. Morita et al. have found that DnaJ (Hsp40) homologous subfamily B member 8 (DNAJB8), a member of the heat shock protein (HSP) 40 family, have the effect of inhibiting the accumulation of erroneous folding toxic proteins, which may be related to the development and metastasis of cancer. Combining DNAJ88 targeted immunotherapy with other standard therapies may effectively cure cancer and will be a new target for colon cancer targeted immunotherapy [85].

Traditional medicine

Traditional Chinese medicine is widely used in various inflammation-related diseases. The main components of the medicinal plant *Scutellaria baicalensis*is are baicalin and scutellarin. The study using human intestinal bacteria group culture and HPLC analysis found that baicalin can be converted to baicalein. Another study shows that baicalin has a limited anti-proliferative effect on cancer cells, while baicalein has a significant anti-proliferative effect on cancer cells, especially on HCT-116 human colon cancer cells, therefore, baicalein is an effective anti-cancer metabolite and has a chemo preventive effect on colon cancer [86-88]. The saponin AST obtained from the medicinal plant *Astragalus* can play a role in anti-tumor and apoptosis promotion in colon cancer cells [89,90]. *Araliaceae ginseng* can prevent and treat many chronic diseases. Several studies have shown that ginsenosides Rg3 and Rh2 in ginseng have anticancer effects, which can reduce the incidence of colon cancer, while protosan diol (PPD) can increase the anticancer effect of the chemotherapeutic agent fluorouracil (5-FU), thereby improving the overall condition of patients [91-93]. Guan Chang Fu Fang (GCFF) is extracted from the three plants of *Agrimonia pilosa Ledeb.*, *Patrinia scabiosaefolia* and *Solanum nigrum L.*, which is similar to the original ginseng diol (PPD). It can also be combined with fluorouracil (5-FU) to treat colon cancer [94,95]. However, Wang et al. have indicated that 5-FU can cause intestinal flora disorder and colon damage, and the polysaccharide carboxymethylated sclerotium (CMP) isolated from *Poria cocos* can regulate the balance of intestinal flora and alleviate FU-induced colon injury [96-98]. The main active components of *Sophora flavescens* are alkaloids and brass, and its different components have a good inhibitory effect on the activities of cells such as SW1116, SW620 and SW480, and the ethanol extract of Sophora also inhibited the proliferation of colon cancer HT29 cells [99,100]. Yang et al. have explored that the consumption of *Ganoderma lucidum* mushroom can prevent the occurrence of colon cancer in rodents, so the mechanism of action was studied and it was found that *Ganoderma lucidum* extract regulates secondary bile acids, flora, mucin and propionate associated with colon cancer. It has an impact on colon health [101]. Some prescriptions such as *Shiquan Dabu Decoction, Shenqi Decoction, Qihuang Decoction, Jiedu Sangen Decoction, etc.* can also be used to treat colon cancer, and the mechanism of action can be applied to the method of metabolomics of traditional Chinese medicine. Metabolomics is based on the symptom as the entry point, using prescriptions as the research object, using metabolomics technology to discover and identify the biomarkers of the symptoms, and using the biomarkers of the symptoms as parameters to evaluate the overall efficacy of the prescription. Using this method we can understand the mechanism of action and provide effective help for the treatment of colon cancer [102-104].

Western medicine

The main means of treating colon cancer is surgery, and prevention of postoperative recurrence is also important, so effective postoperative adjuvant chemotherapy is needed. Sadahiro et al. have evidence that 5-fluorouracil (5-FU)

monotherapy and 5-FU plus Oxali Platinum is an effective adjuvant chemotherapy program for colon cancer surgery, especially for adjuvant chemotherapy in patients with stage III colon cancer [105,106]. The new study shows that the combination of three active chemotherapeutic drugs, namely leucovorin, oxaliplatin (XELOX), 5-fluorouracil and irinotecan, can improve the safety and effectiveness of adjuvant chemotherapy and improves patient survival [107]. However, it has been reported that capecitabine and oxaliplatin may induce coronary vasospasm and acute coronary thromboembolism [108,109]. Taking bevacizumab may also form thrombosis, and there are differences between people, black patients are more likely to develop thrombosis than white patients, and are prone to occur with increasing age [110]. Panitumab (P-XELOX) can be combined with oxaliplatin and oral capecitabine to treat colon cancer and advanced liver metastases [111]. Matsuda et al. have found that after treatment with capecitabine, oxaliplatin and bevacizumab in patients with liver metastases with advanced colon cancer, symptoms of hand-foot syndrome (HFS) have emerged [112,113]. Simvastatin combined with irinotecan could overcome the resistance of irinotecan, and the combination of the two in a molar ratio of 2:1 can achieve the best effect to treat colon cancer [114].

Other therapies

In order to treat colon cancer, a colitis-associated colon cancer model of azomethane/dextran sulfate (AOM / DSS) was established in the laboratory, and this model was used to analyze the role of p38γ and p38δ in colon cancer associated with colitis, it can be found that p38γ / δ deletion can reduce tumor formation, but p38 γ / δ deficiency does not have much effect on advanced tumors [115]. Iwanaga et al. have evidence that prostaglandin D2 (PGD2) produced by mast cells can inhibit colitis and subsequent tumor formation, and can be used to prevent and treat colon cancer [116]. Canine uric acid (KYNA) acts as a tryptophan metabolite to inhibit the proliferation of cancer cells such as colon cancer and kidney cancer, and KYNA is considered to be a potential chemo preventive agent for colon cancer [117-119]. The small molecule compound sulfidic can prevent colon cancer from treating pre-stage adenoma, but it is toxic in the cardiovascular and renal systems. Lee et al. have explored that small doses of sulfidic can be used in combination with other chemo preventive agents to treat colon cancer, and can increase its effectiveness [120]. 5-Fu is the most commonly used chemoprevention therapy for the therapy of colon cancer. Fu et al. have noticed that when combined with 5-Fu, antioxidants sometimes do not work for colon cancer patients, but antioxidants can pass regulation of Src-dependent caspase-7 phosphorylation, thereby reducing the apoptosis of 5-Fu in colon cancer, and improving the therapeutic effect [121]. Cytochrome P450 2W1 (CYP2W1) is a monooxygenase that can be detected in 30% of colon cancers, but it is not expressed in non-transformed adult tissues. It can be used as a new treatment for colon cancer [122,123]. Bee venom (BV) has anticancer activity and is a traditional medicine for treating skin diseases, cancerous tumors and rheumatism. Recently, Zhenget al. have evidence that BV can induce apoptosis by activating DR4 and DR5 and inhibiting NF-kB, thereby inhibiting the growth of colon cancer cells [124]. Vitamin D can participate in various physiological functions including immune response in the human body, it can regulate intestinal barrier function and antibacterial peptide synthesis. Epidemiological studies have found that vitamin D supplementation can alleviate the symptoms of colitis and have a protective and therapeutic effect on colon cancer [125].

Xiaet al. have found that laparoscopic surgery has become an alternative treatment for colon-related diseases in recent years, and laparoscopic colectomy has many advantages in postoperative recovery compared with conventional surgery, because inflammation can promote colon cancer recurrence and metastasis, and laparoscopic surgery may also cause postoperative complications. Therefore, doctors should minimize their postoperative complications and improve their survival rate through their own efforts [126,127]. Postoperative intestinal obstruction (POI) is the most common complication after intestinal surgery and is associated with dendritic cells (DCs) and macrophages. Pohl et al. have explored that modifying the intestinal flora can prevent inappropriate activation of these cells. It can be used as a new method to prevent POI [128]. During the patient's hospitalization, for patients with stage III colon cancer, the communication and cooperation between the surgeon and the oncologist can promptly identify postoperative and chemotherapy-related complications, reduce some unnecessary errors and improve patient care strategies in a timely manner [129], and appropriate individual treatment strategies can be used to improve patient survival [130]. Modified FOLFOX is a widely accepted standard of treatment for colon cancer removal. Kotaka et al. have noticed that modified FOLFOX6 can be used as adjunctive therapy for patients with stage II or III colon cancer radical resection, but further research is needed [131]. In addition, elderly patients with locally advanced and metastatic colon cancer need to consider the pharmacokinetics and pharmacodynamics of the drug during treatment, as well as the performance status and assessment of activities of daily living (ADL) or instrumental ADL, and tailored treatment options for each patient and timely return visits [132].

Prevention

People with colon cancer are the result of many factors interacting with obesity, sedentary, diet, alcohol, smoking, low-fiber intake, high-fat diet, sleep, and lack of exercise are all related to the incidence of colon cancer [133-136]. Colon cancer can be prevented to a large extent. By establishing a corresponding mouse model, it is found that dietary adjustment and nutrient intake can prevent colon cancer very well. An important mechanism of action is by regulating the concentration of micronutrients in the target tissue [137], for example, vitamin E is a micronutrient that has the characteristics of preventing colon cancer, and can appropriately increase the intake of vitamin E in the diet, but it cannot be overdose because high alpha-tocopherol intakes from vitamin E supplements can result in decreased blood gamma-tocopherol concentrations, while gamma-tocopherol has a higher ability to prevent cancer than alpha-tocopherol [138,139]. Pomegranate juice and citrus juice can also be

added to the diet, and the polyphenols in the juice have chemo preventive properties against colon cancer [140]. The main ingredient of hot-processed ginger is Shogaols, which has proven to be a very effective anti-cancer agent, and studies have shown that the coupled metabolite of Shogaols and cysteine can be used as a novel dietary preventive agent for colon cancer [141]. Liu et al. have evidence that the main triggers of colon cancer are inflammation and intestinal flora, and regular consumption of broccoli not only has great benefits for our health, but also reduces the risk of cancer and inflammatory diseases, thereby preventing colon cancer [142]. Del Pino-García et al. have found that red wine pomace seasoning has anti-proliferative and antigenic toxic effects, and has the potential to prevent colon cancer [143]. "Mediterranean" and vegetarian diets including oils, olive oil and vegetables and oily fish, have anti-inflammatory effects, prevent intestinal flora imbalance and inflammatory bowel disease, and can prevent the occurrence of colon cancer [144]. In addition, in the diet, a high animal protein diet promotes the binding of bile acids to taurine, and the combination of the two will produce a toxic compound hydrogen sulfide and tumor promoter deoxycholic acid through intestinal flora metabolism, which will promote colon cancer [145,146], so in the daily diet, should avoid high animal protein and other foods. In addition, Zelenskiy et al. have explored that the risk of colon cancer increases with age, and high dietary glucose load (GL) also increases the risk of colon cancer, while the high GL diet in the elderly will triple the risk of cancer, so people should take a low GL diet, especially for the elderly, which can reduce the risk of colon cancer and achieve the purpose of prevention [147]. Fat intake should also be reduced in the daily diet because a high-fat diet promotes inflammation and exacerbates the severity of colitis [148]. In addition, Nurdin et al. have found that dietary fiber supplementation can play a role in preventing colon cancer, and dietary fiber mixtures such as a traditional Indonesian dietary fiber may have a more pronounced effect on colon cancer than single dietary fiber [149]. Dietary emulsifier is a ubiquitous processed food ingredient that can change the composition of the intestinal flora and promote low-grade inflammation in the intestine. Therefore, reducing dietary emulsifier intake can prevent inflammatory bowel disease and colon cancer [150]. In today's society, sedentary behavior is ubiquitous due to work. Cong et al. have evidence that the risk of colon cancer in a sedentary population increases by 30%, therefore, reducing sedentary behavior in daily life and work can prevent colon cancer [151]. When people have symptoms of colitis such as diarrhea and abdominal pain, they should pay attention and go to the hospital for examination [152]. In addition, HAMLET (human alpha-lactalbumin lethal to tumor cells) can be used as a new oral drug for the prevention and therapy of colon cancer, especially those with colon cancers carrying APC mutations [153,154]. The RNA-binding protein HuR, a small molecular target, can be used to prevent colon cancer in high-risk populations with familial adenoma polyposis (FAP) or inflammatory bowel disease (IBD) [155]. At the same time, researchers have found that long-term exposure to antibiotics can thin the intestinal protective mucus layer and increase the risk of colon cancer, so reduce the exposure of antibiotics

such as vancomycin and streptomycin can effectively prevent colon cancer [156]. Colon cancer is a heterogeneous disease caused by at least two precursors, conventional adenoma (CA) and serrated polyps, and Peters et al. have explored that the intestinal flora may play through the development of CAs in the early stages of colon cancer. Therefore, it can further study the early driving factors of intestinal flora in colon cancer and effectively prevent colon cancer [157].

It can be seen from the above that the intestinal flora plays an important role in the disease of colon cancer, which is not only related to the screening diagnosis of colon cancer, but also related to the metastasis, treatment and prevention of colon cancer. The multiple effects of intestinal flora on colon cancer are shown in figure 3. We should constantly study the multiple mechanisms of action of the intestinal flora, which can better control colon cancer and reduce the harm of colon cancer to human health.

Future prospects

Continuous research on colon cancer has found that left and right colon cancers have different clinical and biological characteristics and require continuous efforts to provide personalized treatments. Recent studies have found that intestinal flora can regulate immunity, improve inflammation,
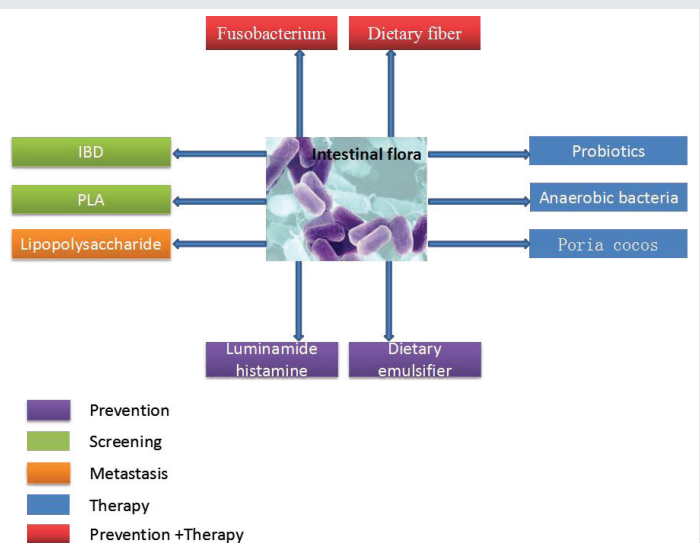
Figure 3: Multiple effects of intestinal flora on colon cancer. (Prevention: Intestinal flora can mediate inhibition of inflammation-related colon cancer through luminalamine histamine production. Reduction of dietary emulsifier intake can alter intestinal flora to prevent colon cancer; Screening: intestinal flora imbalance can lead to IBD, which in turn develops into colon cancer, requiring screening for IBD patients. Intestinal flora can be transmitted to the liver through colon tumors to produce PLA, screening for PLA patients; Metastasis: lipopolysaccharide (LPS) produced by intestinal flora may promote the transfer of colon cancer to the liver; Therapy: probiotics can regulate intestinal flora and its metabolism. Anaerobic bacteria can also be used as a potential active ingredient in probiotic preparations for the treatment of colon cancer. The polysaccharide carboxymethylated coarse powder (CMP) isolated from Poria cocos can regulate the ecological balance of intestinal flora and alleviate 5-FU-induced colon injury.; Prevention and Therapy:using 16S rRNA genome sequencing, it is found that Fusobacterium is a key factor in colon cancer and can be used for the prevention and treatment of colon cancer. Dietary fiber can produce butyrate under the action of intestinal flora, which can inhibit the survival and growth of colon cancer cell lines and can be used to prevent and treat colon cancer).

and inhibit the growth of cancer cells. Intestinal flora has also been shown to be useful in the treatment of pancreatic cancer, breast cancer, liver cancer, lung cancer, bladder cancer, kidney stones, autoimmune diseases, *etc*. In order to better utilize the intestinal flora and understand its mechanism of action, further research is needed.

Conclusion

This article systematically introduces the latest advances in the study of colon cancer and its treatment, and summarizes the advantages and disadvantages of effective methods and methods for screening, diagnosis, treatment and prevention of colon cancer. The methods for treating colon cancer are introduced from the intestinal flora, targeting, Chinese medicine, western medicine and other aspects, respectively, which gives us a more comprehensive understanding of colon cancer. As people's living conditions continue to improve, they are also more concerned about the health of themselves and their families, but the preventive measures in daily life may not completely curb the occurrence of colon cancer. Therefore, effective treatment is particularly important, and prognostic care should also be taken seriously. In recent years, studies have found that intestinal flora not only has a good effect on the treatment of colon cancer, but also plays an important role in the screening, diagnosis, metastasis and prevention of colon cancer. So we can continue and focus on research to achieve better results, better to provide protection for human health.

Acknowledgments

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