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Exploring the Interplay Between Cancer, Health, and Inflammation

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Abstract: Cancer is a complex disease influenced by various factors, including DNA damage, growth signals, and inflammation. Although inflammation has commonly not been considered carcinogenic, increasing evidence indicates its substantial involvement in the onset and progression of cancer, especially in the presence of chronic microbial infections. This review thoroughly analyzes the complex relationship between cancer, health, and inflammation by introducing pathological and physiological features of inflammation. The study explores the various factors that might enhance inflammation, including infections and para-inflammation caused by tissue stress. It will also explore the changing comprehension of microorganisms about health and illness, clarifying their possible influence on the development of several malignancies, including colon, pancreatic, gastric, and prostate cancers. In addition, the study emphasizes the development of new therapy approaches that specifically target chronic inflammations and their associated cancers. This review seeks to enhance the comprehension of the intricate correlation between cancer, inflammation, and human health by combining existing research.

Keywords: Cancer; Tissue stress; Inflammation; Human health; Therapeutic interventions

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1. Introduction

Cancer is a significant global health issue, resulting in a considerable number of diseases and fatalities. During the year 2012, there were an estimated 14 million incidences of cancer that were newly diagnosed and eight million deaths directly linked to the disease. Estimations suggest that the incidence of cancer will increase, reaching around 22 million new cases annually by 2030 [1]. Additionally, it is estimated that there will be around 13 million deaths annually due to cancer. The rise in cancer prevalence is partially attributed to the expansion of the population and the process of aging. Nevertheless, it is expected that alterations in cultural, economic, and lifestyle aspects associated with human growth will also impact and increase the cancer profile in the future [2,3]. Various research has demonstrated a robust correlation between socioeconomic advancement, inflammation,

and cancer. The existing body of literature offers valuable insights that may be used to shape strategies and establish goals to effectively address the burden of cancer. Additionally, it emphasizes the variations in cancer susceptibility and impact among varying degrees of human development. This review seeks to evaluate the worldwide occurrence of cancer concisely, its correlation with inflammation, and the general state of human health, explicitly emphasizing the variations in cancer prevalence among various levels of human development [4]. This review focuses on the relationship between inflammation and cancer in various types and risk factors that affect cancer, as well as the treatments with corresponding outcomes that include disabilities and life expectancy cases.

Knowledge of the underlying health elements affecting cancer is essential since the elements of health can significantly affect the possibilities of cancer in terms of early detection and survival rates [5]. The causes of cancer include nursing factors like the type of diet, exercise regimes, and tobacco use, as well as environmental conditions and heredity [6]. Lack of a healthy diet and physically inactive lifestyle are some of the significant factors that lead to obesity. This fact has been widely accepted as a precursor to several diseases and cancers. Furthermore, smoking is associated with instances of lung cancer as well as various other kinds of cancer. If these risk factors are further defined, they can reduce total body cancer [7]. Additionally, knowing of risks originating from genetics can help integrate the methods of individualized medicine in preventive and therapeutic practices, thus improving the efficacy of prevention measures and drugs. Understanding the factors affecting health requires further identification and scrutiny to make possible changes regarding the approaches of public health interventions that would allow for the unique needs and concerns of various populations to be addressed. This results in better diagnosis and effective management of cancer and lowered incidence of the disease [8].

Inflammation has also been directly linked to the risk of new cancer events and enhanced mortality rates, according to multiple studies [9]. That is why the exact pathogenic mechanism of many long-term illnesses, like stress or cancer, is called chronic low-grade inflammation. Chronic psychological stress leads to sustained elevation of circulating cytokines in the blood, which is responsible for mild peripheral and central inflammation [10,11]. NF-kB, STAT3, and mTOR pathways regulate the synthesis of cytokines, which provoke inflammation and further modulate their activity [12]. The studies regarding the fact that the NF-κB/STAT3 oncofetal gene for FAT10 upregulation is unfavorable to the p53 tumor suppressor gene that is overexpressed with a significantly higher rate of enhancement [13]. One of the other molecular changes identified as having a direct link with high chances of an individual developing tumors is the alteration or complete knockout of p53 protein that results from *TP53* gene mutations. Also, Romeo et al., in their recent study in 2009, confirmed that the end-of-life experiences of patients can be measured by the quality-of-life index and ACE. This study also revealed the same as the study conducted by Noman on how Mutant p53 proteins facilitate the survival of cancer cells through increased ROS production, synthesis of pro-inflammatory cytokines, activation of mTOR, suppression of autophagy, and suppression of UCP2. They also noted that the p53 distribution usually occurs in a dispersed manner, and as for the currently described standard p53 scattering pattern, certain conditions were meant to decrease the action of mutated TP53 in supporting the survival of the cancerous cells [12]. Moreover, the compounds also stimulated the said pro-inflammatory and cancer-promoting cytokines and had a positive reinforcement toward tumor promotion [12].

Stress, hypoxic cancers, metabolism, anti-cancer therapy, cancer-inducing inflammation, angiogenesis, cytokine- production, and so on can be the possibility of the cause [14]. They affect tumor development

depending on cell proliferation and increase the invasiveness of the cancer cells through the epithelial-mesenchymal transition. Furthermore, VEGF and its receptors show an increase in tumor angiogenesis. The following research works provided preeminence of the points above, all of which aid the integration of technology in the learning and teaching process [15,16].

Additionally, one should note that when cancer cells produce more pro-inflammatory cytokines, it may result in multiple drug resistance; this is likely attributed to an autocrine feedback mechanism [14]. This is because chronic stress or cancer will place the body on a pro-inflammatory status, which then triggers other stress responses. This condition can change the cancer biology and be associated with neuroinflammation. Neuroinflammation refers to a condition that involves monocyte activation, microglia activation, and disruption of the blood-brain barrier (BBB) [17,18]. This then caused an aggregation of macrophages in the lymph nodes and splenic spaces by stress releasing them in the brain by continued release of catecholamine [19]. It is these cells that later become hyperinflammatory, and they facilitate the migration of cells into the brain [17-19]. In this context, sustained inflammation increases the up-regulation of high cell adhesion molecules on the cerebral endothelium to facilitate the attachment of monocytes and their diapedesis through the endothelium. Lastly, this results in the metamorphosis of the monocytes into cells with strong microglia features. For this reason, we can find out that the monocyte infiltration caused by chronic stress and CCR2-dependent is not related to the damage to the BBB [20]. MIF has been reported to be up-regulated under conditions of chronic stress, to directly facilitate the recruitment of monocytes by engaging the CCL2/CCR2 signaling pathway, and is also mandatory for maintaining chronic neuroinflammation [21-23]. The interactions between inflammation, human stages of development, and cancer are unpredictable yet diverse. It is, therefore, important for public health stakeholders to better understand these interactions to develop and implement better strategies and interventions that can help reduce the occurrence of cancer and improve treatment outcomes.

1.1. Cancer and health

Malignant diseases of the cancer category are common and manifested by the proliferation and ongoing proliferation of abnormal cells. If this proliferation is to go unchecked, it can lead to death. Cancer can often develop in any of the body's organs or tissues. Over a hundred types of cancer are termed after the body part where and/or from where they arise. Lung cancer arises from cells found in the lungs, whereas brain cancer arises from cells found in the brain [24]. The main categories of cancer include as follows.

Carcinomas are malignant neoplasms arising from the epidermis or the epithelial tissues surrounding internal organs. Examples include breast, lung, and colorectal cancer. Sarcomas are cancerous tumors that originate from connective tissues.

Leukemias are cancerous growths that develop in the hematopoietic tissue, particularly the bone marrow. This leads to the overproduction and release of abnormal blood cells into the circulatory system. Lymphomas and myelomas are tumors that originate from the defense system. Neoplasms are CNS cancers that originate in the tissues of the brain and spinal cord [25].

1.2. Cancer epidemiology

Cancer is a prominent cause of morbidity and mortality on a global scale. The WHO documented roughly 14 million cases of cancer and around 8 million deaths caused by cancer in 2012. The expected burden is set to rise, as forecasts indicate a yearly increase of 22 million new cases and 13 million fatalities by 2030. The

increase in this phenomenon can be attributed to various variables, such as the expansion of the population and the aging of individuals, along with changes in lifestyle and the environment linked to socioeconomic progress. Cancer incidence remains an area that shows relative distribution differences by geographical areas, age, gender, and social status. The universal types are common in developed nations, such as breast and prostate cancer, based on advanced diagnostic methods and increased life expectancy. On the other hand, economically developed countries are less likely to be affected by these infections causing cancer, such as cervical cancer from viruses and liver cancer from viruses [26].

Some of the leading well-identified causes of cancer that affect humanity globally include tobacco smoking, misuse of alcohol, poor diet, tendency to perform little or no exercise, and exposure to viruses. Suppose there is any single social vice that remains the most significant cause of cancer deaths. Smoking, which accounts for about 22 percent of all cancer-related deaths. In addition, Human exposure to hazardous substances at the workplace, such as carcinogens, radiation, and environmental toxins, increases the likelihood of cancer significantly. The best approach to address this health threat is a holistic approach that includes prevention, timely diagnosis, treatment, and support for the patient. Preventable risk factors, which require strategies that can be changed, controlling over-vaccination, screening, and promoting access to medical care services, are vital for reducing the likelihood of cancer and improving results [27].

2. Inflammation and its physiological role in the body

Inflammation, defined by the literal meaning of the word being an abbreviation for “inflammatory,” a term meaning “to flame,” is a critical function in the body that serves the purpose of protecting cell membranes from damage or infection by pathogens [28,29]. Inflammation is a vital human body condition, though it continues as a chronic disease. Inflammation is related to diseases with lengthy intervals, such as neurological disorders, cancer, and cardiovascular illnesses. Inflammation is an elaborate process of coordinated and dynamic events involving a cascade of clear and well-orchestrated events, such as responses within cells and blood vessels and the release of specific mediators [30,31]. The mechanisms involve the migration of leukocytes, plasma, and substances towards the site of inflammation. Immune cells secrete various chemicals and signaling molecules, such as histamine, cytokines, and free radicals. Each of these chemicals promotes inflammation [29]. Inflammatory responses consist of two distinct stages: major and minor. There are different mechanisms at play in each phase.

2.1. Acute inflammation

Inflammatory responses can occur at the vascular and cellular levels during the acute inflammatory phase. When the tissue is injured or invaded by microorganisms, vascular events commence — the vessels dilate and become hyperpermeable. This enables inflammatory mediators to move in and results in the formation of interstitial edema. The ability of cells to pass through the circulatory system and invade other tissues is essential for inflammatory reactions [32]. Some chemical messengers involved in the trigger of leukocyte migration include microbial endotoxins, the C5a complement component, interleukins, and the secretions from basophil. It is recognized that these cells are the first responders at sites of severe inflammation. The invasion of the immune system is a complex phenomenon characterized by leukocyte interactions with the lining of blood vessels, which is found in postcapillary veins [33]. This process involves several cellular activities, such as the

capture, rolling, and firm adhering of leukocytes to the endothelium lining of tiny blood arteries. Some CAMs are explained as follows: intercellular adhesion molecular-1 (ICAM-1), intercellular adhesion molecular-2 (ICAM-2), integrin, and selectin, which are involved in these actions. The selectins can be classified into three families: P-selectin and E-selectin, which are on endothelial cells, and L-selectin, which is on leukocytes. It is also necessary to mention the interaction between the white blood cells and the endothelium due to the high affinity between the human protein-integrating protein CDII/CDI8, present in the white blood cells, and the CAMs, located in endothelial cells [34]. Once adherence is established, white blood cells send out pseudopods through the intercellular spaces of the endothelial row and penetrate the sub-endothelial basement lamina. It can be called white blood cell invasion and transendothelial migration [35].

2.2. Chronic inflammation

Mononuclear cells, particularly monocytes and lymphocytes, fibroblast proliferation, collagen fiber synthesis, connective tissue growth, and the eventual creation of granulomas are hallmarks of chronic inflammation [36]. In chronic inflammation, inflammatory cells enter the damaged area and produce ROS, RNS, proteases, and so on. These species are responsible for tissue destruction. Diseases of the inflammatory bowel, rheumatoid arthritis, and cancer are among the chronic inflammatory illnesses linked to mutations in the *p53* gene [36].

2.3. Key inflammatory mediators

Many different chemical mediators released by damaged tissues, inflammatory cells, and the bloodstream actively regulate the inflammatory response. Thromboxanes, leukotrienes, and prostaglandins are eicosanoids; peptides like bradykinin histamine and serotonin are all part of this class of chemical mediators. Although additional cell types can secrete cytokines, the primary sources of cytokine release include vascular cells, fibroblasts, and endothelial cells, among others [37].

2.4. Mechanisms of inflammation

Complex molecular and cellular mechanisms contribute to inflammation and the immunological system's reaction to pathogens or damaged tissues [38]. At the outset, chemical signals released by damaged or sick tissues attract several immune cells to the site of inflammation, including lymphocytes, macrophages, and neutrophils [39]. These cytokines, chemokines, and prostaglandins are just a few of the pro-inflammatory substances released by these cells. By increasing vascular permeability and inducing vasodilation, these substances bring additional immune cells to the affected area. The primary signaling pathways for inflammation are NF-κB, STAT3, and MAPKs [40]. Essential proteins for the immune response, such as inflammatory cytokines, are controlled by these pathways [41]. Also, warning signs activate multi-protein complexes called inflammasomes, and they play an essential role in producing cytokines like interleukin-1β (IL-1β) that enhance inflammation. Imbalance in these pathways can result in long-term inflammation and have a role in developing several types of cancers, such as gastric, liver, colorectal, prostate, and breast cancer (**Figure 1**) [42].

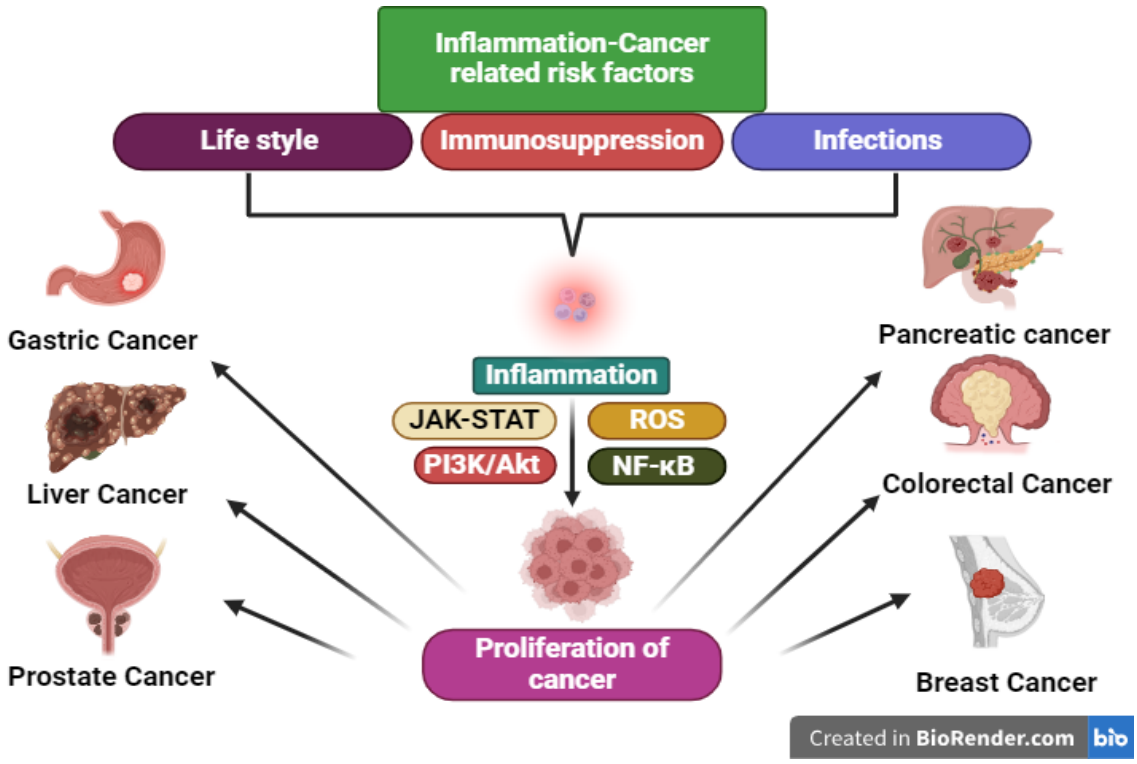

Figure 1. Role of inflammation in the development of several types of cancers such as gastric cancer, liver cancer, colorectal cancer, prostate cancer, and breast cancer

3. Link between inflammation and cancers

In 1863, Rudolf Virchow made the initial connection between inflammation and cancer. He noticed the presence of leukocytes in cancerous tissues, indicating that cancer may potentially arise in areas of long-lasting inflammation. In the last 150 years, the understanding of this correlation has dramatically progressed. At first, it was believed that substances that cause irritation and tissue damage, leading to inflammation, could promote cell growth and contribute to cancer formation [43]. Nevertheless, it is currently acknowledged that other variables beyond cell proliferation influence the distinctive aberrant growth of cancer [44]. These factors include growth hormones, DNA damage chemicals, an active stroma, and an inflammatory environment [45]. In contrast, inflammation in typical circumstances typically subsides on its own because of the creation of anti-inflammatory cytokines. Unregulated chronic inflammation can disturb regular cellular processes, resulting in the development of different types of cancer (**Table 1**). Additional evidence substantiating this connection is derived from research indicating that most cancerous tissues display an inflammatory element in their surrounding environment. This condition is characterized by changes in the structure of tissues, the development of new blood vessels (angiogenesis), the invasion of white blood cells (leukocytes), a significant presence of tumor-associated macrophages (TAMs), and elevated levels of signaling chemicals called cytokines and chemokines [45].

Table 1. Interconnections between inflammation and different types of cancers

No	Type of cancer	The primary cause of inflammation	Inflammatory pathway	Reference
1	Gastric cancer	Helicobacter pylori	Activation of MEK/ERK, NF-κB, and β-catenin pathways	[78,79]
2	Liver cancer	Hepatitis B (HBV) and C (HCV)	Mediated by CD8+ T cells, NK cells, and macrophages producing ROS and nitrogen compounds	[54,80]
3	Pancreatic cancer	Smoking, genetic predisposition, and infections	Activation of NF-κB pathway	[57,81]
4	Colorectal cancer	Inflammatory bowel disease (IBD) leads to chronic intestinal inflammation	Immune cells produce cytokines, ROS, and RNS, causing DNA damage	[69,82]
5	Breast cancer	Abundance of Methyl bacterium and disruptions in estrogen metabolizing bacteria	Chronic inflammations cause disruptions in a cellular pathway	[69,83]

3.1. Gastric cancer

Helicobacter pylori produces one instance of cancer associated with inflammation [46]. By creating virulence factors, particularly cytotoxin-associated gene (Cag) A, *H. pylori* causes inflammatory reactions in the host [47]. Host inflammatory protein pathways, such as MEK/ERK, NF-κB, and β-catenin, are activated by this factor. About 70% of stomach adenocarcinomas, chronic gastritis, and mucosa-associated lymphoid tissue (MALT) lymphomas are caused by *H. pylori*, the first bacteria to be classified as a carcinogen by the WHO [48]. Research conducted on animal models has shown that mice infected exclusively with *H. pylori* display more widespread tumor profiles in comparison to germ-free and antibiotic-treated controls [48]. This indicates that *H. pylori* alone may not be enough to cause cancer and is likely to interact with other factors. Gastric cancer growth has been associated with Epstein-Barr Virus (EBV) infection, which is marked by aberrant gene methylation, specifically affecting *RUNX1*, *RBM5*, and *PSME1* [48]. Environmental variables, such as smoking, along with the host's genetic susceptibility (particularly, differences in genes encoding IL-1B, IL-10, and TNF) and interactions between specific bacterial virulence factors (cagPAI, T4SS, CagA), have an impact on the outcome of infection [49]. Despite a decline in the occurrence of stomach cancer in recent years as a result of enhanced knowledge about its causes and better treatment decision-making, it continues to be the second most common cause of cancer-related fatalities globally [50].

3.2. Liver cancer

Primary liver cancer, known as hepatocellular carcinoma (HCC), was the third leading cause of cancer-related deaths worldwide [51]. Liver inflammation and damage are associated with about 90% of HCC cases. There is a substantial correlation between chronic inflammation in the liver and the development of hepatic fibrosis, cirrhosis, and, finally, HCC [52]. Influenza with Hepatitis B and C together causes increased inflammation of the liver and factors the incidence of hepatocellular carcinoma (HCC) by more than twenty. He et al. found that HBV and HCV preferentially target $CD8^+$ T cells and natural killer (NK) cells to cause inflammation and liver injury. Some of the resulting inflammatory mediators include macrophages and neutrophils, reactive oxygen species (ROS), and nitrogen compounds. These factors increase the DNA damage connected with HCC and other forms of cancer [53,54]. *Helicobacter hepaticus* and other microorganisms involved in the digestive system are also proven to be related to liver cancer [55]. This is supported by the appearance of tumors and activation of

the NF-κB signaling pathway after introducing *H. hepaticus* in the gastrointestinal tract [56].

3.3. Pancreatic cancer

This aggravates inflammation of the pancreatic tissue and subsequently leads to an increased risk of pancreatic cancer as well as an increased number of pancreatic stellar cells [57]. Various causes are involved in developing long-term pancreatitis; some of them are effects of the environment, including smoking, heredity, the existence of metabolic disorders, and infections [58]. Research of the past done on experimental human and animal models suggests that certain types of bacteria may be behind the inflammation usually detected in pancreatic cancer patients [59]. The studies have revealed a strong relationship between the existence of periodontal infections and an individual more vulnerable to pancreatic cancer [60]. The 5-year survival rate of pancreatic cancer is among the lowest being at 3%–7%, and this is an inferior figure [61]. Bacterial identification may lead to the development of the specific medication against these periodontal germs, as well as the identification of the biomarkers useful for distinguishing high-risk individuals — such a discovery could contribute to total cancer inception prevention [62].

3.4. Colorectal cancer

CRC is the third most diagnosed cancer worldwide and is found to be more common in IBD patients, a chronic inflammatory condition that is on the rise. Among them, there are indicator features of inflammation in the intestines associated with IBD: the infiltration of immune cells — macrophages, neutrophils, and others [63]. Patients with IBD often have inflammation and ulcerations, and the cells produce cytokines, as this production enhances free radicals, proteolytic enzymes, and inflammatory reactions [61,64].

RNS and ROS are excessive in inflammatory bowel diseases, which have been suggested to promote tumor growth in the intestinal tract [65]. DNA damage due to ROS/RNS accumulation and external mutagen activation leads to cancer cell migration and spreading to adjacent tissues [66]. Furthermore, comparing the molecular signals produced in inflammatory bowel disease shows remarkable similarities with those produced in colorectal cancer. It is a critical factor that promotes tumor development in colorectal cancer. Cytokines are defined as the collection of molecules, whereas the one referred to as interleukin [67]. Diversity, an imbalance in the gut microbial community, relates to inflammation in inflammatory bowel disease (IBD) and colorectal cancer (CRC) risk. Genome sequencing studies have demonstrated an association between a particular bacterial species to be involved in the development of colon cancer. This bacterial species has higher quantities in the tissues of patients with this disease [68]. Its exact role is not clearly understood, but it significantly affects disease progression [69].

3.5. Breast and prostate cancer

The leading cause of cancer-related mortality in women is breast cancer, whereas in men, it is prostate cancer [70]. Inflammation and bacteria have been implicated in the development of various illnesses in previous research [71]. Cancer patients show a dramatic decrease in the presence of Methyl bacteria in breast tissue, which is linked to tumors that have a higher likelihood of spreading. Disruptions in bacteria that participate in estrogen metabolism can lead to an elevation of estrogen levels in the bloodstream, thereby raising the probability of developing breast cancer [72,73]. As could be expected, there invariably exists inflammatory cells in the rectal vicinity together with prostate cancer in men [74]. Anaerobic bacteria may make themselves noticeable if the tumor

grows and reduces oxygen levels in the body. Although it has been challenging to prove that bacteria have a role in prostate cancer, there is a link between inflammatory changes and prostate infection [75]. This link has the potential to lower the prostate's protective barrier, which in turn can aid in the progression of cancer. The risk of developing a prostate infection is associated with shifts in the urinary tract's microbial composition [76,77].

4. Therapeutic interventions for cancers

Cancer treatment involves a comprehensive strategy that includes different approaches to therapy and nutritional recommendations. Chemotherapy involves using platinum-based compounds and other drugs, causing tumor cells to undergo programmed cell death and toxicity. However, the effectiveness of chemotherapy can be affected by the microorganisms in the gut [84,85]. This would imply that probiotics can improve treatment regimens while reducing the side effects of chemotherapy. Another strength of cancer care that has made rapid progress in cancer treatment is immunotherapy, a remarkably immune checkpoint inhibitor. The relevance of bacterial composition to patient clinical outcomes stems from the evidence that the gut microbiome can alter the pharmacologic actions of drugs.

People should consume more fruits, vegetables, and fiber-rich food to manage and prevent cancer. Lignans and isothiocyanates, other micronutrients found in the diet, have anti-cancer properties. This demonstrates that some foods have potential in the treatment of cancer. In summary, there is an opportunity for better cancer treatment outcomes and better overall health of patients by combining two medical approaches, immunotherapy, and chemotherapy, and making dietary adjustments [83].

5. Conclusion

In conclusion, this review has provided in-depth knowledge of the link between cancer, health, and inflammation, focusing on various mechanisms underlying cancer progression. This study has emphasized the importance of examining chronic microbial infections and inflammation in therapeutic approaches since they play a part in the initiation and progression of cancer. This study is critical because it focuses on the many factors contributing to cancer development through inflammation and demonstrates the role of bacteria in promoting tumor growth. Investigating these relationships in the future will empower the creation of novel treatment paradigms that focus on the cancer cells and target the cause of inflammation. This will help the research community develop better ways of managing cancer in the future. This may result in better patient outcomes and a more evolved approach to cancer.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Ferlay J, Soerjomataram I, Dikshit R, et al., 2015, Cancer Incidence and Mortality Worldwide: Sources, Methods and Major Patterns in GLOBOCAN 2012. International Journal of Cancer, 136(5): 359–386.

[2] Fidler MM, Soerjomataram I, Bray FJI, 2016, A Global View on Cancer Incidence and National Levels of the Human

Development Index. International Journal of Cancer, 139(11): 2436–2446.

[3] McGuire S, 2016, World Cancer Report 2014. Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer, WHO Press, 2015. Advances in Nutrition, 7(2): 418–419.

[4] Fidler MM, Bray F, Soerjomataram I, 2018, The Global Cancer Burden and Human Development: A Review. Scandinavian Journal of Public Health, 46(1): 27–36.

[5] Clinton SK, Giovannucci EL, Hursting SD, 2020, The World Cancer Research Fund/American Institute for Cancer Research Third Expert Report on Diet, Nutrition, Physical Activity, and Cancer: Impact and Future Directions. The Journal of Nutrition, 150(4): 663–671.

[6] Pati S, Irfan W, Jameel A, et al., 2023, Obesity and Cancer: A Current Overview of Epidemiology, Pathogenesis, Outcomes, and Management. Cancers, 15(2): 485.

[7] Zhang CH, Xu DK, Long J, et al., 2023, Human Resource Allocation in Centers for Disease Control and Prevention at County-level and its Equity in Chongqing Municipality, 2019–2021: An Online Survey. Chinese Journal of Public Health, 39(12): 1620–1624.

[8] Rooney MM, Miller KN, Plichta J, 2023, Genetics of Breast Cancer: Risk Models, Who to Test, and Management Options. The Surgical Clinics of North America, 103(1): 35–47.

[9] Nost TH, Alcala K, Urbarova I, et al., 2021, Systemic Inflammation Markers and Cancer Incidence in the UK Biobank. European Journal of Epidemiology, 36(8): 841–848.

[10] Miller ES, Apple CG, Kannan KB, et al., 2019, Chronic Stress Induces Persistent Low-grade Inflammation. American Journal of Surgery, 218(4): 677–683.

[11] Rohleder N, 2014, Stimulation of Systemic Low-grade Inflammation by Psychosocial Stress. Psychosomatic Medicine, 76(3): 181–189.

[12] Orazi GD, Cordani M, Cirone M, et al., 2021, Oncogenic Pathways Activated by Pro-inflammatory Cytokines Promote Mutant p53 Stability: Clue for Novel Anticancer Therapies. Cellular and Molecular Life Sciences, 78(5): 1853–1860.

[13] Choi Y, Kim JK, Yoo JY, 2014, NFKB and STAT3 Synergistically Activate the Expression of FAT10, a Gene Counteracting the Tumor Suppressor p53. Molecular Oncology, 8(3): 642–655.

[14] Kartikasari AER, Huertas CS, Mitchell A, et al., 2021, Tumor-induced Inflammatory Cytokines and the Emerging Diagnostic Devices for Cancer Detection and Prognosis. Frontiers in Oncology, 2021(11): 692142.

[15] Yadav A, Kumar B, Datta J, et al., 2011, IL-6 Promotes Head and Neck Tumor Metastasis by Inducing Epithelial–mesenchymal Transition via the JAK-STAT3-SNAIL Signaling Pathway. Molecular Cancer Research, 9(12): 1658–1667.

[16] Chang WP, Lin CC, 2017, Relationships of Salivary Cortisol and Melatonin Rhythms to Sleep Quality, Emotion, and Fatigue Levels in Patients with Newly Diagnosed Lung Cancer. European Journal of Oncology Nursing, 2017(29): 79–84.

[17] Wohleb ES, McKim DB, Sheridan JF, et al., 2015, Monocyte Trafficking to the Brain with Stress and Inflammation: A Novel Axis of Immune-to-brain Communication that Influences Mood and Behavior. Frontiers in Neuroscience, 2015(8): 447.

[18] Sun Y, Koyama Y, Shimada S, 2022, Inflammation from Peripheral Organs to the Brain: How Does Systemic Inflammation Cause Neuroinflammation? Frontiers in Aging Neuroscience, 2022(14): 903455.

[19] Weber MD, Godbout JP, Sheridan JF, 2017, Repeated Social Defeat, Neuroinflammation, and Behavior: Monocytes Carry the Signal. Neuropsychopharmacology, 42(1): 46–61.

[20] Hu H, Yang X, He Y, et al., 2022, Psychological Stress Induces Depressive-like Behavior Associated with Bone Marrow-derived Monocyte Infiltration into the Hippocampus Independent of Blood-brain Barrier Disruption. Journal of Neuroinflammation, 19(1): 208.

[21] Vignjevic PS, Budec M, Markovic D, et al., 2016, Macrophage Migration Inhibitory Factor is an Endogenous Regulator of Stress-induced Extramedullary Erythropoiesis. Histochemistry and Cell Biology, 146(3): 311–324.

[22] Gregory JL, Morand EF, McKeown SJ, et al., 2006, Macrophage Migration Inhibitory Factor Induces Macrophage Recruitment via CC Chemokine Ligand 2. Journal of Immunology, 177(11): 8072–8079.

[23] Nasiri E, Sankowski R, Dietrich H, et al., 2020, Key role of MIF-related Neuroinflammation in Neurodegeneration and Cognitive Impairment in Alzheimer's Disease. Molecular Medicine, 26(1): 34.

[24] Wild CP, Stewart BW, Wild C, 2014, World Cancer Report 2014. World Health Organization Geneva, Switzerland.

[25] Bray F, Ferlay J, Soerjomataram I, et al., 2018, Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians, 68(6): 394–424.

[26] Wolf AMD, Oeffinger KC, Shih TY, et al., 2023, Screening for Lung Cancer: 2023 Guideline Update from the American Cancer Society. CA: A Cancer Journal for Clinicians, 74(1): 50–81.

[27] Siegel RL, Miller KD, Wagle NS, et al., 2023, Cancer Statistics, 2023. CA: A Cancer Journal for Clinicians, 73(1): 17–48.

[28] Isailovic N, Daigo K, Mantovani A, et al., 2015, Interleukin-17 and Innate Immunity in Infections and Chronic Inflammation. Journal of Autoimmunity, 2015(60): 1–11.

[29] Abdulkhaleq LA, Assi MA, Abdullah R, et al., 2018, The Crucial Roles of Inflammatory Mediators in Inflammation: A Review. Veterinary World, 11(5): 627–635

[30] Serhan CN, Dalli J, Colas RA, et al., 2015, Protectins and Maresins: New Pro-resolving Families of Mediators in Acute Inflammation and Resolution Bioactive Metabolome. Biochimica et Biophysica Acta, 1851(4): 397–413.

[31] Uttara B, Singh AV, Zamboni P, et al., 2009, Oxidative Stress and Neurodegenerative Diseases: A Review of Upstream and Downstream Antioxidant Therapeutic Options. Current Neuropharmacology, 7(1): 65–74.

[32] Anwikar S, Bhitre M, 2010, Study of the Synergistic Anti-inflammatory Activity of Solanum Xanthocarpum Schrad and Wendl and Cassia fistula Linn. International Journal of Ayurveda Research, 1(3): 167–171.

[33] Nguyen TT, 2012, Systems Biology Approaches to Corticosteroid Pharmacogenomics and Systemic Inflammation, thesis, The State University of New Jersey.

[34] Porter S, 2013, Tidy's Physiotherapy E-Book. Elsevier Health Sciences, Amsterdam.

[35] Goljan EF, 2013, Rapid Review Pathology: With Student Consult Online Access. Elsevier, Philadelphia.

[36] Kumar V, Abbas AK, Aster JC, 2013, Robbins Basic Pathology. Elsevier Health Sciences, Amsterdam.

[37] Seta F, Bachschmid M, 2012, Cyclooxygenase Pathway of the Arachidonate Cascade. Published online, eLS.

[38] Mantovani A, Dinarello CA, Molgora M, et al., 2019, Interleukin-1 and Related Cytokines in the Regulation of Inflammation and Immunity. Immunity, 50(4): 778–795.

[39] Lawrence T, Natoli G, 2011, Transcriptional Regulation of Macrophage Polarization: Enabling Diversity with Identity. Immunology, 11(11): 750–761.

[40] Roszer T, 2015, Understanding the Mysterious M2 Macrophage through Activation Markers and Effector Mechanisms. Mediators of Inflammation, 2015: 816460.

[41] Lamkanfi M, Dixit VM, 2014, Mechanisms and Functions of Inflammasomes. Cell, 157(5): 1013–1022

[42] Medzhitov R, 2008, Origin and Physiological Roles of Inflammation. Nature, 454(7203): 428–435.

[43] Shacter E, Weitzman SA, 2002, Chronic Inflammation and Cancer. Oncology, 16(2): 217–232.

[44] Rubin DC, Shaker A, Levin MS, 2012, Chronic Intestinal Inflammation: Inflammatory Bowel Disease and Colitis-associated Colon Cancer. Frontiers in Immunology, 2012(3): 107.

[45] Coussens LM, Werb Z, 2002, Inflammation and Cancer. Nature, 420(6917): 860–867.

[46] Fox JG, Wang TC, 2007, Inflammation, Atrophy, and Gastric Cancer. The Journal of Clinical Investigation, 117(1): 60–69.

[47] Wang F, Meng W, Wang B, et al., 2014, Helicobacter pylori-induced Gastric Inflammation and Gastric Cancer. Cancer Letters, 345(2): 196–202.

[48] Mueller D, Tegtmeyer N, Brandt S, et al., 2012, c-Src and c-Abl Kinases Control Hierarchic Phosphorylation and Function of the CagA Effector Protein in Western and East Asian Helicobacter pylori strains. The Journal of Clinical Investigation, 122(4): 1553–1566.

[49] Ekstrom AM, Held M, Hansson LE, et al., 2001, Helicobacter pylori in Gastric Cancer Established by CagA Immunoblot as a Marker of Past Infection. Gastroenterology, 121(4): 784–791.

[50] Peek RM Jr, Crabtree JE, 2006, Helicobacter Infection and Gastric Neoplasia. The Journal of Pathology, 208(2): 233–248.

[51] El-Serag HB, Rudolph KL, 2007, Hepatocellular Carcinoma: Epidemiology and Molecular Carcinogenesis. Gastroenterology, 132(7): 2557–2576.

[52] Bishayee A, 2014, The Inflammation and Liver Cancer, in Inflammation and Cancer: Advances in Experimental Medicine and Biology, 816. Springer, Basel, 401–435.

[53] Buchmann P, Dembek C, Kuklick L, et al., 2013, A Novel Therapeutic Hepatitis B Vaccine Induces Cellular and Humoral Immune Responses and Breaks Tolerance in Hepatitis B Virus (HBV) Transgenic Mice. Vaccine, 31(8): 1197–1203.

[54] Nakamoto Y, Guidotti LG, Kuhlen CV, et al., 1998, Immune Pathogenesis of Hepatocellular Carcinoma. The Journal of Experimental Medicine, 188(2): 341–350

[55] Jackson S, Bartek J, 2009, The DNA-damage Response in Human Biology and Disease. Nature, 461(7267): 1071–1078.

[56] Fox JG, Feng Y, Theve EJ, et al., 2010, Gut Microbes Define Liver Cancer Risk in Mice Exposed to Chemical and Viral Transgenic Hepatocarcinogens. Gut, 59(1): 88–97.

[57] Algul H, Treiber M, Lesina M, et al., 2017, Mechanisms of Disease: Chronic Inflammation and Cancer in the Pancreas—A Potential Role for Pancreatic Stellate Cells? Gastroenterology & Hepatology, 4(8): 454–462.

[58] Kleeff J, Whitcomb D, Shimosegawa T, et al., 2017, Chronic Pancreatitis. Nature Reviews Disease Primers, 3(1): 1–18.

[59] Mima K, Nakagawa S, Sawayama H, et al., 2017, The Microbiome and Hepatobiliary-Pancreatic Cancers. Cancer Letters, 2017(402): 9–15.

[60] Fan X, Alekseyenko AV, Wu J, et al., 2018, Human Oral Microbiome and Prospective Risk for Pancreatic Cancer: A Population-based Nested Case-control Study. Gut, 67(1): 120–127.

[61] Tenesa A, Dunlop MG, 2009, New Insights into the Aetiology of Colorectal Cancer from Genome-wide Association Studies. Nature Reviews: Genetics, 10(6): 353–358

[62] Mackner LM, Greenley RN, Szigethy E, et al., 2013, Psychosocial Issues in Pediatric Inflammatory Bowel Disease: Report of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition. Journal of Pediatric Gastroenterology and Nutrition, 56(4): 449–458.

[63] Grivennikov SI, Greten FR, Karin M, 2010, Immunity, Inflammation, and Cancer. Cell, 140(6): 883–899.

[64] Benhayon D, Youk A, McCarthy FN, et al., 2013, Characterization of Relations among Sleep, Inflammation, and Psychiatric Dysfunction in Depressed Youth with Crohn Disease. Journal of Pediatric Gastroenterology and Nutrition, 57(3): 335–342.

[65] Stokkers PC, Hommes DW, 2004, New Cytokine Therapeutics for Inflammatory Bowel Disease. Cytokine, 28(4–5): 167–173.

[66] Greten FR, Eckmann L, Greten TF, et al., 2004, IKKbeta Links Inflammation and Tumorigenesis in a Mouse Model of Colitis-associated Cancer. Cell, 118(3): 285–296.

[67] Hussain SP, Hofseth LJ, Harris CC, 2003, Radical Causes of Cancer. Nature Reviews: Cancer, 3(4): 276–285.

[68] Francescone R, Hou V, Grivennikov SI, 2015, Cytokines, IBD, and Colitis-associated Cancer. Inflammatory Bowel Diseases, 21(2): 409–418.

[69] Neurath MF, 2014, Cytokines in Inflammatory Bowel Disease. Nature Reviews: Immunology, 14(5): 329–342.

[70] Popivanova BK, Kitamura K, Wu Y, et al., 2008, Blocking TNF-alpha in Mice Reduces Colorectal Carcinogenesis Associated with Chronic Colitis. The Journal of Clinical Investigation, 118(2): 560–570.

[71] Atreya R, Mudter J, Finotto S, et al., 2000, Blockade of Interleukin 6 Trans Signaling Suppresses T-cell Resistance against Apoptosis in Chronic Intestinal Inflammation: Evidence in Crohn Disease and Experimental Colitis in vivo. Nature Medicine, 6(5): 583–588.

[72] Kai Y, Takahashi I, Ishikawa H, et al., 2005, Colitis in Mice Lacking the Common Cytokine Receptor Gamma Chain is Mediated by IL-6-producing CD4+ T Cells. Gastroenterology, 128(4): 922–934.

[73] Ng SC, Benjamin JL, McCarthy NE, et al., 2011, Relationship between Human Intestinal Dendritic Cells, Gut Microbiota, and Disease Activity in Crohn's Disease. Inflammatory Bowel Diseases, 17(10): 2027–2037.

[74] Izcue A, Hue S, Buonocore S, et al., 2008, Interleukin-23 Restrains Regulatory T Cell Activity to Drive T Cell-dependent Colitis. Immunity, 28(4): 559–570.

[75] Cox JH, Kljavin NM, Ota N, et al., 2012, Opposing Consequences of IL-23 Signaling Mediated by Innate and Adaptive Cells in Chemically Induced Colitis in Mice. Mucosal Immunology, 5(1): 99–109.

[76] Yen D, Cheung J, Scheerens H, et al., 2006, IL-23 is Essential for T Cell-mediated Colitis and Promotes Inflammation via IL-17 and IL-6. The Journal of Clinical Investigation, 116(5): 1310–1316.

[77] Fujino S, Andoh A, Bamba S, et al., 2003, Increased Expression of Interleukin 17 in Inflammatory Bowel Disease. Gut, 52(1): 65–70.

[78] Lyon DE, Mohanraj L, Kelly DL, et al., 2014, Health Promoting Life-style Behaviors and Systemic Inflammation in African American and Caucasian Women Prior to Chemotherapy for Breast Cancer. Health Promotion Perspectives, 4(1): 18–26.

[79] Coussens LM, Werb Z, 2002, Inflammation and Cancer. Nature, 420(6917): 860–867.

[80] Kochi T, Shimizu M, Shirakami Y, et al., 2015, Utility of Apc-mutant Rats with a Colitis-associated Colon Carcinogenesis Model for Chemoprevention Studies. European Journal of Cancer Prevention, 24(3): 180–187.

[81] Hardaway AL, 2015, Adipocyte-induced Inflammation in Prostate Tumor Progression in Bone: Role of CXCR2 and Osteopontin Signaling Axes, thesis, Wayne State University.

[82] Ohnishi S, Hiramoto K, Ma N, et al., 2021, Chemoprevention by Aspirin against Inflammation-related Colorectal Cancer in Mice. Journal of Clinical Biochemistry and Nutrition, 69(3): 265–271.

[83] Armstrong H, Bording-Jorgensen M, Dijk S, et al., 2018, The Complex Interplay between Chronic Inflammation, the Microbiome, and Cancer: Understanding Disease Progression and What We Can Do to Prevent It. Cancers, 10(3): 83.

[84] Johnstone TC, Park GY, Lippard SJ, 2014, Lippard, Understanding and Improving Platinum Anticancer Drugs—

Phenanthriplatin. Anticancer Research, 34(1): 471–476.

[85] Bai, LK, Gao CZ, Liu QH, et al., 2017, Research Progress in Modern Structure of Platinum Complexes. Journal of Medicinal Chemistry, 2017(140): 349–382.

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