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Investigation the types cancer and role of opportunistic fungi in development

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Abstract :

«Cancer» is a serious and devastating «disease and one of the most common causes of death». In recent decades, the risk of developing various types of cancer has increased, enabling scientists to discover new methods of prevention and treatment to reduce mortality rates and thus enable its prevention in the near future. Based on previous studies, a clear link has been found between» pathogenic fungal« infections and the development of «cancer». This link is often seen in immunocompromised individuals, such as the elderly, children, those with HIV/AIDS, diabetes, and cancer patients.

Fungi are eukaryotic organisms that infect humans, causing skin and systemic diseases. They are transmitted through the inhalation of fungal spores. *Candida*, on the other hand, coexists with the gastrointestinal tract and skin, multiplying under certain conditions and entering the bloodstream when introduced into the body through medical devices such as catheters and organ transplants.

There are several different genetic and environmental factors that participation in the occurrence of cancer. Opportunistic fungi and the infections they cause are among the most important factors in the occurrence of the disease. Previous studies have shown that the most common fungi involved in the development of cancer are the *Candida* group, with its various species, such as *Candida albicans*, *Candida tropica*, and *Candida glabrata*, as well as various species of syngamous and cystic fungi. Fungal strains exhibit differences depending on the location of the tumor, and this is a starting point for exploring the role of fungi in the development of cancer through complex mechanisms, opening up horizons for innovative therapeutic strategies.

This article focuses on the role and mechanism of fungal infection in the occurrence of various types of cancer in humans, with an emphasis on the role of nutrients in fungal growth, spread, invasion, and cancer pathogenesis.

Keywords: cancer, fungal infection, immunocompromised , Opportunistic fungi.

الاستقصاء في انواع السرطان ودور الفطريات الانتهازية في تطوره

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مستخلص:

يعد السرطان مرض خطير ومدمر واحد اكثر اسباب الوفاة شيوعا ، في العقود الاخيرة زاد ارتفاع مخاطر الاصابة بأنواع مختلفة من السرطان بحيث مكن العلماء من اكتشاف طرق جديدة للوقاية والعلاج لتقليل معدل الوفيات وبالتالي تمكين الوقاية منه في المستقبل القريب . بناء على الدراسات السابقة وجد هناك صلة واضحة بين العدوى الفطرية المسببة للأمراض وتطور السرطان غالبا ما يرى هذا الارتباط لدى الاشخاص ضعيفي المناعة مثل كبار السن والاطفال والمصابين بفايروس نقص المناعة المكتسب (الايدز) ومرضى السكري والسرطان .

تعرف الفطريات بانها كائنات حية حقيقية النواة تصيب البشر وتسبب امراضا جلدية وجهازية وتنتقل عن طريق استنشاق الجراثيم الفطرية اما المبيضات فهي تتعايش مع الجهاز الهضمي والجلد وتتكاثر في ظل ظروف معينة وتنتقل الى الدم عند ادخالها الى الجسم عن طريق ادوات طبية مثل القسطرة وعمليات زرع الاعضاء.

هناك عدة عوامل وراثية وبيئية مختلفة تساهم في حدوث السرطان ، وان احد اهم عوامل الخطر هي الانواع الفطرية الانتهازية والعدوى التي تسببها ، بينت دراسات سابقة على ان اكثر الفطريات شيوعا والتي تشارك في تطور السرطان هي مجموعة المبيضات بأنواعها المختلفة مثل *Candida alicans,Candida tropica,Candida glabrata* فضلا عن انواع مختلفة من الفطريات التزاوجية والكيسية وتظهر سلالات الفطريات اختلافات اعتمادا على موقع الورم وتعد نقطة انطلاق لاكتشاف دور الفطريات في تطور السرطان من خلال اليات معقدة والتي تفتح افاقا لاستراتيجيات علاجية مبتكرة .

ركزت في هذه المقالة على دور والية العدوى الفطرية في حدوث انواع مختلفة من السرطان لدى البشر والتركيز على دور العناصر الغذائية في نمو وانتشار الفطريات وغزوها وتسببها في حدوث مرض السرطان .

الكلمات المفتاحية : السرطان، العدوى الفطرية، ضعيفي المناعة، الفطريات الانتهازية.

Introduction

Fungal infections pose a major threat to immunocompromised individuals, leading to increased rates of infection and mortality [1]. Fungi are eukaryotic organisms that form different sites in the human body. Fungi are represented by three main divisions: cystic, basidiomycete, and chytridiomycete , which greatly affect the health of the host and the occurrence and development of cancerous tumors [2].

Cancer tumors have a unique complex structure represented by bacteria, viruses, and fungi, and these organisms participate in tumor formation and development [3]. Cheng et al. (2024) showed that fungi affect tumor formation through several factors, including host immunity, biologically active metabolites, and genetic and epigenetic factors, all of which contribute to the enrichment of fungi in tumor tissues or the transformation from symbiotic fungi to pathogenic fungi]4] . The fungi that can transform from symbiotic lifestyles to pathogenic lifestyles such as colorectal cancer depend mainly on the pH, saliva flow rates, oxygen concentration, the immune and health status of the host, and others such as the use of antibiotics [5]

Le et al. (2023) pointed out the role of fungal infection in the occurrence of different types of cancer, including oesophageal, stomach, colon, rectum, lung, cervical, and ovarian cancer, in addition to other factors such as »age, smoking, diet, saturated fats, body weight, alcohol consumption, exposure to pollutants, and radioactivity«. These factors vary according to region and geographical location. Previous studies have shown that fungal infection can not only promote cancer, but can contribute to its treatment [5]. The most common fungal genera involved in cancer are *Fusarium verticilliodes, Aspergillus flavus, Aspergillus parasiticus, Candida glabrata*, and *Candida tropica* [4].

The current article aims to identify the role of fungal infection in each type of cancer and the fungal causes of each, in addition to the role of nutrients in the growth and reproduction of fungi and thus the development of cancer.

Fungal infections

About one billion people worldwide are affected by fungal infections that affect the skin, nails and hair, tens of

millions are affected by candidiasis and more than 150 million by other fungal diseases, the severity of the infection ranges from mucosal to cutaneous or severe systemic infections leading to death [6].

Fungi are known as eukaryotic organisms that infect humans and cause skin and systemic diseases and are transmitted by inhaling fungal spores, while Candida coexists with the digestive system and skin and multiplies under certain conditions and is transmitted to the blood when introduced into the body through medical devices such as catheters and organ transplants [7].Cancer patients treated with chemotherapy and other patients with weak immunity are at risk of fungal infections, which are a major cause of illness and death in cancer patients due to low neutrophil counts and exposure to fungal pathogens such as *Aspergillus* and *Fusarium* species, but most of them are caused by *Candida* species. Microbial infections can not only promote cancer but can help in its treatment. »*Candida*« is one of the genera most closely linked to cancer, such as *Candida glabrata, Candida tropica,* and other species such as *Aspergillus flavus, Aspergillus parasiticus, Fusarium verticilliodes*. It is necessary to distinguish between fungal infections and cancer[8].

Predictions of fungal species in cancerous tumors

Tumors are complex ecosystems consisting of cancer cells, immune cells, fibroblasts, and microbes. Tumor microbes are a good and integrated component of the tumor, which includes bacteria and fungi, which are determined by the type of cancer in the tumor tissue. In fact, each type of tumor contains a distinctive microbial composition. Tumor microbes can be used for multiple purposes, including distinguishing between normal and cancerous tissues, distinguishing between benign and malignant cancers, and between cancer patients who respond to drugs from those who do not respond to drugs, and between patients with a positive prognosis and those with a poor prognosis. Multiple types of yeasts, candida, and other types of fungi have been found that differ according to the type of cancerous tumors [9]. Figure (1) Types of cancers and the fungi that cause them.

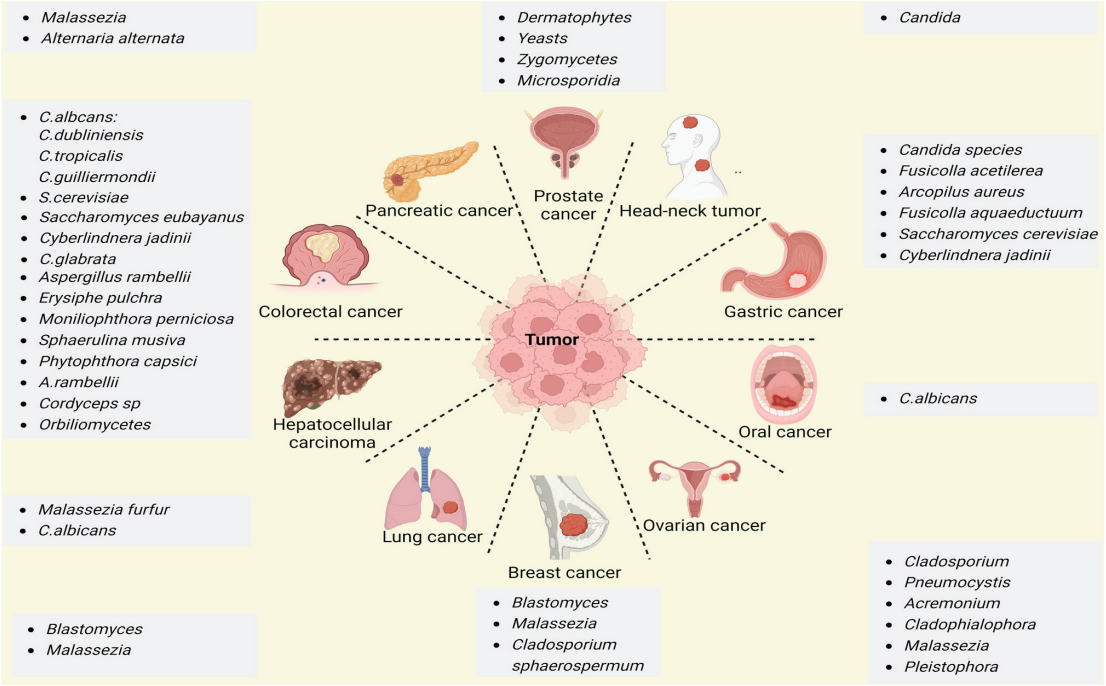

Figure (1)

Types of cancers and the fungi that cause them.(Cheng *et al.*,2024)

Risk factors associated with fungal infections

A wide range of risk factors contribute to the susceptibility of immune-compromised patients to fungal infections, including

1. Immunocompromised individuals undergoing chemotherapy, such as cancer patients, diabetics, AIDS patients, and others.

2. Neutropenia Low neutrophil counts significantly increase the risk of invasive

infections, especially *Aspergillus* and *Candida* species.

3. The use of broad-spectrum antibiotics can facilitate the development of opportunistic fungal infections.

4. Underlying diseases associated with cancer, such as diabetes and chronic lung disease, from a weak immune response.

Fungal pathogens exploit the weak immune status of their hosts by adhering to host tissues, as fungi produce substances that facilitate their adhesion to cells and epithelial tissues, which allows colonization and invasion, in addition to the formation of biofilms and immune evasion strategies, which in-

hibit the phagocytosis process and allow for continuation and spread. Moreover, the metabolites produced by fungi may affect the biological pathways that control the growth of cancer cells. For example, some fungal compounds may inhibit topomerase enzymes that play an important role in cancer cell division or activate signalling pathways that lead to cancer cell death. The diagnosis of fungal infection is of great importance through culture and sensitivity tests or serological tests and molecular methods [1].

Genetic and epigenetic factors of fungi

Fungi switch from commensal to pathogenic lifestyles. *Candida albicans* can colonize the intestine by activating the expression of the pro-inflammatory protease Saps specific to fungal hyphae and adhesion to cell surfaces Hyr1 [10]. Exposure of *Candida albicans* to the mammalian intestine can induce a growth shift that is driven by a transcription factor into a symbiont. These fungi can activate or repress iron uptake genes involved in virulence or colonization via the *Sef1/Sfu1*, *Wor1* genes. *Blastomyces dermatitis* suppresses the production of TGF-α, which can stimulate adhesion and pathogenic transformation. *Aspergillus fumigates* may activate a stress response program that is required for virulence. It is worth noting that the cAMP pathway plays an important role in inducing certain genes during transformation. Several *Candida* species that cause enteritis can produce more phospholipases. In addition, methylation H3K4 by *Sef1* is required for *Candida albicans* virulence through control of reactive oxygen species[11].

Other fungal mechanisms of tumorigenesis

There are several mechanisms that fungi possess that enable them to cause tumors, and through interactions between bacteria and fungi, they are linked to the formation of a pathogenic biofilm that acts as a barrier to protect the microbiota from the host immune system and potentially enhances the inflammatory response, Which may be involved in the occurrence of colon and rectal cancer. Metabolites produced by fungi which has an important impact in the occurrence of »hepatocellular carcinoma«, such as aflatoxin produced by species of the genus *Aspergillus* [12], by generating highly mutagenic DNA.

Candida albicans also generates nitrosamines and converts ethanol to acetaldehyde, an electrophilic and genotoxic substance that can affect DNA and protein repair and cause oxidative stress and lead to DNA damage. These substances work to raise levels of Reactive Oxygen Species (ROS) to stimulate mitochondrial dysfunction, which is associated with cytotoxicity. In addition, acetaldehyde and ethanol cause synergistic production In cells, which leads to disruption of the immune barrier [13]. The transformation of *Candida albicans* from yeast to filamentous form also stimulates B-cells to produce immunoglobulin's IgA , which can regulate fungal symbiosis in the intestine and bind to fungal hyphae to limit its spread [14]. The vesicles produced by extracellular fungi which has an important impact on the development of the disease, as they carry pigments, carbohydrates, proteins, nucleic acids and lipids, and are closely associated with virulence factors. They play a role in regulating fungal communities and enhancing the ability to cause diseases. They produce cytokines and enhance the production of TNF-α and TGF-β by phagocytic cells [4].

The role of fungal infection in oral cancer

Oral cancer develops in different parts of the human mouth including the tongue, cheeks, lips, gums, palate, salivary glands, tonsils and pharynx are also susceptible to cancer, but such cases occur less frequently [8].The main risk factors that promote the development of oral tumors were found to be alcohol consumption, viral infection and excessive exposure to ultraviolet rays for lip cancer[15], in addition to poor oral hygiene and smoking, which promotes the formation of keratin in the oral mucosa and diet [16]. Fungi such as *Candida* species are usually found in the mouth and are harmless under normal conditions. However, they can transform into a pathogenic form, causing oral candidiasis, which is the main fungal infection that occurs in the oral cavity and is usually caused by *Candida albicans* or other *Candida* species [17] This infection can range from mild to severe depending on the host's immunity. Candidiasis has long been associated with cancer treatment or complications of treatment. It was later discovered that this disease may be involved in the development of oral cancer [18]. A study

conducted in Taiwan revealed that individuals with Candida infection were more likely to develop oral cancer, especially in immunocompromised hosts [19]. *Candida* fungi have been linked to the development of cancer through the production of hydrolytic enzymes that metabolize alcohol into acetaldehyde. Acetylcholine is known to be a human carcinogen. *Candida* species possess alcohol dehydrogenase enzymes, which are necessary to convert ethanol into acetylcholine, a cell wall protein that is essential for fungal growth and metabolism [20].

Moreover, acetylcholine may interact with host cell proteins and stimulate the immune response. Its effect on cells is mainly due to oxidative stress, cell damage, cytokine induction, protein adducts or DNA residues, DNA cross-linking, or chromosomal aberrations. These events lead to mutations within the host DNA and disruption of protein function essential for normal host function and cell division, which in turn leads to tumor development and progression. Another mechanism by which *Candida* species help in tumor induction comes from their ability to invade host tissues and produce nitrosamines, which have been found to cause cancer in animal models. Nitrosamine compounds have been found to activate primary tumors and cause tissue dysfunction, as shown in Figure (2).

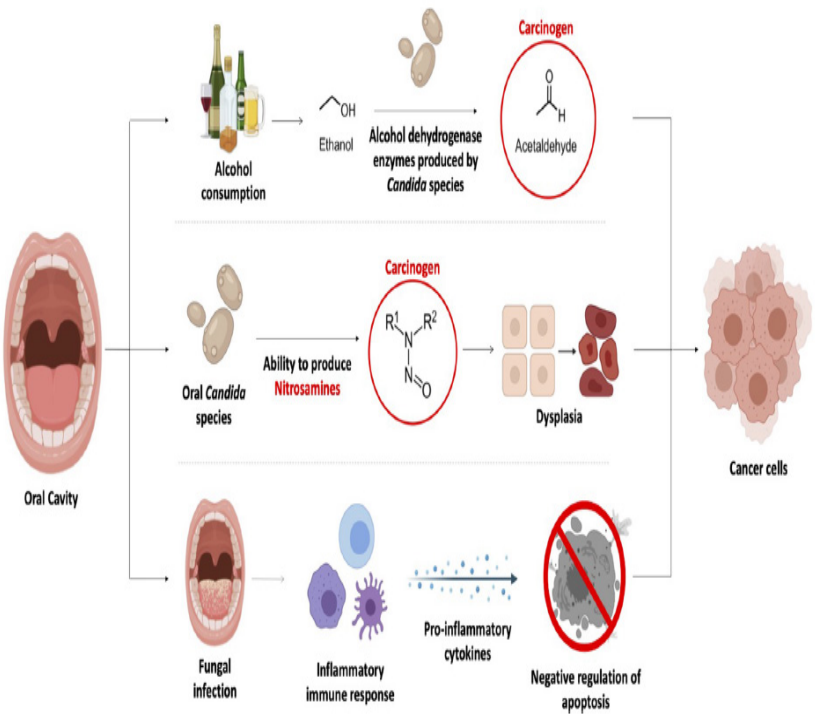

Figure (2)
The different ways in which fungal species participate in the development of oral cancer.
(Wu *et al.*,2024)

They showed that activated nitrosamines can mutate a primary cancer causing gene in the laboratory. They used PEC plasmids containing the primary cancer-causing gene *C-Ha-ras*, which is involved in regulating cell division in the human body and N3H3T3 cells [21]. Furthermore, *Candida* has the ability to produce biofilms, readily adhere to cell surfaces, and invade oral epithelial cells. These traits are virulence factors that play a major role in tumor development, especially through infection and inflammation. During the inflammatory process, cytokines such as IL-6, IL-17A are produced by T helper cells (Th17), which in turn activate the wnt signalling pathway and the nuclear factor-κB signalling pathθ way. Overexpression of »pro-inflammatory cytokines such as IL-6« is a pivotal point in tumorigenesis through negative regulation of apoptosis, which strongly affects cell cycles [22].

The "role of fungal infection in oesophageal cancer"

"Oesophageal cancer" ranks as the sixth leading cause of cancer-related deaths, and the eighth largest cause of cancer globally. Histologically, this disease is classified into two categories: oesophageal adenocarcinoma, which affects the lower part of the oesophagus, and oesophageal squamous cell carcinoma, which affects the middle and upper part of the oesophagus. There are several factors that influence the onset of the disease, including "smoking, drinking alcohol, consuming hot beverages and foods, malnutrition, and exposure to pathogenic and opportunistic microorganisms". The fungus *Candida albicans* is one of the most common species associated with people with oesophageal cancer [8]. *Candida albicans* is one of the most common strains associated with oesophageal cancer [8]. According to a study by [23], patients with weakened immune systems are more likely to develop oesophageal candidiasis. The disease is caused by several mutations that ultimately affect the pathways that produce interleukin-17. One of these «mutations» is an acquisition mutation, where genetic analysis amplifies the "immune" response of "Th1" cells, ultimately reducing interleukin-17 production[8].

The "role of fungal infection in gastric cancer"

"Gastric cancer" ranks as the fourth

leading cause of cancer and the second leading cause of death in all malignant tumors worldwide. Gastric cancer is classified into four types: sporadic gastric cancer, early gastric cancer, gastric stump cancer, and hereditary diffuse gastric cancer. The factors for this type are smoking, alcohol consumption, blood type A, mycotoxins, and infections. A study has shown that fungi constitute about 70% of the digestive tract of adults and their number is increasing [4]. The presence of these fungi may contribute to gastric cancer, as it was found that the increase in *Candida* is associated with the »enrichment of genes involved in cytokine interactions, host immunity, and inflammation , including IL-1A, IL-1B, IL-6» [24].

The "role of fungal infection in colorectal cancer"

"Colorectal cancer" is the most common type of cancer worldwide, and it is the third leading cause of cancer and death. Colorectal cancer is classified into three distinct categories. "Most point mutations cause this type of cancer and occur in the genes *APC, Dcc, Tp53, kRAS*. Point mutations also occur in another allele of the mutated gene". This inherited form is divided into two groups: FAP (familial adenomatous polyposis) and HNPCC (Hereditary non-polyposis CRC). This causes »mutations in DNA repair proteins« such as (PMS2, PMS1, MLH6, MLH1, MSH2) [8]. "Environmental" and genetic risk factors play an important role in determining colorectal cancer. Non-modifiable risk factors are classified, such as race, gender, age, cystic fibrosis, and cholecystectomy, in addition to non-modifiable risk factors such as obesity and diet. Smoking, alcohol, diabetes, and insulin resistance, and among the fungi associated with colorectal cancer are *Candida albicans , Phoma , Malassezia , Trichosporon, Cladosporium, Histoplasma ,Cryptococcus*, and *Aspergillus* [25].

The role of fungal infection in pancreatic cancer

Pancreatic cancer is one of the most deadly cancers worldwide and the burden is mainly attributed to the fact that the probability of cure is relatively low and the majority of patients are diagnosed in stages III and IV of cancer [26]. A study indicated that obesity, malnutrition, diabetes, chronic pancreatitis and excessive alcohol con-

sumption are associated with tumor formation in the pancreas [27] A study showed that there is an abundance of fungal species in tumor tissues that can accelerate pancreatic tumorigenesis and that Lectin activation also contributes to the increased emergence and spread of pancreatic cancer [28].

"**The role of fungal infection in liver cancer**"

"Liver cancer ,"specially "hepatocellular carcinoma", has become the third leading cause of cancer-related deaths. Previous studies have shown the diversity and increase of fungi and yeasts in patients with "hepatocellular carcinoma". The abundance of *Candida albicans* was significantly higher in patients with "hepatocellular carcinoma" in stages III and IV than in stages I and II. Abnormal colonization by fungi leads to metabolic changes and accelerates the progression of hepatocellular carcinoma [29]. In addition, many fungi such as *Aspergillus flavus* and *Aspergillus parasiticus* can be found widely in various crops such as cereals, oil seeds, nuts and spices, where the liver is the main target organ and the most harmful type of aflatoxin, such as exposure to high doses of it leads to acute hepatitis and even death and can cause immune- suppression, nutritional disorders and tumors. It is known that the oxidation of aflatoxin is an essential part of the process of genotoxicity and thus in the development of cancer, as it is metabolized in the liver by CYP450 enzymes and converted to an epoxide [30]. This metabolite has a strong affinity for DNA, which leads to the formation of additional products that enhance DNA mutations and participation in the occurrence of hepatocellular carcinoma. Aflatoxin-B may synergize with other risk factors such as hepatitis-B infection, which increases the risk of developing hepatocellular carcinoma [30].

The "role of fungal infection in lung cancer"

Lung cancer is one of the most common causes of "cancer" death and men are more susceptible to infection than women. One of the main causes of "lung cancer" is the disruption of molecular pathways of lung cells, which alters normal cell growth, differentiation and programmed cell death. In general, lung cancer exists in two forms, the first is known as "non-small cell lung cancer", which consti-

tutes 85% of cases, and small cell lung cancer constitutes 15%. Many internal and external factors are risk factors for lung cancer, including "smoking, arsenic in drinking water, radon gas, tuberculosis, chronic obstructive pulmonary disease", HIV infection, and mutations in the *BRAF*, *KRAS*, *EGFR* genes, etc. One of the risk factors for lung cancer is "immunocompromised" people who become susceptible to lung diseases through exposure to opportunistic fungi such as »*Aspergillus*«, *Cryptococcus* and "*Pneumocystis*". It has also been proven that patients with pulmonary aspergillosis who receive corticosteroids are susceptible to pneumonia and increased exacerbation of the disease. Cancer. A study has shown that opportunistic dimorphic fungal pathogens such as *Talaromyces marneffei* are the causative agent of Talaromycosis and thus are susceptible to lung cancer [8]. as shown in Figure (3).

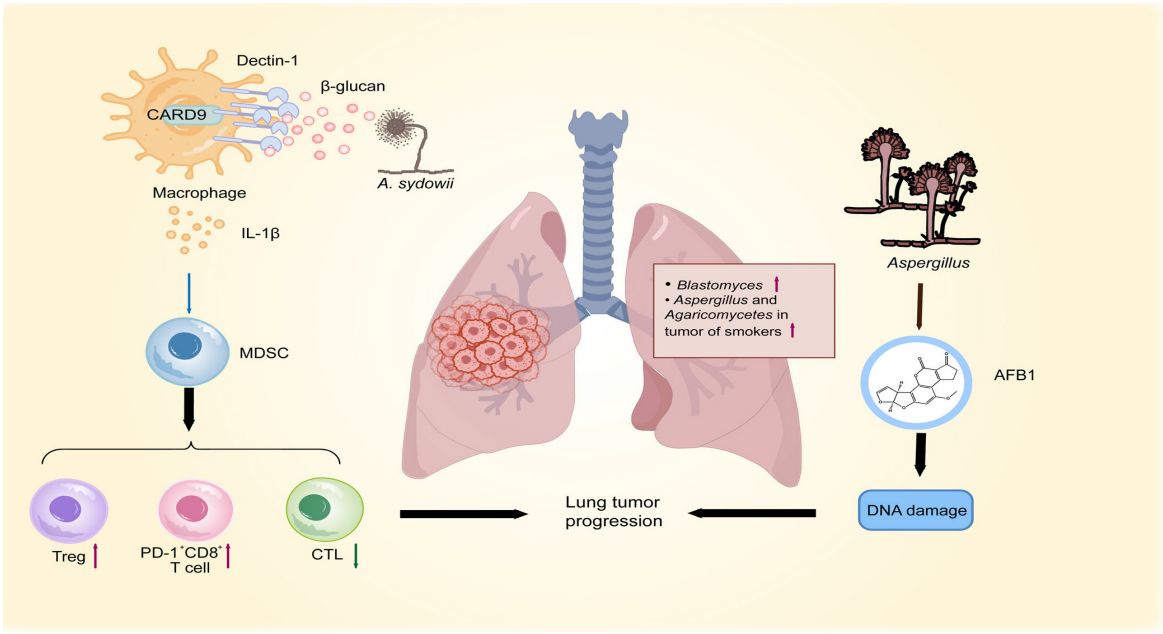

Figure (3)
The functional role of fungi in the development of lung cancer (Wu *etal.*,2024)

The "role of fungal infection in cervical cancer"

"Cervical cancer" is the third most common type of cancer in the female reproductive system. There are a number of factors that increase the risk of cervical cancer, including multiple births, obesity, sexual behaviour, diet,

multiple births, "prolonged use of hormonal contraceptives, poor socioeconomic status, smoking, multiple pregnancies, and the presence of bacterial, fungal, and viral causes". The most common fungal species that cause inflammation and cervical cancer are *Candida*, *Malassezia*, *Sporidiobolaeae*, and *Saccharomyces* [31].

The "role of fungal infection in ovarian cancer"

Ovarian cancer ranks seventh among the types of cancer that affect women. Ovarian cancer is divided pathologically into two types: epithelial ovarian cancer and reproductive ovarian cancer. Risk factors include continuous "ovulation, hormonal factors such as family history, genetic predisposition such as mutations in genes, race, and diet" (low fiber intake, vitamin D, obesity, smoking, and alcohol consumption). Several types of fungi have been isolated from ovarian cancer samples such as *Acremonium*, *Cladophialophora* , *Malassezia* , *Microsporidia* , *Candida*, *Cryptococcus*, *Pencillium*, *Rhodotorula gonadotropins* [32].

The "role of fungal infection in breast cancer"

Breast cancer ranks second in prevalence among women over the age of forty, compared to other cancer types. Breast cancer is classified according to its surface receptors into endocrine receptors (estrogen and progesterone receptors). Studies have revealed the presence of fungi in breast cancer tumors such as *Malassezia* and *Blastomyces* in abundance. The most important risk factors are genetic predisposition , family history, breastfeeding , obesity, and others [22].

The role of fungal infection in skin cancer

Skin cancer is the most common type of cancer in white individuals and is classified into melanoma and non-melanoma. There are several factors that lead to skin cancer, including exposure to ultraviolet rays, fair skin, aging, chemicals, exposure to radiation, weak immune system, and fungal infection. Most of the fungi that contribute to skin cancer are *Candida*, such as *Candida albicans*, *Candida tropica*, *Candida glabrata*, and *Candida parapsilosis* was isolated from a patient suffering from skin cancer, in addition to several filamentous fungi belonging to the cyst fungi group and incomplete [33].

Nutritional regulation of mycobiome and cancer development

Previous studies have shown that the associated fungi are involved in regulating the progression of cancer through the secretion of biologically active substances. Diets greatly affect the intestinal metabolic environment, which leads to changing the lifestyle of fungi. A small number of fungi within the tumor can be affected by the abnormal microenvironment after re- programming the tumor metabolism. Nutrients such as "cholesterol, carbohydrates, proteins and minerals play crucial physiological" roles in the growth, reproduction and pathogenesis of invasive diseases of the normal mycobiome. Fungi can specifically sense nutritional changes in the microenvironment and thus produce distinct metabolic products in response, which may act as signalling molecules. They also adapt to their lifestyle, such as in the transformation from symbionts to pathogens. Antifungal factors are manipulated by nutrients and tumor formation. The most important substances are [34]. as shown in Figure (4).

Alcohol consumption

Alcoholic beverages are a special food component worldwide and are often consumed with food. Alcohol contains seven calories per gram consumed and evidence has shown that alcohol consumption contributes to approximately 4% of »cancer« cases worldwide. Alcohol consumption increases the risk of several types of cancer including »colorectal, liver, breast«, etc.[35]. The fungal species can be changed and interact with chronic alcohol consumption [13]. Ethanol produced by *Candida albicans* stimulates the production of methyl-phenaziuq-carboxylic acid and alcohol increases intestinal Th17 cells specific to *Candida albicans*, which migrate to the liver and promote liver disease via IL17a receptor signalling in "Kupffer cells" [29]. Excessive alcohol consumption also causes an imbalance in the fungus and an overgrowth of *Candida*, which leads to fungal "beta-glucan transfer and IL-1B secretion via C-type lectin-like CLEC7A receptors« on »Kupffer cells", which contributes to liver cell damage and promotes the development of ethanol-induced liver disease [13].

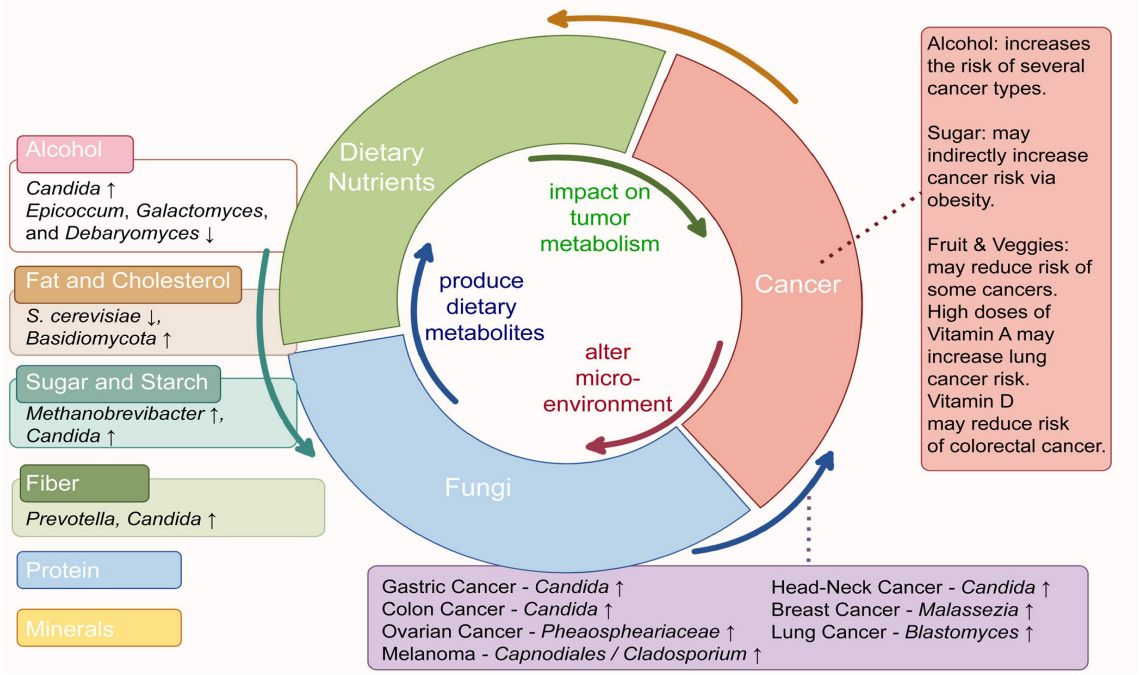

Figure (4) The triple interaction between nutrition, fungi and the host in cancer development (Huet *et al.*,2022)

Fats and "cholesterol"

"Cholesterol" and fats produce more calories per gram, doubling the amount of "carbohydrates". Epidemiological statistics and clinical studies have reported a significant positive association between fat and cholesterol intake and the risk of liver cancer. Obesity has been reported to be associated with intestinal fungi, as "*Candida*" fungi promote fat accumulation and "obesity" by producing lipase and converting "triglycerides" to monoacylglycerol. However, it is still unclear whether fungi, such as bacteria, can contribute to cancer independently of obesity. Dietary fats are a potential source of cancer, and high levels of fat and cholesterol activates the growth and colonization of *Candida*, resulting in candidiasis [36].

Sugars

A polysaccharide consisting of glucose monomers, which is recommended to constitute 45-65% of total calories. Excessive sugar consumption indirectly fuels cancer growth through excessive caloric intake. Glucose, fructose, maltose and gallate were able to induce *Candida albicans* from the

yeast stage to the fungal stage, while »lactose, sorbitol and glycerol« we're not.Given the role of fungi in tumor development, low carbohydrate and caloric restriction have a possible role in slowing tumor stimulation [30].

Fiber

It is a "complex carbohydrate" and It has been observed that dietary fiber plays a role in preventing obesity and helps reduce the incidence of cancer. "Short-chain fatty acids" fermented from dietary fiber soluble by gut microbes can directly activate »protein-coupled« receptors, inhibit "histone deacetylation" and act as energy substrates to link dietary patterns and gut microbes [37].

Proteins

Nitrogen synthesis or metabolism is the main pathway in protein synthesis in both humans and microbes, including "*Candida albicans*" and "*Aspergillus fumigatus*". Recent studies have shown that nitrogen source can influence the phase transition and "biofilm formation" of *Candida albicans*. *Candida* uses the Csh3-Sps sensor complex to sense extracellular amino acid levels and regulate the secretion of "virulence factors" via genes controlled by"*Stp1*" including the major secreted "aspartyl protease". *Candida albicans* can facilitate "proline" metabolism by expressing "proline"-metabolizing enzymes to promote the transition from yeast to hyphae when ingested by macrophages. Inhibition of »proline« metabolism affects hyphae formation, which impairs the ability of *Candida albicans* to escape from phagocytic cells [38].

Minerals

Lack of "essential vitamins" and "minerals "is one of the factors that increase susceptibility to cancer Furthermore, high-dose vitamin and mineral supplements have not reduced cancer incidence in well-nourished populations, but may even increase their risk. Given the scarcity and necessity of minerals, especially trace elements , for both the host and "fungi", the nutritional tug-of-war between them is more intense than for trace elements. Fungal pathogens have established adaptive mechanisms to overcome mineral deficiency or excess conditions[39]. Minerals including "potassium, calcium, magnesium, iron, and copper" play critical roles in protein structure, enzyme-catalyst interactions, signal transduction pathways, and cellular

physiological homeostasis in both the host and »fungi40] «]. Furthermore, phosphorus nutrition has been found to be another nutrient involved in regulating the target of rapamycin signalling pathway. *Candida albicans* senses oxidative stress in various microenvironments and exerts »virulence« to invade the host [41].

Conclusion

Many fungal species that participation in the occurrence cancer through several mechanisms The connection between nutrition and fungal diseases has been found to play an important role in the development, spread, and invasion of cancer. Tumor development and nutrition are closely linked, as adequate nutritional intake reduces the likelihood of tumor development, while excessive intake may have the opposite effect. This article focuses on the role and mechanism of fungal infection in the occurrence of various types of cancer in humans, with an emphasis on the role of nutrients in fungal growth, spread, invasion, and cancer pathogenesis.

References

1.Leelambigai D , Shanthi T , Beranaitis L.Fungal infection in immunopromised hosts.Global Journal of Research in medical sicences. . 2024; ISSN:2583-3960. Volume 04 Issue 06 Nov-De

DOI: 10.5281/zenodo.14046470

2. Qu J, Chen Q, Bing Z, Shen S, Hou Y, Lv M and Wang T. *C.tropicalis* promotes CRC by down regulating tumor cell intrinsic PD 1 receptor via autophagy. J Cancer.2023;14:1794-1808. doi: 10.7150/jca.79664

3. Yang L, Li A, Wang Y and Zhang Y.. Intratumoral microbiota: Roles in cancer initiation, development and therapeutic efficacy. Signal Transduct Target Ther. 2023 ;8: 35.

https://doi .org/10.1038/ s41392-022-1304.

4.Cheng W, Yunhuan G, Rongcun y. Fungi and tumors: The role of tumorigenesis (Review). International Journal oncology. 2024; 64:52.

DOI: 10.3892/ijo.2024.5640

5. Le N, Jiao N, Tan J, Wang Z, Wu D. Multi kingdom microbiota analyses identify bacterial fungal interactions and biomarkers of colorectal cancer across cohorts. Nat Microbiol . 2023;

7: 238 250. DOI: 10.1038/s41564-021-01030-7.

6.Azevedo M, Cidalia P, Fatima B. Microbes and cancer: Friends or faux. International Journal of Molecular Sciences.2023; 21,3115.

doi: 10.3390/ijms21093115

7.Correa Moreira D, Barbara D, Domenico G, Manoel M. Editorial : Emerging fungal pathogens: perspectives. Frontiers in fungal biology. . Front fungal boil2024;Vol5,14Feb doi: 10.3389/ffunb.2024.1369062

8.Hosseini K, Hosseini A, Florence C, Gwenad R. Role of Fungal Infections in Carcinogenesis and Cancer Development: A Literature Review. Adv Pharm Bull. 2022;12(4),747-75.

DOI: 10.34172/apb.2022.076

9. Zong Z, Zhou F and Zhang L. The fungal mycobiome: a new hallmark of cancer revealed by pan cancer analyses. Signal Transduct Target Ther .2023; 8: 50.

https://doi.org/10.1038/s41392-023-13346

10.Witchley JN, Penumetcha CP, Abon NV, Woolford CA, Mitchell AP ,Noble SM. *Candida albicans* Morphogenesis Programs Control the Balance between Gut Commensalism and Invasive Infection. Cell Host Microbe.2019; 25: 432- 443.

DOI: 10.1016/j.chom.2019.02.008

11.Seelbinder B, Lohinai Z, Vazquez R, Brunke S, Chen X, Mirhakkak M, Escalera S, Dome B, Berta J. Candida expansion in the gut of lung cancer patients associates with an ecological signature that supports growth under dysbiotic conditions.

Nat Commun .2023; 14: 2673. DOI: 10.1038/s41467-023-38058-8

12. Hager, Christopher L., and Mahmoud A. Ghannoum. "The Mycobiome: Role in Health and Disease, and as a Potential Probiotic Target in Gastrointestinal Disease. "Digestive and Liver Disease. 2017; 49: 1171– 6 .

DOI: 10.1016/j.dld.2017.08.025

13. Yang, A, Tatsuo I, Katrin H, Peng C, Lirui W, Cristina L, Sena B. "Intestinal Fungi Contribute to Development of Alcoholic Liver Disease." Journal of Clinical Investigation 2017 ; 127:2829–41.

https://doi.org/10.1172/JCI90562

14.Rushing BR and Selim M I: Aflatoxin B1: A review on metabolism, toxicity, occurrence in food, occupational exposure, and detoxification methods. Food Chem Toxicol . 2019; Feb 124: 81100 -

DOI: 10.1016/j.fct.2018.11.047

15. Gupta S, Gupta R, Sinha N, Mehrotra, R. Relationship between type of smokeless tobacco & risk of cancer: a systematic review. Indian J. Med. Res. 2018;5676.

https://doi.Org/10.4103/ijmr.IJMR.

16. Arzmi H, Dashper S, Cullough M, Polymicrobial interactions of Candida albicans and its role in oral carcinogenesis. J. Oral Pathol. Med. 2019 48, 546–551. https://doi.Org /10.1111/ jop.12905

17. Zhai, B, Ola M, Rolling T, Tosini N, Joshowitz S, Littmann E. High-resolution mycobiota analysis reveals dynamic intestinal translocation preceding invasive candidiasis. Nature Medicine . 2020; 26, 59–64.

https://doi.org/10.1038/s41591-019-07097

18. Sharma, A. Oral Candidiasis: an Opportunistic Infection of AIDS. Int. J. Appl. Dent. Sci. 2019; 5, 23–27. https://doi.org/10.4172/2155- 6113 . 1000 i101

19.Chung LM, Liang JA, Lin CL, Sun LM, Kao CH. Cancer risk in patients with candidiasis: a nationwide population based cohort study. Oncotarget 2019; 8,63562–63573.

https: //doi. Org /10.18632/ oncotarget. 18855

20. Li JQ, Li JL, Xie YH, Shen XN, Han JX, Chen YX , Fang JY. *Saccharomyces cerevisiae* may serve as a probiotic in colorectal cancer by promoting cancer cell apoptosis. J Dig Dis 2020 ; 21: 571 582.

DOI: 10.1111/1751-2980.12930

21. Shukla K, Vun I, Lov I, Laparidis G, Camley C, Ariyawardana A. Role of *Candida* infection in the malignant transformation of oral leukoplakia : a systematic review of observational studies. Transl. Res. Oral Oncol . 2019; 4.

https://doi.org/10.1177/2057178X1982822

22. Huet M, Chen Z,Sadequr R. A review on association of fungi with the development and progression of carcinogenesis in the human body Current Research in Microbial Sciences. 2022; Volume3,100090. https://doi.org/10.1016/j.crmicr.2021.1000

23..Koo S, Kejariwal D, Al-Shehri T, Dhar A, Lilic D. Oesophageal candidiasis and squamous cell cancer in patients with gain-of-function STAT1 gene mutation. United Eur. Gastroenterol. J. 2017;5,625–631. https://doi.org/10.1177/50640616684404.

24. Dohlman A, Klug J, Mesko M, Gao H, Lipkin M, Shen X , Iliev D.

A pan cancer mycobiome analysis reveals fungal involvement in gastrointestinal and lung tumors. Cell 2022; 185: 3807 3822 e12.

doi: 10.1016/j.cell.2022.09.015.

25. Coker OO, Nakatsu GA, Dai RZ., Wu WK, Wong SH, Chan FK, Sung JY. Enteric fungal microbiota dysbiosis and ecological alterations in colorectal cancer. Gut 2019; 68, 654–662.

https: //doi. org/ 10. 1136/gutjnl-2018-317178

26. Eissa M , Lerner L, Abdelfatah E, Shankar N, Canner K, Hasan M, Yaghoobi V, Huang B, Kerner Z, Takaesu F, Wolfgang C, Kwak R, Ruiz M, Tam M. Promoter methylation of ADAMTS1 and BNC1 as potential biomarkers for early detection of pancreatic cancer in blood. Clin. Epigenetics 2024; 11, 1–10.

https: //doi. Org /10.1186/s13148-019-0650-0.

27. Sung H, Jacques F, Rebecca L, Siegel M, Ahmedin J, Freddie B. "Global Cancer Statistics: Estimates of Incidence and Mortality Worldwide for 36 Cancers. in 185 Countries." CA: A Cancer Journal for Clinicians 2021; 71: 209.

https: //doi. Org /10.3322/caac.21660

28. Aykut B, Pushalkar S, Chen R, Li Q, Abengozar R, Kim J, Shadaloey A, Wu D, Preiss P, Verma N. The fungal mycobiome promotes pancreatic oncogenesis activation of MBL. Nature 2019;574:264267. https://doi.org/10.1038/s4158

29. Zhang L, Chen C, Chai D, Li C, Qiu Z, Kuang T, Liu L, Deng W ,Wang W. Characterization of the intestinal fungal microbiome in patients with hepatocellular carcinoma. J Transl Med 2023; 21: 126.

http://www.chictr.org.cn /edit.aspx.

30.Wu D ,Yun-Yuan G , Chen-Has L, Quan Z. "Nutrient fungi host" tripartite interaction in cancer progression .Imetawiley. 2024; Vol.3.Issue2. https://doi.org/10.1017/9781316659373.

31. Delam H, Izanloo S, Bazrafshan R, Eidi A. Risk factors for cervical cancer: an epidemiological review.J Health Sci Surveill Syst 2020;8(3):105-9.

doi: 10.1016/j.idcr.2016.09.016.

32. Banerjee S, Tian T, Wei Z, Shih N, Feldman M, Alwine J, Coukos G , Robertson E. The ovarian cancer oncobiome. Oncotarget. 2024 ; 8: (٢٢) 3622-36245. DOI: 10.18632/oncotarget.16717

33. Brother RP, Daveluy SD. Squamous cell carcinoma mimicking fungal infection. IDCases.2016;6:72-73. DIO: 10.1016/j.idcr.2016.09.016

34. Szóstak N, Luiza H, Anna S,Katarzyna T, Marcin S, Tukasz P, Kaja Z, Piotr K, Anna P."Host Factors Associated With Gut Mycobiome Structure."mSystems2023; 8: e0098622.
https://doi.org/10.1128/msystems.00986-

35.Rumgay, H, Neil M, Pietro F, and Isabelle S. "Alcohol and Cancer: Epidemiology and Biological Mechanisms." Nutrients 2021; 13: 3173. https//:doi.org/١٠,٣٣٩٠/nu١٣٠٩٣١٧٣.

36 Sun S, Li S, Kai W, Shanshan Q, Xinyue Z, Xiaomin H, Wei C. "The Gut Commensal Fungus, *Candida parapsilosis*, Promotes High Fat Diet Induced Obesity in Mice." Communi-.cations Biology2021 ; 4: 1220
https://doi.org/10.1038/s42003-021-

37. Martin-Gallausiaux C, Ludovica M, Herve M, Pierre L ,Nicolas L. Mechanisms and functional importance in the Gut .Proccedings of the Nutrition Society.2021;80:37-49. DOI: https://doi.org/10.1017/S0029665120006916

38. Silao, F., Meliza W, Kicki R, Axel W, Björn B, Klas U, and Per O. "Mitochondrial Proline Catabolism ActivatesRas1/cAMP/PKA-induced Filamentation in *Candida albicans*." PLoS Genetics 2019; 15: e1007976. https//:doi.org/١٠,١٣٧١/journal.pgen١٠٠٧٩.

39.Liu XY, Wang XY, Li RY, Jia SC., Sun P, Zhao M, Fang C. Recent progress in the understanding of complement activation and its role in tumor growth and anti-tumor therapy Biomed Pharmacother. 2017; 91,446–456. https://doi.org/10.1016/

40. Liu Y, Ou Y, Sun L, Li W, Yang J, Zhang X, Hu Y. Alcohol dehydrogenase of *Candida albicans* triggers differentiation of THP-1 cells into macrophages. J. Adv. Res. 2019 ; 18, 137–145. https://doi.org/10.1016/j.jare.2019.02.005

41. Narunsky Haziza L, Sepich GD, Livyatan I, Asraf O, Martino C, Nejman D, Gavert N, Stajich J, Amit G, González A. Pan cancer analyses reveal cancer type-specific fungal ecologies and bacteriome interactions. Cell 2022; 185: 3789 3806 e17.
DOI: 10.1016/j.cell.2022.09.005