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Pathology and pharmacology of lung cancer, stomach cancer and colorectal cancer

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Abstract. Cancer, a term that strikes fear and concern in the hearts of millions around the globe, stands as one of the most formidable diseases of our time. It has been responsible for an alarming escalation in the number of fatalities annually, casting a dark shadow over the world's health statistics. The insidious nature of cancer is further highlighted by the fact that it is no longer confined to the elderly, and it is increasingly affecting younger individuals, defying traditional age-related patterns. However, there is still no cure for cancer, so the development of cancer drugs is particularly important. When looking to the future, the relentless march of technological advancement offers a beacon of hope. With each breakthrough in fields such as genomics, immunotherapy, and nanotechnology, the possibility of defeating cancer is getting closer and closer. This research will cover the history of cancer, introduce three different types of cancer, their pathology and pharmacology.

Keywords: Cancer; Pathology; Pharmacology.

1. Introduction

Cancer has plagued people for many years and is still incurable, which is becoming increasingly prevalent among younger generations. It is a disease characterized by the loss of growth control in one or more cells, resulting in either a solid mass of cells called a tumor or a liquid form of cancer, such as those affecting the blood or bone marrow [1]. There is a theory called Humoral theory which use four humors to predict how the cancer form. Because of some religious reasons, people nearly know nothing about cancer. Afterwards, many theories about cancer such as Lymph theory, Chronic irritation theory and Trauma theory were proposed, and it was not until the discovery of oncogenes and tumor suppressor genes in the mid-20th century that progress was made in cancer treatment.

With the discovery of more and more carcinogens and viruses for example Hepatitis B or C viruses, Epstein-Barr viruses and Human papilloma viruses (HPVs) that cause cancer, cancer screening and treatment have been developed [2]. Curing cancer has always been a matter of great concern. In the multidimensional field of cancer treatment, monoclonal antibody technology has become a hot topic in research and clinical application due to its unique targeting and therapeutic effects. These antibodies can accurately recognize and bind to specific receptors on the surface of cancer cells, thereby blocking its binding to signaling molecules and cutting off the pathways of signal transduction within cancer cells. The treatment strategy for HER2 positive tumors has undergone a revolutionary change. In addition, the application of nanotechnology in cancer treatment is becoming increasingly widespread, especially in the design of drug delivery systems. The development of drugs targeting specific molecular pathways is also becoming a hot research topic. This research introduces pathology and pharmacology of lung cancer, stomach cancer and colorectal cancer.

2. Lung cancer

Lung cancer is diagnosed more frequently than any other form of cancer and is the primary cause of cancer-related fatalities. It is projected that by 2035, the number of annual lung cancer deaths will approach 3 million worldwide, largely due to prevalent tobacco consumption and an increasing number of elderly individuals [3]. The likelihood of developing lung cancer is affected by

environmental factors, particularly cigarette smoking, and by occupational hazards in industries such as mining, shipbuilding, petroleum refining, and those involving asbestos [3]. Individuals who smoke cigarettes constitute 85–90% of all lung cancer diagnoses, with 15% of smokers eventually being diagnosed with the disease [3]. Even non-smokers are at an elevated risk of lung cancer due to exposure to tobacco smoke. Exposure to secondhand smoke can increase the risk by approximately 30%, with the level of risk being proportional to the length of time exposed [3].

2.1. Pathology of lung cancer

2.1.1. Small cell lung carcinoma.

About two-thirds of small cell lung cancer (SCLC) cases manifest as a mass around the hilum of the lung. SCLC is found in the area surrounding the bronchi, with the cancer cells infiltrating the submucosa of the bronchus and the surrounding tissue. The obstruction of the bronchus is most often due to compression from all sides, although in some rare instances, lesions can develop within the bronchial lumen itself. Since SCLC is commonly diagnosed through transbronchial biopsy or cytological examination, it is not common to see it presented as a specimen for surgery. The cancerous cells are diminutive, exhibiting a shape that ranges from round to spindle-like, with minimal cytoplasm. Their nuclei contain delicate, granular chromatin, and their nucleoli are either not present or barely noticeable [4]. The nuclei may demonstrate a pattern of molding against each other and a smearing effect on the chromatin, which can be quite evident due to damage from manipulation during biopsy processing.

2.1.2. Non-small cell lung carcinoma.

Large cell carcinomas are typically located at the outer parts of the lung, but central occurrences are also possible. Upon visual inspection, they often present as sizable, necrotic growths. A diagnosis of large cell carcinoma is one that rules out other types, specifically requiring the absence of squamous or glandular features as confirmed under a microscope. Under the microscope, these tumors are characterized by clusters and layers of large, polygonal-shaped cells featuring nuclei with a vesicular appearance and distinct nucleoli [4].

The development of cancer in the bronchial tubes is viewed as a complex, multi-stage process that involves the transition of normal bronchial lining into various forms of abnormalities. This progression includes stages such as an overgrowth of basal cells, a change in cell type to squamous cells, the development of abnormal cell formations, and eventually carcinoma in situ. AAH represents a growth within the bronchioloalveolar region that is similar to non-mucinous BAC [4]. AAH is seen as a localized increase in the number of mildly abnormal, cube-shaped to short, pillar-like epithelial cells that line the air sacs and the small airways. There might also be a minor thickening of the walls between these air sacs.

2.2. Pharmacology of lung cancer

2.2.1. Cetuximab.

Monoclonal antibodies that attach to the outer part of the EGF-R stop the receptor from connecting with EGF, its signal molecule, which in turn halts the transmission of signals inside the cell. These antibodies can naturally summon immune cells by linking their constant Fc region to particular receptors on these cells. Cetuximab is a hybrid monoclonal antibody of the IgG1 class that binds competitively to the external region of the EGF-R, as shown in Figure 1 [5]. The EGF-R and IGF-1R signaling pathways play crucial roles in cellular communication. When activated, EGF-R triggers key signaling cascades such as the Ras-Raf-Mek pathway and another involving the PI3K, Akt, and mTOR components. These pathways can influence cell behaviors -such as growth and survival. There is a possibility of interaction or cross-talk between these pathways and those controlled by IGF-1R and c-MET, as well as the LKB1-AMPK signaling route [5].

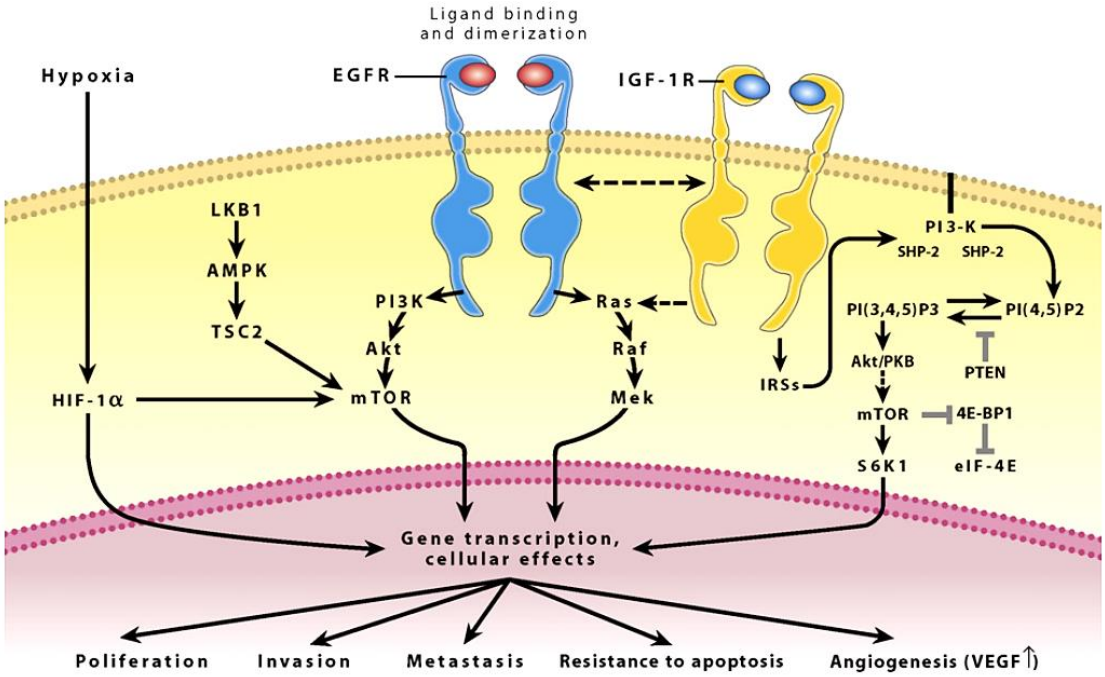

Figure 1. The EGF-R and IGF-1R signaling pathways [5].

2.2.2. Bevacizumab.

Bevacizumab is a monoclonal antibody that strongly binds to VEGF, as shown in Figure 2 [6]. Receptor tyrosine kinases (RTKs) are proteins that span the cell membrane, having a part that sticks out to catch signaling molecules and another part inside the cell that acts as an enzyme. When they latch onto their specific signaling molecules, most RTKs pair up and switch on by adding phosphate groups to themselves on tyrosine amino acids. This activation switches on many cells signaling pathways that encourage cell growth, survival, and the formation of new blood vessels in response to certain triggers. Mis activation of RTKs, either by mutation, overproduction, or abnormal signaling molecule creation, is a common characteristic in the development and worsening of human cancers, and it's believed to be a primary way that cancer cells hijack normal growth regulation [6].

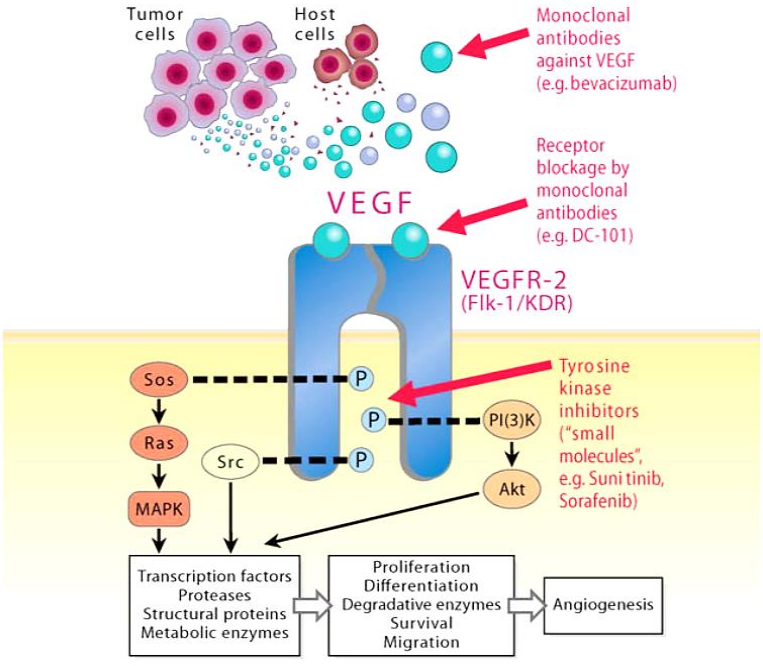

Figure 2. Signaling pathways triggered by VEGF [6]

3. Stomach cancer

Even with improved diagnostic methods, gastric cancer is often identified at a stage where it has already penetrated the muscularis propria. This is because the symptoms in the early phase are often unclear and not specific, with the typical signs of anemia, weight loss, and aversion to meat-based foods manifesting only in later stages of the disease. The effectiveness of surgical intervention and chemotherapy is quite restricted in later stages of the disease, and there is a shortage of precise molecular markers for targeted treatments. Given the bleak outlook for stomach cancer, with a five-year survival rate of approximately 20%, it is crucial to reassess the findings from epidemiological and experimental research to develop effective primary prevention strategies [7].

3.1. Pathology of stomach cancer

Gastric cancer denotes malignant growths originating from the area that spans from the gastroesophageal junction to the pylorus. The vast majority (about 95%) of these tumors originate from the epithelium and are classified as adenocarcinoma, while Aden squamous, squamous, and undifferentiated carcinomas are less common [8]. The highly differentiated intestinal-type is composed of cohesive malignant cells that arrange into tubular, gland-like formations prone to ulceration. In contrast, the poorly differentiated diffuse-type is marked by an infiltration and stiffening of the gastric wall, resembling a leather bottle, without forming a distinct tumor mass [7]. It originates from precancerous conditions like gastric atrophy and intestinal metaplasia, being affected by environmental elements such as H. pylori infection, obesity, and dietary habits. The diffuse-type is the predominant histological subtype in regions where the disease is prevalent, occurring more often in women and younger individuals, and is linked to blood type A, suggesting a genetic predisposition.

The progression to invasive gastric carcinoma is characterized by a gradual, multi-step process that unfolds across a spectrum of precancerous conditions. A sequence of histological modifications occurs within the gastric lining, encompassing atrophic gastritis with a reduction in parietal cell count, intestinal metaplasia, and dysplasia, culminating ultimately in carcinoma. This progression from metaplasia to dysplasia and then to carcinoma is particularly pertinent to the intestinal-type gastric cancer, which evolves through an aggregate of genetic mutations akin to the process observed in colorectal cancer.

3.2. Pharmacology of stomach cance

3.2.1. Anti-HER2.

Trastuzumab is an engineered human-like monoclonal antibody of the IgG1 class, which targets the external region of the HER2 protein. This medication attaches firmly, disrupting the cell signaling initiated by HER2 and triggering an immune response that destroys cancer cells with excessive HER2 expression. Trastuzumab emtansine is a type of antibody-drug conjugate that fuses trastuzumab with the tubulin inhibitor emtansine through a stable linking mechanism. Once inside HER2-positive cells, the release of the cytotoxic emtansine metabolites leads to the halting of cell division and the initiation of cell death [9]. Trastuzumab deruxtecan represents an innovative class of HER2-targeting antibody-drug conjugates, formed by connecting a humanized monoclonal antibody to a topoisomerase I inhibitor via a cleavable peptide bond. According to phase I clinical trials, the safety, tolerability, and efficacy of trastuzumab in the treatment of advanced gastric cancer or gastroesophageal junction cancer patients with HER2 overexpression were evaluated [10].

3.2.2. Nanotechnology.

The field of cancer treatment, detection, and medication administration has been dramatically revolutionized by nanotechnology, particularly through the use of nanoparticles. These nanoparticles are typically synthesized by controlling the structural properties of a variety of polymers, inorganics, and organic substances. Polymeric nanoparticles possess distinctive architectures capable of encapsulating or incorporating drug molecules, resulting in the formation of nanocapsules or nanospheres. They are extensively utilized as vehicles for chemotherapeutic agents, owing to their

capacity to enhance the efficacy of cancer treatments. This is achieved by overcoming the limitations associated with drugs, including their low solubility, inadequate permeation, brief duration of action, instability, and potential toxicity [11]. Metal-based nanoparticles have attracted considerable interest for their potential as innovative treatments in gastric cancer. The fabrication of these nanoparticles typically involves a process of reduction and capping of metal precursor compounds, including substances like silver nitrate, gold halides, zinc acetate dihydrate, and copper nitrate, among others. Polymeric nanoparticles serve as carriers to encapsulate and accurately transport chemotherapeutic agents directly to the tumor, enhancing the effectiveness of gastric cancer treatment. In contrast, metallic nanoparticles directly target and eliminate cancer cells, leveraging their distinctive physicochemical characteristics [12].

4. Colorectal cancer

Colorectal cancer, ranking as the third most frequently identified form of cancer and the third highest contributor to cancer-related fatalities in the United States, has seen a decline in its occurrence rate [13]. When viewed on a worldwide scale, it stands as the second biggest killer for men and the third for women in terms of cancer mortality. While the majority of colorectal cancer instances occur without a familial pattern, less than ten percent are attributed to inherited cancer conditions [14]. Most colorectal cancers originate from precancerous conditions such as adenomatous polyps, which can progress to adenocarcinomas.

4.1. Pathology of colorectal cancer

4.1.1. Adenocarcinoma.

Adenocarcinomas represent the most prevalent form of cancer. The majority of these tumors are of moderate differentiation and do not exhibit distinctive pathological characteristics. Colorectal cancers often display a cribriform pattern, marked by central necrosis, which is a helpful diagnostic feature when identifying metastatic tumors, especially when the primary colorectal source remains undetected. Dysplastic changes can be observed in the surrounding mucosa. However, it is common for the invasive cancer to erase evidence of any original polyp that might have given rise to it [15].

4.1.2. Mucinous adenocarcinoma and medullary carcinoma.

This refers to a variant of adenocarcinoma characterized by the production of extracellular mucin. For a tumor to be classified as such, it should contain a mucinous component constituting at least 50% of its total volume. Mucinous adenocarcinomas are often linked to microsatellite instability. It is unclear if mucinous tumors are associated with a more favorable prognosis [16]. This subtype of colorectal cancer, which was incorporated into the World Health Organization's classification system in 2000, is significant. It is defined by a distinctive microscopic appearance, typically found in right-sided tumors, featuring extensive cell clusters and a prominent presence of tumor-infiltrating lymphocytes [17].

4.2. Pharmacology of colorectal cancer

Growing understanding of the cancer-HGF-MET pathway link has pinpointed it as a potential target for therapy. A range of strategies to inhibit HGF-MET are being explored, utilizing novel monoclonal antibodies and small molecules with distinct modes of action. These approaches target HGF either by preventing its activation and synthesis or by disrupting its interaction with MET receptors. Some agents compete with MET for binding (acting as MET antagonists), while others impede the tyrosine kinase activity within MET (as MET TKIs). These treatments have not been linked to severe side effects, although a few patients have experienced issues such as fatigue, loss of appetite, allergic responses, swelling, skin eruptions, and a decrease in neutrophil counts [18]. Numerous ongoing clinical trials are investigating the role of HGF/c-MET targeted agents as part of colorectal cancer treatment strategies [19]. The generation of HGF depends on the processing of its precursor form, known as pro-HGF, a process that is facilitated by a group of natural inhibitor proteins known as HGF

activator inhibitors (HAIs). Elevated amounts of HAI-1 are noticed in individuals with non-cancerous growths when compared to those suffering from prostate cancer, whereas HAI-2 levels are found to be reduced in aggressively invasive and advanced prostate cancer cells [20]. Molecules that contend with HGF for MET binding led to the abnormal formation and breakdown of MET dimers. A range of antibodies, such as onartuzumab, DN-30, and ABT-700, have been engineered for this purpose [19].

5. Conclusion

This research introduces the history of cancer and discusses the pathology and target therapy of three different types of cancer. The above-mentioned drugs and treatment methods have the advantage of effectively inhibiting tumor cell activity, proliferation, and metastasis. It can also be used for the treatment of various cancers. However, there are also drawbacks with significant side effects, such as allergic reactions, swelling, and rash. Trastuzumab deruxtecan can even cause interstitial lung disease. Some drugs have high costs, such as cetuximab, trastuzumab emtansine and onartuzumab. Long term use of cetuximab and trastuzumab can lead to drug resistance and affect treatment efficacy. As mentioned in this research, nanoparticles have played a certain innovative role in cancer treatment through technological development. In the future, more technology combined with existing drug therapies may improve the efficiency of cancer treatment and reduce its side effects.

References

[1] S. Nussbaumer, P. Bonnabry, J. L. Veuthey, et al. Analysis of anticancer drugs: a review, Talanta 85 (2011) 2265 - 2289.

[2] A. Sudhakar, History of cancer, ancient and modern treatment methods, Journal of cancer science & therapy 1 (2009) 1.

[3] V. C. Broaddus, J. D. Ernst, T. E. King Jr, et al. (Eds.). Murray & Nadel's textbook of respiratory medicine, Elsevier Health Sciences, 2021, pp. 1018 - 1028.

[4] W. D. Travis, E. Brambilla, H. K. Müller-Hermelink, et al. Pathology and genetics of tumours of the lung, pleura, thymus, and heart. WHO Classification of Tumours, 3rd Edition, 10 (2004) 344.

[5] W. C. Dempke, T. Suto, M. Reck, Targeted therapies for non-small cell lung cancer, Lung cancer 67 (2010) 257 - 274.

[6] W. C. Dempke, V. Heinemann, Resistance to EGF-R (erbB-1) and VEGF-R modulating agents, European journal of cancer 45 (2009) 1117 - 1128.

[7] S. Nagini, Carcinoma of the stomach: A review of epidemiology, pathogenesis, molecular genetics and chemoprevention, World journal of gastrointestinal oncology 4 (2012) 156.

[8] M. Sarbia, K. F. Becker, H. Höfler, Pathology of upper gastrointestinal malignancies, In Seminars in oncology 2004 pp. 465 - 475.

[9] G. D. Lewis Phillips, G. Li, D. L. Dugger, et al. Targeting HER2-positive breast cancer with trastuzumab-DM1, an antibody–cytotoxic drug conjugate, Cancer research 68 (2008) 9280 - 9290.

[10] K. Shitara, H. Iwata, S. Takahashi, et al. Trastuzumab deruxtecan (DS-8201a) in patients with advanced HER2-positive gastric cancer: a dose-expansion, phase 1 study, The Lancet Oncology 20 (2019) 827 - 836.

[11] F. Carreiró, A. M. Oliveira, A. Neves, et al. Polymeric nanoparticles: Production, characterization, toxicology and ecotoxicology, Molecules. 25 (2020) 3731.

[12] L. Tamayo, H. Palza, J. Bejarano, et al. Polymer composites with metal nanoparticles: synthesis, properties, and applications, In Polymer composites with functionalized nanoparticles 2019 pp. 249 - 286.

[13] R. L. Siegel, K. D. Miller, A. Jemal, Cancer statistics, 2018, CA: a cancer journal for clinicians 68 (2018) 7 - 30.

[14] F. Bray, J. Ferlay, I. Soerjomataram, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA: a cancer journal for clinicians 68 (2018) 394 - 424.

[15] D. Treanor, P. Quirke, Pathology of colorectal cancer, Clinical oncology 19 (2007) 769 - 776.

[16] C. C. Compton, Colorectal carcinoma: diagnostic, prognostic, and molecular features, Modern Pathology 16 (2003) 376 - 388.

[17] J. Jessurun, M. Romero-Guadarrama, J. C. Manivel, Medullary adenocarcinoma of the colon: clinicopathologic study of 11 cases, Human pathology 30 (1999) 843 - 848.

[18] H. N. Mo, P. Liu, Targeting MET in cancer therapy, Chronic diseases and translational medicine 3 (2017) 148 - 153.

[19] Y. H. Xie, Y. X. Chen, J. Y. Fang, Comprehensive review of targeted therapy for colorectal cancer, Signal transduction and targeted therapy 5 (2020) 22.

[20] C. H. Tsai, C. H. Teng, Y. T. Tu, et al. HAI-2 suppresses the invasive growth and metastasis of prostate cancer through regulation of matriptase, Oncogene 33 (2014) 4643 - 4652.