ISSN 2618-1584 Vol. 4, Issue 4: 44-47, DOI: 10.25236/FMSR.2022.040407

Research progress of antitumor peptides

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Abstract: *In recent years, with the progress of medical research and the continuous emergence of new antitumor drugs, they have antitumor activity peptides have attracted extensive attention in the field of antitumor drug research and development because they are not easy to produce drug resistance, wide sources, high bioavailability in vivo, good specificity, easy synthesis and low synthesis cost. In this paper, the peptides with antitumor activity from various sources are sorted and analyzed, in order to improve the reference for the in-depth research of antitumor peptides and the development of new drugs.*

Keywords: *peptide, cancer,antitumor, activities, treatment*

1. Introduction

Peptides are a kind of substances that naturally exist in animals, plants or microorganisms, animal or plant proteins can also produce peptides through protease hydrolysis. In addition, peptides can also be produced by artificial chemical synthesis or Bioengineering. Polypeptides are amino acids that are linked together by amide bonds, that is, peptide chains to form compounds. They are intermediate products of protein hydrolysis. They are often formed by dehydration and condensation of 2 to 100 amino acid molecules. Generally, peptides composed of 2 to 10 amino acids are called oligopeptides; Peptides composed of 10 to 50 amino acids are called polypeptides; Peptides composed of more than 50 amino acids are called proteins. The function of polypeptide involves various fields of hormones, nerves, cell growth and reproduction. Its importance is to regulate the functional activities of various system organs and cells in the body. Its greatest feature is that it has strong activity, diversity and special biological functions.

Cancer is a disease characterized by abnormal cell growth out of control caused by a series of mutations, which lead to the abnormal expression of gene products necessary to regulate cell proliferation, survival and growth activities. Therefore, cancer from the most basic biological defects of cells: the ability to respond to growth signals, participate in cell death procedures to eliminate unnecessary, redundant or damaged cells, and the ability to form new blood vessels and invade tissues. For clinicians and researchers, the grandest challenges is how to maintain normal and healthy tissue while eliminating tumor cells. Although significant progress has been made in the treatment of cancer in recent years, most cancer treatments involve surgery, chemotherapy, radiotherapy and hormone therapy, which have hardly changed in the past decade [1]. For example, conventional chemotherapy targeting cancer cells (such as DNA alkylating agents) can also damage normal healthy growing cells, but may not eliminate quiescent or non proliferating cancer cells [2,3]. In addition, drug resistance may also occur in the process of treatment. It may be that the abnormalities of drug transporters or detoxification enzymes affect the interaction between drugs and their targets. The defects of DNA repair mechanism and apoptosis or death pathway may also lead to the emergence and development of cancer drug resistance. As one of the diseases that seriously threaten human life and health worldwide, cancer is also the disease with the highest clinical, social and economic burden. The burden of cancer treatment is increasing in both developing and developing countries [4-6]. It is estimated that in 2020, the number of new cancer cases in the world will be 19.3 million, and about 10 million people have died of cancer. Statistics show that the number of women with breast cancer exceeds lung cancer as the most common cancer in 2020. At present, lung cancer, liver cancer, gastric cancer, breast cancer and colon cancer are the five leading causes of death, followed by esophageal cancer, pancreatic cancer and prostate cancer. Since 2020, the number of deaths from gastric cancer has increased by nearly 14000. Cervical cancer surpassed tongue cancer as the ninth most common cancer. Overall, the top 14 cancer types accounted for nearly 75% of newly diagnosed cases in 2020. Lung cancer, liver cancer, gastric cancer, breast cancer and colon cancer are the five leading causes of death in 2020, followed by

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esophageal cancer, pancreatic cancer and prostate cancer. In 2020, the number of deaths from gastric cancer decreased by 14000. The incidence rate of liver cancer changed from the third highest in 2008 to the second highest in 2020.

2. Antitumor peptides Manuscript

Even if the initial treatment is successful, the risk of cancer recurrence remains a problem for patients. Because drug resistance may occur during treatment, it is necessary to constantly look for new anticancer drugs. Compared with traditional small molecule chemical drugs, peptide drugs have many advantages [7,8]. Peptide drugs have selectivity, specificity and effectiveness. They are usually small molecule drugs and degrade into amino acids. It is less likely to show unwelcome drug-drug interaction. In addition, peptide drugs are less likely to accumulate in vivo due to their short half-life[9-11]. In addition, the cost of peptide synthesis is relatively low and easy to modify. Peptides are widely used in diagnosis and cancer treatment, especially in the development of antitumor drugs. In recent years, many small molecular peptides with antitumor activity have been found. This paper reviews all kinds of peptides with antitumor activity, and briefly summarizes the structural transformation and biological activity research of antitumor peptides, so as to provide new ideas for the research and development of peptide antitumor drugs.

2.1. Natural antitumor peptides

Antitumor peptides from natural sources widely exist in plants, animals, microorganisms or marine organisms, and can be directly extracted from natural organisms by modern extraction and separation technology or enzymatic hydrolysis technology [12]. The author consulted the relevant research of natural antitumor peptides in recent years, as shown in Table 1.

Table 1: Antitumor peptides of natural origin

Name	Source	Activities	Mechanism
Melittin [13]	Bee venom	Inhibit ovarian epithelial cancer cells and the proliferation of glioma cells	Inhibit the oxidative phosphorylation process of tumor tissue, so as to inhibit tissue metabolism
Meretrix polypeptide[14]	Meretrix	Inhibit the growth of A549 cells in a dose - and time-dependent manner	Inhibit tumor growth by promoting apoptosis and anti metastasis
Gecko polypeptide[15]	Gecko	inhibited the proliferation of HepG2 cells in a time, and dose-dependent manner	Related to the activation of caspase apoptosis pathway
hemiasterlin[16]	Sponge	Inhibit skin cancer, lung cancer, prostate cancer and colon cancer	Inhibit the polymerization of tubulin and the proliferation of tumor cells
Dolastatin10[17]	Sea hare	Inhibit lung cancer, breast cancer	It can non competitively inhibit the binding site between vinblastine and microtubules, thus strongly affecting microtubule polymerization and microtubule dependent guanosine acid hydrolysis
Scorpion venom polypeptide[18]	Scorpion	It can effectively down regulate oncogenes in H22 liver cancer and promote tumor vascular growth	The compound may have both cytotoxic and antiangiogenic effects
cryptophycins-1[19]	Monilia	It has inhibitory effect on breast cancer, colon cancer and pancreatic cancer xenograft in mice	By causing the depolymerization of tubulin, the cells stagnate in G2 / M phase, destroy the stability of microtubules and induce apoptosis
Vglycin[20]	Pea	Inhibition of colon cancer	Down regulated the expression of CDK2 and cyclin D1
lunasin[21]	soybean	Proliferation of non-small cell lung cancer cell line H661	Inhibit the phosphorylation level of retinoblastoma protein
Ganoderma lucidum peptide[22]	Ganoderma lucidum	It can induce apoptosis of human hepatoma HepG2 cells in vitro	It may be related to the down-regulation of Bcl-2 and survivin expression, the up-regulation of p53 expression and the activation of Caspase-3

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2.2. Antitumor peptides from other sources

Although peptides with antitumor activity can be extracted and sorted out in animals and plants, and their activity is good, the content of peptides in most animals and plants is low, so it is difficult to extract on a large scale. At present, most active peptides are synthesized artificially, with low cost and large quantity, which can meet the needs of use. In addition, anti-tumor peptides can also be screened by phage display technology or computer simulation technology. As shown in Table 2, the author summarizes the relevant research of anti-tumor peptides from unnatural sources.

Table 2: Antitumor peptides from other sources

Name	Source	Function and mechanism
Cyclic peptide CDCRGDCFC[23]	Phage display technology	Selectively bind to integrin receptors $\alpha_v\beta_3$ and $\alpha_v\beta_5$
MDSC specific binding peptide[24]	Phage display technology	Scavenging MDSC cells and improving antitumor immunity
P160[25]	Phage display technology	Affinity for breast cancer cells
YWCS[26]	Synthetic	Inhibition of breast cancer cell migration
SVS-1[27]	Synthetic	Kill lung cancer cell A549
TPVN[28]	Computer simulation screening	Inhibiting proliferation of breast cancer cells
TOVN		
TPVNP		
TOVNO		
MTPVNPG		
EMTPVNP		

3. Conclusions

Many peptides, whether from natural sources or other sources, have shown significant antitumor activity, and play an antitumor role in a variety of ways. Peptides with antitumor activity have attracted extensive attention in the field of antitumor drug research and development because they are not easy to produce drug resistance, wide sources, high bioavailability in vivo, good specificity, easy synthesis and low synthesis cost. This paper collates and analyzes the research of antitumor peptides from various sources, so as to improve the reference for the in-depth research of antitumor peptides and the research and development of new drugs. In the future, it is expected that more antitumor peptides will enter clinical research as soon as possible and benefit mankind.

References

[1] Albericio F, Kruger HG. The rapeutic peptides. Future Medicinal Chemistry. 2012, 4(12) :1527-1531.
[2] Roderich D S , Andi M .Nonribosomal Peptide Synthesis-Principles and Prospects. Angew Chem Int Ed Engl. 2017 Mar 27;56(14):3770-3821.
[3] Vlieghe P, Lisowski V, MartinezJ, etal. Synthetic the rapeutic peptides: science and market. Drug Discov Today.2010,15(1–2):40–56.
[4] Yeaman MR, Yount NY. Mechanisms of antimicrobial peptide action and resistance. Pharmacol Rev .2003,55(1):27–55.
[5] Hoda M , Zahra M, Maryam Y, et al. Antimicrobial Peptides: Features, Action, and Their Resistance Mechanisms in Bacteria. Microb Drug Resist. 2018;24(6):747-767.
[6] Holohan C, Van Schaeybroeck S, Longley DB, et al. Cancer drug resistance: anevolving paradigm. Nature Reviews Cancer.2013,13(10):714–26.
[7] R.J. Boohaker, M.W. Lee, P. Vishnubhotla, et al. Bentham Science Publishers The Use of Therapeutic Peptides to Target and to Kill Cancer Cells.Current Medicinal Chemistry.2012, 19:3794-3804.
[8] Kalyanaraman B., Joseph J., Kalivendi S., Wang, S., et al. Doxorubicin-induced apoptosis:

ISSN 2618-1584 Vol. 4, Issue 4: 44-47, DOI: 10.25236/FMSR.2022.040407

implications in cardiot oxicity. Mol. Cell Biochem. 2002, 119-124.
[9] Naumov G N., Townson J. L., MacDonald I. C., Wilson, et al. Ineffectiveness of doxorubicin treatment on solitary dormant mammary carcinoma cells or late-developing metastases. Breast Cancer Res. Treat. 2003, 82, 199-206.
[10] Bray F, Ferlay J, SoerjomataramI, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394424.
[11] Zhang S, Sun K, Zheng R, et al. Cancer incidence and mortality in China 2015. J Natl Cancer Center 2020. Br J Cancer.2014, 111:1014–1020.
[12] WANG C C , LIU M, CHENG L Y, et al. A novel polypeptide from Meretrix meretrix Linnaeus inhibits the growth of human lung adenocarcinoma. Exp Biol Med (Maywood), 2012, 237(4): 442-450.
[13] Islam Rady , Imtiaz A Siddiqui , Mohamad Rady , Hasan Mukhtar. Melittin, a major peptide component of bee venom, and its conjugates in cancer therapy. Cancer letter. 2017,402:16-31.
[14] Wang H, Wei J, Wu N, et al. Mere15,a novel polypeptide from meretrix, inhibits adhesion, migration and invasion of human lung cancer A549 cells via down-regulating MMPs [J] Pharmaceutical Biology,2013,51(2) : 145-151.
[15] Ying Song , Jian-Gang Wang, Rui-Fang Li, et al. Gecko crude peptides induce apoptosis in human liver carcinoma cells in vitro and exert antitumor activity in a mouse ascites H22 xenograft model. J Biomed Biotechnol. 2012; 743573.
[16] Hilary J, John E, et al. Cytotoxic peptides hemiasterlin, hemiasterlin A and hemiasterlin B induce mitotic arrest and abnormal spindle formation. Cancer Chemotherapy Pharmacol.1997,39:223–226
[17] Ruoli Bai, George R, et al. Dolastatin 10, a powerful cytostatic peptide derived from a marine animal: Inhibition of tubulin polymerization mediated through the vinca alkaloid binding domain. Biochemical Pharmacology.1990,39(12): 1941-1949.
[18] AmmarAlmaaytahaQosayAlbalasb. Scorpion venom peptides with no disulfide bridges: A review.Peptides. Peptides. 2014,51: 35-45.
[19] Kevin M. Gardinier,James W. Leahy. Enantio specific Total Synthesis of the Potent Antitumor Macrolides Cryptophycins 1 and 8. J. Org. Chem. 1997, 62, 21, 7098–7099.
[20] Gao C, Sun R, XieY R, et al. The soy-derived peptide Vglycin inhibits the growth of colon cancer cells in vitro and in vivo . Exp Biol Med (Maywood), 2017, 242(10): 1034-1043.
[21] Mcconnell E J, Devapatla B. cancer cell proliferation by suppressing phosphorylation of the retinoblastoma protein. Oncotarget,2015,6(7):4649-62.
[22] Chunhua Wang , Dongmei Lin , Quan Chen, et al. Polysaccharide peptide isolated from grass-cultured Ganoderma lucidum induces anti-proliferative and pro-apoptotic effects in the human U251 glioma cell line. Oncol Lett. 2018 ,15(4):4330-4336.
[23] Ruoslahti E. Vascular zip codes in angiogenesis and metastasis [J]. Biochem Soc Trans, 2004, 32: 397-402.
[24] Qin H, Lerman B, Sakamaki I, et al. Generation of a new therapeutic peptide that depletes myeloid-derived suppressor cells in tumor-bearing mice [J]. Nat Med, 2014, 20: 676-681.
[25] Rodrigo Q, Bluma F, Salomao F, et al. Initial studies of radiolabeling and biodistribution of peptide p160 analog with technetium-99m.Journal of Nuclear Medicine,2008 ,5(49) .
[26] AK Singh, R Singh, F Naz, Structure Based Design and Synthesis of Peptide Inhibitor of Human LOX-12:In Vitro and In Vivo Analysis of a Novel Therapeutic Agent for Breast Cancer. PloS one, 2012,7(2).
[27] Sinthuvanich,C.,Veiga,A.S.,Gupta,K., et al. Anticancer β-hairpin peptides:Membrane-induced folding triggers activity.J.Am.Chem.Soc,2012,134:6210–6217.
[28] KN Kirschner, KW lexa, et al. computational design and experimental discovery of an antiestrogenic peptide derived from α-fetoprotein. C.J.AM.CHEM.SOC.2007,129,6263-6268.