

Application Research of Small Molecule Peptide Screening Based on Cancer Cells

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Abstract. With the rapid development of biology, more and more attention has been paid to the research, which is very valuable, about small molecule peptide of which the structure is relatively simple and the molecular weight is small. This paper summarizes the characteristics of small molecular peptide, the screening methods of small molecular peptide and the application of small molecule peptide in the medical field, especially the application of cancer cells.

1. Introduction

Small molecular peptide [1] are fragments of proteins that are widely present in plants and animals. Proteins are absorbed by the body through peptide. For instance, in the intestinal tract, the protein can be better absorbed into the next circulatory system, the blood circulatory system, after it digested by digestive enzymes and translate into small molecule peptide. In other words, it get into the cell in its original form which can be absorbed and utilized by the cell, through osmosis effect.

2. Small Molecular Peptide Properties.

Small molecule peptide has many physiological activities in vivo and are highly active in these compounds. The main physiological characteristics and functions of small molecular peptide are: small molecule peptide can transport nutrients in human body. After loading the nutrients needed by the body, small molecular peptides transport them to the tissues and organs of the human body so that they can be absorbed by the body. It acts as a tool and transporter;

Avoiding the capillary wall [2] and mucosal barriers, small molecule peptide can penetrate the cells. This property makes most cell diseases, that are incurable because the drugs cannot penetrate the cells, curable; Small molecule peptides change the transmission of genetic information by altering the transcription of DNA; Small molecular peptides can improve the permeability of biological membrane (capillary wall, red cell wall, gastrointestinal mucous membrane and alveolar, glomerular basement membrane, meninges). This property makes the biological membrane able to absorb nutrients and excrete toxins effectively, and to resistant pathogens invasion in a certain extent; Small molecular peptides can participate in the synthesis of enzymes and improve the enzyme activity [3], thereby it enhances the function of the enzyme and ultimately ensure the stability of the enzyme. This paper will study the application of small molecule peptide screening in cancer cells.

3. Tumor Suppressants

In the 1980s, Saus discovered a tumor suppressant in its own antigen when studying the pulmonary - renal hemorrhage syndrome. This suppressant has the effect of obstructing the formation of tumor blood vessels [4] and the effect of inhibiting endothelial cell proliferation in tumor blood vessels. Although tumor suppressants have a good inhibitory effect on tumor activity, we rarely used it in clinical medicine. Because it has a very large molecular weight and the anti-tumor mechanisms of it is not clear which lead to a lot uncontrollable side effects.

With the deep research in tumor suppressant, we found the 19 peptide which located near the end of 185-203 C. 19 titanium is characteristic of inhibiting tumor proliferation and promote apoptosis of

tumor, direct anti-tumor effect of a region. It has the characteristics of inhibiting tumor proliferation and promoting tumor apoptosis. It is the area that suppress tumor directly.

19 peptides have rapidly developed into a new anti-tumor target [5] therapeutic drug because of its unique function and effect. It's much better than other endostatin. For example, it has obvious resistance to breast cancer tumor cells and prostate cancer. 19 peptide can enhance the ability of melanoma cells in adhesion, and can effectively inhibit the proliferation of melanoma cells. At present, people usually choose direct synthesis method to get anti-tumor peptide, but we usually use genetic engineering to get 19 peptide. The purification of 19 peptide usually requires medium containing peptides. In clinical application, 19 peptides are commonly used through intravenous injection, because its molecular weight is very low and the drug safety is high. If multiple targets are pulled by 19 peptides, the drug can be delivered directly to the tumor cells [6], and then improve the efficiency of medicine [7].

4. Screening of Small Molecular Peptides.

Currently, there are two common methods for screening small molecule peptides.

One is the combinatorial chemical peptide library method that is one bead one peptide chain, and the other is the phage display peptide library method.

The combinatorial chemical peptide library technology was proposed by Lam first. The theory is to synthesize natural and unnatural amino acids on resin beads, and then synthesized the peptide chain of amino acids according to the need [9]. One bead has only one peptide chain on it, but one experiment can screen tens of thousands of peptides, so its screening efficiency is very high. The phage display peptide library method can also be used to screening small molecule peptides. But we usually use the former method. Because the chemical peptide library technology can be randomly added to the non-natural amino acids in the process of peptide chain synthesis, the selected peptide chains are not easy to be hydrolyzed, and the structure is stable.

Foreign experts and scholars have been successful in adopting combinatorial chemical peptide library technology. A variety of small molecular peptides were screened, and these small peptides were associated with cell adhesion. Pennington used the (du-h) prostate cancer cell line to screen in an environment of nearly 1.5 million peptides. He obtains two sequences, DNRIRLQKXX (rx-1) and lnivs-vngrhx (ru-1), and they were both related to the cell adhesion. The two amino acid peptides screened by Dereck are kikmviswkg (hyd-1) and kmviywkag (rz-3). These cells support the adhesion of prostate cancer cells and weaken the adhesion between cancer cells and extracellular matrix proteins. The small molecule cDGXGXXc screened by Aina can be specifically adhered to ovarian cancer cells.

5. The Role of Small Molecule Peptides in Tumor Suppression.

The role of small molecular peptides in tumor suppressor [10] is very important, especially p53, which is mainly used for reconstruction. P53 was obtained in cells of mice infected with SV40. In recent years, people have paid more and more attention to p53, a gene that is mainly used in tumor suppressor. Through continuous research, the research on influencing factors is very prominent.

The tumor suppressive function of p53 is that it can induce apoptosis. The research on p53 focuses on the transcription level. In recent years, the transcription factors found in p53 are RREB1, BLIMP1, YB1, BCL6, etc. The function of transcription factors is different because they are in different parts of the body. It can be divided into regulator type, constitutive type, signal dependent type and cell selective type. In conclusion, the function of p53 as a transcription factor is diverse.

The apoptotic stimulant used in p53 is the ASPP family. It's made up of iASPP, ASPP2 and ASPP1. IASPP is the member that mainly act as a suppressor, which can specifically suppress the effort of p53. At the same time, iASPP was found to be overexpressed in a variety of cancers, including hepatocellular carcinoma, leukemia, ovarian cancer, pituitary adenoma, and non-small cell lung

cancer. The results indicated that the key factors that suppress the effort of p53 in normal tumor suppression may be related to the high expression of IASPP in tumor cells.

According to Ahn, the binding domain in p53 may combine with iASPP to change the location of the sub-DNA and affect the apoptosis activity of p53. Among them, the affinity between IASPP and p53 domain is high. P53 structure domain includes proline (Pro), N the transcriptional activation structure domain (TAD), would (L) structure, the structure of the DNA binding or core domains (CD), the basic structure domain (BD) and oligomers, area (OD). Up to now, their effort to the activity of p53 has been confirmed except for the linker (L) domain.

6. Development and Prospect.

In recent years, the research on small molecular peptides has become more and more extensive in China. Products based on small molecular peptides are also incorporated into people's lives. The characteristics of small molecule peptides are strong activity and diversity. In food, small molecular peptides are extracted from lactic acid bacteria, which can be made into natural and non-toxic preservatives. In the manufacture of cosmetics, many small molecule peptides and their sub-peptides are adopted, because small molecule peptide can regulate the metabolism of skin cell better, also can repair damaged cell, delay skin senescence thereby; In medicine, small molecular peptides can be used to make antihypertensive drugs and can also be used to make drugs for immunological diseases such as serum disease. The application of small molecule peptide plays an increasingly important role in building a better life.

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References

- [1]. Maeshima Y,Colorado PC,Torre A,et al.Distinct antitum or properties of a type IV collagen domain derived from basement membrane[J].J Biol Chem,2000, 275(28):21340-21348.
- [2]. Chadderton NS, Stringer SE. Interaction of platelet factor 4 with fibroblast growth factor 2 is stabilized by heparan sulphate [J]. Int J Biochem Cell Biol, 2003, 35(7):1052-1055.
- [3]. Maeshima Y,Sudhakar A,Lively JC,et al.Tumstatin,an endothelial cell-specific inhibitor of Protein synthesis[J].Science,2002,295(5552):140-143.
- [4]. Siddiqui MM,Rais-Bahrami S,Turkbey B,et al.Comparison of MR ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer[J].JAMA,2015,31(4) : 390-397.
- [5]. Vargas HA,Wassberg C,Fox JJ,et al. Bone metastases in castration-resistant prostate cancer: Associations between morphologic CT patterns,glycolytic activity and androgen receptor expression on PET and overall survival[J] .Radiology,2014,271(1) :220-229.
- [6]. Skovgaard D,Persson M,Kjaer A. PET imaging of urokinase-type plasminogen activator receptor (uPAR) in prostate cancer: Current status and future perspectives[J].Clin Transl Imaging,2016,4(6) : 457-465.
- [7]. Afaq A, Batura D, Bomanji J. New frontiers in prostate cancer imaging: Clinical utility of prostate-specific membrane antigen positron emission tomography [J] .Int Urol Nephrol, 2017, 49(5): 803-810.

- [8]. Pawlotsky JM. The results of phase III clinical trials with telaprevir and boceprevir presented at the liver meeting 2010: a new standard of care for hepatitis C virus genotype 1 infection, but with issues still pending [J]. *Gastroenterology*, 2011, 140:746-754.
- [9]. Jauregui LE, Babazadeh S, Seltzer E, et al. Randomized, double-blind comparison of once-weekly dalbavancin versus twice-daily linezolid therapy for the treatment of complicated skin and skin structure infections [J]. *Clin Infect Dis*, 2005,41: 1407-1415
- [10]. Kvols LK, Oberg KE, O'Dorisio TM, et al. Pasireotide (SOM230) shows efficacy and tolerability in the treatment of patients with advanced neuroendocrine tumors refractory or resistant to octreotide LAR: results from a phase II study [J]. *Endocr Relat Cancer*, 2012, 19: 657-666.