

Peptide-Based Therapy against Esophageal Cancer Cell Line

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Received: 14 August, 2018; **Accepted:** 16 August, 2018; **Published:** 19 August, 2018

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Copyright: © 2018 Goudarzi F, Peptide Therapy on Esophageal Cancer Cell Line. Int J Gastroenterol Hepatol; 1(1): 1-4.

Introduction

Along with advances in genomic research and biotechnology, pharmaceutical companies have developed protein and peptide drugs for the treatment of various diseases [1]. The importance of peptides as a mediator of biological activity in the body and its specific roles in the body has determined the important role of the drug for them in the pharmaceutical industry because peptides have biological effects and very little toxic side effects compared to other related drugs. The importance of this issue in the pharmaceutical industry is so high that major pharmaceutical companies operating in the field of the production of old medicines, in recent years, turned to peptide drugs.

Nisin

Lantibiotics are a group of peptides. They are small and heat-resistant peptides and have lantionone and methyl-lantionone amino acids in their structure [2]. Nisin is a

subgroup of the lantibiotics and has +4 charges. Nisin is a soluble polypeptide with 34 amino acid with a $(C_{143} H_{230} N_{42} O_3)$ formula.

Cancer

Cancer is a dangerous growth of the body tissue by the rapid division of the cells. Cancer is basically a genetic disorder. The fate of the cell at any time is controlled precisely by growth factors, environmental messages, and some proteins. Mutations that lead to changes in any of the factors affecting the fate of the cell lead to a precarious regulation that regulates the growth and reproduction and differentiation of the cells and can lead to cancer [3].

Gastrointestinal cancers

Gastrointestinal cancers are the most common cancers in the world [4,5]. Environmental and heritable factors are the causative agents of these tumors. Lifestyle related factors such as eating habits, physical

Goudarzi F (2018) Peptide Therapy on Esophageal Cancer Cell Line. *Int J Gastroenterol Hepatol*; 1(1): 101.

activity, smoking, alcohol and exposure to contaminants have an important role in the development of these cancers [6,7]. According to the Iranian Ministry of Health, cancer is the third most common cause of death in Iran. Compared with western countries, the prevalence of squamous cell carcinoma in esophagus and gastric cancer is higher in Iran [8, 9]. Esophageal and gastric cancers, which are the cause of the highest deaths associated with cancer in Iran, have the highest prevalence in the northern parts of the country, including Ardebil [10,11]. Gastric cancer is the leading cause of half of the cancers and also accounts for more than half of the deaths associated with cancer in Ardabil [12].

Esophageal cancer

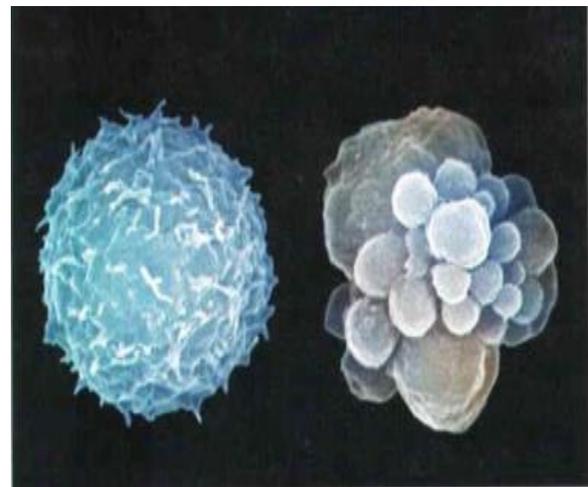
High-invasive esophageal cancer is a common cancer worldwide. Over the past two decades, the incidence and mortality of esophageal cancer has increased significantly [13]. In addition to the eastern parts of the Caspian Sea coast, which has the highest incidence of esophageal cancer in the world, other parts of the country have different rates of this cancer from 3 to 15 thousand cases per 100,000 people. Having a family history of esophageal cancer, social and economic status, and poor diet are among the factors that affect esophageal cancer [14]. This cancer occurs more often in men over 50 years of age. Esophageal cancer is the same malignant tumor in the esophagus (Figure. 1), which is of two types: carcinoma and adenocarcinoma; these two types of cancer are different from each other under the microscope. The most deadly cancer in the upper parts of the digestive tract is cancer of the esophagus [15,16]. Recent experiments

suggest that chemotherapy may have a similar surgical effect. In spite of these escalation therapies, esophageal cancer remains a challenge for researchers [16,17].

Figure (1): Microscopic Image of Esophageal Cancer Cells



Figure (2): Apoptotic cells. Apoptotic cells break down without releasing cellular components that can damage the surrounding cells.



Apoptosis

Apoptosis is a planned cell death that is essential for the growth and appropriate

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function of living organisms (Figure. 2). Dying cells are contracted and dense, then split, and eventually small apoptotic membrane bodies surrounded by other cells. In the apoptotic cells, the nucleus is compressed and the DNA is fragmented, but in this case, the intracellular components are not released into the environment. The nucleus congestion and the surrounding cells of the apoptosis show that this type of cell death is well controlled [18,19].

The effect of nisin on esophageal cancer cell line

Nisin peptide was treated by MTT and Neutral Red assays on esophageal (KYSE-30) cancer cells. The results of this assays showed that nisin have cytotoxic effect on KYSE-30 cell line. the IC50 value of this peptide was 130 μ M after 72h. The cytotoxicity of nisin is dependent on concentration and time. Nisin has cytotoxic effect on this cell line by apoptosis [20].

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