MEDS Clinical Medicine (2022)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2022.030713
ISSN 2616-1907 Vol. 3 Num. 7

Discussion on Related Genes and Genetic Susceptibility of Esophageal Cancer in Kazakh

Yongshuai Zhang

Xinjiang Applied Vocational and Technical College, 62 West Beijing Road, Kuitun 833200, Xinjiang, China

Keywords: Esophageal cancer; Kazakh; Oncogene

Abstract: Xinjiang is a high incidence area of esophageal cancer. In particular, Kazakhs are a high incidence of esophageal cancer population. At present, the proportion and mechanism of environmental and genetic interactions as risk factors for esophageal cancer have not been well understood. The occurrence and development of tumors are the result of environmental exposure and genetic susceptibility. This article aims to explore the relationship between P53, RB gene and the pathogenesis of esophageal cancer in order to explore its genetic variation and lay the foundation for future prevention and research of esophageal cancer.

1. Introduction

Esophageal cancer is one of the most common gastrointestinal malignancies in the world, with about 300,000 deaths each year. The epidemiological characteristics of esophageal cancer showed significant regional differences and ethnic differences. The incidence of esophageal cancer in high incidence area is 500 times higher than that in low incidence area [1]. The incidence of esophageal cancer in Xinjiang Kazakh residents is the highest, with an incidence rate of 155.9 / 100,000, and the mortality rate (88.7 / 100,000) is much higher than that of other ethnic groups in the same region (22.3 / 100,000). This is a malignant tumor that needs prevention and treatment in the region.[2]

Xinjiang is a multi-ethnic living area and a high incidence area of esophageal cancer. The mortality of esophageal cancer in Xinjiang was 13.05 %. The incidence of esophageal cancer is different in different races. Among all ethnic groups in China, the prevalence of Kazak is the highest, far more than 14.94 ‰, followed by Uygur and Han. The lifestyle and habits of Tajiks are similar to Kazakhs and are the lowest in China. [3] Kazakh is a northern region of Xinjiang, is a nomadic people-based nation. The incidence of esophageal cancer is different between different regions and different ethnic groups, indicating that environmental factors play an important role in the occurrence of esophageal cancer. However, even in places with similar high incidence and environmental exposure factors, only a few patients with esophageal cancer will occur, and there are obvious family reunions. An epidemiological survey of high incidence areas of esophageal cancer in China showed that: nearly 36 % of esophageal cancer family history, 21 % of esophageal cancer family history in low incidence areas also have a family history. It indicates that genes are also involved in the occurrence and development of esophageal cancer [4]. At present, the proportion and mechanism of environmental and genetic interactions as risk factors for esophageal

cancer have not been well understood. The occurrence and development of tumors are the result of environmental exposure and genetic susceptibility. In this paper, the Kazakh esophageal cancer related genes P53, RB, CYP, HPV, survivin, matrix metalloproteinase and BCL-2 were discussed.

2. Kazakh esophageal cancer related genes

2.1 P53 and RB

P53 is the most extensive and systemic anti-tumor gene. Abnormal expression of P53 gene in tumors is a common phenomenon, and it is also a prognostic indicator of many tumors. P53 protein has a high expression level in the pathogenesis and development of esophageal cancer in Kazakh, which is related to the invasion and clinical stage of esophageal cancer. RB and P53 are two major tumor suppressors. Tumor suppressor genes usually use their protein product nucleoprotein to regulate cell growth. If the tumor suppressor gene loses its function, it may promote malignant transformation of cancer cells. The expression of RB in tumor tissues is more, indicating that the inactivation of RB plays an important role in the development of esophageal cancer, and the role of RB in Kazakh esophageal cancer is also significantly different from other ethnic groups.

2.2 CYP

Cytochrome P450 (CYP) is a protein containing hemoglobin and sulfide hydroxyl, which is widely distributed in the body. It plays an important role in carbon assimilation, hormone synthesis, degradation of exogenous substances, tumor precursor activity and other processes, of which more than 60 % is metabolized by CYP450 [5].

2.3 Human papillomavirus

The pathological morphology of esophageal carcinoma is similar to genital warts. The detection rate of HPV in high incidence areas is higher than that in low incidence areas. In this paper, the infection of HPVdna in 318 cases of esophageal cancer in Xinjiang Kazakh area was analyzed. The results showed that HPVdna infection was related to esophageal cancer in Xinjiang Kazakh area, which was an important cause of esophageal cancer. In this paper, HPV-18,31,45E7 in Han patients with esophageal cancer were studied. The results showed that HPV18 was the most common type in Xinjiang Han population. In the Kazakh region, the detection rate of HPV18E7 genotype is higher, indicating that HPV18E7 has a certain relationship with its occurrence.

2.4 Surviving protein

Active proteins have a certain inhibitory effect on apoptosis and are of great significance to the development of tumors. The content of survival protein in Kazakh esophageal cancer was significantly higher than that in adjacent tissues [6], indicating its inhibitory effect on tumor cell apoptosis.

2.5 Matrix Metalloproteinases

Matrix metalloproteinase is a protease composed of most extracellular matrix except polysaccharides. It is a major anti-tumor cell membrane matrix. The increase in its expression level indicates tumor invasion and metastasis. The results showed that the expression level of mmp-7 protein in Kazakh esophageal cancer tissues was significantly higher than that in adjacent tissues, suggesting that there was a certain correlation between mmp-7 and tumor invasion and metastasis.

2.6 BCL-2

The current study of BCL-2 gene, BCL2 gene cleavage and BCL2 expression in tumor tissues have shown that overexpression of BCL-2-2 gene will hinder the normal apoptosis of cells, increase cell variation and viral infection. The expression of BCL-2 in esophageal cancer of Han and Kazak patients increased with the decrease of differentiation, indicating that the expression of BCL-2 in esophageal cancer is an early event in tumorigenesis. There is a certain correlation between the degree of differentiation of esophageal cancer, but there is no significant difference between different countries.

3. Related aspects of genetic susceptibility to esophageal cancer in Kazakh

Esophageal cancer in northern Xinjiang has a high ethnic aggregation rate, suggesting that in addition to environmental carcinogenic factors, there are also differences in genetic susceptibility between Kazakhs and Hans. Environmental exposure factors are closely related to the occurrence of esophageal cancer. In addition, genetic susceptibility such as abnormal gene methylation, copy number changes, and single nucleotide polymorphism changes also play an important role in the development of esophageal cancer. Deficiency of vitamins and trace elements is considered a key factor in environmental exposure to esophageal cancer. Changes in vitamin and trace element metabolism-related genes and genetic susceptibility of metabolism-related genes are key targets for the interaction between tumor environment and genetic factors. In recent years, it has become a hot spot in the study of risk factors and etiology of esophageal cancer.

According to the existing literature, the methylation types and levels of hypermethylated genes in esophageal cancer cells are significantly different among populations and races in different regions, indicating the genetic susceptibility of the population to the disease. It suggests that population genetic sensitivity and environmental exposure factors play a special role in the occurrence and development of esophageal cancer. In recent years, the relationship between CYP gene polymorphism and induced disease susceptibility has been paid more and more attention. The polymorphism of CYP2E1 RSA I gene locus is associated with the occurrence of esophageal cancer in Kazakhs, while CYP2E1-C1 / C1 gene locus is closely related to smoking and alcohol abuse. Therefore, in the prevention and treatment of esophageal cancer, health education should be strengthened to control the external environment, lifestyle and other adverse factors to prevent cancer.

All biological characteristics of the human body are maintained by the specific gene coding of the corresponding protein. Therefore, gene coding and human genomics are considered to be the hope of explaining all biological characteristics and human functions. When a specific gene undergoes gene mutation, abnormal methylation, and specific gene sequence variation, it will inevitably lead to abnormal gene function, resulting in the corresponding coding protein variation between different groups, which is called genetic susceptibility. We believe that the change of genetic susceptibility of human riboflavin transporter genes is the root cause of abnormal riboflavin metabolism in human nuclei, which leads to national, individual, and regional differences in the results of riboflavin diet intervention experiments.

4. Summary and outlook

Xinjiang is a high incidence area of esophageal cancer. The incidence and mortality of esophageal cancer in Kazakh are higher than those in other regions. The cause of esophageal cancer is unclear. There are many studies on the factors that cause esophageal cancer, including environmental factors such as nitrosamines, diet overheating, trace element deficiency and genetic

susceptibility. Some sensitive genes were found, such as K-ras, MTHFR, PLCE1 and so on. Furthermore, viral factors such as HPV infection are also considered to be related to the pathogenesis of tumors. However, domestic, and foreign studies have confirmed that tumors, as a multi-oncogenic factor and multi-gene target mutation, are caused by environmental exposure and genetic susceptibility.

Kazakh esophageal cancer is a multi-factor comprehensive disease caused by living habits, including living standards, geography, economy, health, genetics, and other factors. Many studies have shown that the predisposing factors of high incidence of esophageal cancer can be prevented and treated by daily eating habits. Tumor is a disease associated with environmental exposure and genetic susceptibility. Therefore, the study of riboflavin metabolism-related enzymes and genes may be the key to discovering riboflavin deficiency-induced tumorigenesis. With the in-depth research and development of various national scientific research projects and the support for the health cause in the western region, the pathogenesis of esophageal cancer can be further elucidated, and the gene therapy for patients with esophageal cancer can be accurately carried out to promote the development of clinical cancer treatment.

Acknowledgments

This work was supported by Key Scientific Research Project of Xinjiang Applied Vocational and Technical College (NO: XYZY2020KZD0002)

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