Study of variability of p53, pRB genes and ribosomal cistrones activity during colon cancer

Nino Chigvinadze

Ivane Javakhishvili Tbilisi State University, Faculty of Exact and Natural Sciences, Department of Biology, Division of Genetics.
E-mail: nino_chigvinadze@yahoo.com

Summary of master's thesis.

Scientific Managers:
Professor Tinatin Jokhadze;
Doctor of biology Tamuna Buadze

The colon cancer (CC), as well as other oncologic diseases, belongs to genetically predicated multifactic diseases. The carcinogenesis is associated with a range of genetic phenomena that occur in a certain group of genes, have a gradual nature and involve interaction between gene suppressors and oncogen. Special interest is generated by genes - pRb and p53, whose mutations begin to involve a consistent cascade of events that ultimately lead to tumor development. The established connection between pRb and p53 genes (Nevins J. 2001). It is shown that the system of the nuclear organisators (threads of satellites acrocentric chromosomes containing ribosomal cistrons) involved in the neoplastic vulnerability of tumors. This system is one of the key components of the cell protein-synthesizing apparatus and is associated with p53 gen (James, 2014).

It is known that in pathologies the activity of the protein-synthesizing apparatus of cells can be varied in different ways.

This above shows the importance of studying the variability of the genes and products of genes involved in carcinogenesis and the effectiveness of ribosomal cystrons in the cells of patients with colorectal cancer. The relevance of this topic is due to the fact that such studies have not been conducted in Georgia.

Consequently, the goal was - on the one hand, the study the variability of products of pRb and p53 genes, and on the other hand, the variability of activity ribosomal cistrones in the case of colon cancer

In the framework of the grant project was conducted:

1. Evaluation of variability of p53 and pRb gene products in patients with CRC.
2. Evaluation of functional genomic parameters (structural-quanitative disorders of chromosomes) and activity of ribosomal cistrones (cytogenetic part) in patients with colon cancer.

Material and methods

The peripheral blood by individuals with CRC was used as a material for the study; as a control - peripheral blood by healthy groups.

P53 and PRB gene products have been evaluated by the ELISA method.

For cytogenetic studies were used the methods: peripheral blood lymphocytes cultivation; Methods of measuring quantitative, structural disorders and fragile sites of chromosomes; The method of silver impregnation to reveal active nuclear organizers.

The results

Most of the patients with colon cancer generally had a low content of P53 and PRB proteins. The content of protein P53 was varied within 95-155 in different individuals (in control group - within 290-510).

The ccontent PRB protein in the majority of patients was within 105-390 and was significantly lower than the control group.

The results show that in the majority of patients there is a mutation of p53 and pRb genes. This corresponds to the opinion (point of view) of the role these genes in the development of tumors. It should be noted that a number of patients have high levels of P53 and PRB proteins that are higher than the control indicator. The findings indicate that the involvement of these genes in cases of different tumors Probably has a different character. At the next stage of working is the level of genome stability by patients with CRC was determined . As a result of the analysis show, the patients with colon cancer is characterized general instability of genome. The quantitative (to be registered the frequencies of cells with aneuploidy and polyploidy) and structural (the frequency of cells with chromosomal aberrations and fragile sites) violations (disorders) of chromosomes have increased. In particular, (the) frequencies of cells with aneuploidy in lymphocytes cultures of patients it was 19,7±1,8% (in control group of healthy donors - 6,7±0,9%); the frequencies of cells with chromosomal aberrations - 6,7±0,9% (in control - 1,7±0,4%). The results obtained are indicated that: the patients with CRC is characterized Increased level of chromatin condensation. In addition, as the chromosomal fragility test indicates, changed the distribution of damaged chromosomes by groups, what should be a specific feature for a tumor of this type. To evaluate the intensity of synthetic processes in the cells of patients with colon cancer, the activity of ribosomal cistrones has been studied: frequency – Ag positive acrocentric chromosomes and intensification of its inclusion in associations. It was found that the total value of Ag positive acrocentric chromosome (single and double scale) per cell in CRC patients does not differ from that for healthy people. At the same time, for cells of CRC patients, the predominance of active NORs of a large size is specific, which indicates the activation of additional ribosomal genes. The results obtained are also confirmed when using the associative activity test of acrocentric chromosomes, and indicate that the intensity of synthetic processes in cells patients with CRC is increased in comparison with the control index of healthy people.

Thus, on the basis of conducted studies we can conclude that:

1. The role of mutations in P53 and PRB genes in colon cancer patients may be muted in case of specific tumors.

2. Against the background of general high instability, the genome of patients with CRC is characterized by the presence of specific areas of the greatest vulnerability (damageability).

3. The cells of patients CRC are characterized by a high level of intensity of synthetic processes, which is provided by additional activation of ribosomal cistrones.

Recommendation:

Proceeding from the fact that a significant part of cases of colon cancer is of a family nature, it would be advisable to study the variability of the functional characteristics of the genome, as well as study

heterozygous carriers of P53 and PRB genes in relatives of patients, which would create opportunities for early identification and prevention of high-risk groups