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Carcinogenesis as a Process of the Reverse Evolution (Hypothesis)

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Keywords:
carcinogenesis; evolution; genome instability; malignant tumors; metastases

Abstract.

The hypothesis about carcinogenesis process as a cell reverse evolution process is proposed. The process of transition of the cells functioning programs from its daughter forms to the plesiomorphic ones (those that cell used evolutionarily earlier) occurs under the conditions of genomic instability as a result of mutations. We suppose this transition to occur in the process of a cell malignant transformation as a result of the repair genes damage in the cell genome. The process consists in the mutational destruction of the existing cell functioning and management programs resulting in the unlocking and the bringing into action ancestral forms of the cell functioning programs. As a result, in each replication cycle the cell takes a step back in evolutionary terms. This leads at first to the formation of colonies of such cells (malignant tumor), and later to the cells which are metastases.

Problem statement and analysis of the recent research

Carcinogenesis as a process has been under study for a long time. Recently oncologic diseases formation has been associated with stem cells modification into tumorous stem cells [6]. It is known which processes occur in cells that transform constantly, however, issues about causes, reasons and mechanisms of these processes have not been studied and clarified yet.

Cell malignant change is known [1, 6] to be associated with its genome instability. Moreover, this instability is probably a result of some genes damage as a consequence of mutagenesis (such genes as p53, RB1BRCA1, BRCA2 and others are mentioned the most often) [2]. These genes can take part in repair process of DNA cells.

There is different number of repair genes in genotype cells of different individuals since mutagenesis of genes damage is random process. Eventually, different number of gene repair is destroyed in different cells of a person. Destruction of all repair genes in some stem cell means this cell malignization. Malignant cell can be present when the number of repair cells was bigger at birth. According to our calculations people whose number of repair genes was less than 3 can get oncologic disease in early childhood, and average age of this disorder for people having 8 repair genes in genotype can be more than 100 years.

Thus, repair deficiency causes genotype destruction, so leads to the gradual destruction of the mechanism in cancerous cell. Such thoughts allow making a conclusion that numerous aspects of carcinogenesis should be analyzed taking into account the theory of cybernetics.

Hypothesis proposed in this paper can be important and interesting for research resulting from the above mentioned information.

Hypothesis. What happens to the cell in the process of malignant transformation? We consider the deficiency of repair genes to create genome instability, which manifests itself in the fact that each subsequent information reading from DNA cell at translation or reduplication causes DNA cells damage with some probability (and much higher than in cells with undamaged repair genes). So, the process of further genes damage in the cell occurs with increasing rate.

According to cybernetics, DNA nucleotide sequence is a set of programs determining the structure and functions of cells. Damage of these programs causes inability to perform cell functions. However, cells which are transformed can function in a different way than original stem cells. What can explain this? We think that we should talk about evolution to give the answer to this question.

During evolution, changes of organisms occurred as a consequence of nucleotide sequence in the genotype of these organisms causing changes in the program of cell functioning. Probably, old programs were not eliminated. They were maintained but were blocked and were not performed. It is suggested that old programs are maintained in nucleotide sequence of organisms as introns.

Thus, cell genotype is a set of programs, part of which functions and is registered on exons, another part of it is blocked and registered on introns.

We consider that due to the destruction of original program of cell functioning, the program in introns is released. To be more precise it is the cell functioning program of the type which preceded the given one in the evolutionary sense. Thus, the cell retreats in evolutionary plan.

As a consequence of gene instability associated with long-lasting mutagenesis of gene programs, such programs which evolutionarily occurred later (we shall name them the daughter ones), would be destroyed earlier than programs which evolutionarily occurred earlier (we shall name them plesiomorphic ones).

As genome instability does not disappear, the programs which occurred earlier will eventually break and, and a cell "makes" one more "step" towards plesiomorphic forms. Thus, program transition from daughter to plesiomorphic forms continuously occurs in the transforming cell, that is the reverse evolution of cells occurs.

What does the reverse evolution cause? We consider the cell to return sooner or later to such stage of evolution, which corresponds to the level of cellular colonies able to unlimited growth. This is a cancerous tumor and it corresponds to the evolution stage which was named "Morula" by Haeckel [5].

The continuation of the reverse evolution of malignant cell has to return cell to the stage which corresponds to Cytaea [5] according to Haeckel determination. Unicellular organisms are formed, which are able to move actively in water medium. These are the cells which are called metastases.

Discussion. The hypothesis which is proposed in this paper allows explaining some important facts which appear at tumor progression. So, cancerous stem cells going beyond the control of systems limiting proliferation may be associated with destroyed (original) daughter programs, and these cells work according to the undestroyed programs of plesiomorphic forms. However, biochemical signals of plesiomorphic organism differ from signals of healthy organism. As a consequence cancerous cells either do not react or react differently than those cells in which modification does not appear. The reverse evolution in plesiomorphic form continues in the course of time and the difference between primary signals of original organism and signals of its plesiomorphic forms increases. Thus, the control of organism over cells loses. Similar reasoning is provided in this paper [4]. There is an assumption that "cancerous stem cells stop responding to outer signals and control under the influence of mutation".

At first sight, the hypothesis has serious drawback associated with such fact that the reverse evolution of cells may cause complete destruction of nucleotide sequences and death.

However, as a result of the reverse evolution cell passes to programs of plesiomorphic forms formed in other conditions than modern one. It is considered [3] that organisms existed in anaerobic environment in archaea and the Proterozoic. Oxygen was poison for organisms which existed at that time. These organisms were anaerobic and processes of catabolism and anabolism occurred differently than in daughter anaerobic organisms which appeared in Cambria. Cells could use oxygen only after oxygen content in oceans exceeded Pasteur point (oxygen tension was 1.59 millimeter of mercury), it occurred between from 620 to 1000 millions years ago. This is only assumption.

According to above mentioned facts cells of these anaerobic organisms used other schemes of life activity than cells of modern organisms. There is an assumption that mechanisms of integrity maintenance of genome in these cells (and therefore, in modern cells of malignant tumors and their metastases) were principally other, reckoned on existence in difficult conditions: water temperature could reach 50° C, ultraviolet irradiation (ozonic screen did not exist at that time) and others [3].

It should be concluded that if hypothesis is right, high resistance of tumors and metastasis to hypoxia and, probably, an attempt of metastasis to move to hypoxia zone and necrosis must be one of its consequences.

References

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