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Perspectives of using of somatic cells fusion process in some aspects of carcinogenesis

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Abstract

Normal somatic cells sensitive to carcinogenic effects and capable of proliferation form firstly a binuclear cells (dikaryons) and then hybrid cells (mononucleated synkaryons) by means of fusion with another cells of the same organism, in particular with differentiated and non-differentiated cells of corresponding tissue or with cells capable to migrate.

In all probability, during the perforation of the plasma membrane, i.e., after the formation of pores, induced by different carcinogenic (and noncarcinogenic) agents and factors, the total negative charge of plasma membrane changes (decreases) and the cells develop the ability to come closer to each other, which will probably be the prerequisite to a fusion process. On the other hand, it is not excluded that perforation can assist the fusion of only neighboring cells.

Initially, a set of chromosomes in a precancerous cell retains, even for a short time, the condition of tetraploidy. Because of cell fusion generates tetraploidy, it potentially might cause chromosomal instability.

The article emphasizes a possibility of using the fusion process in different aspects of carcinogenesis (therapy, prevention, etc.).

Keywords: Fusogeny; Dikaryons; Synkarions; Malignization.

1. Perspectives on Cancer's Resolution

It is established that a cancer cell in contrast to normal analogues, needs comparatively lower concentrations of serum, calcium ions, oxygen, and glucose for its proliferation. Decrease in the limiting concentrations of substances necessary for growth makes the cancer cell proliferation process less dependent on the chemical composition of the environment. This circumstance gives the cancer cell a selective priority in competition with normal cells.

Moreover, in contrast to normal analogues, a cancer cell possess a comparatively high resistance to some adverse influences. Moreover, in contrast to normal analogues, a cancer cell possesses a comparatively high resistance to some bad influences (chemo-, radiotherapy, etc.); In other words, as compared with normal cells, the cancer cell has only one weak side, particularly, it enters into fusogenic processes much easier, or easier produces dikaryons, trikaryons and polykaryocytes. Some tumorous cell lines are so fusogenic, that they fused spontaneously more efficiently than in the presence of fusogenic agents and factors. It is exactly this last feature of a cancer cell that can be used in the cellular therapy for cancer. Unfortunately, no other way is visible!

After fusogeny, together with dikaryons arise giant polynuclear cells, so-called polykaryocytes . Polykaryocytes formed after endomitosis (mitosis without cytotomy) are functionally active. Unlike from these cells, polykaryocytes formed after fusogeny process, from the genetic standpoint seemingly present a certain deadlock. In most cases they are

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nonviable and imperfect cellular formations, i.e., they do not enter the S-phase of a cellular cycle and mitosis and die quickly. Appearance in certain tissues and organs of the cells of such morphology can signify presence of conditions for cells' hybridization.

As a consequence of nonviability of polykaryocytes, formed by mean of fusion process, our supposition is that it would be necessary to produce simultaneous transformation of tumor cellular substrate to the stage of nonviable polykaryocytes. If this could be achieved, there might be a dissociation of tumor substrate and considerable reduction of the mass of the tumor or even its full resolution.

How might the transformation of tumorous cells into the stage of nonviable polykaryocytes be achieved? It would be ideal to have such chemical substance or biological agent (for example, virus) that would be capable of tropism towards a particular tissue or organs together with strong fusogenic properties. For this aim, it is possible to use PEG, lysolecithin, polyarginin, glyceril monooleate, electric fields, virus Sendai or other viruses with fusogenic abilities and so on.

On such possibility of cellular therapy for cancer we informed the scientific community already in 2000 [5]. This view has been established sufficiently to use virus-induced cell fusion to kill cancer cells as a therapeutic approach [6]. Since this idea failed to attract proper attention in due time, we represented it in 2017 and 2020 [3,7].

2. Perspectives on Cancer's Prevention

Given that a tumorous cell represent a hybrid cell [1,2], originated because of the spontaneous or induced fusion of two normal somatic cells and the subsequent karyogamy, it can be assumed that inhibition of the approaching, contact and the further adhesion process of normal somatic cells, will suffice for preventing this fatal disease. In technical terms, this is a considerably easily performed process as against the manipulation in the genome of somatic cells at the molecular level (for dehybridization) or the repression of the genes being responsible for malignant transformation.

To achieve the set objective, it would be ideal to use the cell plasma membranes' stabilizing substances (to avoid plasma membranes perforations by different agents and factors) or the low-molecular disaggregants (for inhibition of adhesion of somatic cells). Said substances might be administered to the macro organism permanently, in the course of life, in small, harmless doses (for example, with drinking water and food). The expected outcome would be the creation in the body of the conditions when somatic cells are incapable of close contact with each other (nor injurious for organism). This will completely exclude the fusion of cells and then nuclei and reduce thus to a minimum the possibility of cancer cells development.

In the case of cancer prevention the following circumstance should be especially underlined: if the cancer patients manage to overcome the disease or to prolong for a definite term their life as a result of conducted therapy (chemotherapy, radiotherapy, etc.), for which reliable statistics are available, the positive outcomes of cancer prevention can hardly be fixed. In other words, the fixing of cancer prevention outcomes by means of inhibition of somatic cell fusion would, possibly, take several years or even decades.

3. Short-term test on carcinogenicity

Currently, in the world every year, there are synthesized nearly 10000 new chemical combinations, which are used in pharmacology, industry, food industry, agriculture and so forth. An absolute majority of these substances are not verified on carcinogenicity, mutagenicity, teratogenicity and so on.

For investigation of carcinogenic abilities of different chemical substances, the most informative, so far, are the chronic experiments in two species of laboratory rodents (for example, mice and rats). Nevertheless, these tests are expansive and take great deal of time. At the same time, extrapolation of the results obtained in animals to human population has a rather probabilistic character.

The principal obstacle of short-term tests are trials in carcinogenicity is a deficiency of modern knowledge of most important questions of carcinogenesis, in particular, on mechanisms of initiation, promotion and progression stages and critical and cellular, sub-cellular and molecular events, which take place on these stages.

As we believe, the substances and factors that induce the cells' fusion are potentially oncogenic ones. The positive fusogenic effect (i.e., appearance of two- and polynuclear hetero- and homokaryons) of all the known carcinogenic

agents and factors with negative controls can confirm the existence exactly this mechanism in malignization and also allows to use this method for the determination of carcinogenicity of certain chemical substances and other dubious factors in an oncogenic respect [8,9]. It is necessary to emphasize that approximately such results were received in 1993, by Baldwin and Lucy [10].

Well-known chemical carcinogens (for example, polycyclic aromatic hydrocarbons) possess a weak fusogenic effect and infrequently induced the formation of dikaryons with high oncogenic potency. In our view, this fact is an experimental basis of malignant tumor origin as proposed by the karyogamic theory of carcinogenesis. Thus, revealed reverse correlation between fusogenic and carcinogenic abilities: the higher the fusogenic activity of this or that substance, the lower its carcinogenic activity and vice versa. In particular, in the case of high fusogenic ability of the substance (for example, PEG), formation of unviable giant polykaryocytes was induced and the carcinogenic effect was less manifested; and vice versa: carcinogenic effect was higher in the presence of low fusogenic activity of the substance, because of the formation of mainly dikaryons with high oncogenic potency.

On our opinion, fusogenic test may be used for the determination of carcinogenicity of certain chemical substances. In a case of positive results (independently of fusion process intensity), this test allows us to identify full carcinogens and initiators (but not promoters).

One can make as even wider conclusion: those substance and influences, which induce somatic cells' fusion (or cells' membranes' perforations) are probably potential oncogenic agent.

4. Conclusion

The article highlights and underlines different aspects of carcinogenesis, where the somatic cells fusion phenomenon can be used both theoretically and practically. For example, fusion phenomenon can be used in cellular therapy of cancer by producing of giant nonviable polykaryocytes; the inhibitory means of the somatic cells' fusion can be used for cancer prevention; to develop a short-term fusogenic test for carcinogenicity, the capability of somatic cells' fusion for identifying different substances with carcinogenic potency can be used.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

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