Development of a skin benign tumor, cancer and melanoma from the view point of morphofunctional zones

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Abstract

Development of a benign and malignant skin tumor in a morphofunctional zone in many respects depends on the quantity of cambial cells, which excite an electric field at their division, due to which the inactive Src-kinase, participating in a formation of the cytoskeleton and a differentiation, is expressed in cells. Decrease in cells number to 8 leads to formation of a benign tumor, and up to 6 – to malignant as this quantity of cambial cells can't express enough inactive Src-kinase, necessary for a normal cytoskeleton formation. The skin melanoma can develop without decrease in cambial cells number due to sharp redistribution between shares of inactive and the active Src-kinase, thus the cytoskeleton formation and cell differentiation fall.

Key words: *morphofunctional zones, stem cells quantity, skin benign tumor, cancer, and melanoma*

Formation of a benign tumor, cancer and melanoma of skin is intimately connected with the structural organization of skin. In norm the skin epithelium consists of morphofunctional zones, in which two subunits with 12 cambial cells in each occur. Proliferation and differentiation of cambial cells and their offspring happen in these structures [5, 8]. Each subunit is presented by cambial cells of one type which unite in groups of 3 cells and begin to divide [11]. As soon as their number reaches 12, the accumulation of cambial cells quantity stops in spite of the fact that these cells continue to divide (Figure 1).

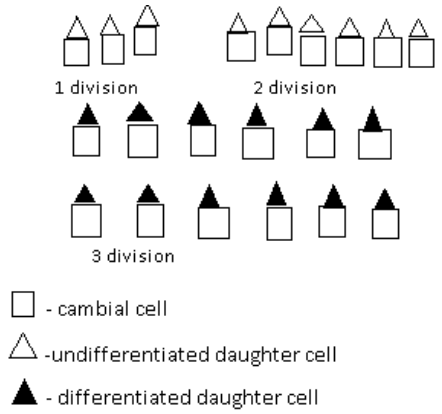

Figure 1. The scheme of cambial cells quantity regulation

Really, the main axis of cambial cells is directed vertically in relation to a basal membrane therefore the mother cells which turned out at their division, situate on a basal membrane, and daughter – over them. In mother cells the negatively charged chromatin has more dense structure, than in daughter due to action of the growth factors, which are in a basal membrane and have spastic properties. It leads to redistribution of the superficial charges between these cells and to emergence of an electric field [8]. Because the cambial cells are grouped in 3, 6 pairs of mother and daughter cells turn out during the first and second division. But such number of cells pairs aren't enough for exciting of an electric field necessary for a differentiation of the daughter cells. Therefore at contact with a basal membrane, 6 undifferentiated daughter cells become cambial. Then at the following division when the number of cambial cells reaches 12, the daughter cells, which are over the mother, begin to stretch by the electric field forces. At the same time the loci of chromosomes, fixed to the nucleus membrane, are stretched, which makes available these sites for a transcription [5].

Therefore, the electric field arising at 12 cambial cells division, makes the differentiating impact on daughter cells and at the same time interferes with further increase in cambial cells number. The field which is turning out at 6 cambial cells division doesn't make a differentiation of daughter cells [9].

In the other subunit of a morphofunctional zone there are similar processes, but the cambial cells in it enter into a proliferation a bit later, than in the first. In spite of the fact that in each subunit processes of a proliferation and differentiation are rather autonomous, however functionally subunits nevertheless are united in common morphofunctional zone, because at structural and function changes in the first subunit the second begins to react.

Interestingly, on the other side of a basal membrane in a stroma there are the same cambial cells with the similar principles of work. The main function of a stromal morphofunctional zone comes down to relaxation of epithelial cells cortex due to the own growth factors, without which epithelial cells can't be stretched by an electric field forces [10].

Thus, 12 cambial cells in each subunit provide a normal differentiation of daughter cells in a morphofunctional zone. Decrease in cambial cells number to 6 in one zone subunit can lead to origin of a malignant tumor. The weak electric field excited at division of such quantity can't stretch daughter cells and provide their differentiation. Because the stroma isn't changed during this period, 12 stromal cambial cells at the expense of their growth factors provide a relaxation of 6 epithelial cells cortex not only in a similar epithelial subunit, but also in another, which cells by this moment entered into mitosis. So, during the tumor process formation, two subunits of an epithelial morphofunctional zone with 6 cambial cells in each, work simultaneously. However the differentiation of daughter cells in the first and second subunits doesn't occur because weak fields don't interact with each other and can't stretch daughter cells (Figure 2 a).

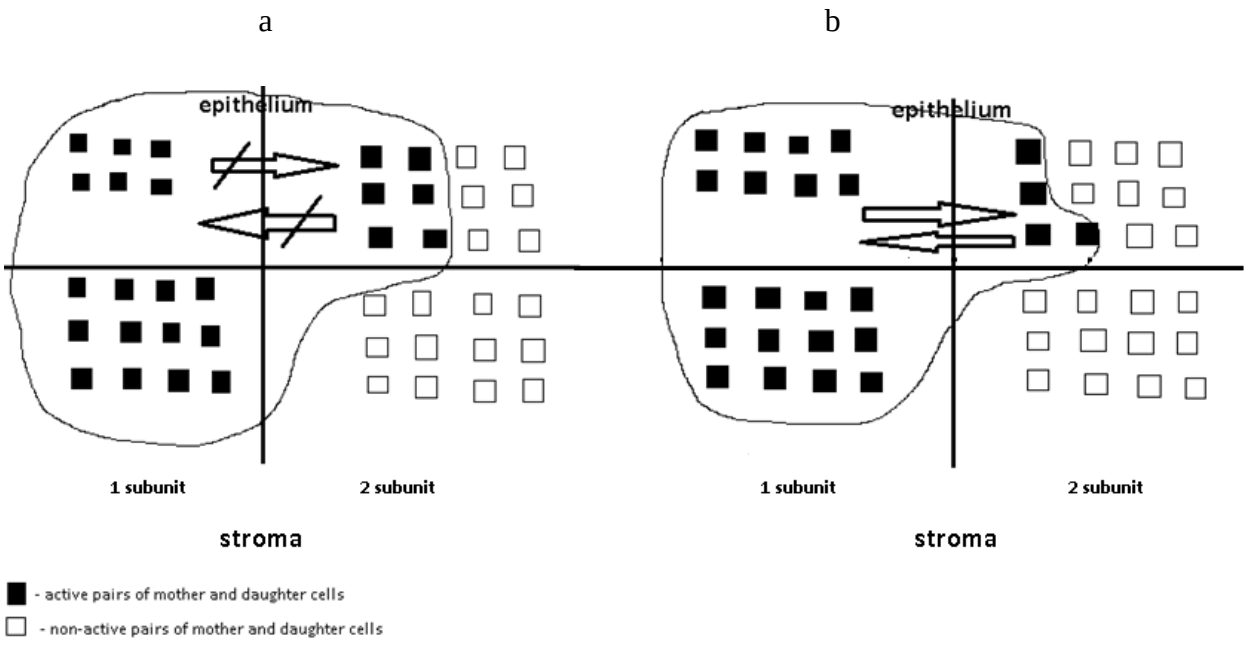

Figure 2.The scheme of cancer (a) and benign tumor development (b)

When forming a benign tumor the number of cambial cells in one subunit falls up to 8 (Figure 2 b). The electric field, excited at their division, is above threshold level (6 cells), therefore the differentiation of cells in this subunit is carried out. Besides, 12 stromal cambial cells will additionally relax a cortex of 4 cells in the other subunit. In spite of the fact that the field excited at 4 cambial cells division is below threshold level, the differentiation of daughter cells in the second subunit will also occur, because the electric field of the first subunit is higher than threshold and it summarizes with weaker field of the second subunit. At the same time the cells, which are in the weaker field deviate more strong, forming specific vectors of polarization. In each proliferative process the quantity of such vectors increases by 4 [9]. Thus, there is a special type of a symmetry, characteristic for non-cancer growth – radial-ray [4].

So, the existence of normal or tumor processes in tissues to a large extent depends on cambial cells quantity in morphofunctional zones.

Really, the electric field, excited at cambial cells division, stretches the daughter cells and potentiates in them an expression of an inactive form of Src-kinase, which participates in the formation of a cytoskeleton, especially of microtubules and acts as a cross-link protein, connecting molecules of a tubulin through SH2 domain [7]. Then microtubules together with the intermediate microfilaments stretch a cell nucleus, which finally leads to a differentiation of a cell. The quantity of cambial cells equal to 6 is critical because such excited electric field does not stretch the daughter cells, which leads to a small expression of inactive Src-kinase. In this case the cytoskeleton of a cell and a differentiation suffers.

Interestingly, Src-kinase in the inactive form participates also in a melanogenesis because it is one of donors of nucleophilic groups, which are necessary for activization of a tyrosinase. The latter gains ability to oxidize tyrosine only at the reduction of the copper ions entering in its active center, and this occurs at the expense of thiol groups. Therefore, both processes: melanogenesis and a cytoskeleton formation need in inactive Src-kinase [7].

It is known that inactive Src-kinase is a redox-sensitive molecule and easily is oxidized under the influence of various oxidants including UV radiation (UV) [1, 2, 3]. At the strong long UV the majority of inactive Src-kinase passes into the active form, which doesn't take part in the formation of a rigid protein network of microtubules and the intermediate filaments, which stretch a cell nucleus. Along with it the formation of DOPA and DOPA-quinone from tyrosine amplifies, which leads to increase in synthesis of a tyrosinase. The latter for its activization uses the increased number of SH groups of the proteins which are in melanosomes [7]. As a result of fast falling in a portion of inactive Src-kinase and increase in quantity of a tyrosinase, the formation of cytoskeleton and differentiation of cells begin to suffer sharply, which can lead to the development of a low-differentiated skin tumor - melanoma. In this case the quantity of cambial cells can remain on normal level but there is only a redistribution between the shares of inactive and active forms of Src-kinase towards increase of the active [6, 7] .

Thus, melanoma can arise due to strengthening of tyrosinase synthesis during the massive action of UV, followed by falloff of a share of inactive Src-kinase and dropping of a cytoskeleton formation and differentiation. The quantity of cambial cells at the same time is not changed, but the main condition of a malignant tumor development is met: a share of inactive Src-kinase is not higher than the level, which is created by 6 cambial cells, at which the differentiation is absent.

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