

Viability and glucose metabolism of cancer cells with different metastatic potential under deadhesive growth

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A distinctive feature of cancer cells that facilitates metastatic dissemination is resistance to anoikis (a caspase-dependent cell death process triggered by extracellular matrix detachment) the mechanisms of which remain unclear.

The study aimed to investigate the viability and indices of glucose metabolism of cancer cells with different metastatic potential under deadhesive and adhesive growth.

Materials and Methods. In the study, there were used two variants of Lewis lung carcinoma cells with different metastatic potential (LLC and LLC/R9). The cells were cultured under standard in vitro conditions on a deadhesive and adhesive substrate for 3 days. The number of cells was determined using the vital dye trypan blue in a hemocytometer. The level of apoptosis was determined by flow cytometry using propidium iodide. The level of lactate and glucose in the incubation medium was measured using a biochemical analyzer.

Results. It was shown that the growth of both variants of cancer cells as a deadhesive culture was accompanied by a significant decrease in the number of viable cells by more than 33% ($p < 0.01$) compared with that for their adhesive growth. The deadhesive growth of highly metastatic LLC cells caused a decrease in the number of both dead cells (by 56%, $p < 0.01$) and apoptotic cells (by 29%, $p < 0.01$) compared with adhesive growth conditions, indicating the presence of the subpopulation of the cells which are resistant to anoikis. In contrast to LLC, deadhesive growth of low-metastatic LLC/R9 cells caused an increase in the number of apoptotic cells by 80% ($p < 0.005$), without affecting the number of necrotic cells. Deadhesive growth of LLC/R9 cells was accompanied by a decrease in both the

level of glucose consumption and the level of lactate production. Thus, the level of glucose in the incubation medium was 12.6% ($p < 0.05$) higher, and the level of lactate 10% ($p < 0.05$) lower than that of these cells grown in adhesive culture. At the same time, the level of glucose and lactate in the incubation medium of LLC cells was almost the same for their adhesive and non-adhesive growth.

Conclusions. A comparative analysis of the studied parameters showed that under deadhesive growth low metastatic LLC/R9 cells (as opposed to highly metastatic LLC cells) are characterized by reduced glycolysis and increased sensitivity to anoikis. The stability of the glycolysis intensity in LLC cells during the transition to deadhesive growth conditions allow them to maintain a high level of synthesis of antioxidant enzymes and, consequently, to neutralize reactive oxygen species, causing both resistance of these cells (at least in part) to anoikis as well as their high metastatic potential.