DOI 10.36074/logos-18.08.2023.26

RELATIONSHIP BETWEEN THE INTENSITY OF GLYCOLYSIS AND THE METASTATIC POTENTIAL OF CANCER CELLS

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Despite significant advances in treatment methods and the development of new therapeutic drugs, cancer remains one of the most serious diseases. Anti-tumor therapy, particularly antimetastatic therapy, is still relevant. It is known that, compared with normal cells, cancer cells are characterized by an intensification of glycolysis and an increase in glucose uptake to ensure high proliferative activity. Meanwhile, the question of the relationship between the intensity of glycolysis and the metastatic potential of tumor cells remains open. Therefore, understanding the metabolic processes in metastatic cancer cells may lead to the development of new, more effective therapeutic methods.

The aim of the study was to determine the rate of glucose uptake and lactate production by cancer cells with different metastatic potential during 1 day of anchorage-dependent growth in vitro under standard incubation conditions.

In the work, two variants of Lewis lung carcinoma cells (LLC and LLC/R9), which differ in their metastatic potential *in vivo*, were used. Even though these cell lines are of the same genesis, LLC/R9 cells are characterized by triply lower metastatic potential compared to LLC cells: the growth of LLC/R9 cells *in vivo* causes 3 times lower number and volume of lung metastases compared to LLC. Cells of both LLC variants were obtained from the National Bank of Cell Lines and Tumor Strains of the IEPOR NAS of Ukraine.

Both cell variants were maintained *in vitro* under standard conditions in RPMI 1640 incubation medium (Sigma-Aldrich, USA) supplemented with 10% fetal calf serum, 2 mM L-glutamine, and 40 μg/ml gentamicin at 37°C in humidified conditions, 5% CO_2.

For the study, the cells were planted in Petri dishes and incubated for 1 day without changing the incubation medium. For each cell line, the study was performed in 4 replicates. After 1 day of anchorage-dependent growth of LLC and LLC/R9 the number of cells (viable and dead) was determined by direct counting in a hemocytometer using a 0.4% solution of trypan blue vital dye (Sigma-Aldrich, USA). Determination of glucose and lactate levels in the incubation medium of cancer cells was performed on a ChemWell 2910 biochemical analyzer (Awareness Technology, USA) using commercial kits according to the manufacturer's protocols. The glucose

consumption rate and lactate production rate were calculated taking into account the change in the number of living cells during their growth.

It was shown that the rate of glucose consumption by LLC/R9 cells was equal to 18.2×10-9±3.5×10-9 mmol/cell/day and was significantly higher by 90% ($p<0.01$) compared with this indicator for LLC cells. (9.6×10-9±1.4×10-9 mmol/cell/day).

The high rate of glucose consumption by cancer cells was accompanied by the active production of lactate, the production rate of which was significantly higher by 80% ($p<0.05$) for LLC/R9 cells than for LLC cells (32.6×10-9±6.8×10-9 mmol/cell/day and 18.05×10-9±2.1×10-9 mmol/cell/day for LLC/R9 and LLC, respectively).

Conclusions. The results showed that the intensity of glycolysis in the low-metastatic variant of Lewis lung carcinoma cells (LLC/R9) is significantly higher than in the highly metastatic variant (LLC).

Acknowledgement:

Galina SOLYANIK thank for the financial support of the Project ”Biophysical and biochemical characteristics of metastatic circulating cells as potential targets of antimetastatic therapy” NRFU 2021.01/0229.