SENSITIVITY OF CLONOGENIC HUMAN MEDULLOBLASTOMA TUMOR CELLS TO INFLUENCE OF ANTITUMORAL PREPARATION "ARGLABIN": INNOVATIVE APPROACH

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Introduction. One of breakthrough directions in the field of modern antitumor therapy of malignant human brain tumors is isolation and proliferation characteristic of clonogenic tumor cells and development of new antitumor preparations, influencing selectively on these cells. Research results of influence on clonogenic human medulloblastoma cells *in vitro* by antitumor preparation "Arglabin" prove that clonogenic cells can be a target for antitumor therapy.

Material and research methods. We developed technology of isolation and proliferation characteristic of clonogenic and nonclonogenic human medulloblastoma cells by cell cloning method *in vitro* (fig. 1). Experiment designs: 1) isolation of primary culture of medulloblastoma tumor cells from bioptic tumor material; 2) influence of arglabin on heterogeneous population of medulloblastoma cells in monolayer *in vitro*. After 24 hour cell cloning; 3) influence of arglabin on clonogenic medulloblastoma tumor cells in clones *in vitro*. Arglabin was injected into clonogenic medulloblastoma cells population for 2 days of cloning when colonies contained individual cells. Fixation and analysis of clones were carried out for 10 days of cloning.

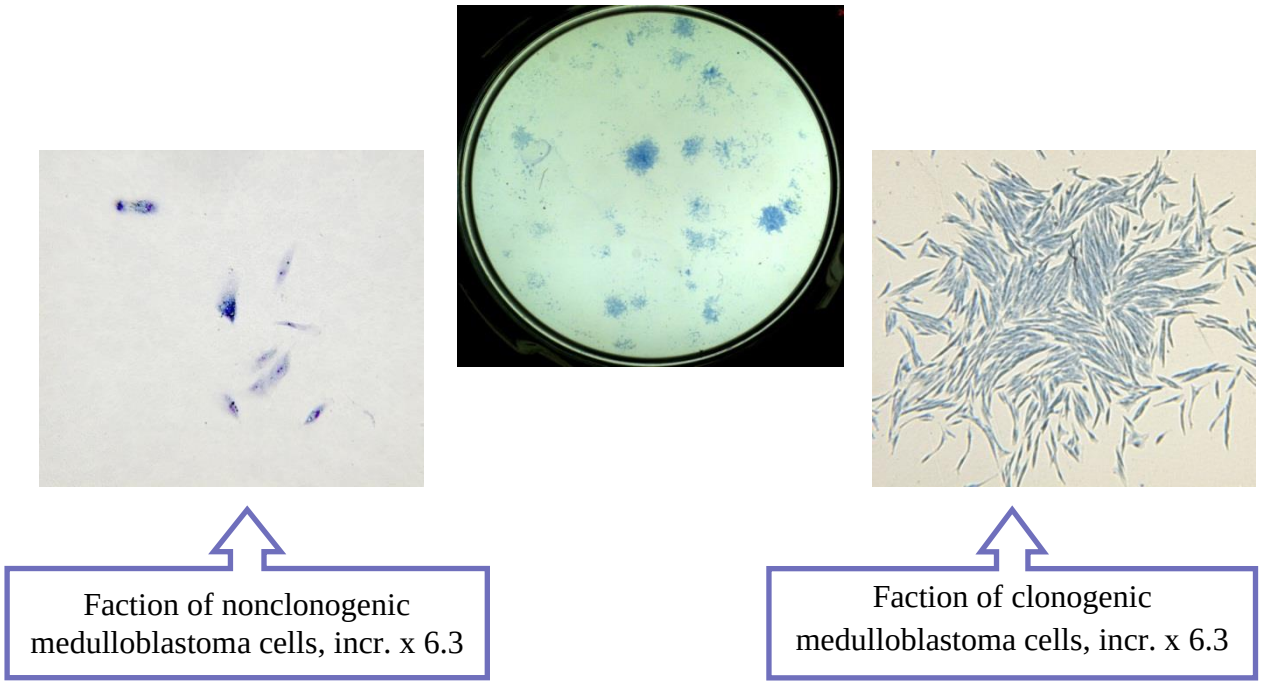
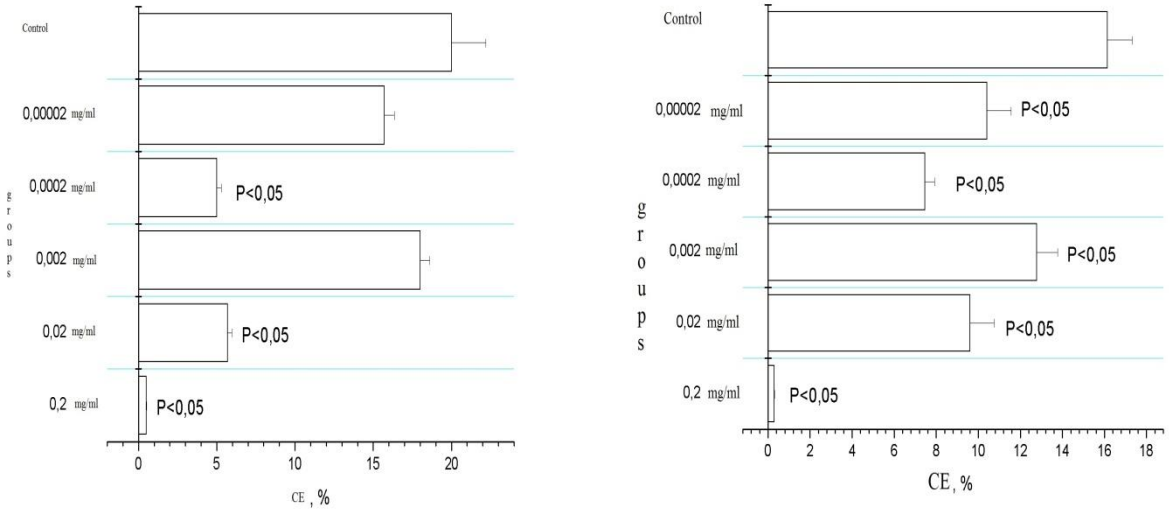


Fig. 1. Method of cloning in vitro human medulloblastoma cells

In terms on model *in vitro* the therapeutic dose of arglabin made 0.2 mg/ml (250 mg/m^2), which reduced by serial dilution method in 10 times. Final doses of arglabin made 0.2; 0.02; 0.002; 0.0002 and 0.00002 mg/ml. Indexes of proliferation and survival of clonogenic cells were defined: 1) proliferation (cloning efficiency, CE) of clonogenic cells was estimated on ability of clonogenic tumor cells to form multicellular colonies (not less than 50 cells). Cloning efficiency (CE, %) was counted as ratio of full-rate (> 50 cells) colonies on Petri dishes to count of cell seeding; 2) survival (LD, %) - as ration of CE in dose to CE in control.

Research results. Influence of preparation "Arglabin" on clonogenic human medulloblastoma cells was first researched. The obtained data testified the perspective application of preparation "Arglabin" as effective antitumor agent to inhibit proliferation of clonogenic medulloblastoma cells (fig. 2).



A *B*

Fig. 2. Cloning efficiency of clonogenic tumor cells after influence of preparation "Arglabin" on heterogeneous population of human medulloblastoma cells in monolayer in vitro (A) and on clonogenic cells in clones in vitro (B)

Selective influence of arglabin on clonogenic medulloblastoma cells, which expressed in death of clonogenic cells in clones' center was shown and testified to possibility of their use as target for antitumor therapy.

Colonies of nonclonogenic cells (abortive clones), which probably more sensitive to influence of arglabin in therapeutic dose were isolated among multicellular colonies of clonogenic medulloblastoma cells, and their death is caused by apoptosis mechanisms. Their share among clones of clonogenic cells increases in process of dose reduction of arglabin.

Conclusion. The further studying properties of clonogenic tumor cells will allow passing to qualitatively new level of search of pharmacological targets and development of new antitumor preparations.