Tomsk National Research Medical Center of the Russian Academy of Sciences
National Research Tomsk State University

The 22nd International Charles Heidelberger Symposium on Cancer Research

Proceedings of the International Symposium

17–19 September 2018

Publishing house of Tomsk University
2018

Conclusions

The data obtained showed that exposure of normal brain tissue to temozolomide and dexamethasone significantly affected the normal brain ECM, creating the appropriate microenvironment for tumor cells proliferation and invasion, thereby promoting tumor relapses.

Keywords: glioblastoma, chemotherapy, extracellular matrix, invasion, proteoglycan.

This work has been supported by a Russian Science Foundation (RSF grant № 16-15-10243). Tsidulko A.Y. was supported by scholarship of Russian Federation President for young scientists (SP-5435.2018.4). Microscopy was performed at the Microscopy Center of the Institute of Cytology and Genetics, SB RAS, Russia

CNA LANDSCAPE OF BREAST TUMOR, CONNECTION WITH THE EFFICIENCY OF NEOADJUVANT CHEMOTHERAPY

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The research involved 80 patients diagnosed with breast cancer (BC). Biopsy samples were collected before treatment. We studied the tumor tissue using the CytoScan HD Array (Affymetrix, USA) microarray to evaluate the CNA landscape. We studied the frequency of segmental and numerical CNA occurrence and their association with the efficiency of neoadjuvant chemotherapy (NAC).

Introduction

Deletions and amplifications of chromosome regions and individual chromosomes are called Copy Number Aberrations (CNA). These types of cytogenetic disorders may affect the expression of genes; generally, in cases of deletions, the expression of genes located in the deleted regions is decreased, and it is increased in the cases of amplifications [1, 2]. CNA are especially widespread in solid tumors of various localizations, namely in breast tumors[3]. CNA is most frequently observed in the 1q, 8q, and 16q regions of a breast tumor.

Only a few studies have reported an association between CNA and NAC in BC. Thus, the study of the CNA landscape of breast tumor before treatment and evaluation of the association between CAN and NAC response is of great importance.

Material and Methods

We examined 80 patients with histologically verified breast cancer (BC) in IIA – IIIB (T1-3-N0-3M0) stages. The patients were in the age range of 28–68 years (median age: 48.2±2.4). The patients received 2-4 courses of chemotherapy according to the FAC, CAX regimens or taxotere monotherapy in the neoadjuvant mode. The efficiency of preoperative chemotherapy was evaluated according to the WHO [3] criteria using findinga of ultrasound imaging and/or mammography. According to the international recommendations, we formed the groups of the patients whose tumors stabilized or progressed after the preoperative chemotherapy (NAC no-response group), and the patients with partial regression (positive response group) [4]. Biopsy samples taken before treatment were used as the material for the study. We extracted DNA from breast tumor tissues using QIAamp DNA mini Kit (Qiagen, Germany). Microarray analysis was carried out using the CytoScanTM HD Array high-density microchips manufactured by Affymetrix (USA).

Results

At the first stage, we analyzed the frequency of segmental chromosome anomalies for each chromosome in each patient. The study showed that the highest frequency of the amplifications (more than 60.0% of the patients) was detected on the long arm of the 1 chromosome in the following locuses: 1q32.1, 1q32.2, 1q32.3, 1q42.13, 1q42.2, 1q43. The biggest frequency of deletions (more than in 58.0% of the patients) was found in these locuses: 16q21, 16q23.2, 16q23.3, 17p13.1, 17p12. We also found the locuses with the complete absence of segmental chromosome anomalies – the absence of the amplifications is the case for the *4p13, 13p13-13p11.1, 14p13-11.1,*

14q11.1, 15p13-11.1, 15q11.1, 21p13-11.1, 21q11.1, 22p13-11.1 locuses; the deletions are absent in the *1q23.2, 1q25.3, 8q23.2, 8q23.3, 8q24.11, 13p13, 13p12, 13p11.2, 13p11.1, 14p13, 14p12, 14p11.2, 14p11.1, 14q11.1, 15p13, 15p12, 15p11.2, 15p11.1, 15q11.1, 21p13, 21p12, 21p11.2, 21p11.1, 21q11.1, 22p13, 22p12, 22p11.2, 22p11.1* locuses. We also found the regions with neither deletions nor amplifications: *13p13-13p11.1, 14p13-11.1, 14q11.1, 15p13-11.1, 15q11.1, 21p13-11.1, 21q11.1, 22p13-11.1.* Then all patients were divided into two groups depending on their response to NAC: group 1 – patients with no response to NAC, group 2 - patients with objective response to NAC (partial or complete regression of tumor after treatment). The frequency of CNA occurrence in patients with stable disease or cancer progression is shown in Figure 1.

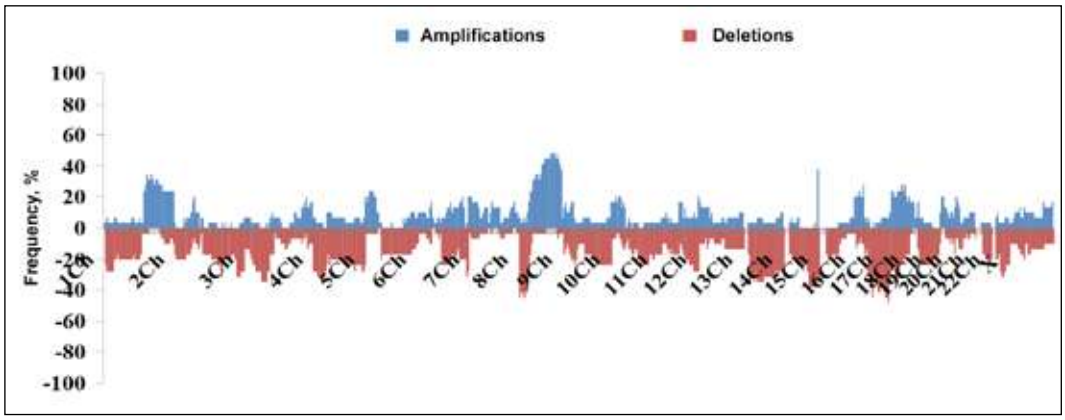

Figure 1. CNA occurrence frequency in the patients with stabilizing or progressing. Note: the horizontal axis – the cytobands and chromosomes from 1 to X; the vertical axis – the frequencies of deletions (below the X-axis) and amplifications (above the X-axis) for each cytoband

The locuses with simultaneous absence of CNA are: *13p13-11.1, 14p13-11.1, 14q11.1, 15p13-11.1, 15q11.1, 21p13, 21p12, 21p11.2, 21p11.1, 21q11.1, 22p13-11.1.* The maximum frequency of amplification occurrence (48.3% or more) was detected in the *8q22.3, 8q23.2, 8q23.3, 8q24.13* regions. It should be noted that the highlighted locuses with high frequency of amplifications occurrence showed the absence of deleted regions. The biggest amount of deletions (44.8-48.3% and more) in this group was detected in the *8p23.3, 8p21.3, 8p21.2, 16q21, 17p13.1, 17p12, 17p11.2* cytobands. The frequency of CNA occurrence in patients with partial or complete regression of tumor is shown in Figure 2.

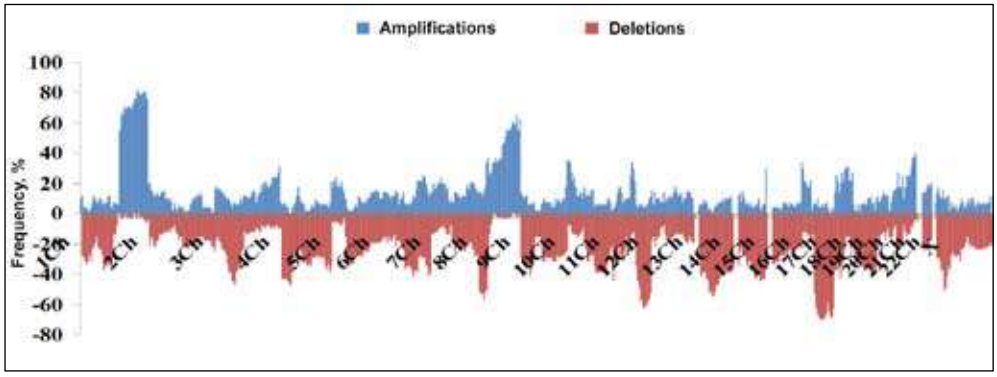

Figure 2. The frequency of CNA occurrence in patients with partial or complete regression of tumor. Note: the horizontal axis – the cytobands and chromosomes from 1 to X; the vertical axis – the frequencies of deletions (below the X-axis) and the amplifications (above the X-axis) for each cytoband

The maximum frequency of amplification occurrence (60.0% and more) was detected in the long arm of the 1 chromosome *1q21.3-44* and in the cytobands. The maximum number of deletions (60.0% and more) in this group was detected in the *11q22.3-23.3, 16q12.2, 16q21-24.2, 17p13.3-11.2* locuses.

The analysis found the cytobands, in which the difference in frequencies of chromosome anomaly occurrence between the groups with or without objective response to NAC reached a maximum value of 35% and more. The biggest difference in the frequency of amplification occurrence between the groups was shown on the long arm of the 1 chromosome *1q23.1-44*, and the biggest difference

in the frequency of deletion occurrence between the groups was in the *11q22.1-23.2, 16q22.2, 16q22.3, 16q23.1, 18p11.21* regions. We also calculated the numerical chromosome anomalies.

Conclusions

The data obtained may be used to predict the efficiency of NAC. The patients with amplifications on the long arm of the 1 chromosome and/or deletions in certain cytobands of the 11, 16, 18 chromosomes are more likely to respond to NAC.

The study is funded by the Russian Science Foundation № 17-15-01203 «Metastatic breast tumor clones»

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THE EFFECT OF ALKYLOXYBENZENES ON THE THERMAL DENATURATION OF PROTEINS OF THE COLON CARCINOMA CELL LINE HT-29

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Using a cellular thermal shift assay (CESTA), we showed that alkyloxybenzenes (AOB) have intracellular target proteins in mammalian cells with which they can be bound to. Data were obtained on the change in the properties of proteins under the influence of AOB in physiological concentrations.

Keywords: alkyloxybenzenes, 4-hexylresorcinol, 5-heptylresorcinol, cells of the colon carcinoma cell line large HT-29, the cellular thermal shift assay.

Alkyloxybenzenes (AOB) are mainly synthesized by microorganisms [1], so their concentration increases with infectious diseases in the blood, as well as in intestinal contents in dysbacteriosis. Microorganisms increase the synthesis of AOB under stress, which increases the resistance of these cells. A number of researchers believe that the mechanism of protection of microorganisms AOB is their ability to change the native functions of enzymes [3]. Cells of the colon cancer show resistance to stress, probably as a result of contact with AOB, which are synthesized by the microflora of the colon.

Material and Methods

The material for study was the HT-29 cell lines (colon carcioma). In the work we used the techniques: CESTA [2], polyacrilamide gel electrophoresis (PAGE), staining with silver nitrate. Chemically synthesized AOBs were used: 4-hexylresorcinol, 5-heptylresorcinol.

Results

Figure 1 shows that at a temperature ranging from 55 °C to 65°C, the number of proteins unrelated to the ligand (lanes under number 1) is slightly more (a protein with a molecular mass in the range of 50 and 37 kDa) compared to that after AOB treatment. It should be noted that after heating until 75 °C, this effect is not detected, while proteins treated with AOB are seen. It can also be noted that proteins incubated with 0.2 μM 5-heptylresorcinol compete in the intensity of the bands with a control at a temperature ranging from 55 to 65°C, and an increase in the intensity of staining is observed with increasing temperature.