

# **Correlations between lymph concentrations of cytokines and morphometric parameters of mesenteric lymph nodes after breast cancer chemotherapy**

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The experiment was conducted on 60 female Wistar rats weight 250-300 g. Two groups of animals were formed: group 1 – control (intact animals); group 2 – breast cancer; group 3 – breast cancer chemotherapy (after 6 months from the moment of induction of breast cancer). Animals were removed from the experiment 6.5 months after induction of breast cancer under anesthesia (i.p., 40 mg/kg Nembutal). Breast cancer was induced by the introduction of N-methyl-N-nitrosourea (MNU) 5 times with an interval of 7 days, subcutaneously in the region of the 2nd breast on the right. The course of chemotherapy included: 15 mg/kg of 5-fluorouracil and 2.5 mg/kg of methotrexate (Ebewe, Austria, intraperitoneal on days 1 and 8), 3 mg/kg of cyclophosphane (Biochemistry, Russia, intraperitoneal daily once, 14 days). Lymph was taken from the cistern of the thoracic lymphatic duct. Concentrations of 24 cytokines in lymph were assessed by flow fluorimetry using Bio-Plex Pro Rat Cytokines 24-Plex Assay (Bio-Rad, USA). Spearman r rank was done to estimate correlation.

In contrast to the breast cancer group without treatment, a correlation between IFN interferon and small lymphocytes (the number of which is increased) and macrophages in germinal centers (table 1) and mitotic dividing cells in the medullary substance was revealed, which may be associated with the action of IFN $\gamma$ , which has an immunomodulating and antitumor effect, enhancing cytotoxic reactions mediated by T-lymphocytes. This can also be indicated by a correlation in the germinating centers of immunoblasts with MIP-1 $\alpha$  and an increase in the number of small lymphocytes in the thymus-dependent zone of the lymph nodes against the background of a decrease in its area.

Table 1. The parameters of spirmean r-rank estimated between thoracic lymph cytokines levels and morphological and cellulae parameters of mesenterial lymph node after breast cancer chemotherapy

Parameter	Group	IL-5	IL-12	IL-17	IL-18	GRO/K C	IFN $\gamma$	M-CSF	MIP-1a	MIP-3a	MCP-1
Герминативные центры вторичных лимфоидных узелков											
Immunoblasts	bc	-	-	-	-	0.95	-	-	-	-	-
	ct	-	-	-	-	-	-	-	0.98	-	-
Medium lymphocytes	bc	-	-	-	-	-	-	-	0.9	-	-
Small lymphocyte	ct	-	-	-	-	-	0.9	-	-	-	-
Macrophage	ct			-	-		0.98				
Reticular cells	bc	-	0.95	-	-	-	-	-	-	-	-
Mitosis	bc	0.98	-	-	-	-	-	-	-	-	-
Паракортикальная зона											
Macrophage	bc	-	-	-	-	-	-	-	-	-	0.95
Reticular cells	bc	-	-	-	-	-	-	0.9	-	-	-
Mast cells	bc	0.95	-	-	-	-	-	-	-	-	-
Мозговые тяжи											
Medium lymphocytes	bc	-	-	-	-	-	-	-	0.9	-	-
Immunoblasts	ct	-	-	-	-	-	-	0.98	-	-	-
Mature plasma cells	ct			0.98	-						
Mitosis	bc	0.9	-	-	-	-	-	-	-	-	-
	ct	-	-	-	-	-	0.98	-	-	-	-
Neutrophils	ct	-	0.9	-	-	-	-	-	-	-	-
Мозговые синусы											
Small lymphocyte	bc	-	-	-	-	0.9	-	-	-	-	-
Immunoblasts	bc	-	-	-	-	-	0.89	-	-	0.89	-
Mature plasma cells	bc			-	-	0.97					
	ct	-	-	-	0.9	-	-	-	-	-	-

Note. bc, rats with breast cancer; ct - rats after breast cancer chemotherapy.

An effect on the immune system can also be indicated by a correlation in the medullary substance of interleukin IL-17 with mature plasma cells (the number of which is increasing). Interleukin IL-12 correlates with neutrophils in the medullary substance. After chemotherapy breast cancer interleukin IL-18 has a direct relationship with mature plasma cells in the medullary sinuses. Like interleukin IL-12, interleukin IL-18 promotes the preferential differentiation of T-helpers 0 into T-helpers 1. In addition, IL-18 leads to the formation of GM-CSF and, thus, enhances leukopoiesis.

Thus, the study of the correlation of the concentration of cytokines lymph of the thoracic duct with structural changes in the mesenteric lymph nodes revealed dependencies aimed at increasing the immunomodulatory and antitumor action of cytokines.