

Correlations between lymph concentrations of cytokine and cell morphometric parameters of mesenteric lymph nodes in rats with chemically induced breast cancer

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The study was done on 40 female Wistar. Animal was divided into: control (intact) group and BC group. BC was induced by injection 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 side.

Rats were removed from the experiment 6.5 months after induction of BC under anesthesia.

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.

Table 1 summarized the estimated correlations between the concentrations of lymph cytokines and the morphological parameters of the mesenteric lymph node. It was found that the increased area of the germinal centers of lymphoid nodules and medullary substance positively correlates with the number of mitotic cells in germinal centers (the number of which is increasing) and medullary substance with IL-5.

Correlation of middle size lymphocytes of germinative centers and medullary cords with chemokine MIP-1 α and correlation of the number of immunoblasts with GRO/KC cytokine, which determines the chemotaxis of immunocompetent cells, may also indicate the preservation of the activity of local immune response.

Structural changes in the lymph nodes can also indicate maintaining activity of the local level of the immune response. In the paracortical zone, which plays a key role in the antitumor immune response, structural signs of maintaining the local immune response are also noted: the area of the paracortical zone remains at the level of the intact group, the number of macrophages is increased, and positively correlated the number of macrophages with chemokine MCP-1 is revealed.

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

Parameter	Group	IL-4	IL-5	IL-6	IL-12	GRO/KC	IFN γ	M-CSF	MIP-1a	MIP-3a	MCP-1
<i>Germinative centers of secondary lymphoid nodules</i>											
Immunoblasts	BC	-	-	-	-	0.9	-	-	-	-	-
	BC	-	-	-	-	0.95	-	-	-	-	-
Medium size lymphocytes	In	-	-	-	-	-	0.9	-	-	-	0.9
	BC	-	-	-	-	-	-	-	0.9	-	-
Reticular cells	BC	-	-	-	0.95	-	-	-	-	-	-
Mitosis	In	-	-	-	-	-	0.95	-	-	-	-
	BC	-	0.98	-	-	-	-	-	-	-	-
<i>Paracortical zone</i>											
Macrophage	In	-	0.97	-	-	-	-	-	-	-	0.97
	BC	-	-	-	-	-	-	-	-	-	0.95
Reticular cells	BC	-	-	0.9	-	-	-	0.9	-	-	-
Mast cells	BC	-	0.95	-	-	-	-	-	-	-	-
<i>Medullary substance</i>											
Medium size lymphocytes	BC	-	-	-	-	-	-	-	0.9	-	-
Small size lymphocyte	In	0.95	-	-	-	-	-	-	-	0.97	-
Immunoblasts	In	0.89	-	-	-	-	-	-	-	-	-
Macrophage	In	-	-	-	-	-	-	0.95	-	-	-
Mitosis	BC	-	0.9	-	-	-	-	-	-	-	-
<i>Medullary sinuses</i>											
Small lymphocyte	In	-	-	-	0.9	-	-	-	-	-	-
	BC	-	-	-	-	0.9	-	-	-	-	-
Immunoblasts	BC	-	-	-	-	-	0.89	-	-	0.89	-
Immature plasma B cells	In	-	-	-	-	0.9	-	-	-	-	-
Mature plasma B cells	In	-	-	-	0.9	-	-	-	-	-	-
	BC	-	-	-	-	0.97	-	-	-	-	-
Reticular cells	In	-	-	-	-	-	-	-	0.97	-	-

Note. In, control (intact) group; BC, breast cancer group

Positive correlation of reticular cells with IL-6 may be due to its production by tumor cells and serve as one of the factors of growth and progression of the tumor. This can be indicated by the correlation of the number of reticular cells with M-CSF, which affects phagocytic activity, and may also be due to the growth of the primary tumor, and metastases in the lymph nodes. The revealed correlation of the number of mast cells, as factors contributing to homeostasis in the immune system, with IL-5, may also indicate a continuing activity of the local immune response aimed at antitumor protection. The positive correlation of the number of small lymphocytes and the number of mature plasma B cells with GRO/KC chemokine, noted in the medullary sinuses, may be associated with the migration of small lymphocytes and mature plasma B cells from the lymph node. Increased production of IFN γ is positively correlated with the number of immunoblasts in the medullary sinuses. In addition, the number of immunoblasts in the medullary sinuses in the group of animals with BC also significantly correlates with the chemokine MIP-3 α .

Thus, with chemically induced BC a study of the correlation of cytokines of the lymph of the thoracic duct with morphological changes in the mesenteric lymph nodes revealed a number of dependencies that may be due to a local immune response in the lymph nodes directed on antitumoral protection.