

## Lymphocytopoietic Factor in Lymph

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### Summary

The evidences which suggest the presence of a lymphocytopoietic factor in rat thoracic duct lymph are summarized briefly. The intravenous injections of the extracted materials from lymph plasma into syngeneic recipient rats resulted in the massive proliferation of lymphoid cells predominantly in the thymus dependent areas and thymic cortex, suggesting that the target cells for the factor are not marrow-derived (B) cells, but thymus derived (T) cells. The existence of a thymus is not necessarily required for the production or secretion of the factor. The augmenting effect of the factor on T cell functions, eg. local graft-versus-host reaction and helper activity of plaque forming response to sheep erythrocytes, is mentioned. The physicochemical characteristics of the factor are nondialysable and heat-stable glycoprotein molecules. The roles of lymph humoral factor in T cell-differentiation or proliferation are discussed.

We have recently found evidence which suggests the presence of a lymphocytopoietic factor in lymph collected from lymphocyte-depleted animals (1). This indicated that the lymph plasma collected from the lymphocyte-depleted animal might contain some biologically active substances, which play an important role in lymphocytopoiesis and the differentiation of lymphocytes. The partially purified material was extracted from the thoracic duct lymph which was collected from normal syngeneic rats as described in the preceding paper (2). The physicochemical characteristics of this extract are a non-dialysable and heat stable glycoprotein molecule. The intravenous injection of the lymph extract into normal syngeneic Wistar rats resulted in increase in weight of lymphoid tissues. Histologically a massive proliferation of large pyroninophilic lymphoid cells and an increase in mitotic index was detected predominantly in the thymus-dependent areas and thymic cortex. Similar lymphocytopoietic activity, but to a lesser extent than lymph extract, was also detected

in lymph plasma, serum and serum extract. The lymph extract was shown to be non-immunogenic in syngeneic rats. These findings suggested that the effects of the lymph extract on lymphoid cell proliferation are due to the presence of a lymphocytopoietic factor in body fluid, particularly in the lymph. This suggestion led us to investigate the role of such a humoral factor in lymph in stimulatory lymphocytopoiesis and/or in the maturation of immunocompetent T cells in periphery.

The biological characteristics of a lymph humoral factor were further investigated (3). The lymph extract from normal rats failed to stimulate lymphocytopoiesis in the spleen and lymph node of the thymectomized, irradiated and marrow reconstituted rat (B rat). This suggests that 'target' or responsive cells for the factor are not marrow-derived (B) cells, but thymus-derived (T) cells. The present observations do not throw sufficient light on the origin or mechanism of formation of the factor. However, the very presence of lymphocytopoietic activity in the lymph extract or lymph plasma may reflect the production site, e. g. the lymph node, since lymph always flows within lymph node through lymph sinuses in the direction of efferent lymphatics and its metabolites or secreted materials may be released into lymph plasma. The possibility arises that cells responsible for factor-production or secretion might be reticular cells or macrophages which remained intact in the lymph node of lymph-drained rats, or lymphocyte-subpopulation which release Ia antigen or its components from the surface membrane.

The role of thymus humoral factors in T cell differentiation has been emphasized by a number of workers. However, in our study, the lymph extract from the lymphopenic

lymph-drained B rats showed similar high lymphopoietic activity to those of normal rats (3), indicating that the existence of a thymus is not necessarily required for the production or secretion of the factor. Thus, it seems reasonable to speculate that a variety of thymus independent factors, e. g. lymph humoral factor, are involved in the further maturation of immature T cells and/or expansion of T cell-subpopulations outside the thymus in the periphery at several different stages. In fact, the augmenting effect of lymph extract on T cell function, particularly in local GvHR and helper activity of plaque forming response to sheep erythrocytes were observed (4). It remained necessary to demonstrate the activity of lymph extract on T cell marker-differentiation *in vitro* and on reconstitution in well-controlled T cell deficiency states *in vivo*. Moreover, there is the problem of the relationship of lymph humo-

ral factor with various factors secreted from macrophages, thymus cells or other, by activated T cells.

### References

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