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PHENOTYPIC CHARACTERIZATION OF TARGET CELLS FOR PRODUCTIVE INFECTION BY THE RADIATION LEUKEMIA VIRUS. RELATIONSHIP TO THE IMMATURE LYMPHOID CELLS ASSOCIATED WITH "THYMIC NURSE CELLS".

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In C57BL/Ka mice, thymic lymphomas can be induced by inoculation of the Radiation Leukemia Virus (RadLV) that was originally extracted from radiation-induced lymphomas of the same mouse strain[1]. The selective localization of the neoplastis process within the thymus suggests a critical and specific interaction between RadLV and T-lymphocyte differentiation[2].

A. TARGET CELLS FOR PRODUCTIVE INFECTION BY RadLV

An in vitro infectious center detection assay has been developed in order to estimate, in lymphoid cell subpopulations,the numbers of target cells susceptible to productive infection by RadLV[3].It was demonstrated that the frequency of such target cells is very low (about 1 in 50000 thymocytes) in young adult thymus.

To determine the phenotypic characteristics of these thymus target cells, various thymocyte subpopulations were prepared by using a battery of cell separation methods: cortisone treatment, 1g sedimentation, density gradient centrifugation, cell sorting (with a FACS III). Most of target cells were found highly corticosensitive, large and of medium density. They were recovered among the ^{3}HTdR spontaneously incorporating cells. FACS III sorting experiments demonstrated that target cells expressed H-2 and Thy-1 membrane antigens;however,they were not more frequent among the highly Thy-1 expressing cells[4].

B. VIRUS PRODUCING THYMUS LYMPHOID CELLS AFTER RadLV INOCULATION

The first virus antigen producing cells were detected by immunofluorescence in the subcapsular zone of the thymus as early as 2 days after Rad LV inoculation[5]. By using the infectious center detecting assay, it was shown that these first virus-producing cells represent 1 in 10000 to 1 in 30000 thymus cells. Electron microscopy demonstrated that these cells were blast cells selectively located within the 3-5 outer cell layers of the thymus subcapsular zone[4].

These cells were found to be associated with the peculiar lymphoepithelial complexes, described by Wekerle et al. as "Thymic Nurse Cells"[6]. Indeed TNC_s were isolated from RadLV inoculated thymuses by enzyme dissociation and repeated 1g sedimentation. By electron microscopy, budding viral particles were selectively seen in blast cells located in TNC_s. The infectious center detection assay demonstrated that virus producing cells were 300 X more frequent in lymphoid cells associated with TNC_s than in the whole thymus cell population[7].

C. DISCUSSION

The results strongly implicate that RadLV can infect productively a very immature (and numerically small) blast cell subpopulation of the thymus cortex. These target cells start sustaining viral production when they are located within lymphoepithelial complexes (or TNC_s) of the subcapsular zone.

TNC_s have been considered as the site of penetration of bone marrow derived primitive "lymphoid cells" at the earliest step of thymic lymphopoiesis. Therefore and on the basis of our data, we propose that, within the intrathymic T cell lineage, susceptibility to RadLV infection is expressed during the surface reorganization of T cell precursors (i.e. prothymocytes) when they undergo the first step of intrathymic differentiation. This interaction between RadLV and a very immature T cell subset could be one of the critical events leading to the selective development of RadLV-induced lymphomas within the thymus.

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