It is well known that the activation of lymphoid cells differ significantly depending on their lineage/subset and differentiation stages. Among the variety of cytokines characterized until today, essentially all the cytokines appear not to be strictly specific to any of the subset of lymphocytes. For example, all the interleukins including IL-2, IL-4 and IL-5 are not specific for B or T lymphocytes. The multiple target specificity is a general property of interleukins and cytokines. The most typical examples may be IL-1 and IL-6 having a very broad target specificity.

Many interleukins show B cell activation or differentiating activities, besides the activities on T cells. IL-1, IL-2, IL-4, IL-5 and IL-6 are the examples. Among these, IL-2 and IL-4 are known to act on the immature B cells, while IL-5 and IL-6 seem to activate the mature B cells.

We have comparatively studied IL-4 and IL-2 systems, because of their principal involvement in the B and T cell activation, respectively. IL-4 is known to augment the immunoglobulin production particularly of IgE class. At the same time, IL-4 induces the expression of low affinity Fc receptor for IgE (FcεRII). This FcεRII is deeply involved in the physiological and pathological B cell activation in human.

1)  Because of the affinity to IgE, this receptor and the soluble receptor (IgE binding factor) is considered to play various important regulatory roles in IgE metabolism. FcεRII gene expression is mainly induced on B cells and monocyte/macrophages by appropriate inducing stimuli. In activated or pathological condition, T cells and eosinophils also express FcεRII. While IL-4 is a general inducer of FcεRII on all these cell types, γIFN counteracts the IL-4 action to induce FcεRII and IgE production by B cells. However, γIFN enhances the expression of FcεRII on non-B cells including monocyte/macrophages and eosinophiles, based on the study using cell lines.

2)  FcεRII is identical to the B cell activation actigen CD23, which is known to be strongly expressed on B lymphoblastoid cell lines transormed by Ebstein-Barr virus (EBV). The involvement of FcεRII in the B cell transformation is suggested. The biological role of FcεRII is still unclear, despite the suggestive evidence for its relationship to BCGF system. The possible antigen presenting or processing role of FcεRII/CD23 on dendritic cell types is also suggested.

The role of FcεRII/CD23 on B cell activation appear to be similar to that of IL-2R/p55(Tac), which is constitutively expressed on HTLV-I-induced transformation of T cells. While FcεRII/CD23 induction by IL-4 and other cytokines are one of the key activation steps of B cells, IL-2R/p55(Tac) induction is that of T and LGL/NK lineages.

These two activation markers can be expressed on both B and T cell lineages, although FcεRII and IL-2R/p55(Tac) is primarily expressed on B and T cell subset respectively. For examples, some of the EBV(+) B cell lines and HTLV-I(+) T cell lines express both of the receptors. Furthermore, activation of IL-2R and FcεRII may induce the expression of the other receptors, indicating the presence of cooperative relationship between these two receptor systems.

There is also evidence indicating the involvement of ADF (ADF-derived factor) with potent reducing activity and co-cytokine activity in lymphocyte activation. The network of the activation through different cytokines and the specific receptor system may determine and finely regulate the activation of various lymphocyte subsets including B cells.
The Association of Progressive Follicular Transformation (PFT) and Lymphocytic and Histiocytic (L and H) Hodgkin's Disease: A Labeled Monoclonal Antibody Study

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In the early 1960s, we redefined the pathology of Hodgkin's disease and described six new histologic types with lymphocytic and histiocytic Hodgkin's of diffuse and nodular types having the most favorable prognosis. The new approach was based on the concept of host factors interrelating with the formation of Reed-Sternberg (RS) cells. At the Rye Conference, unfortunately, nodular and diffuse L and H types were condensed into the lymphocyte-predominant type in an attempt to simplify the terminology and ease the burden for clinicians. This change obscured the importance of nodularity. The concern over the origin of nodularity was also lost. In the late 1970s, Poppema proposed the possible origin of nodularity of this type of Hodgkin's disease in reactive follicles. In the decade of the 1980s, we have received biopsy material on 80 consultative cases that were interpreted as either nodular or diffuse types of L and H Hodgkin's disease. Of these, the majority of the nodular type exhibited some degree of PFT with follicular infiltration and fragmentation associated with the formation of L and H variants of RS cells typical of L and H Hodgkin's disease.

Using labeled antibodies, four dramatic abnormal changes were found: 1) the presence of abnormal mononuclear and polyploid variants of RS cells of the L and H type often at the edge of the infiltrated follicles that mark with the follicular center cell antibody (LN1); 2) the heavy infiltration of the fragmented disrupted follicles by cells marking as T-cells with the pan T-cell antibodies (UCHL1, Leu-22, or MT-1); 3) the L and H variants of RS cells as well as the large noncleaved cells in follicular centers marked with three antibodies, the antibody for follicular center cells (LN1), the antibody for lymphocytes (leukocyte common antibody - LCA), and the pan B-cell antibody (L26); 4) the nodular lymphocytic expansions that comprise the nodular L and H Hodgkin's disease areas predominantly mark as B-cells with the pan B-cell antibody (L26), but are always associated with varying proportions of T-cell using the pan T-cell antibodies (UCHL1 and Leu-22).

The results of an immunoreactive staining study now in progress for acid cysteine-proteinase inhibitor, a new marker for dendritic cells will also be reported.

The morphologic changes in this study confirm the distinctness of the nodular and diffuse morphologic types of L and H Hodgkin's disease. The marking of the L and H variants of RS cells in both diffuse and nodular types with the antibodies for lymphocytes (LCA), B-cells (L26), and follicular center cells (LN1) support the distinctive nature of this process as a B-lymphocytic process of follicular center cell origin. The frequent association of PFT, with nodular L and H Hodgkin's disease, supports a strong association of these two processes and the likely origin of L and H Hodgkin's disease in infiltrated altered follicles.