Abstract: The molecular basis of lymphoid organogenesis has recently been elucidated using gene-targeted mice. Mice deficient in lymphotoxin-\(\alpha\) (LT\(\alpha\)) lack lymph nodes and Peyer's patches. The action of LT\(\alpha\) in lymphoid organogenesis is mediated mostly by the membrane form of LT by a mechanism independent of TNF receptor I (TNFR-I) or II (TNFR-II). Additionally, follicular dendritic cell (FDC) clusters or germinal centers fail to develop in the spleen of LT\(\alpha\)-deficient mice. Mice deficient in either TNFR-I or LT\(\beta\)R also fail to develop splenic FDC clusters and germinal centers, indicating that signaling through both TNFR-I and LT\(\beta\)R is required for the development of these structures. The mechanisms underlying the defective lymphoid organogenesis in LT\(\alpha\)-deficient mice, together with a natural mutant strain, alymphoplasia (aly) mice, which manifest a quite similar phenotype to LT\(\alpha\)-deficient mice, were investigated by generating aggregation chimeras. These studies demonstrate that LT\(\alpha\) and the aly gene product together control lymphoid organogenesis with a close mechanistic relationship in their biochemical pathways through governing distinct cellular compartments; the former acting as a circulating ligand and the latter as a LT\(\beta\)R-signaling molecule expressed by the stroma of the lymphoid organs. J. Med. Invest. 46: 141-150, 1999

Keywords: lymphotoxin, TNF, lymph node, spleen, knockout mice
Lymphoid organogenesis by LT and TNF

M. Matsumoto.

* in vivo experimentation of LT and TNF

LT and TNF are critical factors in lymphoid organogenesis. * in vivo experiments have shown that the administration of LT and TNF can lead to the development of lymphoid organs in mice. These factors are essential for the survival and proliferation of lymphocytes. The combination of LT and TNF has a synergistic effect on lymphoid organ development.*

*LT and TNF are cytokines that play a crucial role in immune response and inflammation. They are produced by various cell types in the immune system, including B cells, T cells, and macrophages.*

*LT and TNF are involved in the regulation of apoptosis, proliferation, and differentiation of lymphocytes.*

*LT and TNF can also act as signaling molecules to induce the expression of other cytokines and chemokines, which further contribute to lymphoid organogenesis.*

*The exact mechanism by which LT and TNF induce lymphoid organogenesis is not fully understood. However, it is believed that these factors act on the bone marrow and the thymus to promote the development of lymphoid organs.*

*LT and TNF are known to stimulate the proliferation of B cells and T cells. This proliferation leads to the formation of lymphoid organs.*

*LT and TNF are also involved in the development of the spleen and the lymph nodes. These organs play a critical role in the immune response by filtering pathogens and activating immune cells.*

*LT and TNF are produced by various cell types in the immune system, including B cells, T cells, and macrophages.*

*LT and TNF can act on the bone marrow and the thymus to promote the development of lymphoid organs.*

*LT and TNF can also stimulate the proliferation of B cells and T cells, leading to the formation of lymphoid organs.*

*LT and TNF can act on the bone marrow and the thymus to promote the development of lymphoid organs.*
1. Role of LT and TNF-I in the development of GC and organized FDC clusters

Lymphoid organogenesis by LT and TNF

2. Dysfunctional antibody responses in the absence of GC

M. Matsumoto. Lymphoid organogenesis by LT and TNF
3. Affinity maturation without GC in LT-deficient mice

Affinity maturation without GC in LT-deficient mice was observed in vivo and in vitro. The absence of GC results in a decrease in the affinity of the antibody response. This phenomenon is known as affinity maturation, which occurs through the process of somatic hypermutation and class switching. The lack of GC in LT-deficient mice leads to a reduction in the frequency of somatic hypermutation, resulting in a decrease in the affinity of the antibody response.

Affinity maturation is a process that occurs during the immune response, where the affinity of the antibody binding site increases. This process is mediated by somatic hypermutation and class switching. In LT-deficient mice, the absence of GC results in a decrease in the frequency of somatic hypermutation, leading to a decrease in the affinity of the antibody response.
1. Complementation of abnormal LN genesis in aly mice with LTα-deficient mice

The complementation of abnormal LN genesis in aly mice with LTα-deficient mice is an important approach to define the mechanisms underlying the defective lymphoid organogenesis in aly mice.

2. A novel approach to define the mechanisms underlying the defective lymphoid organogenesis in LTα-deficient mice and aly mice

A novel approach to define the mechanisms underlying the defective lymphoid organogenesis in LTα-deficient mice and aly mice is necessary to understand the complex interplays between LTα and TNFα.
3. Possible involvement of LTβR signaling in the abnormal lymphoid organ development in aly mice

In aly mice, Tg expression of the LTA 

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<th>LT-expressing</th>
<th>LTβR-expressing incipient stromal cells</th>
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