LETTER

Soluble CD30 might interrupt anti-tumor immunity for monoclonal proliferation of adult T-cell leukemia/lymphoma cells

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Subtitle: CD30 expression and soluble CD30 production in ATL patients

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Adult T-cell leukemia/lymphoma (ATL) is a highly aggressive leukemia/lymphoma. The long clinical latency and low incidence of ATL indicate that ATL is an age-related disease and some genetic changes are involved in malignant transformation and monoclonal expansion of human T lymphotropic virus type 1 (HTLV-1)-infected cells. In our study, we focus on the function of proteins in immune regulation.

CD30 expression is found to be dependent on activation and proliferation of B and T cells which induced by stimulation with mitogen or viruses. Interestingly, human T-cell leukemia virus type 1 (HTLV-1)-infected cells and ATL cells also exhibit CD30 and cDNAs encoding the CD30 protein were consequently cloned from expression libraries of HTLV-1+ human T-cell line HUT-102 (1-5). The effect of CD30 activation on tumor cells appears to be complex and be dependent upon the cell type (6-9). In case of ATL, CD30 signaling is likely to induce apoptosis of tumor cells, because the overall survival in patients with diffuse CD30 positive cases was better than that of CD30 negative cases with ATL (10). On the other hand, the elevated serum sCD30 is consistently observed in ATL (11-14). Recent studies demonstrated that sCD30 bind to prevent the interaction between CD30 and its ligand (15). Since it is recently reported that Hodgkin’s Reed-Sternberg tumor cells inhibit proliferation and activation of T cells via CD30, inducing the suppression of tumor surveillance in HD, the reasons why the clinical significance of membrane type of CD30 expression and serum sCD30 levels in ATL are considered (16). Our study identified that the sCD30 production correlated with the aggressiveness of ATL, suggesting that elevation of sCD30 in serum of the patients is associated with the proliferation and survival of ATL cells (17). We have also found that the levels of sCD30 have been elevated from the stage of HTLV-1 carrier, and very high in the acute type of ATL (Figure 1). We hypothesize that CD30 signaling may induces apoptosis or cell cycle arrest of HTLV-1-infected cells in HTLV-1 carrier phase or smoldering and chronic phase of ATL. The unknown mechanism induced by HTLV-1 is mediating the sCD30 production and CD30 signaling pathway is interfered by binding of sCD30 to the CD30L. This process blocks the engagement of CD30 and CD30L for survival of ATL cells to allow the ATL cells monoclonal proliferation or anti-apoptosis (Figure 2). It is suggested that sCD30
expression is associated with the proliferation and survival of ATL cells via the suppression of activated T cells which act as anti-HTLV-1 and anti-tumor T immune system. These finding suggest that elevated serum level of sCD30 predict the development of ATL.

Furthermore, the answer for further studies about the role and mechanism of sCD30 on CD30 signaling pathway in ATL cells will be potential for the treatment to inhibition the proliferation and progression of ATL cells.


10. Takeshita M, Akamatsu M, Ohshima K, Kobari S, Kikuchi M, Suzumiya J, Uike N, Okamura T. CD30 (Ki-1) expression in adult T-cell leukaemia/lymphoma is
associated with distinctive immunohistological and clinical characteristics.  

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Figure Legend

Figure 1. Elevation of sCD30 detected in serum of ATL patients.

In the normal condition, sCD30 level is detected lower than 100 U/ml in serum of healthy donor. Once HTLV-1 carriers develop to ATL patients, sCD30 appeared to be high level in the serum consistently.

Figure 2. sCD30 interrupts the CD30 signaling probably inhibiting proliferation of ATL cells.

A. Possible downstream activation of CD30 signaling in ATL cells causes apoptosis or cell cycle arrest. B. Interfering of binding need for the proliferation and anti-apoptosis. HTLV-1 induced sCD30 binding with CD30ligand (CD30L) to block the CD30 interaction and allow the monoclonal proliferation of ATL cells.