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Short Communication Open Access

Mutualism among HTLV-1-Infected Different Type of Cells or among Other Virus-Infected Cells

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Short Communication

Japan is an endemic area of Human T-cell leukemia virus type 1 (HTLV-1), which is the first discovered retrovirus associated with human disease, especially adult T cell leukemia/lymphoma (ATL). Only two to five percent of HTLV-1-infected carriers develop to ATL more than 50 years after the infection [1]. This is the reason why ATL was described in Japan where the life expectancy is one of highest countries in 1977 [2,3].

HTLV-1 is transferred from mother to infant and integrated into T cells, B cells and dendritic cells (DCs) [1,4,5]. The long term survival of HTLV-1 in the host is ensured by infecting stem cells and other long lasting cells, such as memory T cell.

Once the HTLV-1-infected T cells transform to ATL cells, ATL stem cells acquire monoclonal proliferation rather than undergo senescence [6]. However, they must evade not only host immune system but also their apoptosis (activation-induced cell death) [6-8]. We observed that Phytohemagglutinin stimulation suppressed cell growth of peripheral blood mononuclear cells from patients with ATL but not from HTLV-1 carriers (Figure 1). Because Bangham, et al. reported that Tax-positive CD4+ cells increases with time *ex vivo* [9], Tax could play an important role for survival or cell death of HTLV-1-infected cells. Tax is a trans-activator of HTLV-1 genome and a variety of cellular gene [10]. Furthermore, T cell activation cooperates with Tax for cellular gene expression [11]. Accordingly, our observation suggests that Tax is preferentially expressed in HTLV-1-infected cells to proliferate and survival, while Tax-expression should be defective in ATL cells because Tax may cause apoptosis of ATL tumor cells *in vivo* [12].

We previously treated a patient who was thought to be an early phase of ATL development [13]. Interestingly, the biopsy specimen from cervical lymph node showed that CD4+ T cells proliferated surrounding Epstein Barr virus (EBV)-infected CD30+ large cells (Figure 2). It is speculated that they may respond to chemokines and cytokines and migrate to their niche where other types of cells infected with HTLV-1 or another virus may support their survival and proliferation each other. They could overcome their apoptosis and cellular senescence in the microenvironment together. Other HTLV-1-infected cells may also help them and immature DCs and CD30-CD30L interaction impaired cytotoxic T-cell activation [14]. We would like to call this situation "Mutualism", which is the way two different viruses-infected cells, particularly HTLV-1 and EBV [15], or different types of HTLV-1-infected cell, Tax-expressing cells and Tax-non-expressing tumor cells, exist in relationship in which mutual benefits.

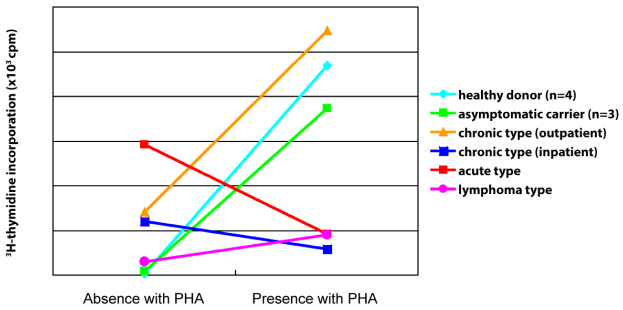

Figure 1: Various cell responses to PHA-P. Peripheral blood mononuclear cells (PBMCs) from ATL patients, HTLV-1 carriers, and healthy donors are incubated for 72 hours at the presence or absence with Phytohemagglutinin (PHA-P) stimulation. Cell proliferation status were measured using 3H-thymidine incorporation.

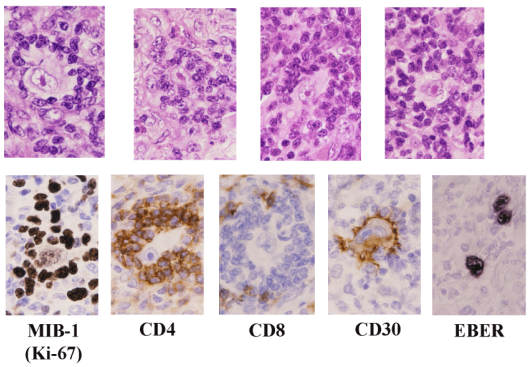

Figure 2: CD4+ T cells surrounding CD30+ cells. Biopsy specimen from HTLV-1-infected lymphoma patients (adult T-cell leukemia/lymphoma) showed the proliferating CD4+CD8- T cells (MIB-1, Ki-67) surrounding Epstein Barr virus (EBV)-infected CD30+ cells (EBER).

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