Journal of Hematology & Thromboembolic Diseases

Takemoto and Pornkuna, J Hematol Thrombo Dis
2014, 2:5
http://dx.doi.org/10.4172/2329-8790.1000164

Short Communication Open Access

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

Shigeki Takemoto[1,2*] **and Ratiorn Pornkuna**[1,3]

[1]*Department of International Cooperation, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan*

[2]*Clinical Laboratory, National Hospital Organization Kumamoto Medical Center, Kumamoto, Japan*

[3]*Institute for Clinical Research, National Hospital Organization Kumamoto Medical Center, Kumamoto, Japan*

[*]**Corresponding author:** Dr. Shigeki Takemoto, M.D., Ph.D., Chief of Clinical laboratory, National Hospital Organization Kumamoto Medical Center, 1-5 Ninomaru, Kumamoto 860-0008, Japan, Tel: +81-096-353-6501; Fax: +81-096-325-2519; E-mail: takemots@kumamed.jp

Rec date: Sep 09, 2014, **Acc date:** Oct 07, 2014, **Pub date:** Oct 20, 2014

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.

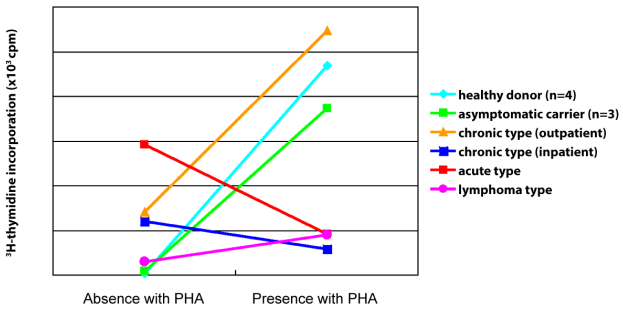

Figure 1: Various cell responses to PHA-P. Peripheral blood mononuclear cells (PBMCs) from ATL patients, HTLV-1 carriers, and healthy donors are incubated for 72 hours at the presence or absence with Phytohemagglutinin (PHA-P) stimulation. Cell proliferation status were measured using 3H-thymidine incorporation.

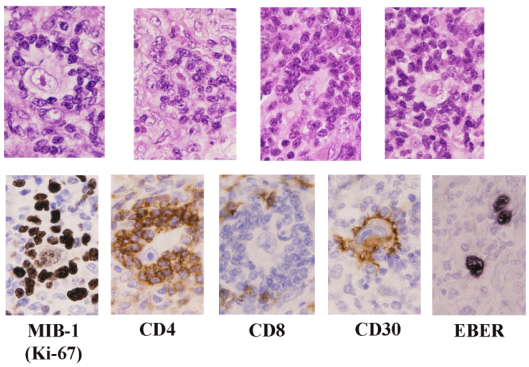

Figure 2: CD4+ T cells surrounding CD30+ cells. Biopsy specimen from HTLV-1-infected lymphoma patients (adult T-cell leukemia/lymphoma) showed the proliferating CD4+CD8- T cells (MIB-1, Ki-67) surrounding Epstein Barr virus (EBV)-infected CD30+ cells (EBER).

Acknowledgements

We would like to thank Prof. Yoshio Haga for supporting our study, and the member of the Department of Hematology at NHO Kumamoto Medical Center and the Department of Hematology and Respiratory Medicine, Kochi Medical School, Kochi University for collaboration. All authors declare no competing financial interests for the present study.

References

1. Yamaguchi K (1994) Human T-lymphotropic virus type I in Japan. Lancet 343: 213-216.
2. Uchiyama T, Yodoi J, Sagawa K, Takatsuki K, Uchino H (1977) Adult T-cell leukemia: clinical and hematologic features of 16 cases. Blood 50: 481-492.
3. Pornkuna R, Wongkhantee S, Jinathongthai S, Shimogawa S, Takemoto S (2014) Effect of blood transfusion on supportive therapy of elderly patients at Kumamoto, Japan as compared with Khon Kaen, Thailand.
4. Ceccaldi PE, Delebecque F, Prevost MC, Moris A, Abastado JP, et al. (2006) DC-SIGN facilitates fusion of dendritic cells with human T-cell leukemia virus type 1-infected cells. J Virol 80: 4771-4780.
5. Jain P, Manuel SL, Khan ZK, Ahuja J, Quann K, et al. (2009) DC-SIGN mediates cell-free infection and transmission of human T-cell lymphotropic virus type 1 by dendritic cells. J Virol 83: 10908-10921.
6. Pornkuna R, Takemoto S (2014) A lack of cellular senescence, formation of microenvironment, and role of soluble CD30 in development of adult T-cell leukemia/lymphoma. J Hematol Thrombo Dis 2: 151.
7. Pornkuna R, Nishioka C, Takemoto S (2014) What is the role of soluble cytokine receptors in adult T-cell leukemia/lymphoma. J Hematol Thrombo Dis 2: 154.
8. Los M, Khazaie K, Schulze-Osthoff K, Baeuerle PA, Schirrmacher V, et al. (1998) Human T cell leukemia virus-I (HTLV-I) Tax-mediated apoptosis in activated T cells requires an enhanced intracellular prooxidant state. 161: 3050-3055.
9. Asquith B, Hanon E, Taylor GP, Bangham CR (2000) Is human T-cell lymphotropic virus type I really silent? Philos Trans R Soc Lond B Biol Sci 355: 1013-1019.
10. Yoshida M (2001) Multiple viral strategies of HTLV-1 for dysregulation of cell growth control. Annu Rev Immunol 19: 475-496.
11. Lin HC, Hickey M, Hsu L, Medina D, Rabson AB (2005) Activation of human T cell leukemia virus type 1 LTR promoter and cellular promoter elements by T cell receptor signaling and HTLV-1 Tax expression. Virology 339: 1-11.
12. Tamiya S, Matsuoka M, Etoh K, Watanabe T, Kamihira S, et al. (1996) Two types of defective human T-lymphotropic virus type I provirus in adult T-cell leukemia. Blood 88: 3065-3073.
13. Takemoto S (2007) Soluble CD30 in sera of adult T cell leukemia patients. Med J NHO Kumamoto Medical Center 7: 10-14
14. Al-Dahoodi ZM, Takemoto S, Kataoka S, Taguchi H (2003) Dysfunction of dendritic and T cells as the cause of immune suppression in HTLV-I infected individuals. J Clin Exp Hematopathol 43: 43-49
15. Ohshima K, Niino D, Karube K (2014) Microenvironment of adult T-cell leukemia/lymphoma-associated nodal lesions. Int J Hematol 99: 240-248.