

Human Retroviruses and Soluble CD30 Levels of Patients

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Abstract

Human T-cell leukemia virus type 1 infection makes CD4+ T cells transformed into leukemic cells, whereas human immunodeficiency virus make them destroyed. Interestingly, activation of CD30 led to the induction of apoptotic death of anaplastic large cell lymphoma cells, while Hodgkin's lymphoma cells, which constitutively express NF- κ B, were not susceptible to CD30-induced apoptosis. Such a pleiotropic effect of CD30 signaling is dependent on cell type, B-cell or T-cell, and probably different activation status of NF- κ B, constitutive or inducible. Accordingly, CD30 triggering may be responsible for the enhanced retroviral replication and T cell death under the influence of T cell activation and/or NF- κ B activation status, showing high levels of sCD30.

Keywords: Soluble CD30 (sCD30); Human T-cell leukemia virus type 1 (HTLV-1); Adult T-cell leukemia (ATL); Human immunodeficiency virus (HIV); Acquired immunodeficiency syndrome (AIDS)

Short Commentary

Most of people are unfamiliar with retroviruses. There are a broad species infected with them. What are they?

Fifty years ago (In 1960s), some researchers studied on oncogenic viruses in animals. DNA virus and RNA virus composed them. In 1970, Dr. Howard Temin and Dr. David Baltimore discovered an enzyme, reverse transcriptase [1,2]. This finding meant that RNA virus could change a form of genome into DNA [3]. Then scientists around the world were looking for the human retrovirus. However, nobody could detect in a body of human for a decade.

In 1976, Dr. Kiyoshi Takatsuki, et al. noticed a new type of adult leukemia in Japan [4]. The shape and form of leukemic cells are quite unique and nuclear of them look like a flower. In addition, all patients with this type of leukemia were from Kyushu, the south-western part of Japan. Dr. Takatsuki imagined that this leukemia was associated with viral infection. Soon after the publication of new disease as adult T-cell leukemia (ATL) in 1977, Dr. Yorio Hinuma and Dr. Isao Miyoshi found anti-virus antibody in blood of the patients [5]. In fact, the leukemic cell were infected with retrovirus, which is the first discovered human retrovirus, human T-cell leukemia virus type 1 (HTLV-1) [6].

At the time of the first human retrovirus discovery, another catastrophe had just begun. In 1981, gay men suffered from an unusual infectious disease [7]. They showed the symptoms of immune deficiency caused by a decreasing number of CD4+ T cells. It was well known as the early phase of widespread acquired immunodeficiency syndrome (AIDS). Soon after virus was thought as a cause, the third human retrovirus was isolated and identified [8]. Interestingly, the first human retrovirus (HTLV-1) infection makes CD4+ T cells transformed into leukemic cells, whereas the third retrovirus make

them destroyed. This third human retrovirus is human immunodeficiency virus (HIV). Their advances in the field of scientific endeavor of HTLV/ATL are followed by the current study on treatment against HIV/AIDS.

CD30, first described as the Ki-1 antigen on malignant B cells in Hodgkin's lymphoma (HD) [9], is also expressed on normal activated B and T cells [10]. Expression of CD30 is augmented in a number of pathologic conditions including anaplastic large cell lymphoma (ALCL), seminoma and cutaneous lymphoproliferative disorders [9,11]. Because HIV-infected individuals have a 200-fold increased risk of developing lymphomas, particular B cell lymphomas [12], CD30 and the soluble form (sCD30) have been an important biomarker for the development of AIDS-associated B cell lymphoma [13,14]. Interestingly, elevated levels of sCD30 are also shown in serum of patients infected with HTLV-1 [15].

CD30 ligation induces proliferation or apoptosis under the downstream signal transduction [16]. They demonstrated that activation of CD30 led to the induction of apoptotic death of ALCL cells, while HD cells, which constitutively express NF- κ B, were not susceptible to CD30-induced apoptosis. Such a pleiotropic effect of CD30 signaling is dependent on cell type, B-cell or T-cell, and probably different activation status of NF- κ B, constitutive or inducible. CD30+ T cells also play important pathogenic roles during the course of HIV infection and AIDS [17]. It has been reported that HIV replication in CD4+ T cells is enhanced by CD30 triggering. However, HIV infection of CD4+ T cells leads to CD30 expression and is associated with the T cell death. It may be dependent on the T cell activation and retroviral expression status because we observed T cell activation, in which HTLV-1 expression is enhanced, caused the cell growth suppression as well as the reduction of CD30 expression and high level production of sCD30 [18,19]. Accordingly, CD30 triggering may be responsible for the enhanced retroviral replication and T cell death under the influence of T cell activation and/or NF- κ B activation status, showing high levels of sCD30.

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