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Shedding by ADAM10 and ADAM17 is associated with progression of adult T-cell leukemia/lymphoma

Adult T-cell leukemia/lymphoma (ATL) is a retrovirus-associated mature T-cell leukemia/lymphoma. It is speculated that ATL is an age-related disease and some changes are involved in malignant transformation and monoclonal expansion of the HTLV-1-infected cells. We previously reported that HTLV-1-infected cells and ATL cells exhibit CD30 and soluble CD30 (sCD30) is elevated in the sera of patients with ATL. Recently, we also evaluated the levels of sCD30 in ATL patients underwent chemotherapy and allogeneic hematopoietic stem cell transplantation (HSCT) to predict prognosis of ATL patients under 2 different clinical settings; before initiation therapy and before HSCT. Our results suggest that sCD30 may be a useful biomarker in HSCT therapy, because a high sCD30 level before HSCT was implicated in early death after HSCT. In addition, we report that sCD30 elevation was followed by acute crisis from chronic type of ATL. Previously, high levels of soluble proteins including cytokine receptor and membrane-binding protein were observed in patients with ATL. A disintegrin and metalloproteinase (ADAM)10 and ADAM17 worked as sheddases of CD30 as well as the other proteins. ADAM10/17 also cleaved collagen and elastin which are structural proteins of tissues and may cause the tissue injury of important organs. It seems that ADAM10/17 plays a role as oncoproteins for tumorigenesis in ATL.
Table 1. High levels of soluble proteins cleaved by ADAM10/17 in ATL patients.

<table>
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<tr>
<th>Shedding proteins on ATL cells</th>
<th>CD30 [8,15]</th>
<th>ADAM17</th>
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<tr>
<td>*Fas ligand (FasL) [28]</td>
<td>IL-6 receptor (IL-6R) [24]</td>
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<td>CD44 [27,32]</td>
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*This report was demonstrated in HTLV-1 carriers.

Figure 1. Aggressive phenotype of ATL cells. ADAM10 and 17 cleave membrane-bound proteins, ligands and receptors, and fibrous proteins, which are involved in the tumorigenesis, development, and metastasis of tumors. To circulate at elevated levels in HTLV-1-infected patients and to be associated activation of STAT3 signaling [24,25]. CD44 is a broadly distributed cell surface glycoprotein and has been identified as a tumor-promoting molecule that is implicated in cancer cell growth, invasion, and metastasis [26]. In vivo, plasma levels of soluble CD44 (sCD44) were significantly associated with the performance status, total number of involved lesions, and lactic dehydrogenase [27]. As mentioned above, HTLV-1 carriers are known to develop pulmonary complications characterized by T-lymphocytic alveolitis. Sakamoto et al. measured soluble Fas (sFas) and Fas ligand (sFasL) in serum and bronchoalveolar lavage fluid of 16 seropositive asymptomatic HTLV-1 carriers and 32 healthy subjects, and the levels of sFasL were significantly higher in asymptomatic carriers than the control [28].

Accordingly, serum levels of sCD30 may be a marker of matrix metalloproteinases activation on ATL cells (Figure 1). A Disintegrin and metalloproteinase (ADAM)10 and ADAM17 work as sheddases of CD30 as well as the other proteins (sFasL, scCD44, and sIL-6R) as shown in Table 1 [29-32]. ADAM10/17 also cleaves collagen and elastin which are structural proteins of tissues and may cause the tissue injury of important organs. It seems that ADAM10/17 play a role as oncoproteins for tumorigenesis in ATL.

References

