Development of a quantitative simulator of HTLV-1 proviral integration sites

Mitsuaki Takaki[1], Shingo Iwami[1]

1) *Department of Biology, Kyushu University, Fukuoka, JAPAN*

Corresponding Author: Shingo Iwami, siwami@kyushu-u.org

ABSTRACT

Human T-lymphotropic virus type 1 (HTLV-1) is a persistent CD4 T-lymphotropic retrovirus. Most HTLV-1 infected individuals remain asymptomatic, but a proportion develop adult T cell leukemia (i.e., ATL) or inflammatory disease, such as HTLV-1-associated myelopathy (i.e., HAM). Interestingly, the clonality of proviral integration sites are different between ATL and HAM (monoclonal vs. polyclonal). HTLV-1 produces their progeny via cell-to-cell infection or clonal expansion. Only cell-to-cell infection, which requires Tax gene expression, can increase the diversity of the integration sites, but expressing Tax also enhance the risk to be eliminated by Tax-specific cytotoxic T lymphocyte. Recently, it has been shown that Tax is expressed in a minor fraction of leukemic cells at any given time, and importantly, its expression spontaneously switches between on and off states. In this study, we developed a simulator which could describe clonality of proviral integration sites depending on Tax expression profiles. This simulator enables us to predict the clonality, and therefore the disease progression.

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