Identification Of Host Restriction Factors Blocking HIV-1 Replication

Professor Akihide RYO
Professor, Department of Microbiology
Graduate School of Medicine
Yokohama City University

Abstract

Recent findings have revealed roles played by intrinsic cellular restriction factors that target HIV-1 replication. BST2/Tetherin is an interferon-induced host protein that restricts the release of progeny virions from infected cells, while the HIV-1 accessory protein Vpu antagonizes this restriction. Although the activity of Vpu is regulated by the phosphorylation on its Ser52 and Ser56 residues, the precise regulatory mechanism for the phosphorylation-dependent Vpu function remains elusive. We have found that SCYL2 (also known as CVAK104) facilitates BST2-dependent restriction of viral release by antagonizing HIV-1 Vpu. The forced expression of SCYL2 results in the reduction of virus particle release from wild-type HIV-1-infected cells in a BST2-dependent manner, but not from cells infected with Vpu-deficient HIV-1. Interestingly, SCYL2 facilitates the dephosphorylation of Vpu on both Ser52 and Ser56 by recruiting protein phosphatase 2A (PP2A). Conversely, the targeted depletion of SCYL2 results in the enhancement of the Vpu phosphorylation, thereby facilitating its function and resultant viral particle release. Moreover, SCYL2 is found to be induced by type I interferon and play a key role in interferon-mediated viral restriction. These results indicate that SCYL2 serves as a cofactor for BST2-mediated viral restriction by suppressing Vpu phosphorylation.

Selected Publications


