

## Special Issue for CURRENT HIV RESEARCH

*Guest Editor: Kenzo Tokunaga, Ph.D.*

**Hot Topic issue: Vpu and BST-2/tetherin**

### **Aims and Scope:**

BST-2/tetherin is a recently identified third interferon-inducible restriction factor (following the discovery of APOBEC3G and TRIM5 $\alpha$ ) that blocks the production of enveloped viruses by tethering them to the plasma membranes of the virus producing cells. HIV-1 is, however, armed with an accessory protein, viral protein U (Vpu), that counteracts the inhibitory activity of BST-2/tetherin by downregulating this restriction factor through transmembrane interactions and leading to its degradation. SIV that does not carry Vpu employs Nef as a tetherin antagonist, suggesting that blocking BST-2/tetherin activity has been an essential viral strategy throughout the evolution of primate lentiviruses. In this review, we will focus on recent advances in the molecular mechanisms of this newly discovered host-pathogen interaction and of its species specificity, and discuss how viruses and hosts have battled through the acquisition of their defensive proteins.

### **Key words:**

HIV-1, Vpu, BST-2/tetherin, interaction, downregulation, degradation, evolution

### **Tentative Subtopics:**

- Vpu's lentiviral evolution.
- Transmembrane interactions between Vpu and BST-2/tetherin.
- Sites of action of Vpu in BST-2/tetherin downregulation.
- $\beta$ TrCP dependency of Vpu-induced downregulation of CD4 and BST-2/tetherin.
- Role of ESCRT protein in Vpu-induced downregulation of BST-2/tetherin.
- BST-2/tetherin's role in cell-to-cell transmission.
- Species-specific effects of SIV Nef/gp41 and HIV-1 Vpu on BST-2/tetherin.
- Structural basis of HIV-1 tethering.
- Intracellular logistics of BST-2/tetherin.
- Vpu interference with innate cellular immune mechanisms.

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