Abstract

PSGL-1 Restricts HIV-1 Infectivity by Blocking Virus Particle Attachment to Target Cells [†]

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Abstract: P-selectin glycoprotein ligand-1 (PSGL-1) is a dimeric, mucin-like, 120-kDa glycoprotein that binds to P-, E-, and L-selectins. PSGL-1 is primarily expressed on the surface of lymphoid and myeloid cells and is up-regulated during inflammation to mediate leukocyte tethering and rolling on the surface of endothelium for migration into inflamed tissues. Although it has been reported that PSGL-1 expression inhibits human immunodeficiency virus type 1 (HIV-1) replication, the mechanism of PSGL-1-mediated anti-HIV activity remains to be elucidated. Here, we report that PSGL-1 in virions blocks the infectivity of HIV-1 particles by preventing the binding of particles to target cells. This inhibitory activity is independent of the viral glycoprotein present on the virus particle; the binding of particles bearing the HIV-1 envelope glycoprotein, vesicular stomatitis virus G glycoprotein, or lacking a viral glycoprotein, is impaired by PSGL-1. Mapping studies show that the extracellular, N-terminal domain of PSGL-1 is necessary for its anti-HIV-1 activity, and the PSGL-1 cytoplasmic tail contributes to its inhibition. In addition, we demonstrate that the PSGL-1-related monomeric E-selectin-binding glycoprotein CD43 also effectively blocks HIV-1 infectivity. HIV-1 infection, or the expression of either Vpu or Nef, downregulates PSGL-1 from the cell surface; the expression of Vpu appears to be primarily responsible for enabling the virus to partially escape PSGL-1-mediated restriction. Finally, we show that PSGL-1 inhibits the infectivity of other viruses such as murine leukemia virus and influenza A virus. These findings demonstrate that PSGL-1 is a broad-spectrum antiviral host factor with a novel mechanism of action.

Keywords: virus release; innate immunity; antiviral factors

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