Abstract

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

Yajing Fu 1,2,3,*, Sijia He 3, Abdul Waheed 4, Deemah Dabbagh 3, Zheng Zhou 3, Benjamin Trinité 5, Zhao Wang 3, Jieshi Yu 6, Dan Wang 6, Feng Li 6, David N Levy 5, Hong Shang 1,2, Eric O Freed 4,* and Yuntao Wu 3,*

1 Key Laboratory of AIDS Immunology of National Health Commission, Department of Laboratory Medicine, The First Affiliated Hospital, China Medical University, Shenyang 110122, China; hongshang100@hotmail.com
2 Key Laboratory of AIDS Immunology, Chinese Academy of Medical Sciences, Shenyang 110001, China
3 National Center for Biodefense and Infectious Diseases, School of Systems Biology, George Mason University, Manassas, VA 20110, USA; she3@gmu.edu (S.H.); dabbagh.deemah@gmail.com (D.D.); zzhou6@masonlive.gmu.edu (Z.Z.)
4 Virus-Cell Interaction Section, HIV Dynamics and Replication Program, NCI-Frederick, Frederick, MD 21702 USA; waheedab@nih.gov
5 Department of Basic Science, New York University College of Dentistry, New York, NY 10010, USA; bt32@nyu.edu (B.T.); dnlevy@nyu.edu (D.N.L.)
6 Department of Biology and Microbiology, South Dakota State University, Brookings, SD 57007, USA; zhaowang2007@outlook.com (Z.W.); jieshi.yu@sdsstate.edu (J.Y.); dan.wang@sdsstate.edu (D.W.); feng.li@sdsstate.edu (F.L.)
* Correspondence: fufu80@sina.com (Y.F.), efreed@nih.gov (E.O.F.), ywu8@gmu.edu (Y.W.)
† Presented at Viruses 2020—Novel Concepts in Virology, Barcelona, Spain, 5–7 February 2020.

Published: 17 June 2020

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

© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).