Control of cell surface density of HIV coreceptor GPR15/BOB by phosphorylation-dependent 14-3-3 protein binding

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Cell surface density of the viral receptors critically determines the rate of infection of viruses. A variety of G protein-coupled receptors act as coreceptors for HIV entry. However, molecular mechanisms that regulate cell surface density of these coreceptors are not fully understood. GPR15/BOB, a putative chemokine receptor, was previously identified as a coreceptor for HIV and SIV and has been suggested to be involved in the HIV/SIV-associated pathogenesis. We report here that the steady-state cell surface expression of GPR15 is substantially promoted by the binding of 14-3-3, a phospho-recognizing scaffolding protein, to the receptor C-terminus upon phosphorylation of the C-terminal penultimate serine residue. The 14-3-3 protein binding interfered with the interaction between the endoplasmic reticulum (ER) retention signal of GPR15 and the coatomer protein complex I (COPI), which resulted in the release of the receptor from the ER retention pathway and its delivery to the cell surface. These results provide novel mechanistic insights into the role of phosphorylation signaling in controlling the cell surface density of an HIV coreceptor.

Biography

Sojin Shikano has completed his Ph.D from Tokyo University and postdoctoral studies from UT Southwestern Medical Center and Johns Hopkins University. He is currently an Assistant Professor in the University of Illinois at Chicago.