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Sugar-binding protein may play a role in HIV infection

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Specific types of "helper" T cells that are crucial to maintaining functioning immune systems contain an enzyme called PDI (protein disulfide isomerase).

This enzyme affects how proteins fold into specific shapes, which in turn influences how the T cells behave. PDI also plays a role in HIV infection by helping to change the shape of the surface envelope protein of the virus, enabling the virus to interact optimally with receptors on the T cells, such as the CD4 molecule.

Though it is known that PDI inhibitors can prevent HIV infection, just how this happens has remained a mystery. And though it has been known that PDI, which normally lives inside the cell, can become entrapped on the cell's surface, it has not been understood how this happens.

Now, in a new study, UCLA researchers report that a sugar-binding protein called galectin-9 traps PDI on T-cells' surface, making them more susceptible to HIV infection.

The findings could lead researchers to a potential new target for anti-HIV therapeutics, such as therapies to inhibit PDI or galectin-9.

More information: Galectin-9 binding to cell surface protein disulfide isomerase regulates the redox environment to enhance T-cell migration and HIV entry, *PNAS*, Published online before print June 13, 2011, doi: 10.1073/pnas.1017954108

Abstract

Interaction of cell surface glycoproteins with endogenous lectins on the cell surface regulates formation and maintenance of plasma membrane domains, clusters signaling complexes, and controls the residency time of glycoproteins on the plasma membrane. Galectin-9 is a soluble, secreted lectin that binds to glycoprotein receptors to form galectin–glycoprotein lattices on the cell surface. Whereas galectin-9 binding to specific glycoprotein receptors induces death of CD4 Th1 cells, CD4 Th2 cells are resistant to galectin-9 death due to alternative glycosylation. On Th2 cells, galectin-9 binds cell surface protein disulfide isomerase (PDI), increasing retention of PDI on the cell surface and altering the redox status at the plasma membrane. Cell surface PDI regulates integrin function on platelets and also enhances susceptibility of T cells to infection with HIV. We find that galectin-9 binding to PDI on Th2 cells results in increased cell migration through extracellular matrix via β3 integrins, identifying a unique mechanism to regulate T-cell migration. In addition, galectin-9 binding to PDI on T cells potentiates infection with HIV. We identify a mechanism for regulating cell surface redox status via a galectin–glycoprotein lattice, to regulate distinct T-cell functions.

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