ABSTRACT

A better understanding of the cellular targets of HIV infection in the female genital tract may inform HIV prevention efforts. Proposed correlates of cellular susceptibility include the HIV co-receptor CCR5, peripheral homing integrins, and immune activation. We used a CCR5-tropic pseudovirus to quantify HIV entry into unstimulated endocervical CD4^+ T cells collected by cytobrush. Virus entry was threefold higher into cervix-derived CD4^+ T cells than blood, but was strongly correlated between these two compartments. Cervix-derived CD4^+ T cells expressing CD69, α4β7, or α4β1 were preferential HIV targets; this enhanced susceptibility was strongly correlated with increased CCR5 expression in α4β7^+ and CD69^+ CD4^+ T cells, and to a lesser extent in α4β1^+ CD4^+ T cells. Direct binding of gp140 to integrins was not observed, integrin inhibitors had no effect on virus entry, and pseudotypes with an env that preferentially binds α4β7 still demonstrated enhanced entry into α4β1^+ cells. In summary, a rapid and sensitive HIV entry assay demonstrated enhanced susceptibility of activated endocervical CD4^+ T cells, and those expressing α4β7 or α4β1. This may relate to increased CCR5 expression by these cell subsets, but did not appear to be due to direct interaction of α4β7 or α4β1 with HIV envelope. Mucosal Immunology advance online publication, 15 April 2015; doi:10.1038/mi.2015.28.