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, $\alpha_4\beta_7$, or $\alpha_4\beta_1$ were preferential HIV targets; this enhanced susceptibility was strongly correlated with increased CCR5 expression in $\alpha_4\beta_7^+$ and $CD69^+$ $CD4^+$ T cells, and to a lesser extent in $\alpha_4\beta_1^+$ $CD4^+$ 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 $\alpha_4\beta_7$ still demonstrated enhanced entry into $\alpha_4\beta_1^+$ cells. In summary, a rapid and sensitive HIV entry assay demonstrated enhanced susceptibility of activated endocervical $CD4^+$ T cells, and those expressing $\alpha_4\beta_7$ or $\alpha_4\beta_1$. This may relate to increased CCR5 expression by these cell subsets, but did not appear to be due to direct interaction of $\alpha_4\beta_7$ or $\alpha_4\beta_1$ with HIV envelope.Mucosal Immunology advance online publication, 15 April 2015; doi:10.1038/mi.2015.28.