Abstract

HIV-1-specific IgA has been described in the genital tract and plasma of HIV-1 highly exposed, persistently seronegative (HEPS) individuals, and IgA from these sites has been shown to neutralize HIV-1. This study examines the ability of IgA isolated from HEPS individuals to inhibit transcytosis across a tight epithelial cell layer. A Transwell system was established to model HIV-1 infection across the human mucosal epithelium. The apical-basolateral transcytosis of primary HIV-1 isolates across this mucosal model was examined in the presence and the absence of IgA isolated from the genital tract, saliva, and plasma of HEPS individuals enrolled in both a sex worker cohort in Nairobi, Kenya, and a discordant couple cohort in Italy. In the absence of IgA, HIV-1 primary isolates were actively transported across the epithelial membrane and were released on the opposite side of the barrier. These transcytosed HIV-1 particles retained their ability to infect human mononuclear cells. However, IgA purified from the mucosa and plasma of HEPS individuals was able to inhibit HIV-1 transcytosis. Inhibition was seen in three of six cervicovaginal fluid samples, five of 10 saliva samples, and three of six plasma samples against at least one of the two primary HIV-1 isolates tested. IgA from low risk, healthy control subjects had no inhibitory effect on HIV-1 transcytosis. The ability of mucosal and plasma IgA to inhibit HIV-1 transcytosis across the mucosal epithelium may represent an important mechanism for protection against the sexual acquisition of HIV-1 infection in HEPS individuals.