

## Abstract

The use of antiretroviral therapy (ART) as pre-exposure prophylaxis (PrEP) has gained global attention as a promising HIV prevention strategy in men who have sex with men. Permeability of these agents in the rectal mucosa may be partially regulated by interactions with drug efflux transporters, P-glycoprotein (P-gp), multidrug resistance-associated proteins (MRPs) and/or breast cancer resistance protein (BCRP). The objective of this work was to investigate the expression of drug efflux transporters in recto-sigmoid colon tissues of HIV-infected and uninfected men, and evaluate the association of ART and/or HIV infection with drug transporter expression. MDR1/P-gp, MRPs (1-4) and BCRP mRNA and protein expression were detected in sigmoid colon biopsies of HIV-uninfected individuals. Biopsies from HIV-infected, ART-naïve participants revealed a significant downregulation of P-gp and MRP2 protein levels compared to HIV-uninfected individuals. Biopsies from HIV-infected ART-treated patients showed 1.9-fold higher P-gp protein expression and 1.5-fold higher MRP2 protein expression compared to the ones obtained from the HIV-infected ART-naïve patients. This is a first report demonstrating that HIV infection or ART could alter expression of drug efflux transporters in gut mucosa which in turn could affect the permeability of PrEP antiretroviral agents across this barrier, a highly vulnerable site of HIV transmission.