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Transporter-Dependent Cytotoxicity of Antiviral Drugs in Primary Cultures of Human Proximal Tubular Cells

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Abstract

The role of plasma membrane transporters in the nephrotoxicity of two antiretroviral drugs, cidofovir and tenofovir, was studied in primary cultures of human proximal tubular (hPT) cells. Cells were grown on Transwell filter inserts to maintain epithelial polarity and access to either the apical or basolateral plasma membrane. The function of relevant membrane transporters, organic anion transporter 1 and 3 (OAT1/3), P-glycoprotein (multidrug resistance protein-1; P-gp or MDR1), and organic cation transporter 2 (OCT2), was validated by measurements of apical-to-basolateral and basolateral-to-apical fluxes of furosemide, digoxin, and metformin, respectively. Acute cytotoxicity of cidofovir (0, 10,