Inhibition of renal tubular cells by novel anti-HIV therapeutic agents and interaction with organic anion transporters

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[Background]EFdA (4'-ethynyl-2-fluoro-2'-deoxyadenosine) is a novel anti-HIV therapeutic agent. It has a unique structure and high antiviral activity, and is expected as a revolutionary new drug. TDF (Tenofovir disoproxil fumarate) and TAF (Tenofovir alafenamide) are nucleoside reverse transcriptase inhibitors that have already been clinically applied. TDF is known to cause renal damage after long-term administration. hOAT1 and hOAT3 are organic anion transporters expressed on the proximal tubule of the kidney and act as a cellular uptake pathway for the secretion of drugs. As one of the onset mechanisms of drug-induced renal damage, it is considered that drugs taken into proximal tubular cells via these transporters cause damage by accumulating in the cells. In this study, we investigated the effect of EFdA on renal tubular cells and the possibility of EFdA being taken into the cells via these transporters.

[Results] In the cell viability assay, EFdA, TDF, and TAF showed cell growth inhibition, after 72 hrs. However, no inhibition of substrate uptake by these compounds was observed in S2-hOAT1 cells and S2-hOAT3 cells.

[Discussion] EFdA can cause damage to proximal tubular cells to the same extent as TDF and TAF under pharmacological doses. However, other reports show that EFdA exhibits high antiviral activity at very low concentrations, and it is unlikely that the blood concentration will be high enough to cause kidney damage in clinical practice. It was considered that hOAT1 and hOAT3 are less involved in the damage of EFdA, TDF, and TAF to proximal tubular cells.