

Charles University

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Title of diploma thesis: Study of interactions of antiretroviral drug tenofovir and its prodrug tenofovir disoproxil fumarate with placental nucleoside transporters

Tenofovir (TFV) in the form of ester prodrug tenofovir disoproxil fumarate (TDF) is an essential part of combination antiretroviral therapy. It is often used in the prevention of perinatal HIV transmission. However, precise mechanism(s) involved in transfer of TFV/TDF from mother to fetus are not described in detail. Since these drugs are nucleoside analogues, there is a possibility that the mechanisms of their transplacental passage might include nucleoside transporters (NTs), either equilibrative or concentrative (ENTs/CNTs).

The aim of the diploma thesis was to investigate the role of placental NTs in membrane transfer of TFV and TDF. To address this issue, we performed *in vitro* accumulation in the BeWo cell line derived from placental choriocarcinoma.

By evaluating experiments, we found out that both TFV and TDF might not be substrates of NTs, thus the role of these transporters in TFV/TDF placental pharmacokinetics was not confirmed. Therefore, the drug-drug interactions on NTs are not expected as well as a significant effect of potential variable expression of NTs on transplacental pharmacokinetics of the mentioned drug and its prodrug.