Bilirubin Reduces the Uptake of Estrogen Precursors and the Followed Synthesis of Estradiol in Human Placental Syncytiotrophoblasts *via* Inhibition and Down-regulation of OAT4

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Running title: Bilirubin inhibits and down-regulates OAT4 in PHTCs

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Supplemental Materials

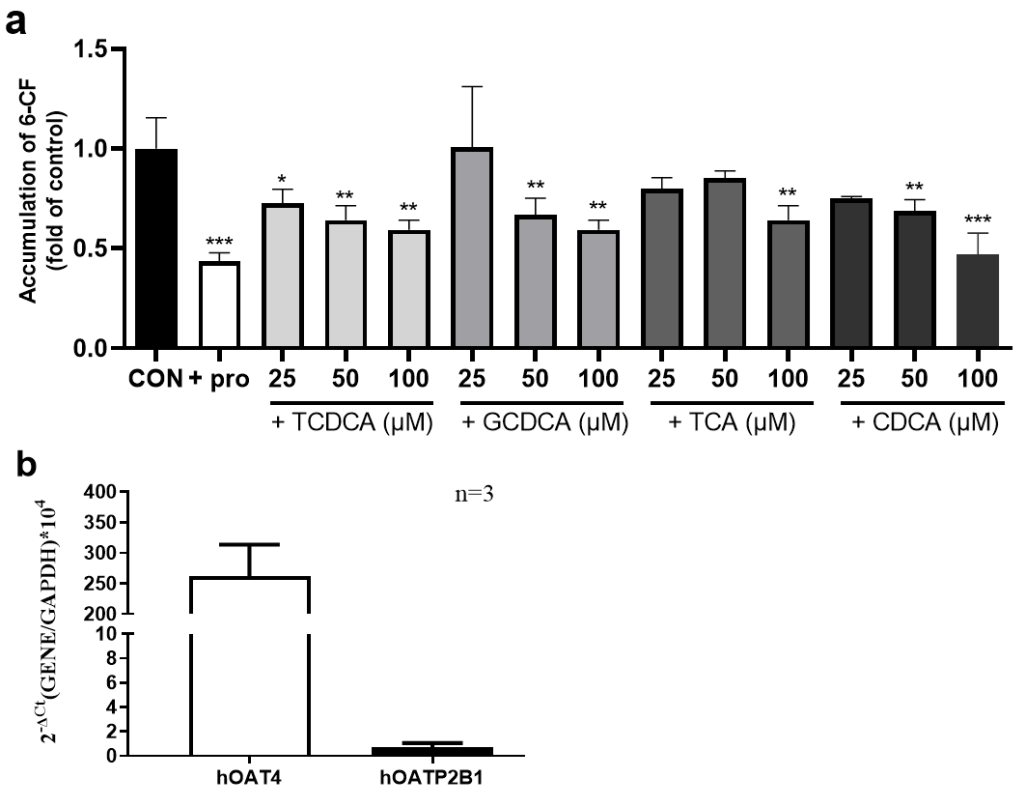

Fig. S1 Inhibitory effects of bile acids on hOAT4-mediated uptake of 6-CF (5 μM) (a) and mRNA expression of OAT4 and OATP2B1 (b) in JEG-3 cell lines. Bile acids including TCDCA, GCDCA, TCA and CDCA performed relatively weaker inhibitory effects on the accumulation of 6-CF in JEG-3 cells. Compared with the accumulation without inhibitors, *P < 0.05, **P < 0.01, ***P < 0.001. All cells were incubated at 37 °C for 3 minutes. The accumulation was expressed as fold of substrate accumulation without those inhibitors. Data were expressed as mean ± SD from three independent experiments conducted in triplicate.

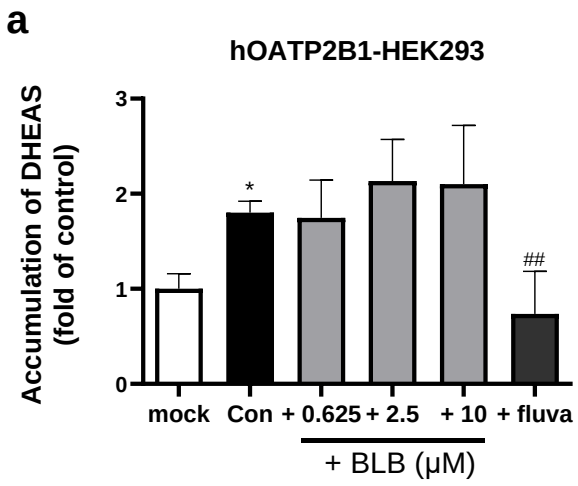

Fig. S2 Identifications of the bilirubin inhibitory effects on OATP2B1-HEK stably transfected cells constructed and preserved in our laboratory in the presence of 10 μM HSA buffer. Function of tested OATP2B1 cells has been identified by its probe substrate (10 μM DHEAS). Compared with the mock cells, *$P < 0.05$; compared with the hOATP2B1-HEK cells without fluvastatin (a classic inhibitor of OATP2B1), $^{\#\#}P < 0.01$. All cells were incubated at 37 °C for 3 minutes. The accumulation was expressed as fold of substrate accumulation without those inhibitors. Data were expressed as mean ± SD from three independent experiments conducted in triplicate.