

**Supplementary Fig. 1.** Interaction of naturally occurring fatty acids and fatty acyl-CoA with hPPAR $\alpha$  based on displacement of hPPAR $\alpha$ -bound BODIPY C16 CoA. hPPAR $\alpha$  complexed with BODIPY C16-CoA as described in the Materials and Methods was titrated with the following ligands: (A) palmitic acid, (B) stearic acid, (C) oleic acid, (D) eicosapentaenoic acid, (E) palmitoyl-CoA, (F) stearoyl-CoA, (G) oleoyl-CoA, (H) eicosapentaenoyl-CoA, (I) lauric acid, (J) lauryl-CoA, (K) clofibrate, and (L) rosiglitazone. The maximal fluorescence emission of BODIPY C16 CoA was measured at 515 nm (excitation at 465 nm). Data are presented as percent change of initial fluorescence plotted as a function of ligand concentration. All values represent mean  $\pm$  S.E.,  $n \ge 3$ .



**Supplementary Fig. 2.** Interaction of naturally occurring fatty acids and fatty acyl-CoA with mPPAR $\alpha$  based on displacement of mPPAR $\alpha$ -bound BODIPY C16 CoA. mPPAR $\alpha$  complexed with BODIPY C16-CoA as described in the Materials and Methods was titrated with the following ligands: (A) palmitic acid, (B) stearic acid, (C) oleic acid, (D) eicosapentaenoic acid, (E) palmitoyl-CoA, (F) stearoyl-CoA, (G) oleoyl-CoA, (H) eicosapentaenoyl-CoA, (I) lauric acid, (J) lauryl-CoA, (K) clofibrate, and (L) rosiglitazone. The maximal fluorescence emission of BODIPY C16 CoA was measured at 515 nm (excitation at 465 nm). Data are presented as percent change of initial fluorescence plotted as a function of ligand concentration. All values represent mean  $\pm$  S.E.,  $n \ge 3$ .