Abstract

While perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) have been studied at length, less is known about the biological activity of other perfluoroalkyl acids (PFAAs) in the environment. Using a transient transfection assay developed in COS-1 cells, our group has previously evaluated a variety of PFAAs for activity associated with activation of peroxisome proliferator-activated receptor alpha (PPARα). Here we use both mouse and human primary heptatocytes to further assess the activity of a similar group of PFAAs using custom designed Taqman Low Density Arrays. Hepatoyctes were cultured for 48 hours in the presence of varying concentrations of 12 different PFAAs or Wy14,643, a known activator of PPARα. Total RNA was collected and the expression of 48 mouse or human genes evaluated. Gene selection was based on either in-house liver microarray data (mouse) or published data using primary hepatocytes (human). Changes in gene expression were more restricted than expected in primary mouse hepatocytes . Genes typically regulated in whole tissue such as Acox1, Me1, Acaa1a, Hmgcs1, and Slc27a1were not altered in mouse cells. Cyp2b10, a gene regulated by the constitutive androstane receptor and a transcript typically up-regulated by in vivo exposure to PFAAs, was also unchanged in mouse hepatocytes. Cyp4a11, Ehhadh, Pdk4, Cpt1b, and Fabp1 were up-regulated as expected in mouse cells. A larger group of genes were differentially expressed in human primary hepatocytes, however, little consistency was observed across compounds with respect to which genes produced a significant dose response. Compound ranking was conducted based on the limited dataset. In mouse hepatocytes, with the exception of PFHxA, the pattern was comparable to that previously observed in our COS-1 reporter cell assay. A similar pattern was observed in human hepatocytes, although PFDA and PFOS showed higher activity than previously observed in COS-1 cells while PFOA showed less activity than