

Effect of Perfluorinated “Forever” Chemicals on the Expression of Intestinal Xenobiotic Transporters

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A class of synthetic chemicals, perfluorinated and polyfluorinated substances (PFAS), have been used for decades in non-stick cookware, fire-fighting foams, textiles, packaging, and cosmetics. PFAS are found in almost the entire U.S population and elevated concentrations may contribute to the development of chronic conditions including hyperuricemia and hypercholesterolemia. Prior studies have demonstrated that PFAS can inhibit the functional activity of the intestinal uric acid transporter, breast cancer resistance protein (BCRP/ABCG2), which may explain a mechanism for increased risk of hyperuricemia. In the current study, we sought to determine whether PFAS chemicals alter expression of BCRP in human intestinal cells. Pharmacological agonists of the AhR (β -naphthoflavone (β -NF) and PPAR γ transcription factors (rosiglitazone, (RG) were used as positive controls that induce BCRP in human Caco-2 cells, a well-studied model of the intestinal barrier. Caco-2 cells were treated with vehicle (0.5% DMSO), various PFAS chemicals (10 μ M, 50 μ M), or β -NF/RG (25 μ M, 100 μ M) for 72 hours. No cytotoxicity was observed at these concentrations. BCRP expression was semi-quantified using SDS-PAGE and Western blot analysis. As expected, β -NF and RG induced BCRP expression. By comparison, at concentrations of 10 μ M, PFAS chemicals did not significantly change BCRP expression. Ongoing studies with PFAS treatments at 50 μ M are being conducted to determine whether PFAS is able to change BCRP expression at higher concentrations. These studies will advance understanding of the interplay of PFAS and BCRP and the risk of developing hyperuricemia in individuals exposed to PFAS. This work was supported by the SOT Intern Program, EMSOP, NIH grants R25ES020721 and R01ES029275, and MARC U T34GM062756.

Influence of PFAS Forever Chemicals on Intestinal Expression of Transporters

