Regulators of the Placental Barrier: Insights from the UPSIDE Birth Cohort

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Placental efflux transporters, such as BCRP and P-gp, regulate fetal exposure to nutrients and xenobiotics, including endocrine disrupting compounds such as per- and polyfluoroalkyl substances (PFAS) and mycoestrogens such as zearalenone (ZEN). While human birth cohort studies have linked maternal exposure to these chemicals with adverse pregnancy outcomes, the extent to which exposure to PFAS or ZEN impacts transporter expression levels in human placentas has not been well characterized. The purpose of this study was to analyze relationships between sociodemographic and clinical factors, environmental chemicals such as PFAS and mycoestrogens, and BCRP and P-gp transporter proteins. Placentas (n=251) were collected at term in the Understanding Pregnancy Signals and Development cohort (Rochester, New York, USA). BCRP and P-gp proteins were quantified in membrane fractions using quantitative targeted absolute proteomics. ZEN and metabolites were measured in placentas, and levels of 5 PFAS chemicals were quantified in second trimester serum samples. Statistical analyses with correlations, nonparametric tests, and regression models using R were conducted to evaluate these relationships. In extended models, there were no significant associations between BCRP/P-gp expression and concentrations of PFAS/mycoestrogens, whereas parity was significantly positively associated with both transporters. Smoking was significantly negatively associated with P-gp levels. Future studies looking at how environmental chemicals impact additional placental transporters including those responsible for fetal delivery of nutrients could help further understand the role of transporters in adverse pregnancy outcomes. Supported by NIH R25ES020721, the Society of Toxicology, and the Ernest Mario School of Pharmacy.