

Poster Number 1

Integrating Transporter Data and Machine Learning Approaches to Predict Drug Transport Across the Placental Barrier

Tong Wang^{1,2}, Xuelian Jia^{1,2}, Lauren M Aleksunes³, and Hao Zhu^{1,2}

¹ Center for Biomedical Informatics and Genomics, Tulane University, New Orleans, LA

² Department of Chemistry and Biochemistry, Rowan University, Glassboro, NJ

³ Department of Pharmacology and Toxicology, Ernest Mario School of Pharmacy, Rutgers University, Piscataway, NJ

Background and Purpose: The placental barrier is crucial for protecting the fetus from damage caused by medications and toxicants. Drug permeability across the placental barrier is dictated in part by the regulation and function of both uptake and efflux transporters. We aimed to integrate drug transporter data with innovative machine learning (ML) approaches to predict drug permeability across the human placental barrier.

Methods: The target activity was the human cord blood-to-maternal blood concentration ratio (CM), which directly reflects overall placental permeability. The transporter data were initially used as descriptors to develop several ML models through a 5-fold cross-validation procedure. Subsequently, the transporter data were used to construct an interpretable neural network (INN) to predict CM and reveal potential routes for drug transport. The neural network was designed to mimic transporters located on multiple membranes (apical and basolateral syncytiotrophoblasts and fetal endothelial cells) within the human placental barrier.

Results: The resulted ML models showed good performance and could predict the drug CM values with coefficients of determination ranging from 0.612 to 0.664. The resulting INN was able to predict CM ratios by activating neurons that represented specific transporters involved in the drug transport routes across the relevant cellular membranes within the placental barrier.

Conclusions: This study provides a novel computational modeling framework that predicts drug placental permeability based on placental transporter functions and regulations, which can be widely applied to assess the risk of drug and toxicant exposures to the fetus during pregnancy. Supported by NIH UC2HD113039 and P30ES005022.