Poster Number 14

SLC and ABC Transporter Expression in Enteroids and Donor-Matched Small Intestine Mucosa

Vicky Sun[1], Kai Wang[1], Jashvant D Unadkat[1], Joanne Wang[1], Edward J. Kelly[1,2], Samuel L.M. Arnold[1]

[1] Department of Pharmaceutics, School of Pharmacy, University of Washington, Seattle, WA

[2] Kidney Research Institute, Seattle, WA

The small intestine is the site of absorption for many orally administered therapeutics and nutrients, and the solute-carrier (SLC) and ATP-binding cassette (ABC) superfamilies of transporters mediate uptake and efflux of many small molecules in the small intestine. Despite the key role of SLC and ABC transporters in drug and nutrient absorption during childhood, the majority of proteomic data have been acquired from adults and transporter abundance in neonates and pediatrics (>1 month - 9 years old) remains under-characterized. To bridge this gap in knowledge, we are developing intestinal crypt cell-derived organoids (enteroids) from neonatal and pediatric intestinal tissue to study drug disposition. Transport studies with enteroids may be most impactful for patients in these age groups, but it remains unclear how well enteroids reflect donor intestinal tissue and age-associated trends in transporter abundance. Published data are largely restricted to mRNA levels and/or activity for a few xenobiotic transporters, neglecting the majority of SLC and ABC transporters that are expressed in these in vitro systems. In this study, pediatric and neonatal enteroids and donor-matched intestine mucosa proteomes were compared to determine whether enteroid monolayers expressed the same proteins at similar abundance to mucosa. In preliminary results, an average of 95 SLC and 17 ABC transporters were identified out of an average of 5,648 proteins in neonatal and pediatric small intestine mucosa and enteroids. Most observed transporters were expressed in both intestine mucosa and enteroids, but the relative abundance of key nutrient and xenobiotic transporters differed between sample types. This work is supported by NIH grant UC2HD113041.