Poster 30 Establishment of an air-liquid interface intestinal organoid monolayer and its characterization for drug absorption and metabolism

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Investigation and prediction of intestinal absorption and metabolism is a key step in the development of orally administered drugs. Even though the Caco-2 model is extensively used and considered as gold standard *in vitro* model, it has several limitations. A major drawback is the lack of cytochrome P450 3A4 (CYP3A4) and therefore Caco-2 models cannot fully recapture the human *in vivo* first-pass metabolism. Biopsy-derived intestinal organoids can overcome these limitations and have been increasingly used in pharmacokinetic studies in recent years. Organoids provide many advantages including cell type heterogeneity, expression of relevant enzymes and scalability to high-throughput assays. In this study we established an air-liquid interface intestinal organoid monolayer and compared it to a submerged culturing condition. In an in-depth characterization of intestinal organoid monolayers derived from duodenum and jejunum biopsies, several advantages of an air-liquid interface culture for intestinal absorption and metabolism studies could be shown. We could demonstrate a reproducible long-term culture and observed physiologically relevant and stable transepithelial electrical resistance values. In comparison to submerged culture conditions we observed distinct differences in cell differentiation, morphology, and most importantly higher expression and activity of drug metabolizing enzymes. Furthermore, the apparent permeability (P_{app}) was evaluated for several compounds from apical-to-basolateral side. This study supports air-liquid interface culture of intestinal organoid monolayers to predict human drug absorption and metabolism.