POLARITY SWITCHING REDUCES PIEZO1-MEDIATED INFLAMMATORY PHENOTYPE OF CONVENTIONAL HUMAN PANCREATIC ORGANOIDS

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Apical-out human pancreatic organoids reveal that conventional organoid cultures may represent a pressure-induced inflammatory state mediated by PIEZO1, suggesting a new model for studying post-ERCP and gallstone-induced pancreatitis.

KEY POINTS

- Polarity switching of human pancreas-derived organoids by Matrigel removal resulted in decreased PIEZO1 expression and reduced expression of pro-inflammatory cytokines CXCL1, CXCL2, CXCL3, and CXCL8.
- Pharmacological activation of PIEZO1 with YODA1 reversed the expression of pro-inflammatory cytokines in apical-out organoids, suggesting PIEZO1 mediates the inflammation-like phenotype in conventional organoids.
- Conventional apical-in organoid cultures may represent a pressure-induced inflammatory state by overexpressing elements of the epithelial innate immune response, while apical-out organoids may provide a more physiologically relevant model.
- Polarity switching led to increased chloride efflux through CFTR and ANO1 due to lack of sustained intraluminal pressure from basal secretion in closed lumens of conventional organoids.
- This work may benefit researchers developing therapeutic options for post-ERCP and gallstone-induced pancreatitis.

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