Bioengineered gut perfusable organoids with *in-vivo*-like complexity and function for precision medicine applications

Marine Meyer[1,*], Pascaline Sirugue[1], Victor Anstett[1], Aline Roch[1], Francesco Piraino[1], Virginie Garnier[1], Sylke Hoehnel[1] and Nathalie Brandenberg[1]

[1] Doppl SA, Lausanne, Switzerland
*E-mail: marine.meyer@doppl.ch

Organoids and microphysiological systems have emerged as powerful tools for modeling human gut physiology and diseases *in-vitro*. However, although physiologically relevant, these systems often lack spatial organization, cell-type diversity, and maturity necessary for mimicking intestinal mucosa. We integrated organoid and organ-on-a-chip technologies to develop a primary human stem–cell-derived perfusable organoid model closely resembling the *in-vivo* cell-type composition and the native architecture of the intestine [1].

This innovative platform facilitates access to both luminal and basal sides, promoting tissue longevity by removing shed cells and promoting enhanced cellular differentiation. Here we introduce a reproducible approach to generate a physiologically mature, human perfusable intestinal organoid system, cultured for up to 20 days. We confirm the cellular heterogeneity of the native intestine as well as the presence of a prominent brush border using immunofluorescence while our standardised barrier integrity assay show leak-tight and stable barrier. Our model can be used for a wide range of applications encompassing studies on nutrient absorption, disease modelling, gut microbia and drug screening. Our technology could be expanded to generate microtissues derived from other organs and incorporate additional microenvironmental components, thus emulating the intricate complexity of the native organ in an *in-vitro* setting. These bioengineered perfusable organoids provide a highly accurate, and functional platform to systematically study human organ physiology and pathology, and for the development of novel therapeutic strategies.

References

[1] Nikolaev M. Et al. Homeostatic mini-intestines through scaffold-guided organoid morphogenesis Nature 585, 574–578 (2020)