

## Generation of intestinal organoids derived from human pluripotent stem cells for drug testing

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Drug absorption via the intestinal tissue is modulated by membrane permeability and metabolism in intestinal epithelial cells (IECs). In drug discovery research, using human IECs to evaluate membrane permeability and metabolic stability can offer very useful information when exploring for drug candidate compounds that have good bioavailability and when trying to predict the fraction absorbed and intestinal availability in humans. Here, we evaluated the pharmacokinetic functions of human IECs differentiated from human induced pluripotent stem cells (hiPSCs) in 3D cultures. As human IECs differentiated in 3D cultures form intestinal organoids and spheroids (herein termed organoids), their morphology makes it difficult to evaluate their pharmacokinetic functions. Therefore, we dissociated intestinal organoids into single cells and attempted to purify human IECs. We found that hiPSC-derived IECs (hiPSC-IECs) expressed the epithelial cell adhesion molecule (EpCAM) and could be highly purified by sorting EpCAM+ cells. The hiP-SC-IEC monolayer showed a high TEER value (approximately 350  $\Omega \times \text{cm}^2$ ). In addition, hiPSC-IECs oxidatively metabolized terfenadine (CYP3A and CYP2J2 substrate) and midazolam (CYP3A substrate). These results indicated that hiPSC-IECs form tight-junction and have cytochrome P450 enzymatic activities. In conclusion, we developed a novel application of hiPSC-derived intestinal organoids for drug testing.

Definitive endoderm
Differentiaition
Activin A

Midgut/hindgut Differentiation Wnt3a, FGF4 Intestinal Differentiation Noggin, EGF R-spondin1

hiPSCs

Definitive Endodermal cells Midgut/ hindgut Intestinal organoids

Schematic drawing of the procedure for diferentiating hiPSCs into intestinal organoids via defnitive endodermal cells and midgut/hindgut cells

사용 제품	Cat #	사용 용도
Recombinant human/mouse/rat Activin A	338-AC	Derivation of hiPSCs
Recombinant human FGF4	235-F4	Derivation of hiPSCs
Recombinant human Wnt3A	5036-WN	Derivation of hiPSCs
Recombinant human R-Spondin1	4645-RS	Derivation of hiPSCs
Recombinant human Noggin	6057-NG	Derivation of hiPSCs
Recombinant human EGF	236-EG	Derivation of hiPSCs
Goat anti-SOX17	AF1924	Immunocytochemistry
Goat anti-FOXA2	AF2400	Immunocytochemistry
Goat anti-EpCAM	AF960	Immunocytochemistry
Goat anti-EphB2	AF467	Immunocytochemistry

## R&D Systems Recombinant Protein

당신의 실험 Quality를 바꿉니다.

종 류	설 명
Retail	5000개 이상의 다양한 종류를 가진 Protein
ProDots	쉽게 Media에 바로 녹여 사용할 수 있는 Protein
TC grade	Tissue culture에 있어 경제적인 가격의 Protein
GMP	Cell therapy 연구에 맞춰진 고품질 GMP Protein
Animal Free	동물 유래 성분을 배제한 효과적인 Protein
Active Biotinylated	Biotinylation의 Activity를 극대화한 Protein
Bulk	합리적인 가격, R&D systems의 고용량 Protein
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