

# Development and application of an immunocompetent human induced pluripotent stem cell-derived intestinal epithelial cell model for hazard assessment of the oral exposure route

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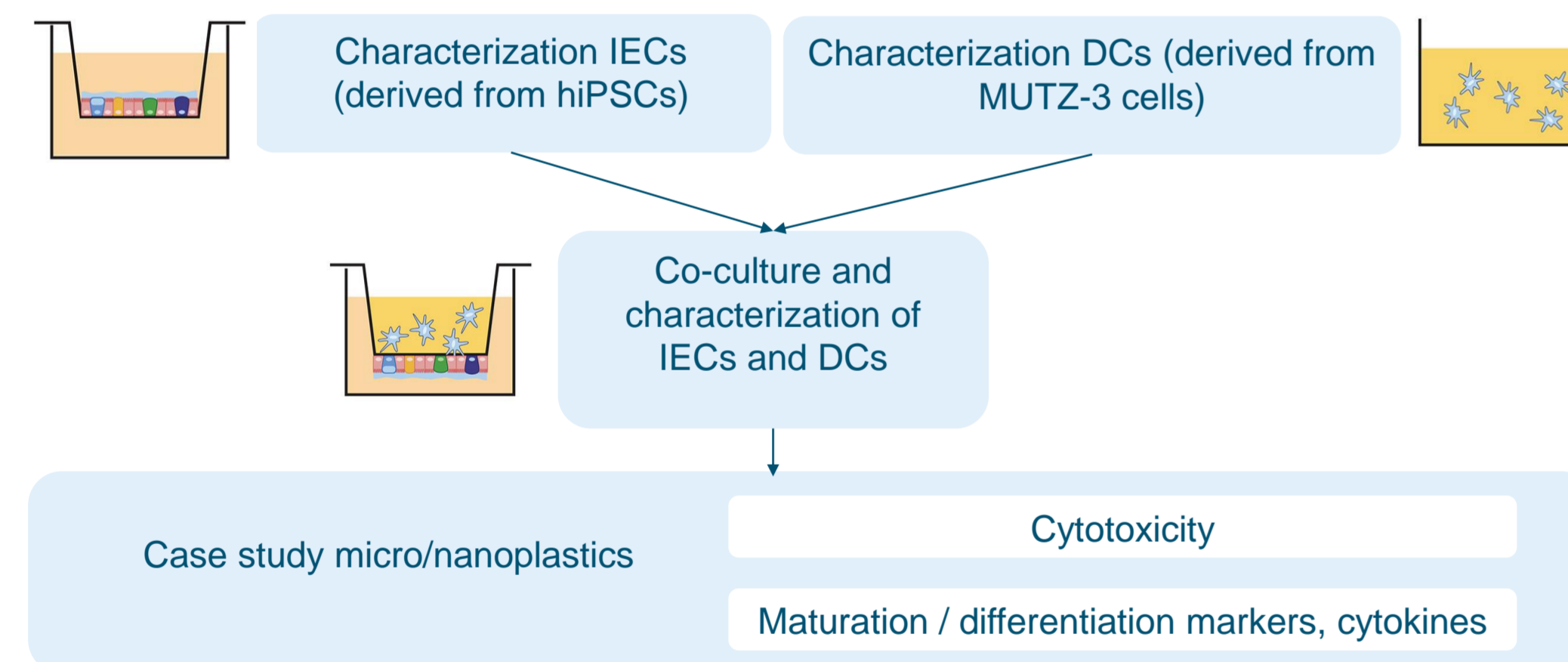
## Background

Human induced pluripotent stem cell (hiPSC)-derived intestinal epithelial cell (IEC) layers have the potential to provide an increasingly improved alternative to cell lines as they differentiate into multiple intestinal cell types that are also present *in vivo*. However, these models currently lack immunocompetence, as they do not contain immune cells like for instance dendritic cells (DCs) that play an important role in intestinal immune responses.

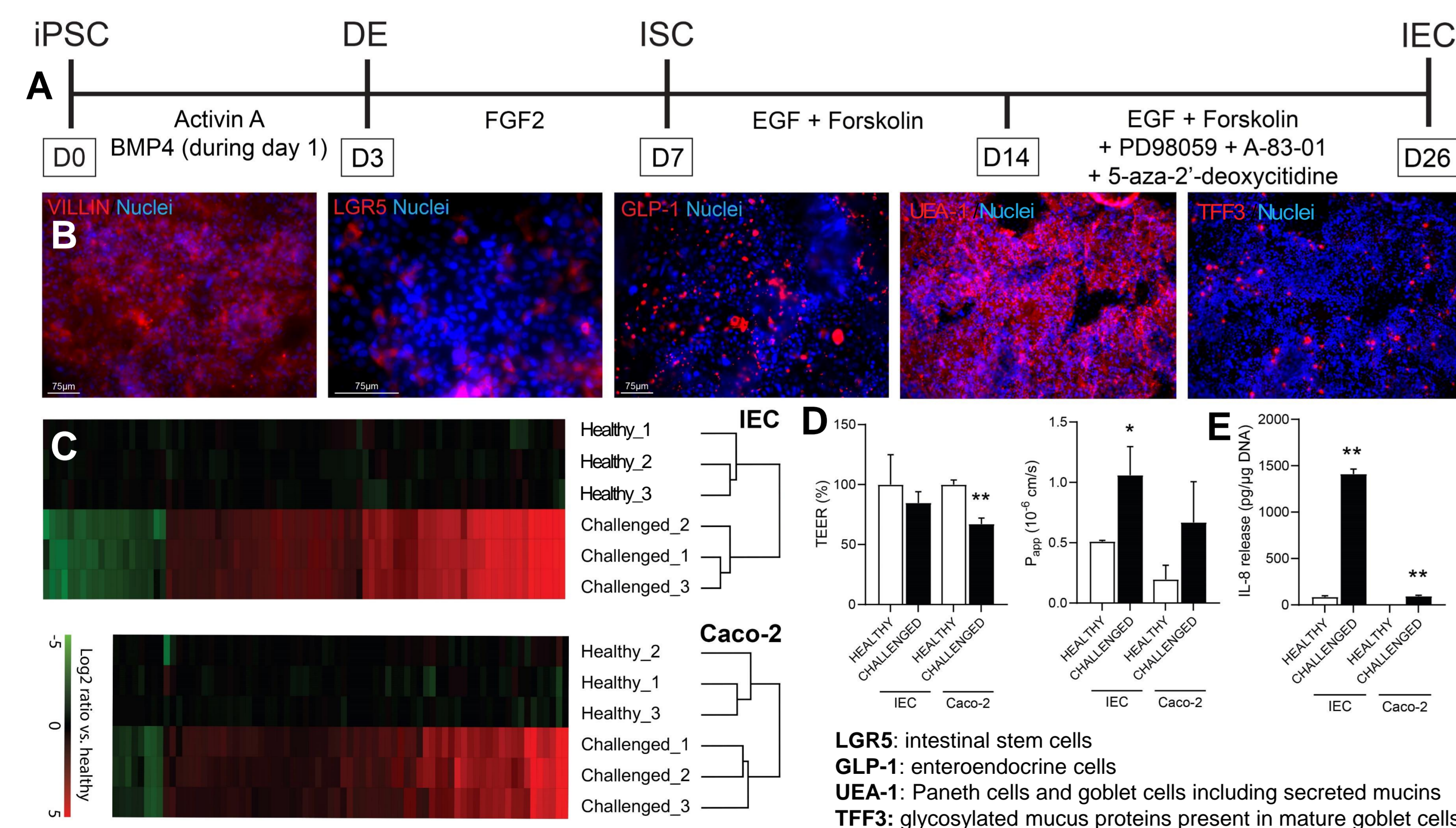
## Objective

To develop and characterize an immunocompetent hiPSC-derived IEC model, by co-culturing IEC layers with MUTZ-3 derived DCs.

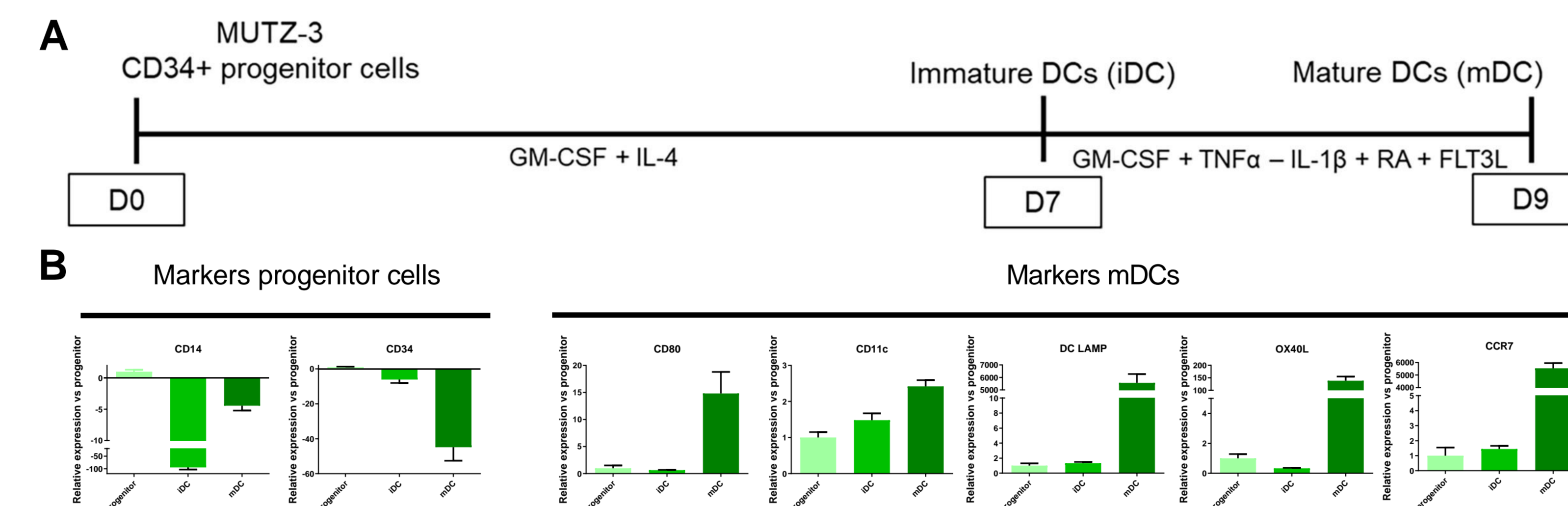
## Study design



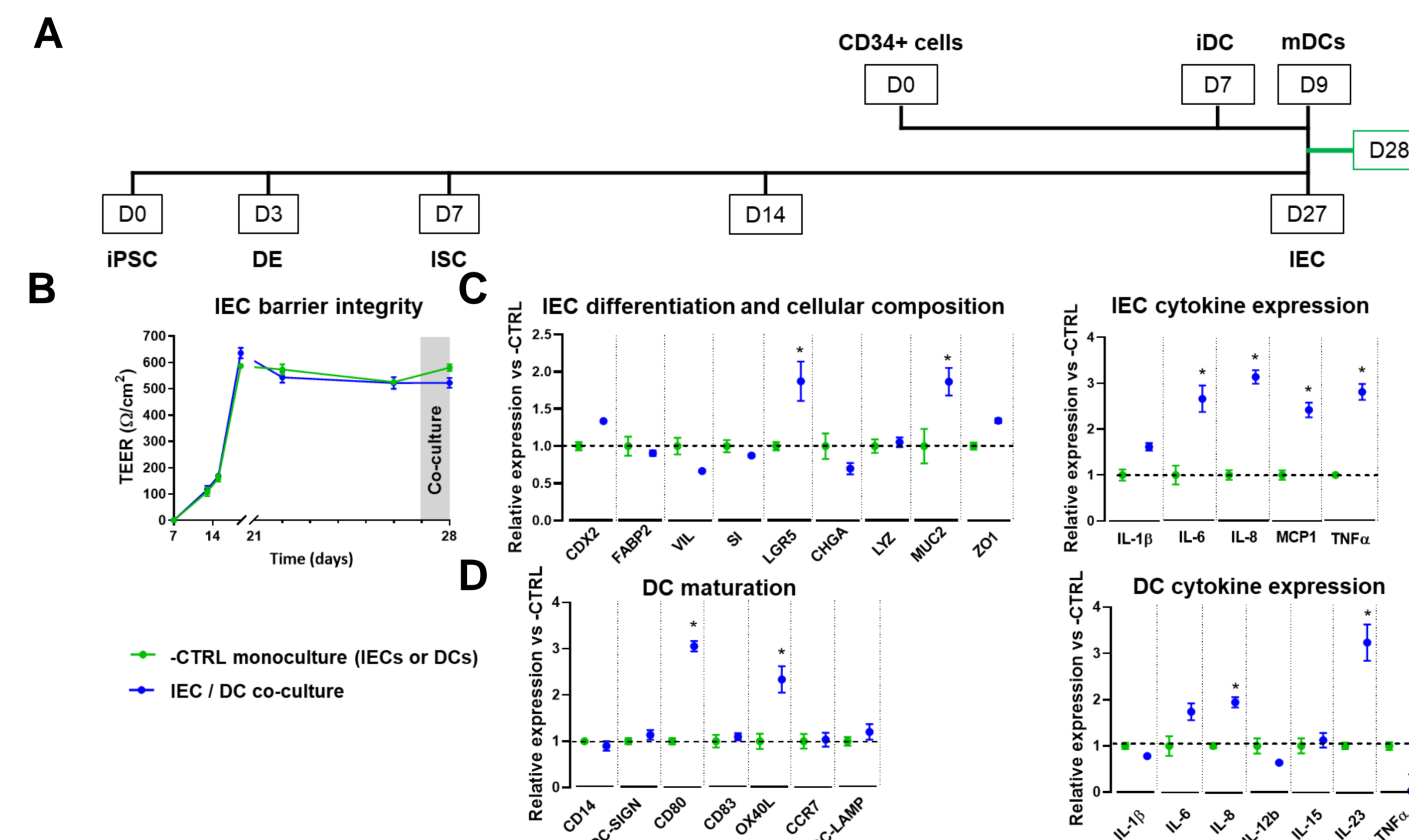
## Results: characterization hiPSC-derived IECs



## Results: characterization MUTZ-3 dendritic cells



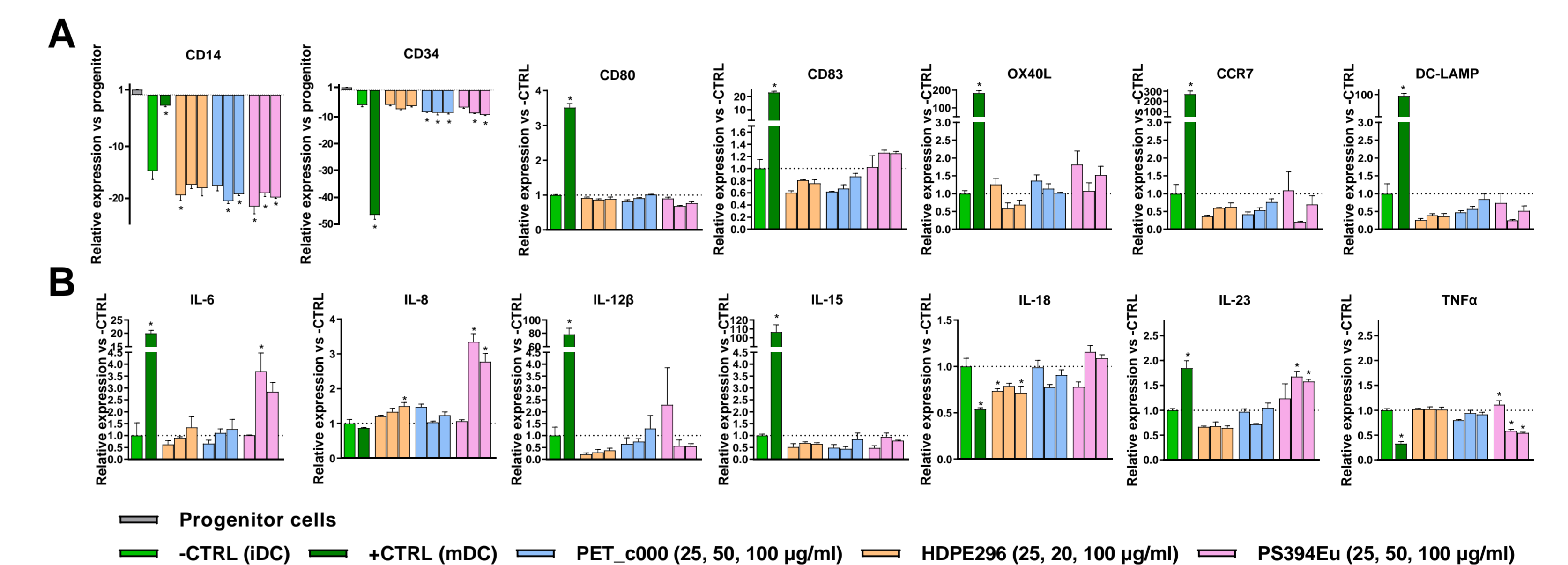
## Results: characterization co-culture model



## Results: exposure of iDCs to microplastics

**Table 1.** Physicochemical data of the micro/nanoplastics for the cell exposure experiment.

Abbreviation	Main polymer composition	Additives	Particle size distribution	Particle shape
HDPE269	High density polyethylene	No	X <sub>10;3</sub> 1.8 $\mu$ m / X <sub>50;3</sub> 4.9 $\mu$ m / X <sub>90;3</sub> 8.7 $\mu$ m	Round
PET_c000	Polyethylene terephthalate	No	X <sub>10;3</sub> 57 nm / X <sub>50;3</sub> 90 nm / X <sub>90;3</sub> 144 nm	Round
PS394Eu	Europium doped polystyrene	No	300 nm	Round



## Conclusions

- hiPSC-derived IEC layers consist of multiple cell types that are present in the intestine *in vivo*
- hiPSC-derived IEC layers have the capacity to induce pro-inflammatory responses when exposed to a pro-inflammatory stimulus
- MUTZ-3-derived DCs express (immature/mature) DC markers when differentiated
- Co-culture of separately differentiated IECs and DCs was successful using an inverted IEC culture technique
- 24h co-culture of IECs and DCs did not appear to negatively affect the differentiation status of the cells and significantly increased cytokine expression in both cell models
- 24h and 48h exposure of iDCs to micro/nanoplastics did not result in strong immunomodulatory effects of any of the materials tested

