NEWCELLS
IN VITRO MODELS TO PREDICT IN VIVO OUTCOMES

iPSC-derived Retinal Pigment Epithelium (RPE): functional cell model for accelerating retinal drug discovery

Superior quality iPSC-derived cells for better predictivity

What you can achieve:

- Generation of functional RPE cells to model healthy and diseased tissue
- Disease model development with isogenic controls
- Gene therapy vector assessment in vitro

What forms the basis of the study:

- Highly differentiated & polarized RPE cells grown on filter inserts
- Cells containing a functional barrier as confirmed by TEER data
- Pigmented RPE cells expressing tight junction proteins and markers for phagocytic function

How can Newcells help

We can accelerate your retinal therapy development with *in vitro* retina disease modelling and gene therapy assessment services on iPSC-derived RPE cells.

iPSC-derived RPE recapitulate the complexity of the retina epithelium

Rigurous production and validation protocols ensure the RPE model provides:

- Pure, highly differentiated, polarized & functional monolayer on Transwell inserts.
- Highly reproducible batches of RPE cells that form tight junctions **(figure 1B)** and TEER, recapitulating the in vivo physiology of the retinal epithelial barrier.
- Well-characterized in vitro model with high expression of RPE-specific markers such as TYRP1, PMEL17 and BEST1 **(figure 1B and 1C)** key proteins for function like phagocytosis of photoreceptor outer segments.
- Derived from the same healthy donor iPSCs as our retinal organoids which allows parallel or comparative assessment of both RPE and neurosensory retina using cells from the same genetic background.

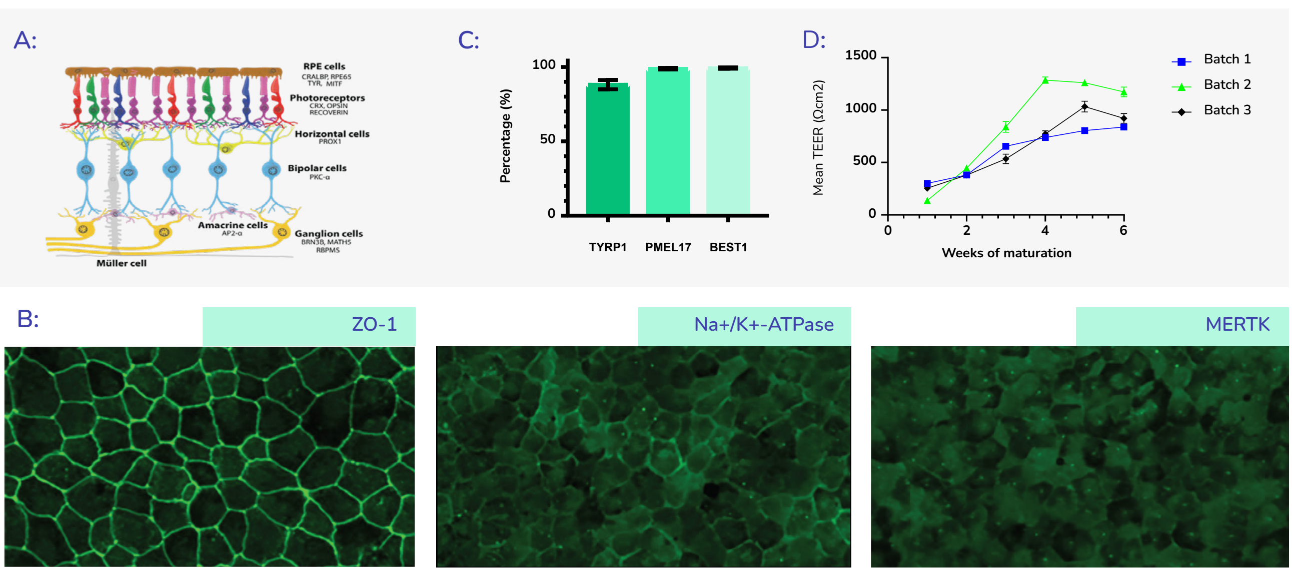

Figure 1: Functional and reproducible model. A) Retina cellular structure B) Fluorescence staining for ZO-1, NA+/K+-ATPase and MERK C) Flow cytometry quantification data for TYRP1, PMEL17 and BEST1 D) TEER profile for three batches of RPE measured over 6 weeks of culture.

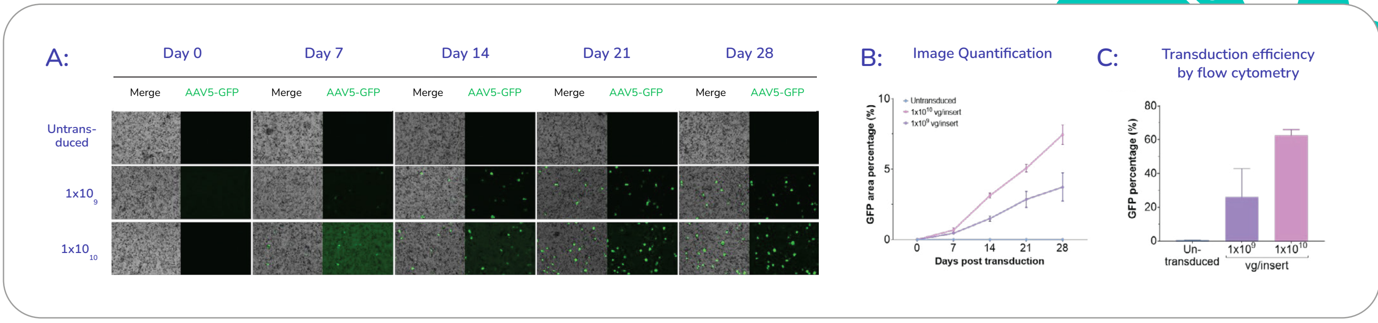

Figure 2: Gene therapy vector efficacy assessment. A) Brightfield and fluorescence imaging of iPSC-derived RPE cells transduced with AAV5-GFP B) Quantification of fluorescence staining plotted using line graph depicting increase in signal with time C) Staining quantification confirmed with flow cytometry.

Gene therapy assessment with iPSC-derived RPE

- This model has been shown to be robust for testing and optimising the transduction of RPE cells with novel gene therapy viral vectors **(figure 2)**.
- Studies include multiple readouts such as fluorescence imaging, image quantification and flow cytometry of transduced RPE cells for quantification of novel vectors' transduction efficiency.
- A rapid and reliable model for in vitro testing of novel gene therapy vectors.

Disease Modelling of inherited retinal diseases

The iPSC-derived RPE model allows to:

- Conserve the genetic aberrations from patient's cells and therefore, can be used to model inherited retinal diseases like AMD, Retinitis Pigmentosa and others.
- Derive RPE cells from iPSCs of patients with low-risk genotype without AMD (F018, F116) and high-risk genotype with advanced AMD (F180, F181).
- Replicate the physiological dysfunctionalities in vitro for quantitative assessment of the disease effects (e.g. ultrastructural changes in cell organelles **(figure 3** – Courtesy: Hallam et al 2017 Stem Cells**)**.
- Gain a deeper understanding of the pathology of the disease and evaluate the efficacy of novel therapeutics in vitro, prior to clinical trials.

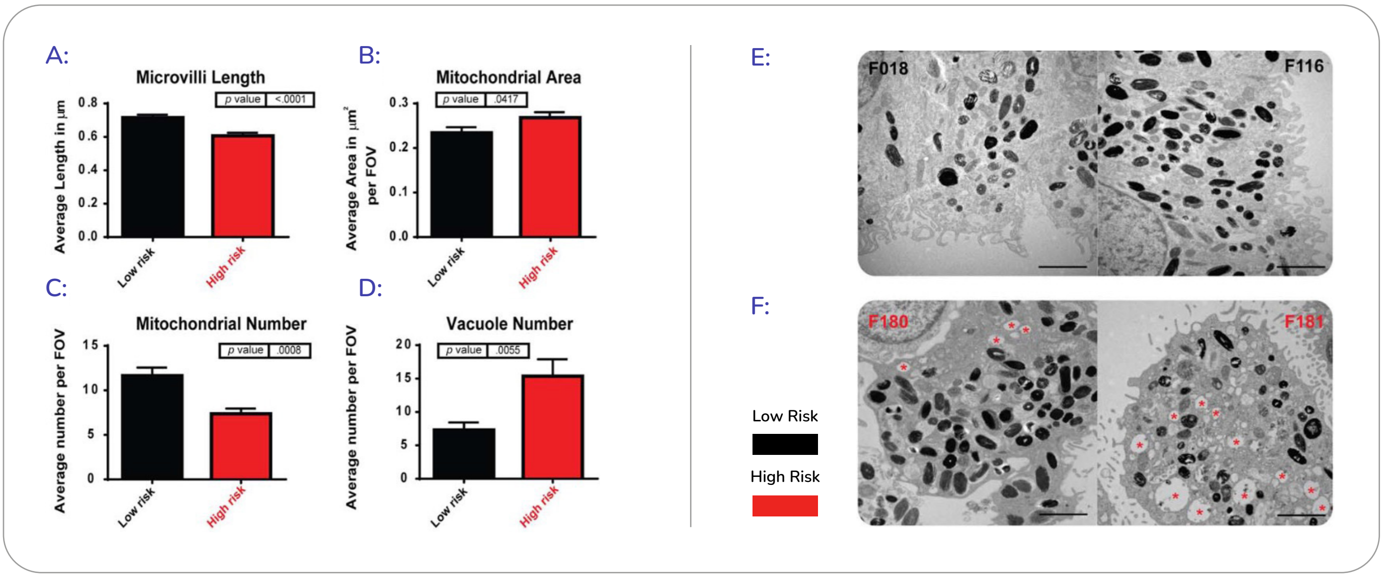

Figure 3: Disease modeling analysis. iPSC-derived RPE generated from high-risk Y402H AMD donors (F180 and F181) show ultrastructural changes when compared to low-risk Y402H donors (F018 and F116). (A): Microvilli length is decreased in high-risk donor RPE. (B): Mitochondrial area was increased in high-risk donor RPE. (C): Mitochondrial number was decreased in high-risk donor RPE. (D): The number of vacuole structures was greatly increased in high-risk donor RPE. (E): Examples of low-risk iPSC-RPE cells: left hand side, F018; right hand side, F116; (F): Examples of high-risk iPSC-RPE cells: left hand side, F180; right hand side, F181; red asterisk indicates vacuoles. Scale bar 52 mm.

Retina Pigment Epithelial Cell Model Offerings			
SKU No.	Offering	Format	Readouts
RSD0000RPE	RPE disease modelling	24-well Transwell	Brightfield imaging, Cell viability (ATP/LDH), Quantitative IF, Gene expression, Transmission (TEM) and Scanning (SEM) electron microscopy (optional), Phagocytosis of photoreceptor outer segment (optional)
RSG0000RPE	RPE gene therapy assessment		Transduction efficiency of viral vector, Cell viability assessment(ATP/LDH), Therapy efficacy using IF and Gene expression

For more information:

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www.newcellsbiotech.co.uk/RPE

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