Retinal Pigment Epithelial Sheet Transplantation for Geographic Atrophy
Financial Disclosure

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Unmet Clinical Need

Normal → Early AMD → Advanced AMD

**Dry (atrophic) AMD**
- 80-90%

**Wet (exudative) AMD**
- 10-20%

**Advanced AMD**
- Dysfunction of retinal pigmented epithelium (RPE)
- Degeneration of Bruch’s membrane
- Accumulation of drusen
- Progressive Loss of RPE and photoreceptors
- Loss of Vision

**Treatment Hypothesis:** Replace damaged RPE on synthetic Bruch’s membrane to prevent vision loss
Dramatic Visual Acuity Improvement after Autologous RPE Transplant

Courtesy Pete Coffey
In-vivo imaging–Human photoreceptor mosaic using Adaptive Optics

Courtesy Pete Coffey
CPCB-RPE1: hESC-RPE Synthetic Substrate Patch

CPCB-RPE1

RPE Cells

Parylene Substrate

H9 hESC-RPE

parylene C substrate

Photoreceptors

Microvilli

RPE cells

Parylene Membrane

Choroid capillaries

Nutrients in

Waste Out

Pete Coffey (UCL + Pfizer) – polyester as substrate
Design of Parylene Membrane Supports Nutrient Exchange and Mechanical Strength

- Thick parylene mesh (6µm) provides mechanical support
- Ultrathin parylene membrane (0.4µm) provides nutrition diffusion zone
Permeability of Parylene C

Parylene thinner than 0.50µm has similar flux and MW exclusion to both natural and previously reported artificial Bruch’s membranes.

MW exclusion limits of submicron parylene

Lu et al, Biomed Microdevices 2012
C. J. Lee et al., Biomaterials, 2006
J. T. Lu et al., Biomaterials, 2007
D. J. Moore et al., IOVS, 2001
CPCB-RPE1: hESC-RPE Synthetic Substrate Patch

**Parylene Membrane**
- Thick parylene mesh (6µm) provides mechanical support
- Ultrathin parylene membrane (0.4µm) provides nutrition diffusion zone

**RPE Cells**
- > 99% Pure
- Express RPE Genes and Carry Out Critical RPE Functions

CPCB-RPE1

[Image of parylene membrane, hESC-RPE cells, and CPCB-RPE1 patch]
CPCB-RPE1: Why Polarized RPE on a Membrane Instead of Suspension RPE cells

Advantage Over Competitors Using Suspension Cells

**Polarized RPE Cells**

- Are non-proliferative
- Do not migrate and remain at the site of implantation
- Show increased neurotrophic growth factor (PEDF) secretion from the apical surface
- Secrete VEGF specifically from the basal surface to promote choriocapillaris survival
- Can integrate with PR outer segments thus promoting efficient phagocytosis of ROS
- Are more resistant to stress
- Have apical and basal domains that promote appropriate transport function.

![PEDF](image1.png)

![Polarized RPE](image2.png)

![Non-Polarized RPE](image3.png)
Optokinetic Behavioral Testing

![Image of mouse in testing apparatus]

![Bar chart showing visual acuity comparison between Par only (n=5) and Par+cells (n=3) groups]
CPCB-RPE1 Cells Survive Post Transplant

**RCS rat retina with CPCB-RPE1**: good RPE survival along the implant

**RCS rat retina with hESC-RPE cell suspension**: Poor RPE Cell Survival

**TRA-1-85**

**RPE-65**

**DAPI**

Human RPE Cell Survival Observed for at Least 6 Mos.

**TRA-1-85**

**RPE-65**

Human RPE Cell Survival

60 days post implantation

TRA-1-85 and RPE-65 were not expressed in the cell clumps (arrow) found in rat’s subretinal space

**Traumatic Retinal Injury**
CPCB-RPE1 Phagocytoses Photoreceptor Outer Segments in the Host Retina

60 days after implantation

ONL

OS

Rho^+ OS

RPE

Phagosomes

Parylene substrate

Phagocytosis not observed in native RCS retina
Delivery of CPCB-RPE1

Delivery in the Yucatan Pig

Complete Pars Plana Vitrectomy
Substrate on the corneal surface

Folding with the tissue injector

Canula Used to Inflate Blister Between Retina and Choroid
Peripheral Retinotomy 1.5 mm

Subretinal implantation with the tissue injector

Blister Evacuated. Perfluorocarbon liquid and laser retinopexy. Air-Oil exchange
Surgical Video-Implantation in Enucleated Porcine Eye
CPCB-RPE1 Survives in the Yucatan Pig Subretinal Space

3 Months after Surgical Implantation

Infrared  FA  OCT
Thank you for your attention