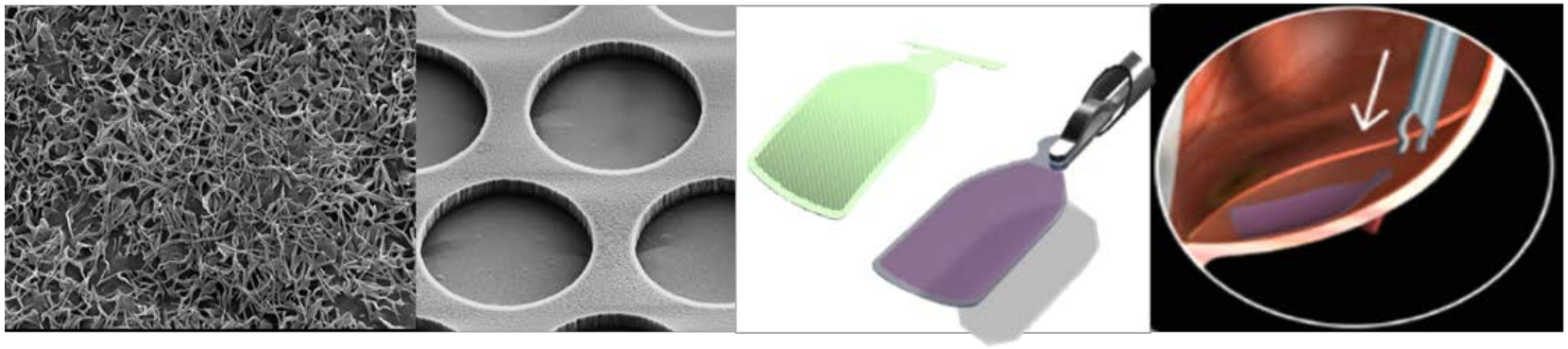
Regenerative Patch Technologies™

Development of a Bio-Engineered Implant for the Treatment of Age-Related Macular Degeneration



Regenerative Patch Technologies LLC

- Clinical Stage Company Formed to Advance Development of Technology from the California Project to Cure Blindness
- Lead Product Target Indication: Advanced Dry AMD
- >$15B Product Opportunity in US
- RPT has Raised $42M in Non-Dilutive CIRM Grant Funding to Fund Development Through IND and Phase 1/2a Clinical Trial
- RPT has Secured Equity Financing from Santen Pharmaceuticals through Santen Ventures
- Phase 1/2a Clinical Trial and One-Year Follow-Up Complete
- Preparing to Initiate Phase 2b Clinical Trial
- FDA Clearance and Agreement on Trial Design and Endpoints
- Issued and Pending World-Wide Patents Cover Product and Implantation Instrumentation

THE CALIFORNIA PROJECT to cure blindness

USC
- Mark Humayun MD PhD
- David Hinton MD

UCSB Macular Degeneration and Stem Cell Centers
- Dennis Clegg PhD
- Lincoln Johnson PhD

Caltech Biology and Chemistry
- Yu-Chong Tai

City of Hope Center for Biomedicine and Genetics GMP Facility
- Joseph Gold

The Dry Form of Age-Related Macular Degeneration: The Clinical Problem

Affects 1 in 8 People Over the Age of 60

- >10 Million with Dry AMD in US
- 196 Million Globally in 2020
- 1.7 Million with Advanced Dry AMD in US
- Incidence Increasing with Aging Population

Source: The Angiogenesis Foundation 2017, Fightingblindness.org

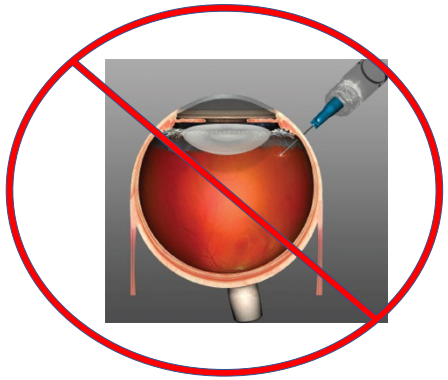
Leading Cause of Blindness in the Elderly

Normal Vision | Macular Degeneration

Leads to:

- Blindness
- Inability to Read, Drive or Recognize Faces
- Loss of Independence
- Increased Falls, Injuries
- Dependence on Caregivers

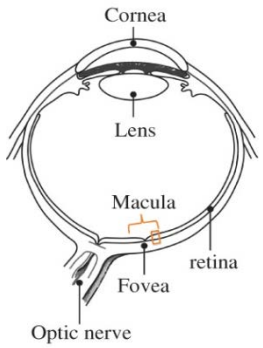
No Approved Therapies for Dry AMD

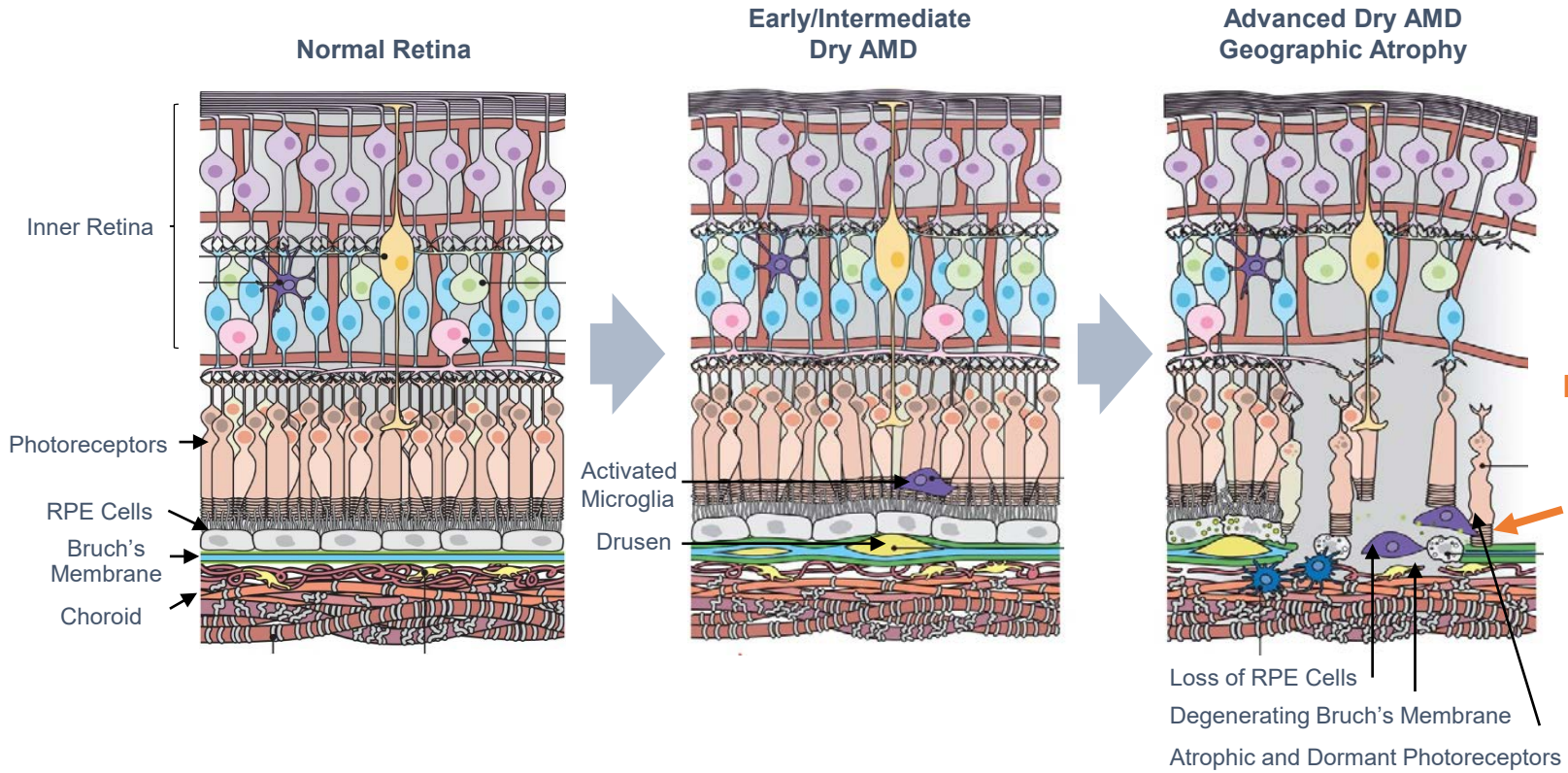


- Conventional Drugs/Biologics to Date Have Failed in the Clinic
- Current Drugs in Clinical Development Designed Only to Slow Progression of Disease

RPT's Implant Addresses the Disease Pathology in Geographic Atrophy, the Advanced form of Dry Age-Related Macular Degeneration

CPCB-RPE1: RPT's Lead Product



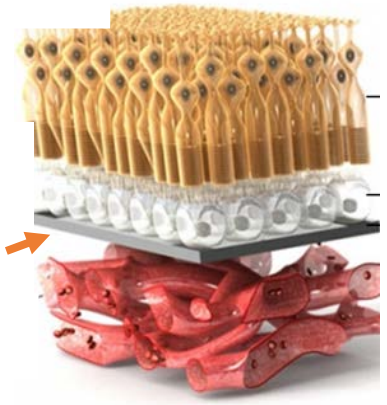


Progression of Dry AMD

Treatment:

Insert Implant of RPE Cells on a Synthetic Bruch's Membrane to Improve Vision or Prevent Vision Loss

Insert RPE Cells on a Synthetic Bruch's Membrane



Implant Provides Metabolic and Structural Support for Photoreceptors

van Lookeren Campagne et al., J Pathol 2014; 232: 151–164

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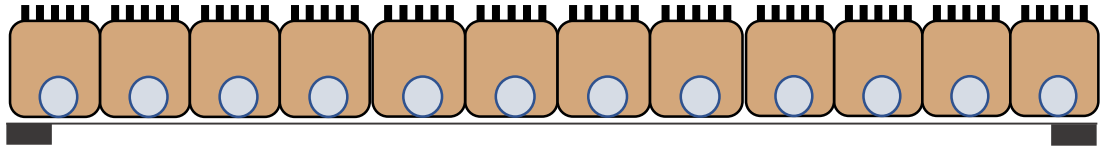
RPT's Lead Product: A Composite RPE Cell-Parylene Membrane Implant

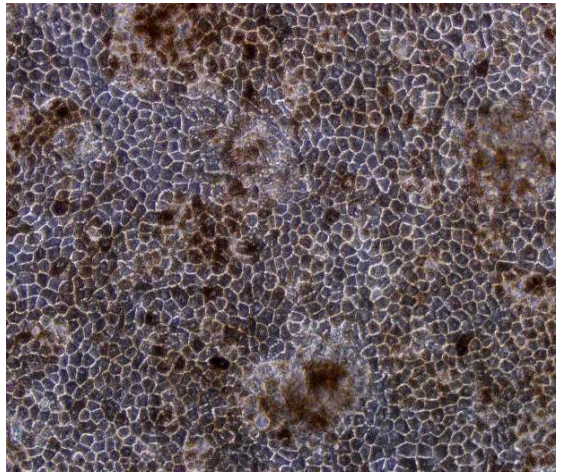
Implant Called CPCB-RPE1



Polarized Healthy RPE Cells:
Replace Dysfunctional RPE Layer in AMD Retina

Ultrathin Diffusible Parylene Membrane:
Replace Degenerating Bruch's Membrane

RPE Cells Produced from Pluripotent Stem Cells



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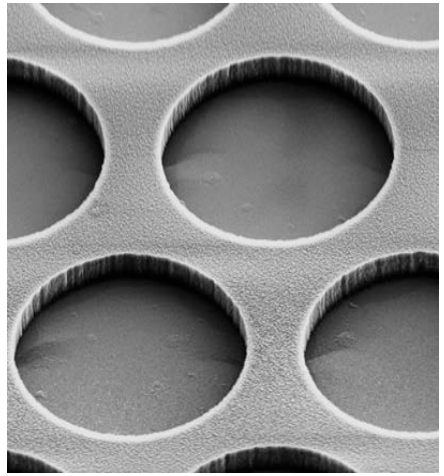
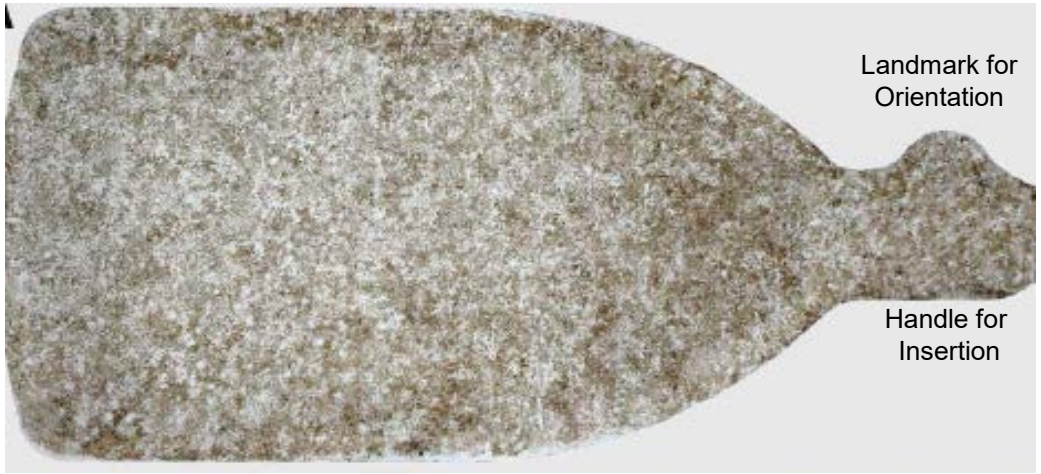
Ultrathin Parylene Membrane



CPCB-RPE1 Implant

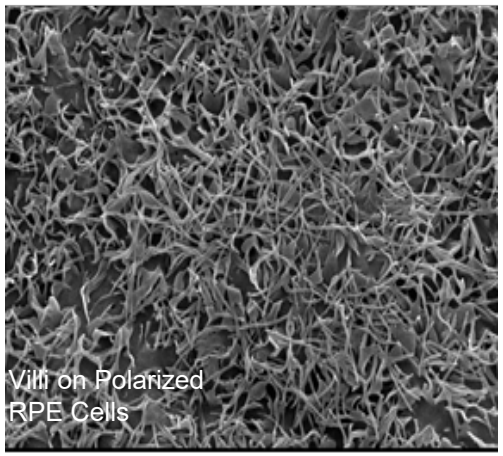


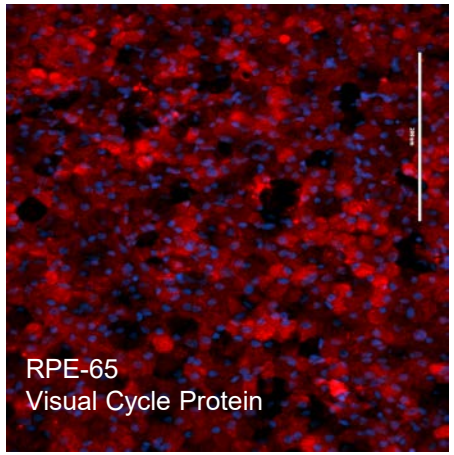
Implant Body

The CPCB-RPE1 Implant Has Two Key Components: RPE Cells and a Parylene Membrane

RPE Cells

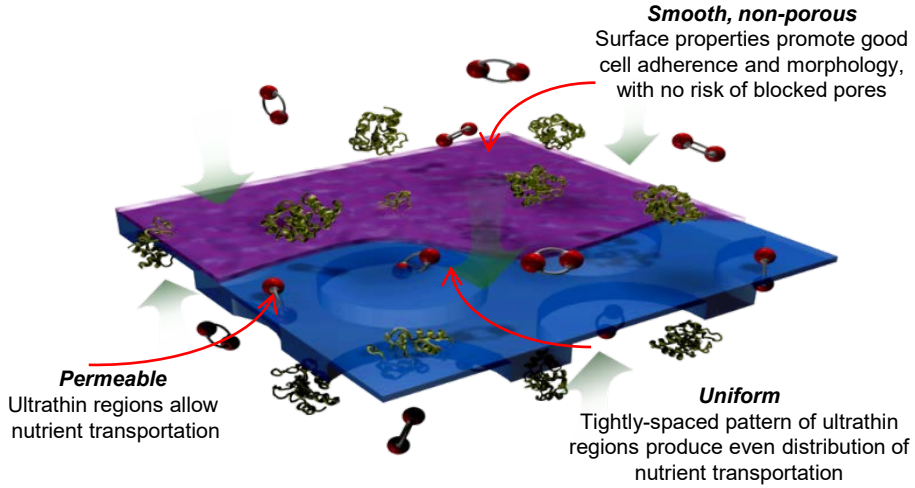
- Derived from Pluripotent Stem Cells
- Polarize to Have Functional Apical and Basal Surfaces as in Native RPE Cells in the Retina
- Execute Mature RPE Cell Function Including Visual Cycle Processing
- Integrate with Photoreceptors to Promote Metabolic and Growth Factor Support





Ultrathin Parylene Membrane

- Healthy Substrate for RPE Cells to Attach and Polarize
- Fabricated with USP Class VI Biocompatible Parylene Monomer
- Used >30 Years in Implantables
- Machined to Precise Thickness to Create Required Diffusion Properties Similar to Bruch's Membrane
- Provides Flat Surface Without Pores to Limit Cell Penetration
- Is Foldable to Reduce Retinotomy Size During Implantation



CPCB-RPE1 Implant: Critical Design Features: Target is Improvement in Visual Function

CPCB-RPE1 Product Designed to:

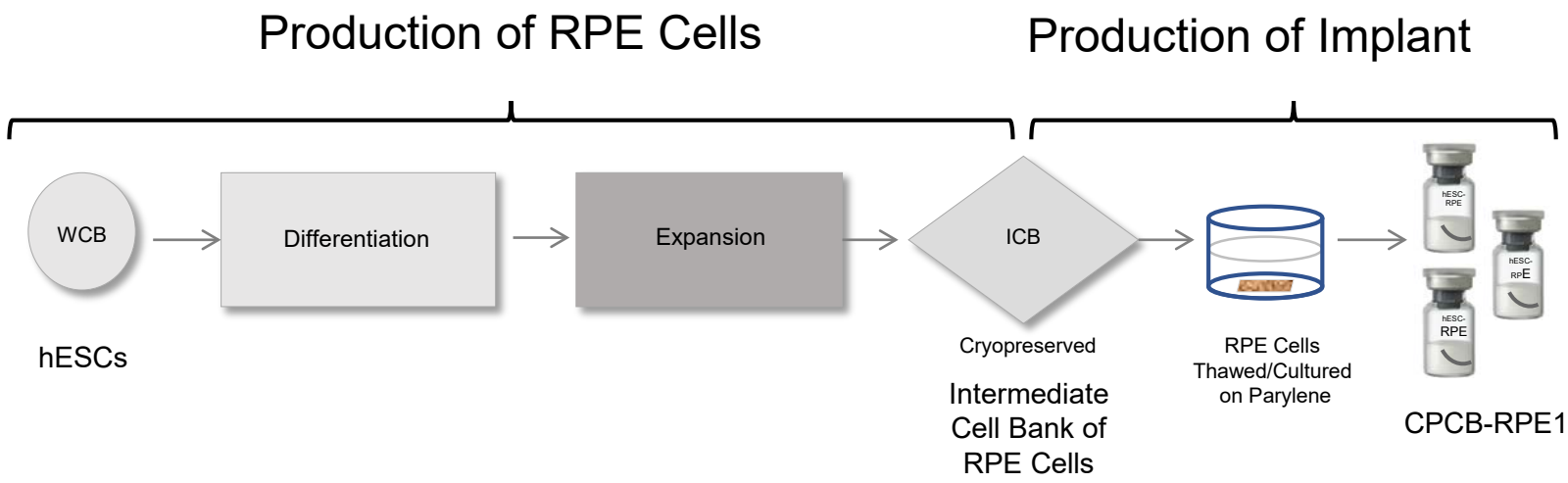
Serve as a Tissue Replacement Therapy to Support the Degenerating Retinal Function in Dry AMD Leading to Vision Improvement

Implications for Development Path

Improvement in Disease Outcome Enables:

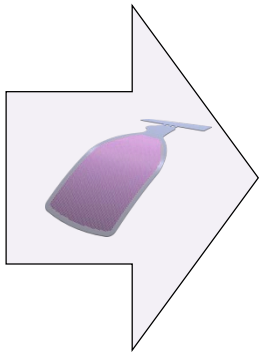
- Decreased Numbers of Patients in Clinical Trials
- Decreased Follow-Up of Patients to Determine Efficacy
- Shorter Development Timelines

CPCB-RPE1 is Produced by a cGMP Batch Manufacturing Process



- Cryopreserved Master, Working and Intermediate Cell Banks Produced, Released and Will Support Future Production
- No Animal Derived Reagents Used in Production
- cGMP Process Implemented Successfully for Phase 1/2a Clinical Trial at City of Hope
- Process Amenable to Automation
- Cryopreserved Formulation of Implant Now Available to Allow Global Distribution
- COGs Support Large Market Potential

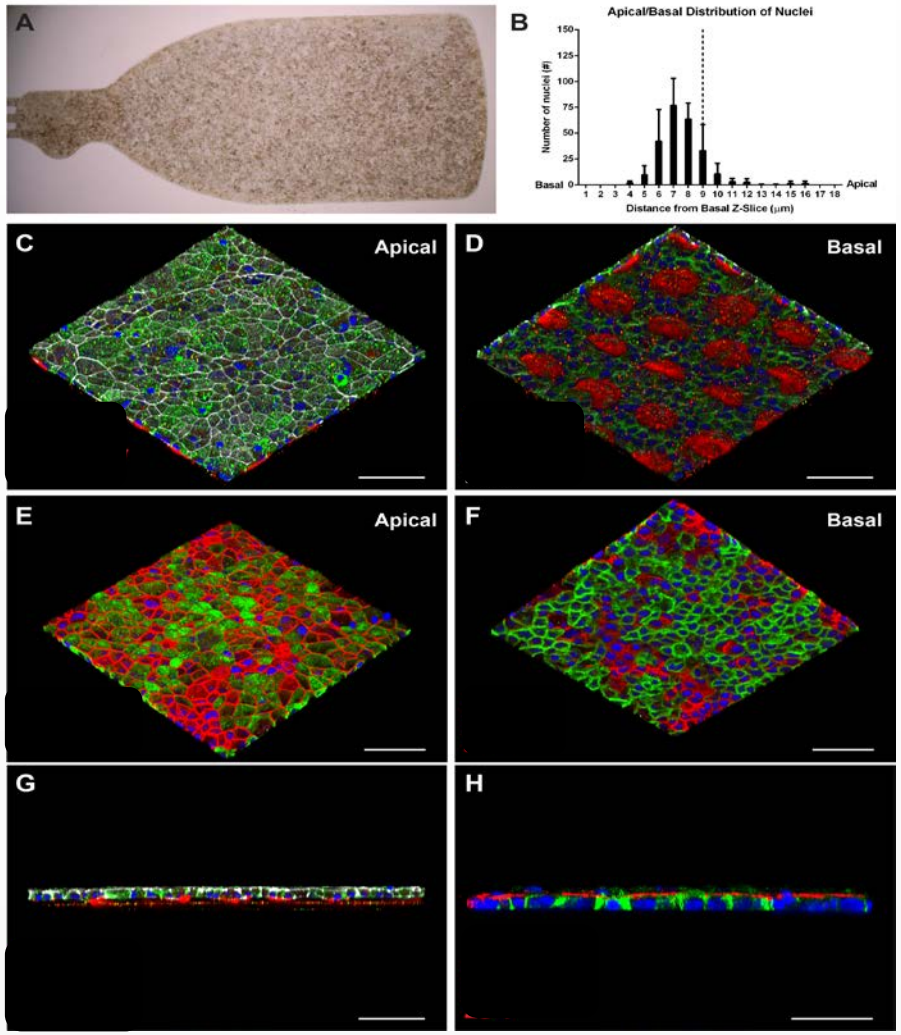
cGMP Manufacturing Facility



Outpatient Surgical Site for Implantation

Cryopreserved and Thawed CPCB-RPE1 Form Polarized Cells with Apical and Basal Structures

Confocal Imaging of Cryopreserved Showing CPCB-RPE1 RPE Cell Polarity Post-Thaw as Assessed for Apical and Basal Markers.



Apical Marker
Basal Marker

Apical Marker
Basal Marker

Apical Marker
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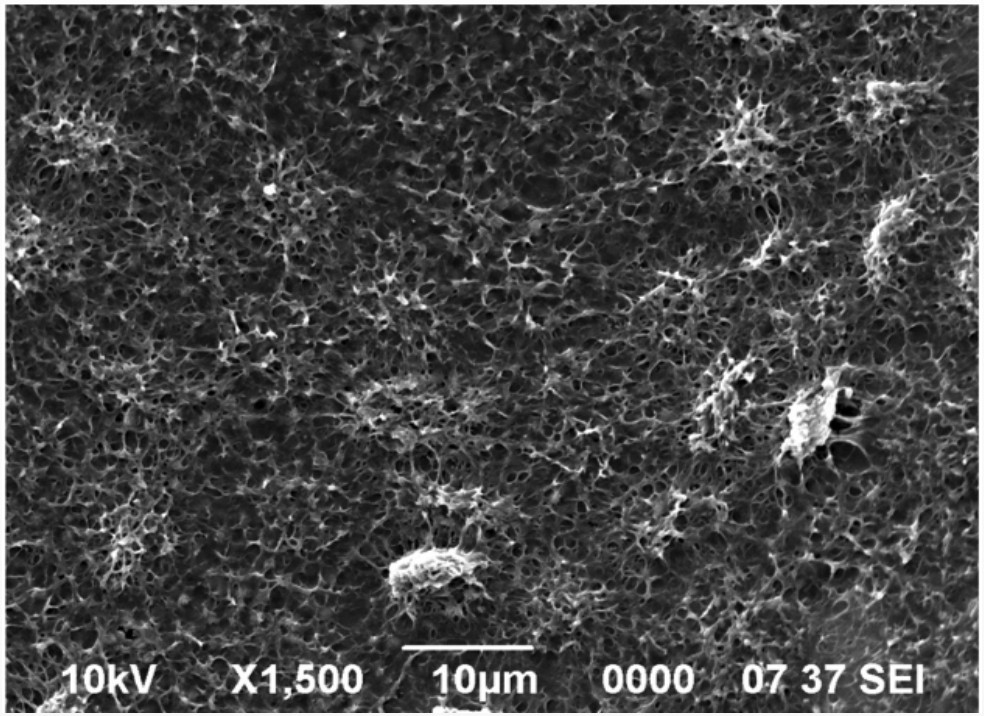
Basal Marker

Apical Villi Development



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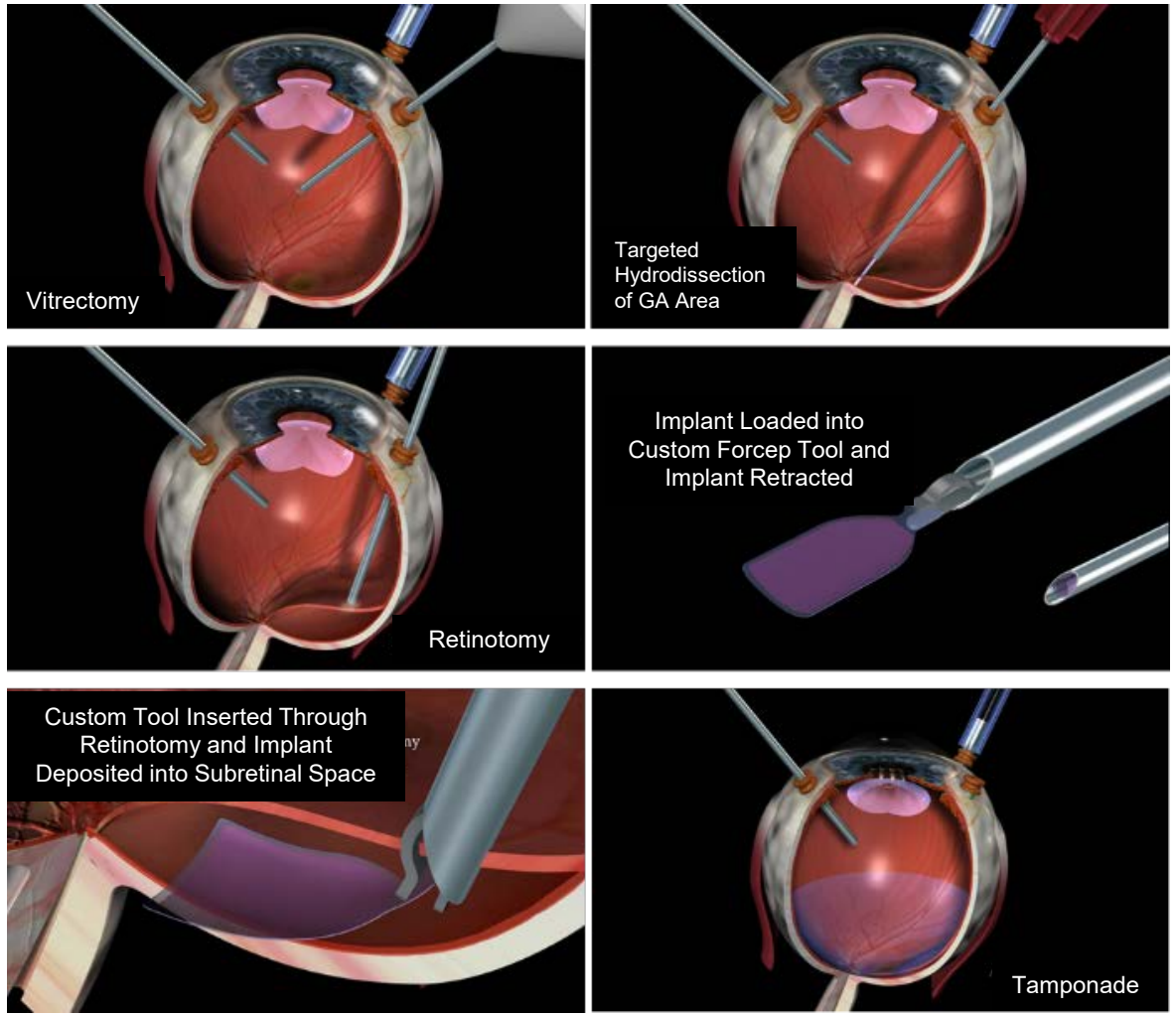
Implant Surgical Delivery:
Uses Well-Established Retinal Surgery Procedures



Custom surgical tool and ability to fold membrane enables delivery through 1.5mm Peripheral Retinotomy

- Uses Well-Established Retinal Surgery Procedures
- Administered as Outpatient Surgery

Regenerative Patch Technologies™

Phase 1/2a Clinical Trial Designed to Establish Safety and Potential Activity of the Implant in Patients with Advanced Disease

Study Design and Population	
Design	Single Arm Open Label Study
Indication	Advanced, Dry Age-Related Macular Degeneration with Significant Geographic Atrophy Involving the Central Fovea
Number of Subjects	16 Subjects
Visual Acuity of Treated Subjects	BCVA ≤20/200; Worst Eye Treated; All Treated Eyes Legally Blind
Dose	One Implant
Immunosuppression	68 Day Couse of Tacrolimus (Day -8 to Day 60)
Primary Endpoint	Test the Safety and Tolerability of CPCB-RPE1 at 1 Year Post Implantation
Secondary Endpoint	Assess Visual Acuity Retinal Function After CPCB-RPE1 Administration

USC Roski Eye Institute, Keck Medicine of USC — PI: Dr. Amir Kashani

Retina Vitreous Associates Medical Group — PI: Dr. Firas Rahhal

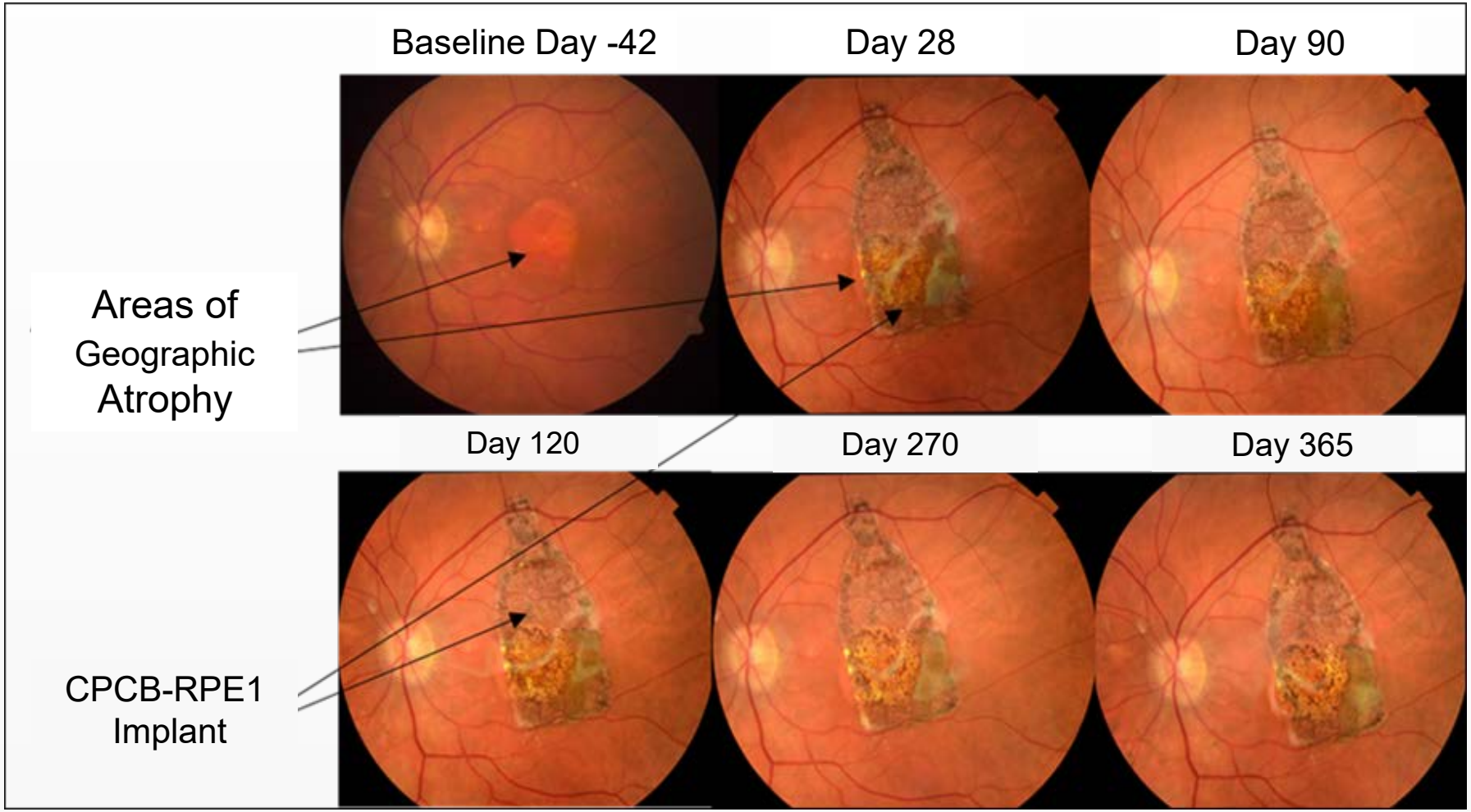
California Retina Consultants, Diseases & Surgery of the Retina, Macula, & Vitreous — PI: Dr. Robert Avery

PI: Dr. Pravin Dugel

RETINA Southern California Desert Retina Consultants — PI: Dr. Clement Chan

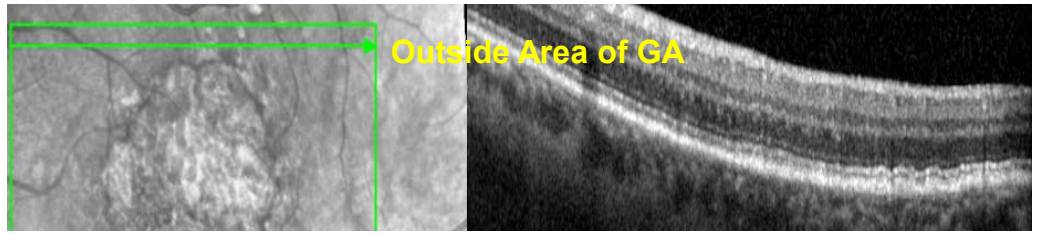
orange county retina — PI: Dr. Sanford Chen

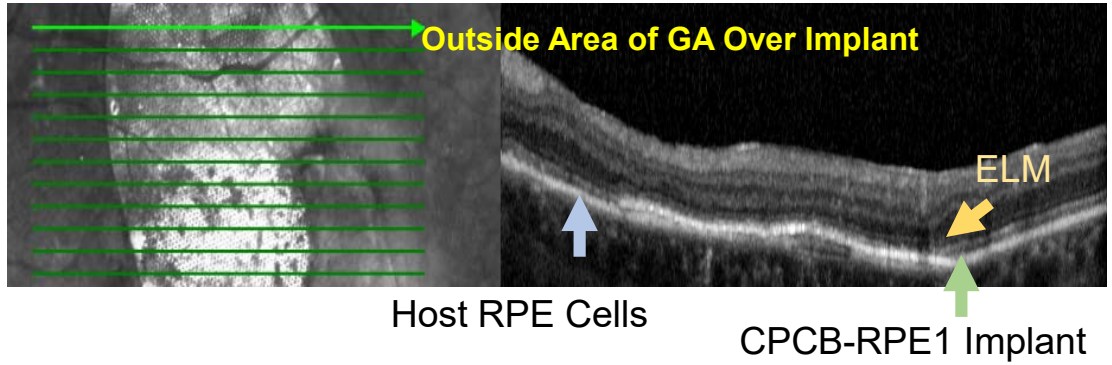
CPCB-RPE1 Implant Delivery Safe and Positioned Over Area of Geographic Atrophy



- Implant Stably Positioned Over Area of GA in All Subjects
- Stable Position of Implant Over Time
- No Evidence of Implant Degeneration
- No Clinical Evidence of Rejection of Allogeneic RPE Cells
- Delivery Procedures Use Techniques Practiced by Most Retinal Surgeons

CPCB-RPE1: Safety Through One Year of Follow-up





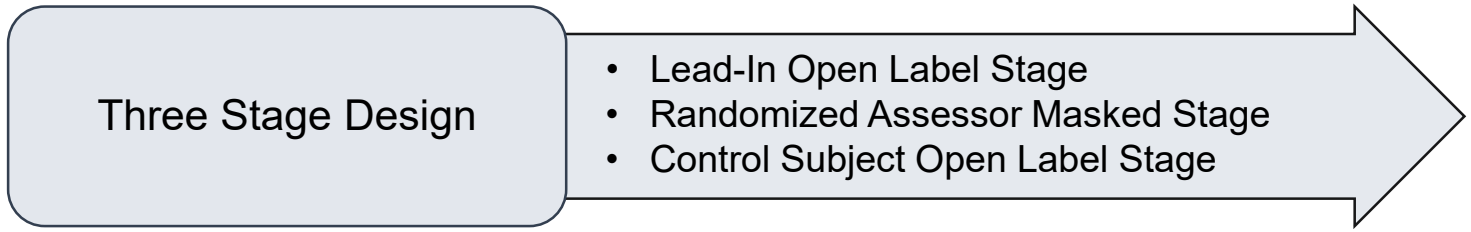
- No Unanticipated Serious Adverse Events Due to Surgery or Implant
- Ocular SAEs Related to Hemorrhage and Edema Confined to 3 of First 7 Subjects in study. No Ocular SAEs Reported in First Year of Follow-up in Subsequent 8 Subjects Due to Better Hemorrhage Prevention
- 68-day Tacrolimus Immunosuppression Regimen Well Tolerated in Most Subjects.
- No Evidence of Rejection of Allogeneic RPE Cells Even with Short Immunosuppression Course
- Good Preservation and Retinal Architecture Even When Implant Placed Over an Area with Intact Host RPE cells.

CPCB-RPE1: Efficacy Through One Year of Follow-up

EDTRS Reading Chart at 1 Meter for Severely Vision Impaired

- Reappearance of External Limiting Membrane Over the Implant in Some Patients
- Best Corrected Visual Activity Stable or Improved in 67% (10/15) of Subjects
- 27% (4/15) Subjects Showed >5 Letter Improvement in BCVA
- Improvements Range from 6-13 Letters
- BCVA Outcomes Superior to That of the Fellow Untreated Eye in Majority of Subjects
- Signals of Efficacy Important for Patients with Advanced Disease that are Legally Blind.

RPT is Preparing for a Phase 2b Clinical Trial: Trial Design



- All Subjects Followed for 12 months for Primary Outcome
- All Subjects Followed an Additional Year for Safety
- Endpoints Cleared by FDA as Registration Endpoints
- Pathway to BLA established

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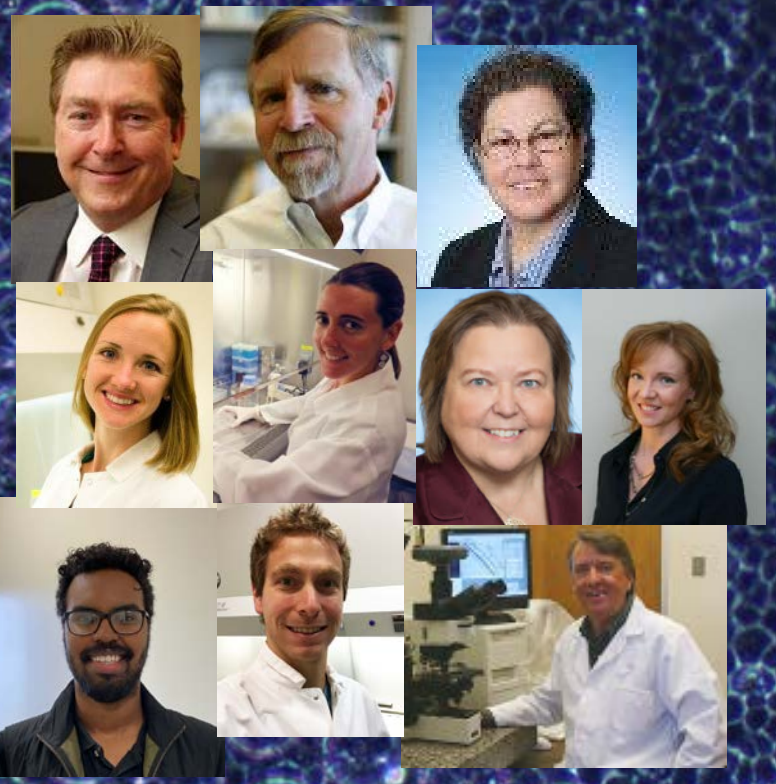

Summary

- Bioengineered Implant Developed as Tissue Replacement Therapy for Advanced Dry AMD
- Implant Produced Under cGMP to Support Clinical Development
- Cryopreserved Formulation Developed to Support Global Distribution
- Phase 1/2a Clinical Trial Shows Feasibility of Delivery with Promising Safety and Efficacy in Subjects With Advanced Geographic Atrophy
- Preparations Ongoing for Phase 2b Clinical Trial

Acknowledgements

Patients and Caregivers

CPCB-RPE1 Team

Mark Humayun, USC
David Hinton, USC
Dennis Clegg, UCSB
Biju Thomas, USC
DanHong Zhu, USC
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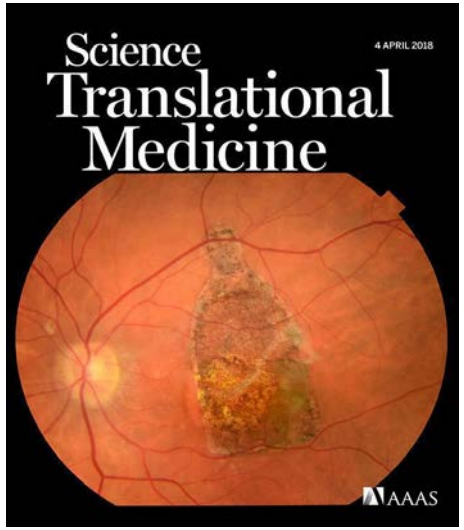
CIRM
CALIFORNIA'S STEM CELL AGENCY

Santen



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

RETINAL DISEASE

A bioengineered retinal pigment epithelial monolayer for advanced, dry age-related macular degeneration

Amir H. Kashani,[1]* Jane S. Lebkowski,[2] Firas M. Rahhal,[3] Robert L. Avery,[4] Hani Salehi-Had,[5] Wei Dang,[6] Chih-Min Lin,[6] Debbie Mitra,[1] Danhong Zhu,[7] Biju B. Thomas,[1] Sherry T. Hikita,[8] Britney O. Pennington,[8] Lincoln V. Johnson,[2,8] Dennis O. Clegg,[8] David R. Hinton,[1,7] Mark S. Humayun[1,9]*

Retinal pigment epithelium (RPE) dysfunction and loss are a hallmark of non-neovascular age-related macular degeneration (NNAMD). Without the RPE, a majority of overlying photoreceptors ultimately degenerate, leading to severe, progressive vision loss. Clinical and histological studies suggest that RPE replacement strategies may delay disease progression or restore vision. A prospective, interventional, U.S. Food and Drug Administration–cleared, phase 1/2a study is being conducted to assess the safety and efficacy of a composite subretinal implant in subjects with advanced NNAMD. The composite implant, termed the California Project to Cure Blindness–Retinal Pigment Epithelium 1 (CPCB-RPE1), consists of a polarized monolayer of human embryonic stem cell–derived RPE (hESC-RPE) on an ultrathin, synthetic parylene substrate designed to mimic Bruch's membrane. We report an interim analysis of the phase 1 cohort consisting of five subjects. Four of five subjects enrolled in the study successfully received the composite implant. In all implanted subjects, optical coherence tomography imaging showed changes consistent with hESC-RPE and host photoreceptor integration. None of the implanted eyes showed progression of vision loss, one eye improved by 17 letters and two eyes demonstrated improved fixation. The concurrent structural and functional findings suggest that CPCB-RPE1 may improve visual function, at least in the short term, in some patients with severe vision loss from advanced NNAMD.

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