Supplementary Material

HLA-matched allogeneic iPS cells-derived RPE transplantation for macular degeneration

Sugita S, et al. *Corresponding author: E-mail: retinalab@ml.riken.jp

Material and Methods

Inclusion and exclusion criteria in age-related macular degeneration (AMD) patients

Table S1 presents the inclusion and exclusion criteria. Briefly, patients with advanced wet AMD in whom anti-VEGF treatment was not effective were included, while patients with any other significant ophthalmologic disease or previous history of malignancy except carcinoma in situ during the last 3 years were excluded. Candidate patients were scored for the existence of subretinal and intraretinal fluid, location and size of the subretinal lesion, and dominant eye and age. After obtaining informed consent, five patients with a high score from two study sites were enrolled. All clinical procedures were performed based on the clinical study protocols. All patients underwent systemic examination including a thorough cancer screening before and at 12 months after the transplantation surgery. The test results of the systemic cancer screening were evaluated by an independent board that consisted of medical oncologists. In one of five patients (Case 4), gastric carcinoma in situ was detected and endoscopic resection was performed prior to the transplantation surgery. No malignancies were detected in the other four cases before the transplantation surgery, and none of the patients were found to have any malignancy at 12 months after the transplantation surgery. Patients were followed up with periodical examinations. In brief, regular ophthalmological examinations including best-corrected visual acuity (BCVA), intraocular pressure measurement with Goldmann tonometry, slit lamp examination, funduscopic examination and spectral-domain optical coherence tomography (SD-OCT) scans were done at every visit. Fluorescein angiography (FA) and indocyanine green angiography (IA), multifocal electroretinogram (ERG) using LE-4100 (Tomey, Nagoya, Japan), and microperimetry using MP-3 (Nidek, Gamagori, Japan) were carried out before surgery and at 3, 6 and 12 months after surgery. The National Eye Institute Visual Functioning Questionnaire 25 (VFQ-25) was administered before and at 1, 3, 6 and 12 months after surgery.

Genome and methylation analyses for iPS cells (iPSC) and RPE cells

We established iPSC from a HLA homozygote healthy donor. Genomic mutation analyses were performed with peripheral blood mononuclear cells of the donor (termed origin), one iPSC line (n=3), QHJI01s04, and two RPE samples that were both differentiated from QHJI01s04 cells. The number of genomic mutations and the sequencing statistics are summarized in Tables S2 and S5, respectively. Tables S3 and S4 show the details of the mutations. For the methylation analysis, we additionally used data from 56 samples for comparison, with 53 selected from normal tissues from GSE31848 (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE31848), two from human eye samples, and one RPE sample purchased from LONZA. The resultant methylation pattern is shown in Fig. 1. Table S6 shows the primers used in Amplicon sequencing to validate the SNVs found in the iPSC and RPE cells.

SNP-genotyping array
CNV analysis was performed using HumanOmnExpress-24 v1.1 (Illumina). We labeled and hybridized genomic DNA (200 ng) on a DNA Beads chip. We generated a final report and performed the cnvPartition CNV analysis (v3.2.0) using GenomeStudio (2011.1) (Illumina). The CNVs were determined using PennCNV [1] (1.0.3), Mosaic Alteration Detection-MAD [2] (1.0.1) and GWAS tools (1.16.1). After comparing the results between the origin and the samples, we were able to extract the CNVs from only the samples.

Whole genome and whole exome sequencing

Whole genome sequencing (WGS) libraries were generated using KAPA Hyper Prep Kit (Roche) or Nextera DNA (Illumina) from 200 ng and 50 ng of genomic DNA, respectively. Whole exome sequencing (WES) libraries were generated using Nimblegen SeqCap EZ Library v3 (Roche) from 1 µg of genomic DNA. Libraries were sequenced on HiSeq2500 (Illumina) using HiSeq SBS Kit v4. All experiments were performed according to the manufacturer’s instructions. After generating FASTQ files with Bcl2fastq (1.8.4), trimming adapter sequences with Trim Galore (0.4.1) and performing a quality filter with Qcleaner (3.1) (Amelieff) in the case of KAPA Hyper Prep Kit, sequencing reads were aligned to the human genome reference (hg19) including the decoy (hs37d5), the plasmid (pCE-hOCT4, pCE-mp53DD, pCE-hSK, pCE-hUL and pCXB-EBNA1) and PhiX sequences using Burrows-Wheeler Aligner (BWA-MEM, 0.7.10 r876) (http://bio-bwa.sourceforge.net/). The duplicate reads were removed using Novosort (1.03.01) (Novocraft Technologies).

Mutation calling and annotation

Mutation (SNV and insertion/deletion) calling on paired samples was performed using Genomon-exome (1.0.1) (http://genomon.hgc.jp/exome/) with Fisher’s exact test (P<0.001, strand ratio ≠0 or 1 variant allele frequency in the founder cells < 0.1) and Genomon (2.0.5) (https://github.com/Genomon-Project) with EB call (Fisher (P-value) >=1.0, EBCall (P-Value) >=4 for WGS, EBCall (P-Value) >=4 for WES, variantPairNum_tumor >=4, P-value (Fisher) realignment >=1.0, strand ratio ≠0 or 1). Mutations that satisfy the following conditions were considered: the ratio of sample alternative allele frequency and control alternative allele frequency >=5 and sample alternative allele frequency >= 0.05. Functional annotation was performed using ANNOVAR 2013 July 28 followed by annotation filters as follows: In the first step, we retained mutations on CDS and splicing regions and excluded synonymous SNVs. Secondly, we then excluded mutations listed in dbSNP 131, ESP 6500 (>0.01), 1000g2014oct (>0.01) and Human Genetic Variation Database (HGVD) (>0.01), if they were not listed in the Catalogue of Somatic Mutations in Cancer (COSMIC) version 74, Cancer Gene Census, Shibata’s list (http://www.pmda.go.jp/files/000152599.pdf#page=8) and the Human Gene Mutation Database (HGMD). The DNA copy number analysis with paired samples was performed using WGS data. CNVs were called using VarScan [3] 2.3.7 (log2_ratio < -0.415 or log2_ratio > 0.322 or Otsu’s threshold [4]) and Delly [5] 0.5.6. (SVLEN > 1500 and Filter == “PASS” and sample|FT == “PASS” and control|FT == “PASS”). Finally, we manually excluded suspicious CNV candidates.

Amplicon sequencing

We designed the primer using primer.py (Amelieff) or the Primer3Plus website (http://primer3plus.com/cgi-bin/dev/primer3plus.cgi) and Primer-BLAST website (https://www.ncbi.nlm.nih.gov/tools/primer-blast/). For the multiplex PCR reaction, we mixed 10 ng of genomic DNA, 200 mM of the primers in the Table S6 and KAPA HiFi HotStart ReadyMix (Roche) with 5% DMSO. The PCR condition was as follows: the initial denaturation was done at 95°C for 5 min, followed by 35 cycles of denaturation done at 98°C for 20 sec, annealing at 60°C for 15 sec, extension at 72°C for 30 sec and final extension at 72°C for 1 min. We purified the amplicon using the 1.8×Agencourt AMPure XP Beads (Beckman Coulter). Subsequently we then generated the sequencing library using KAPA Hyper Prep Kit for Illumina (Roche). The library was sequenced on MiSeq (Illumina) using MiSeq Reagents Kit v2 according to the manufacturer’s instructions. The sequencing reads were aligned to the reference genome used in WGS/WES with the alternative allele frequencies at the targets then calculated.
DNA methylation array

Bisulfite conversion of 500 ng genomic DNA was performed using EZ DNA Methylation Kit (Zymo Research). DNA methylation profiling of the bisulfite-converted DNA was performed using HumanMethylation450K BeadChip (Illumina) according to the manufacturer’s instructions. After exporting methylation data using GenomeStudio (2011.1) and normalizing beta values using BMIQ,[6] we averaged the beta values of 74 genomic blocks at the transcription start sites of cancer related genes as previously described [7], with visualization performed using R (https://www.R-project.org/).

Preparation of iPS-RPE cells and cell quality assessment

The differentiation of iPS cells into RPE cells has been previously described [8]. In the present study, we tested 4 iPS-RPE cell lines for the quality standard and assessment (Tables S8 and S9). The quality of the iPS-RPE cells (morphology, cell viability, RPE-related genes (RPE marker), RPE purity) was assessed according to the list of requirement standards used in our previous report [8] with minor modification. The contamination of undifferentiated cells (Lin28 positive) was evaluated by qRT-PCR. Endotoxin was checked according to protocols in the Japanese pharmacopoeia. The secretion of PEDF and VEGF by iPS-RPE cells was measured in culture supernatants using PEDF ELISA kit (BioVendor) and VEGF-A ELISA kit (eBioscience) [8]. The specific details have been described in our previous study [8].

Phagocytosis of shed photoreceptor rod outer segments

To confirm phagocytic function, iPS-RPE cells (QHJI01s04 line) were cultured with RPE medium in the presence of FITC-labeled porcine shed photoreceptor rod outer segments (ROS, 10 µg/cm²) for 8 hr at 37°C or 4°C as a control. Untreated RPE cells without ROS were also prepared as the control cells. After incubation with FITC-ROS, RPE cells were treated with 0.25% trypsin-EDTA, and phagocytosis was evaluated by microscopy. The specific details have been previously described [8].

Tumorigenicity test

Using immunodeficient mice, iPS-RPE cells (QHJI01s04 line) were tested for tumorigenicity. This test involved the subcutaneous injection of RPE cells with 200 µL Matrigel (BD Biosciences) in NOG mice (CLEA Japan, Inc.). We subcutaneously injected iPS-RPE cells (1 × 10⁶ cells) or HeLa cells (1 × 10⁶ cells, as a positive control) with Matrigel in NOG mice. If the mice survived and had no palpable tumors, they were sacrificed and used to measure the sizes of the transplants at 12 weeks (n=2), 24 weeks (n=1), 42 weeks (n=1), and lifelong (65 weeks, n=2). Matrigel without cells was injected as a negative control. When the size of the transplant was almost the same as that of the Matrigel only vehicle, the transplant was judged as negative for tumorigenic potential. The specific details have been described in our previous study [8].

PCR test for infectious pathogens

To examine infectious pathogens in RPE cell cultures, we performed PCR in the RPE cells. After collecting samples, DNA and RNA were extracted from RPE cells (QHJI01s04 line) (n=2). As per the details in previous reports,[9, 10] multiplex real-time PCR was conducted for the purpose of detecting the following pathogens: herpes simplex virus type 1 (HSV-1), type 2 (HSV-2), varicella-zoster virus (VZV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), human herpes viruses type 6 (HHV-6), type 7 (HHV-7), type 8 (HHV-8), parvovirus B19, BK virus (BKV), JC virus (JCV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus type
1 (HIV-1), type 2 (HIV-2), human T-lymphotrophic virus type 1 (HTLV-1), and type 2 (HTLV-2). PCR was performed with a LightCycler 480 II instrument (Roche, Basel, Switzerland). In addition, we also prepared positive and negative control cells for this PCR. The specific details have been described in our previous study [8].

Mycoplasma tests
In our clinical study of iPS-RPE transplantation, mycoplasma was checked according to the protocols presented in the Japanese pharmacopoeia (mycoplasma sterility tests) [8]. Moreover, in addition to the above tests, we also conducted a novel mycoplasma PCR test (Myco Finder, Nissui Pharmaceutical Co., Ltd.) using transplanted iPS-RPE cells on the day of surgery. As a result, this infection was checked twice in the present clinical study.

Expression of HLA molecules on iPS-RPE cells
To confirm the expression of Human Leukocyte Antigen (HLA) molecules on RPE cells, we examined the expression of HLA-class I (A, B, C) and class II (DR, DQ, DP) on transplanted iPS-RPE cells. Before the assay, RPE cells were prepared with IFN-γ pre-treatment (human recombinant IFN-γ 100 ng/mL, 48 hr). Information for the antibody and the methods have been previously described.[11] The samples were analyzed using FACSCanto™II or FACSARia™II flow cytometer (BD Biosciences, San Jose, CA). Data were analyzed using FlowJo software (version 9.3.1).

Area measurement of window defect lesions in fluorescein angiography images
Fluorescein angiography (FAG) was performed at the Kobe City Eye Hospital and Kobe City Medical Center General Hospital according to the schedule for this study. The Heidelberg Spectralis HRA (Spectralis; Heidelberg Engineering, Heidelberg, Germany) was used to record FAG images at the angle of 25°, which was aimed at the macular region. The images used for window defect evaluation were selected from those obtained at less than one minute after initiation of the imaging. The window defect area was evaluated using the images that are described below.

Evaluation of binarized window defect lesions in the FAG images
Binarization of the window defect lesion in the FAG images was performed using an Otsu method. Briefly, the FAG image was analyzed by the Fiji software (ImageJ version 1.52g, provided in the public domain by the National Institutes of Health, Bethesda, MD, USA; http://imagej.nih.gov/ij/). The selected image was converted to 8 bits. The background brightness of more than six regions were randomly selected by the Oval Selection Tool of the Fiji software sparing retinal veins in the vascular arcade area. The averaged brightness was set at the minimum value in order to minimize the noise in the FAG images. The threshold of each image was then adjusted using the Otsu method under a dark background, with the lesions representing retinal veins removed manually where possible. After the dark background setting was removed in order to convert the binarized image with a white background, the area was selected by the create selection setting from the edit tools so that the window defect area could be measured. This measurement was independently performed three times.
Evaluation of pigmentation in RPEs in the grafted area

A polarization-sensitive OCT (PS-OCT) has been employed in ophthalmic imaging as a way to measure the birefringence of fibrous tissues [12-14]. As polarization scrambling at the RPE via melanin granules has been observed [15, 16], this has been utilized for the segmentation of the RPE [17]. To specifically detect the melanin at the RPE layer in a subject in the present study, we used a clinical prototype of PS-OCT (Tomey Corporation, Nagoya, Aichi, Japan), which provided entropy of local Jones matrices as a measure of spatial randomness of the polarization property by Cloude-Pottier decomposition [18]. The light source was a frequency-swept laser (Axsun Technologies, MA, US) with a center wavelength of 1.05 µm, a wavelength range of 100 nm, and a wavelength scanning rate of 100 kHz. The interferometer of the PS-OCT was based on the depth-encoding method with a similar configuration previously demonstrated with the exception for the wavelength band [19]. The entropy is dimensionless and has a range from 0 (totally uniform) to 1 (totally random polarization property). A lateral range of 6 mm × 6 mm at the macular area was scanned with 1024 × 256 A-scans. Entropy was calculated with a kernel size of 11 (width) × 5 (depth) pixels, which corresponds to 64 µm (width) × 18.6 µm (depth) [18]. Bruch’s membrane line was marked on each B-scan image, and the signal below the line, which corresponds to the choroidal area, was excluded from the analysis. Assuming that only the melanin pigment of RPE caused the polarization scrambling in the inner retina of the subject, the highest entropy in the inner retina above the Bruch’s membrane was extracted for each A-scan and used to create the en face entropy map (Figure S6A), which reflected the melanin distribution of the RPE. The macular entropy was then calculated as a mean of the en face entropy map in a circular region centered at the fovea with a 3-mm diameter. Low entropy area was defined as a ratio of the area where the en face entropy is less than 0.2 to the total area in the same circular region (Figure S6B-D).
Fig. S1. Instrument for iPS-RPE transplantation surgery.

(A) The operator held the upper injector (WRRK-02; Icomes Lab) and placed the tip of the cannula (PolyTip® cannula 25g/38g; MedOne) into the subretinal space. The operator or assistant injected the RPE cell suspension by using the lower foot pedals. The operators were able to control injection speed and read the amount of fluid injected with the middle controller. (B) The cell suspension was loaded in the lower 0.2 mL syringe installed in the upper injector.
Fig. S2. Tumorigenicity tests for iPS-RPE cells.

Before transplantation, we used these iPS-RPE cells to test the tumorigenicity. Immunodeficient mice (NOG mice) were used to test the tumorigenic potential of the RPE cells. To assess the tumorigenicity of iPS-RPE cells (QHJI01s04 line), we conducted tests using subcutaneous transplantation of iPS-RPE cells \((1 \times 10^6)\) or HeLa cells \((1 \times 10^6)\) with 200 µL Matrigel. At 12 weeks, the size of the cell clumps from the iPS-RPE cells were small compared with positive control cells (HeLa cells), even when RPE cells were injected at 24, 42 or 65 weeks. No tumors were observed in these mice. HeLa cells developed a large mass by 12 weeks. \(D \times W \times H\) - Depth \times Width \times Height.
Fig. S3. Expression of HLA class I and class II on transplanted iPS-RPE cells by FACS analysis.

(A) iPS-RPE cells (QHJI01s04 line) constitutively expressed HLA class I (ABC), and RPE cells exposed to IFN-γ greatly expressed class I molecules. (B) Although the iPS-RPE cells did not express HLA class II (DR, DQ, DP), the RPE cells exposed to IFN-γ expressed class II molecules. During the cultures, P3-P6-day14 cultured cells highly expressed HLA class I and II under IFN-γ exposure. In contrast, P3-P6-day28 cells poorly expressed HLA class I and II. P3-day14 indicates 3 passages and a culture time for 14 days. MFI - mean fluorescence intensity.
Fig. S4. Color fundus and IA images of before and 1 year after RPE transplantation in Case 3, 4, and 5.

Fundus images of Case 3 (A), Case 4 (C), and Case 5 (E) before and 1 year after iPSC-RPE transplantation. Pigmented clumps or sheets were observed with some on the retinal surface 1 year after transplantation (white arrows) mostly outside the AMD lesion. In IA images (B, D, F), yellow arrows indicate the presence of polyp lesions before treatment, and polyp lesions at 1 year after transplantation are marked by red arrows. In Case 5, preoperative polyp lesion (yellow in F) caused a hemorrhagic change immediately before surgery (yellow arrowheads, color fundus image), which were stabilized without hemorrhages at 1 year after transplantation.
Fig. S5. Evaluation of epiretinal membrane (ERM) from a transplanted AMD patient, Case 2.

Panel A shows color fundus photographs for pretreatment, and at 4 or 6 months after surgery of the transplanted AMD patient (Case 2). The circles indicate the ERM on the macular area. Panel B shows the OCT images at pretreatment and at 6 months after surgery. We were able to see the diffuse retinal edema together with the ERM on the macular area in Case 2 at 28 weeks. Lower panel in OCT shows removal of the ERM at 31 weeks after transplantation with prompt resolution of the retinal edema. Panel C shows color photographs of the removed ERM that contained pigmented tissues. In addition, quantitative RT-PCR determined that the removed ERM tissues contained inflammatory cells. For the assay, we extracted RNA from the ERM tissue. Results showed that the ERM contained RPE markers such as PEDF and TGFβ2, as well as human primary RPE cells (PC: positive control) and cultured iPS-RPE cells, but not peripheral blood cells (NC: negative control: panel D). On the other hand, these tissues did not contain inflammatory cells such as CD3ε, Iba1, and IFN-γ like human primary RPE cells (NC: panel E), which suggests that immune rejection and inflammatory factors may not be relevant with regard to the outcome. Although RT-PCR showed that the removed ERM contained pigmented cells and was positive for RPE markers, the tissues did not contain any inflammatory cells/factors. This suggests that the ERM was of graft cell origin and that the immune rejection may not have been specifically relevant in the outcome.
Fig. S6. Evaluation of grafted iPS-RPE cells by polarization-sensitive OCT (PS-OCT).

(A) By drawing the border line at Bruch’s membrane, this made it possible to extract the highest entropy value from the upper retina-RPE area (green shaded area) thereby excluding the choroid area (left 2 panels). As a result, the en face image was then created from 256 serial sectional images (right panel). (B) The foveal center was determined for the en face image and the sectional images. This is indicated by the yellow cross on the en face projection image of the OCT intensity and the orange vertical line on the PS-OCT entropy image. The circular region centered at the fovea with a 3-mm diameter was used for the analysis. (C) Mean entropy of the circular region was plotted for 10 healthy volunteers (age 65.1±4.4 years) against age. (D) Mean entropy of the circular region increased over the measured periods of time after transplantation.
Fig. S7. The presence of transplanted cells did not affect the overlying photoreceptors.

In Case 1, there was a substantial amount of pigmented cells observed on the outside margin of the PCV lesion (see color photo in Fig. 3). There was also evidence of these cells in the auto-fluorescence images (white arrows). On the sectional view of the OCT images, the photoreceptor layer on the transplanted RPE cell was not affected and was present and stable at 1 year after transplantation. The vessel shadows correspond to the retinal vessels on each of the fundus images and are indicated by yellow arrows, while the bidirectional white arrows indicate the grafted area. The dotted arrow indicates the same area before transplantation.
Fig. S8. LGIR FACS results after surgery in the AMD patients, Cases 2, 3, 4 and 5.

Cases 2, 3, 4, and 5 did not exhibit any rejection signs in the eye.

1st graph, Case 2: As CD4⁺/Ki-67⁺ double-positive cells in PBMC were increased at 12 weeks, we performed sub-Tenon conjunctival injection of triamcinolone (STTA). After treatment, there was a dramatic decrease in the T cells. Subsequently, this patient received STTA therapy twice (at 16 and 28 weeks).

2nd graph, Case 3: There was no increase in the CD4⁺/Ki-67⁺ or CD11b⁺/Ki-67⁺ double-positive cells in PBMC during the yearlong follow-up. Therefore, we did not administer any anti-inflammatory medications including STTA for this patient.

3rd graph, Case 4: During the yearlong follow-up, LGIR tests were negative, and thus, this patient also did not undergo any further treatment as well.

4th graph, Case 5: Although CD11b⁺/Ki-67⁺ double-positive cells in PBMC temporarily increased at 24 weeks, we did not perform STTA therapy as this case had triamcinolone-related ocular inflammation after surgery (see Fig. S10). During the observation of the eye without treatment, CD11b⁺/Ki-67⁺ double-positive cells decreased at 28 weeks.
**Fig. S9. Sterile endophthalmitis after intravitreal triamcinolone in a transplanted AMD patient.**

Panel A shows slit lamp photographs at one day after surgery in the transplanted patient (Case 5). Severe anterior chamber cells (left panel) and anterior vitreous cells (right) are seen on the day after surgery. The fundus in the right eye was invisible. Panel B shows color fundus photograph at five days. Inflammatory vitreous opacity is observed in the eye. Panel C shows the FACS results before surgery in the AMD patient. We performed LGIR test using the patient’s blood cells, graft RPE cells, along with triamcinolone (TA) in vitro. For the test, CD4+Ki-67+ (proliferative helper T cells) and CD11b+Ki-67+ (proliferative monocytes) were evaluated using flow cytometry. As compared to PBMC plus RPE cells, the CD4+ T cells in PBMC that were exposed to transplanted iPS-RPE cells in the presence of TA were poorly proliferated. On the other hand, there was a great proliferation of the CD11b+ cells in PBMC. Numbers (%) in the histogram indicate double-positive cells (e.g., CD4+Ki-67+). Panel D shows the FACS results after surgery in the patient (Case 5). In the test, there was a great proliferation of both CD4+ and CD11b+ cells in PBMC. In addition, there was also an increase in the cytotoxic T cells, B cells, and NK cells (data not shown) after surgery. Panel E shows the FACS results for the patient, Case 1. For the LGIR test, there was a great decrease observed in both the CD4+ and CD11b+ cells in PBMC, which suggests that TA might be helping to treat this patient’s inflammation. In fact, STTA administration proved to be effective for RPE-related immune rejection for this patient. Therefore, we concluded that the changes in the Case patient were due to TA-related endophthalmitis after IVTA administration.
**Table S1. Inclusion and exclusion criteria in our clinical study.**

### Inclusion Criteria
- Exudative AMD in at least one eye
- Age 50 or over and 85 or under at the time of informed consent
- Subfoveal CNV, scar tissue, or RPE tear but without the need to remove CNV
- BCVA worse than 0.3* and equal to or better than hand motion (*Equivalent to 20/66 by Snellen chart)
- Insufficient effect of anti-VEGF treatments
- With or without fluorescein leakage from CNV by fluorescein angiography
- Able to understand and willing to sign the informed consent form
- Having the HLA haplotype A*24:02, B*52:01, C*12:02, DRB1*15:02, DQB1*06:01, DPB1*09:01

### Exclusion Criteria
- Presence of infectious eye disease
- Presence of retinal disease other than AMD
- Presence of optic nerve atrophy
- Presence of glaucoma with uncontrolled intraocular pressure
- Severe liver disorder (AST or ALT higher than 100 IU/L)
- Severe renal dysfunction requiring artificial dialysis
- Positive for HBV Ag, HCV Ag, HIV antibody, ATL antibody, or serological reaction of syphilis
- Allergic to penicillin, streptomycin, or bovine serum
- Receiving anticoagulation therapy that cannot be discontinued
- History of malignancy except for carcinoma in situ within the last 3 years
- Allergic to indocyanine green or fluorescein
- Pregnancy (including the possibility) or lactation
- Participation in other clinical trial within previous 1 month
- Other condition that limits patient compliance, patient safety, or alters study results

HBV Ag - hepatitis B antigen, HCV Ag - hepatitis C antigen, ATL- Adult T-cell lymphoma
Table S2. Number of SNVs and indels and CNVs found in iPSC and RPE cells derived from QHJI01s04.

| Assay                     | Control | Sample name          | No. of SNVs and indels | No. of CNVs* | Assay details       |
|---------------------------|---------|----------------------|------------------------|--------------|---------------------|
| Whole genome sequencing   | Origin  | RPE-QHJI01s04_P11_P3 | 9                      | 2            | NT                  |
|                           | Origin  | RPE-QHJI01s04_P12_P3 | 15                     | 7            | NT                  |
| Exome sequencing          | Origin  | RPE-QHJI01s04_P11_P3 | 8                      | 2            | NT                  |
|                           | Origin  | RPE-QHJI01s04_P12_P3 | 7                      | 1            | NT                  |
| Whole genome sequencing   | Origin  | QHJI01s04_No01_P12   | 7                      | 1            | NT                  |
|                           | Origin  | QHJI01s04_No35_P12   | 10                     | 4            | NT                  |
|                           | Origin  | QHJI01s04_No70_P12   | 7                      | 2            | NT                  |

*We performed whole genome sequencing and SNP array experiments. -: not found, NT: not tested.
Table S3. Annotation table of SNVs and indels in iPSC and RPE cells derived from QHJI01s04.

| Gene name | Genomon | Genomon2 | Genomon | Genomon2 | Genomon | Genomon2 | Genomon | Genomon2 | Genomon | Genomon2 | Genomon | Genomon2 |
|-----------|---------|----------|---------|----------|---------|----------|---------|----------|---------|----------|---------|----------|
| PTPN5     | x: found. | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| NPHS1     | x | x | x | x | x | x | x | x | x | x | x | x |
| FASTKD1   | x | x | x | x | x | x | x | x | x | x | x | x |
| EXOC2     | x | x | x | x | x | x | x | x | x | x | x | x |
| GDPD2     | x | x | x | x | x | x | x | x | x | x | x | x |
| C7orf72   | x | x | x | x | x | x | x | x | x | x | x | x |
| RPTN      | x | x | x | x | x | x | x | x | x | x | x | x |
| RP1L1     | x | x | x | x | x | x | x | x | x | x | x | x |
| ANKRD12   | x | x | x | x | x | x | x | x | x | x | x | x |
| MUC21     | x | x | x | x | x | x | x | x | x | x | x | x |
| OR2T33    | x | x | x | x | x | x | x | x | x | x | x | x |
| ZNF417    | x | x | x | x | x | x | x | x | x | x | x | x |
| MUC21     | x | x | x | x | x | x | x | x | x | x | x | x |
| ZC3HAV1   | x | x | x | x | x | x | x | x | x | x | x | x |
| MUC19     | x | x | x | x | x | x | x | x | x | x | x | x |
| FAM186A   | x | x | x | x | x | x | x | x | x | x | x | x |
| PLG       | x | x | x | x | x | x | x | x | x | x | x | x |
| ZNF76     | x | x | x | x | x | x | x | x | x | x | x | x |
| MUC4      | x | x | x | x | x | x | x | x | x | x | x | x |
| Gene name | Chr  | Start        | End          | Ref | Alt | Func.refGene | ExonicFunc.refGene                  | Amino_Change                  |
|-----------|------|--------------|--------------|-----|-----|--------------|-------------------------------------|------------------------------|
| PTPN5     | chr11| 18750552     | 18750552     | C   | T   | Exonic       | nonsynonymous SNV                   | p.E487K,p.E511K,p.E519K,p.E543K |
| NPHS1     | chr19| 36317454     | 36317454     | C   | T   | Exonic       | nonsynonymous SNV                   | p.D1230N                     |
| FASTKD1   | chr2 | 170394547    | 170394547    | G   | A   | Exonic       | nonsynonymous SNV                   | p.R684C                      |
| EXOC2     | chr6 | 633058       | 633058       | T   | C   | Exonic       | nonsynonymous SNV                   | p.I60V                       |
| GDPD2     | chrX | 69649509     | 69649509     | C   | T   | Exonic       | nonsynonymous SNV                   | p.T289I,p.T368I              |
| C7orf72   | chr7 | 50135885     | 50135885     | C   | -   | Exonic       | frameshift deletion                 | p.H68fs                      |
| RPTN      | chr1 | 152128232    | 152128232    | T   | C   | Exonic       | nonsynonymous SNV                   | p.N448S                      |
| RP1L1     | chr8 | 10465078     | 10465078     | A   | G   | Exonic       | nonsynonymous SNV                   | p.L2177S                     |
| ANKRD12   | chr18| 9256082      | 9256082      | T   | A   | Exonic       | nonsynonymous SNV                   | p.D916E,p.D939E              |
| MUC21     | chr6 | 30954806     | 30954806     | T   | C   | Exonic       | nonsynonymous SNV                   | p.V285A                      |
| OR2T33    | chr1 | 248436857    | 248436857    | C   | T   | Exonic       | nonsynonymous SNV                   | p.S87N                       |
| ZNF417    | chr19| 58421080     | 58421080     | G   | T   | Exonic       | nonsynonymous SNV                   | p.A189E,p.A188E              |
| MUC21     | chr6 | 30954909     | 30954909     | C   | G   | Exonic       | nonsynonymous SNV                   | p.D319E                      |
| ZC3HAV1   | chr7 | 138732476    | 138732476    | G   | A   | Exonic       | nonsynonymous SNV                   | p.T858M                      |
| MUC19     | chr12| 40879656     | 40879656     | G   | A   | Exonic       | unknown                             | UNKOWN                       |
| FAM186A   | chr12| 50746740     | 50746740     | G   | A   | Exonic       | nonsynonymous SNV                   | p.N1292T                     |
| PLG       | chr6 | 161139775    | 161139775    | G   | A   | Exonic       | stopgain SNV                        | p.W334X                      |
| ZNF76     | chr6 | 35258145     | 35258145     | G   | T   | Exonic       | nonsynonymous SNV                   | p.A179S                      |
| MUC4      | chr3 | 195512767    | 195512767    | T   | G   | Exonic       | nonsynonymous SNV                   | p.N1895T                     |
Table S3. continued

| Gene name | genomicSuperDups | Cancer_geCensus | Shibata list | cosmic74_position (occurrence) | hgmd2015.3 | snp131 | snp138 | esp6500si_all | 1000g2014oct_all | HGVDratio |
|-----------|------------------|-----------------|--------------|--------------------------------|-----------|--------|--------|---------------|-----------------|----------|
| PTPN5     | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| NPHS1     | -                | -               | 1            | -                              | -         | -      | -      | -             | -               | -        |
| FASTKD1   | -                | -               | -            | -                              | -         | rs369748449 | 0.000077 | -             | -               | -        |
| EXOC2     | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| GDPD2     | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| C7orf72   | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| RPTN      | -                | -               | 1            | -                              | -         | -      | -      | -             | -               | -        |
| RP1L1     | -                | -               | -            | -                              | -         | rs200878903 | -         | -             | -               | -        |
| ANKRD12   | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| MUC21     | -                | -               | 1            | -                              | rs9262370 | rs9262370 | -         | -             | -               | -        |
| OR2T33    | Score=0.931148   | -               | 9            | -                              | rs75662887 | rs75662887 | -         | -             | -               | -        |
| ZNF417    | Score=0.936519   | -               | 7            | -                              | rs3810130 | rs3810130 | -         | 0.0998403     | -               | -        |
| MUC21     | -                | -               | 5            | -                              | rs9262380 | rs9262380 | -         | -             | -               | -        |
| ZC3HAV1   | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| MUC19     | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| FAM186A   | -                | -               | 5            | -                              | -         | -      | -      | -             | -               | -        |
| PLG       | -                | -               | 1            | -                              | -         | -      | -      | -             | -               | -        |
| ZNF76     | -                | -               | -            | -                              | -         | -      | -      | -             | -               | -        |
| MUC4      | Score=0.920296   | -               | 12           | -                              | rs2641778 | rs2641778 | -         | -             | -               | -        |

*: not found.
### Table S4. Alternative allele frequencies of SNVs and indels of Origin, iPSC and RPE cells derived from QHJI01s04.

| Gene      | Whole genome sequencing | Exome sequencing |
|-----------|-------------------------|------------------|
|           | Origin | RPE-QHJI01s04_P11_P3 | RPE-QHJI01s04_P12_P3 | Origin | RPE-QHJI01s04_P11_P3 | RPE-QHJI01s04_P12_P3 |
|           | Total | Alt. allele freq. | Total | Alt. allele freq. | Total | Alt. allele freq. | Total | Alt. allele freq. | Total | Alt. allele freq. |
| PTPN5     | 79    | 0.0% | 63    | 36.5% | 63    | 44.4% | 81    | 3.7% | 53    | 43.4% | 33    | 60.6% |
| NPHS1     | 65    | 0.0% | 75    | 44.0% | 67    | 40.3% | 90    | 0.0% | 50    | 40.0% | 57    | 54.4% |
| FASTKD1   | 100   | 1.0% | 100   | 48.0% | 85    | 50.6% | 139   | 0.0% | 259   | 38.2% | 216   | 42.6% |
| EXOC2     | 76    | 0.0% | 127   | 55.9% | 93    | 48.4% | 136   | 0.0% | 105   | 48.6% | 81    | 55.6% |
| GDPD2     | 38    | 0.0% | 37    | 100.0% | 28    | 100.0% | 49    | 0.0% | 56    | 100.0% | 38    | 100.0% |
| C7orf72   | 94    | 0.0% | 94    | 38.3% | 105   | 46.7% | 115   | 0.0% | 189   | 47.6% | 125   | 36.8% |
| RPTN      | 75    | 1.3% | 95    | 20.0% | 79    | 22.8% | 477   | 2.3% | 309   | 1.0% | 269   | 1.9% |
| RP1L1     | 100   | 2.0% | 102   | 15.7% | 75    | 16.0% | 75    | 2.7% | 69    | 1.4% | 56    | 0.0% |
| ANKRD12   | 66    | 0.0% | 115   | 7.8%  | 110   | 0.0%  | 23    | 0.0% | 97    | 2.1% | 92    | 0.0% |
| MUC21     | 83    | 2.4% | 84    | 26.2% | 62    | 41.9% | 92    | 6.5% | 44    | 0.0% | 36    | 0.0% |
| OR2T33    | 77    | 6.5% | 91    | 36.3% | 73    | 45.2% | 303   | 17.2% | 243   | 10.3% | 195   | 17.9% |
| ZNF417    | 31    | 0.0% | 58    | 17.2% | 60    | 36.7% | 64    | 0.0% | 54    | 0.0% | 43    | 0.0% |
| MUC21     | 72    | 1.4% | 62    | 22.6% | 85    | 29.4% | 75    | 4.0% | 46    | 0.0% | 37    | 2.7% |
| ZC3HAV1   | 66    | 0.0% | 87    | 8.0%  | 82    | 11.0% | 117   | 0.0% | 197   | 9.6% | 145   | 11.0% |
| MUC19     | 70    | 1.4% | 93    | 10.8% | 91    | 15.4% | 4     | 0.0% | 0     | 0.0% | 0     | 0.0% |
| FAM186A   | 88    | 5.7% | 68    | 25.0% | 77    | 32.5% | 187   | 2.1% | 124   | 0.8% | 114   | 3.5% |
| PLG       | 78    | 0.0% | 94    | 5.3%  | 87    | 4.6%  | 73    | 0.0% | 136   | 12.5% | 110   | 12.7% |
| ZNF76     | 67    | 0.0% | 75    | 2.7%  | 70    | 5.7%  | 79    | 0.0% | 84    | 3.6% | 55    | 9.1% |
| MUC4      | 149   | 4.0% | 147   | 17.7% | 176   | 22.7% | 543   | 1.8% | 285   | 1.1% | 253   | 1.2% |
### Table S4. continued

| Gene   | Total | Alt. allele freq. | Total | Alt. allele freq. | Total | Alt. allele freq. | Total | Alt. allele freq. | Total | Alt. allele freq. | Total | Alt. allele freq. |
|--------|-------|------------------|-------|------------------|-------|------------------|-------|------------------|-------|------------------|-------|------------------|
|        |       |                  |       |                  |       |                  |       |                  |       |                  |       |                  |
| **Whole genome sequencing** |       |                  |       |                  |       |                  |       |                  |       |                  |       |                  |
| **Origin** |       |                  |       |                  |       |                  |       |                  |       |                  |       |                  |
| PTPN5  | 46    | 2.2%             | 40    | 60.0%            | 59    | 67.8%            | 53    | 60.4%            |       |                  |       |                  |
| NPHS1  | 55    | 0.0%             | 64    | 45.3%            | 60    | 50.0%            | 64    | 40.6%            |       |                  |       |                  |
| FASTKD1| 82    | 0.0%             | 100   | 49.0%            | 71    | 33.8%            | 81    | 51.9%            |       |                  |       |                  |
| EXOC2  | 75    | 0.0%             | 83    | 61.4%            | 63    | 44.4%            | 100   | 46.0%            |       |                  |       |                  |
| GDPD2  | 20    | 0.0%             | 27    | 100.0%           | 32    | 100.0%           | 46    | 97.8%            |       |                  |       |                  |
| C7orf72| 87    | 0.0%             | 86    | 46.5%            | 55    | 56.4%            | 72    | 52.8%            |       |                  |       |                  |
| RPTN   | 73    | 5.5%             | 80    | 18.8%            | 60    | 25.0%            | 85    | 9.4%             |       |                  |       |                  |
| RPI1L1 | 62    | 6.5%             | 78    | 12.8%            | 94    | 8.5%             | 96    | 11.5%            |       |                  |       |                  |
| ANKRD12| 124   | 0.0%             | 71    | 2.8%             | 65    | 3.1%             | 63    | 1.6%             |       |                  |       |                  |
| MUC21  | 48    | 6.3%             | 88    | 10.2%            | 89    | 21.3%            | 76    | 22.4%            |       |                  |       |                  |
| OR2T33 | 71    | 23.9%            | 63    | 27.0%            | 58    | 43.1%            | 65    | 29.2%            |       |                  |       |                  |
| ZNF417 | 39    | 10.3%            | 50    | 32.0%            | 58    | 27.6%            | 51    | 29.4%            |       |                  |       |                  |
| MUC21  | 36    | 0.0%             | 84    | 20.2%            | 70    | 35.7%            | 93    | 11.8%            |       |                  |       |                  |
| ZC3HAV1| 79    | 0.0%             | 73    | 6.8%             | 68    | 8.8%             | 91    | 5.5%             |       |                  |       |                  |
| MUC19  | 84    | 3.6%             | 80    | 8.8%             | 75    | 12.0%            | 81    | 8.6%             |       |                  |       |                  |
| FAM186A| 29    | 6.9%             | 80    | 18.8%            | 98    | 13.3%            | 104   | 13.5%            |       |                  |       |                  |
| PLG    | 100   | 0.0%             | 79    | 7.6%             | 64    | 9.4%             | 91    | 11.0%            |       |                  |       |                  |
| ZNF76  | 56    | 0.0%             | 56    | 21.4%            | 70    | 11.4%            | 57    | 12.3%            |       |                  |       |                  |
| MUC4   | 96    | 4.2%             | 137   | 10.9%            | 158   | 15.8%            | 142   | 8.5%             |       |                  |       |                  |
| **Amplicon Sequencing** |       |                  |       |                  |       |                  |       |                  |       |                  |       |                  |
| **Origin** |       |                  |       |                  |       |                  |       |                  |       |                  |       |                  |
|        |       |                  |       |                  |       |                  |       |                  |       |                  |       |                  |
| PTPN5  | 91891 | 1.7%             | 96516 | 52.1%            | 95007 | 49.5%            |       |                  |       |                  |       |                  |
| NPHS1  | 99839 | 0.5%             | 34727 | 48.5%            | 43004 | 49.8%            |       |                  |       |                  |       |                  |
| FASTKD1| 1351  | 0.4%             | 526   | 58.2%            | 559   | 55.1%            |       |                  |       |                  |       |                  |
| EXOC2  | 63838 | 0.1%             | 9206  | 49.7%            | 12779 | 49.1%            |       |                  |       |                  |       |                  |
| GDPD2  | 24375 | 3.8%             | 6633  | 98.9%            | 7560  | 99.1%            |       |                  |       |                  |       |                  |
| C7orf72| 589   | 1.4%             | 37    | 70.3%            | 41    | 51.2%            |       |                  |       |                  |       |                  |
| RPTN   | 14654 | 37.4%            | 67607 | 49.8%            | 64583 | 49.8%            |       |                  |       |                  |       |                  |
| RPI1L1 | not tested |                      | not tested |                      | not tested |                      | not tested |                      | not tested |                      | not tested |                      |
| ANKRD12| 9712  | 0.0%             | 2588  | 0.2%             | 2993  | 0.2%             |       |                  |       |                  |       |                  |
| MUC21  | 11428 | 22.0%            | 36302 | 17.6%            | 30867 | 17.6%            |       |                  |       |                  |       |                  |
| OR2T33 | 38926 | 39.8%            | 98396 | 36.2%            | 69008 | 36.4%            |       |                  |       |                  |       |                  |
| ZNF417 | 3926  | 39.8%            | 98396 | 36.2%            | 69008 | 36.4%            |       |                  |       |                  |       |                  |
| MUC21  | 18710 | 19.1%            | 53222 | 16.1%            | 45292 | 16.5%            |       |                  |       |                  |       |                  |
| ZC3HAV1| 115807| 0.1%             | 24354 | 9.0%             | 31511 | 8.3%             |       |                  |       |                  |       |                  |
| MUC19  | 119315| 0.1%             | 33410 | 5.2%             | 40150 | 6.9%             |       |                  |       |                  |       |                  |
| FAM186A| 1577  | 0.1%             | 5948  | 4.8%             | 6915  | 8.0%             |       |                  |       |                  |       |                  |
| PLG    | not tested |                      | not tested |                      | not tested |                      | not tested |                      | not tested |                      | not tested |                      |
| ZNF76  | 119315| 0.1%             | 33410 | 5.2%             | 40150 | 6.9%             |       |                  |       |                  |       |                  |
| MUC4   | 22544 | 0.0%             | 5948  | 4.8%             | 6915  | 8.0%             |       |                  |       |                  |       |                  |
Table S5. Sequencing statistics of whole genome sequencing and exome sequencing.

| Sample Name | Library prep kit | Sequence length | Sequencing coverage | No. of sequencing reads | No. of mapped reads |Mapped rate (%) |
|-------------|------------------|-----------------|---------------------|------------------------|-------------------|----------------|
| Whole genome sequencing | KAPA Hyper Prep (PCR Free) | 126bp, PE | 126bp, PE | 126bp, PE | 70.52 | 2239.5M | 2089.7M | 93.3 |
| Whole genome sequencing | Nimblegen SeqCap EZ Library SR v3.0 | 126bp, PE | 126bp, PE | 126bp, PE | 82.75 | 2326.8M | 2207M | 94.9 |
| Whole genome sequencing | Nextera DNA | 126bp, PE | 126bp, PE | 126bp, PE | 79.62 | 2241.4M | 2125.3M | 94.8 |

| Sample Name | Library prep kit | Sequence length | Sequencing coverage | No. of sequencing reads | No. of mapped reads |Mapped rate (%) |
|-------------|------------------|-----------------|---------------------|------------------------|-------------------|----------------|
| Exome sequencing | Nimblegen SeqCap EZ Library SR v3.0 | 126bp, PE | 126bp, PE | 126bp, PE | 98.46 | 89.4M | 86.5M | 96.8 |
| Exome sequencing | Nimblegen SeqCap EZ Library SR v3.0 | 126bp, PE | 126bp, PE | 126bp, PE | 106.92 | 104M | 100M | 96.2 |
| Exome sequencing | Nimblegen SeqCap EZ Library SR v3.0 | 126bp, PE | 126bp, PE | 126bp, PE | 87.08 | 86M | 83.9M | 97.6 |

M: million
Table S6. Primers used in Amplicon sequencing to validate SNVs found in iPSC and RPE cells.

| Gene name | Forward Primer       | Reverse Primer       |
|-----------|----------------------|----------------------|
| PTPN5     | CCCAGAGAACCTTGAGAGAA | GATGCTACTCAATGGCTTTGG |
| NPHS1     | ATGAGAGAGACAGTGAGTGA | GGCGCTGAGACACATATCGAG |
| FASTKD1   | GGAAGGCTCGTGCTGATTTAA | ATCTCGATCTGAAGTGCAAG |
| EXOC2     | AAGAGACTGTGGAGGTTCTCTG | TGTGGACATAATGCTGAC |
| GDPD2     | GTGAGGCGTTACCAGAAAAG | GCAGCCTGAAATCATCCTTC |
| C7orf72   | GAGAACAGACATAACTGCGG | CCAGGACTTAAACCCTGAA |
| RPTN      | TCTGACCATAGTGAGGAATTTT | GTCAACAAAAAGAAGGTCAG |
| ANKRD12   | CCTGAAAAAGAGACATCTAGC | CCTTTTATCTAGCTTCTTTC |
| MUC21     | GAGTCCAGAAGCACCTGCAATG | TTGTGCTGAGTCAGAGGG |
| OR2T33    | TATGGGGACCTACAGGTAAACC | TACTGTCTGCTGACCACTTTC |
| MUC21     | GAGTCCAGAAGCACCTGCAATG | TTGTGCTGAGTCAGAGGG |
| ZC3HAV1   | GAGGGATTCCATCTGTGATACCAC | CGTCGTTATTTGTTAGCCCAAG |
| FAM186A   | GTGAGAGTGATCTCTGAGCTCTG | GATCAGTCTACACCTTTCAGG |
| PLG       | GTAACGGTTGTCTTCAAGCGTG | TAAGGTCTCCATACCTTTGCTTAC |
| ZNF76     | AGATTCCCCCTGTAATGGAAAGGG | GTACGCTTATCTTCCCTCAG |

RPE cells were derived from a QHJ01s04 donor.
| Sample name | Target | Ct value                  |
|-------------|--------|--------------------------|
|             |        | P11 | P12 | P13 | P14 |
| QHJI01s04   | KLF4   | N/D | N/D | N/D | N/D |
|             | MYCL1  | N/D | N/D | N/D | N/D |
|             | Trp53  | N/D | N/D | N/D | N/D |
| LIN28A      | 43.986 | 40.913 | N/D | N/D |
|             | SOX2   | N/D | N/D | N/D | N/D |
| OCT3/4      | N/D   | N/D | N/D | N/D |
| EBNA1       | N/D   | N/D | N/D | N/D |
| WPRE        | N/D   | N/D | N/D | N/D |

P; passage, N/D; not detected
Table S8. Results of quality control tests in iPS-RPE cells.

| No. | Clone | Morphology | Cell Viability (%) (n=3) | RPE Purity-1 (%) | RPE Purity-2 (%) | iPS cells Marker | Infectious Pathogens | Mycoplasma | Sterility Test (EU/mL) | Endotoxin | HLA Haplotype |
|-----|-------|------------|--------------------------|------------------|-----------------|------------------|---------------------|-------------|----------------------|-----------|--------------|
| 1   | QHJI01s0 1-RPE-01 | Passed | 91.0 | Positive | 99.6 | 0.140 | Negative | Negative | Negative | Negative | 0.52 | Same as iPS cells |
| 2   | QHJI01s0 1-RPE-02 | Passed | 87.9 | Positive | 99.1 | 0.144 | Negative | Negative | Negative | Negative | 0.40 | Same as iPS cells |
| 3   | QHJI01s0 4-RPE-01 | Passed | 93.4 | Positive | 99.6 | 0.187 | Negative | Negative | Negative | Negative | 0.39 | Same as iPS cells |
| 4   | QHJI01s0 4-RPE-02 | Passed | 90.1 | Positive | 100 | 0.116 | Negative | Negative | Negative | Negative | 0.35 | Same as iPS cells |

We tested 4 iPS-RPE cell lines for the quality standard and assessment. All cells passed the tests, and thus, we finally picked QHJI01s04-RPE-01 cells for the transplantation. In addition, in vivo tumorigenicity tests were all negative in these 4 lines (see Fig. S3). Specific details for each of the tests are described in our previous report.[8]
Table S9. Results of quality control tests in iPS-RPE cells on transplantation day.

| Case | Transplanted Cells          | Transplantation Day | Cell Viability (%) | Cell Density | Infectious Pathogens | Mycoplasma | Sterility Test | Endotoxin (EU/mL) |
|------|-----------------------------|---------------------|-------------------|--------------|---------------------|------------|---------------|-------------------|
|      |                             | Cell Culture Day    | SV: >70%          | SV: 2 x 10⁶ - 1 x 10⁷ | SV: Not detected | SV: Not detected | SV: Not detected | SV: <3 EU/mL      |
| 1    | QHJI01s01-RPE-01-13, 14     | 3/28/2017           | 91.0              | 5.2 x 10⁶    | Negative            | Negative   | Negative       | 0.41              |
|      |                             | 3/14/2017           |                   |              |                     |            |               |                   |
| 2    | QHJI01s01-RPE-01-15, 16, 17 | 6/27/2017           | 91.1              | 4.2 x 10⁶    | Negative            | Negative   | Negative       | 0.32              |
|      |                             | 6/13/2017           |                   |              |                     |            |               |                   |
| 3    | QHJI01s01-RPE-01-18, 19, 20 | 7/25/2017           | 98.2              | 4.82 x 10⁶   | Negative            | Negative   | Negative       | 0.40              |
|      |                             | 7/11/2017           |                   |              |                     |            |               |                   |
| 4    | QHJI01s01-RPE-01-21, 22, 23 | 9/12/2017           | 84.4              | 4.95 x 10⁶   | Negative            | Negative   | Negative       | 0.297             |
|      |                             | 8/29/2017           |                   |              |                     |            |               |                   |
| 5    | QHJI01s01-RPE-01-27, 28, 29 | 9/21/2017           | 88.8              | 4.28 x 10⁶   | Negative            | Negative   | Negative       | 0.285             |
|      |                             | 9/7/2017            |                   |              |                     |            |               |                   |

On surgery day, we tested iPS cells-derived RPE cells for the quality standard and assessment. All cells passed these tests. Thus, we used the RPE cells for the transplantation in each patient. SV - Standard value.
Table S10. Summary of immunological tests in transplanted AMD patients - LGIR tests.

| No. | Case       | Pre-OPE | OPE | 2W | 4W | 8W | 12W | 20W | 24W | 28W | 36W | 52W | Tested PBMC |
|-----|------------|---------|-----|----|----|----|-----|-----|-----|-----|-----|-----|-------------|
| 1   | al-so-w01  | –       | –   | nt | +  | +  | ±   | nt  | ±   | nt  | –   | –   | n=8         |
| 2   | al-so-w02  | –       | –   | nt | –  | nt | ±   | –   | –   | nt  | nt  | –   | n=7         |
| 3   | al-so-w03  | –       | –   | nt | nt | –  | nt  | –   | nt  | –   | –   | –   | n=6         |
| 4   | al-so-w04  | –       | –   | nt | –  | nt | –   | nt  | –   | nt  | –   | –   | n=6         |
| 5   | osk-al-so-w01 | –   | –   | –  | –  | nt | –   | nt  | ±   | –   | nt  | –   | n=8         |

Plus (+) indicates LGIR tests were positive, plus-minus (±) indicates LGIR tests were suspected positive, and minus (-) indicates LGIR tests were negative.

Pre-OPE (pre-operation) and OPE (operation day) indicate data before transplantation. nt - not tested, PBMC - peripheral blood mononuclear cells.
Table S11. Summary of immunological tests in transplanted AMD patients – RSA tests.

| No. | Case       | Pre-OPE | OPE | 2W | 4W | 8W | 12W | 20W | 24W | 28W | 36W | 52W | Tested serum |
|-----|------------|---------|-----|----|----|----|-----|-----|-----|-----|-----|-----|--------------|
| 1   | al-so-w01  | –       | –   | nt | –  | –  | nt  | –   | nt  | –   | –   | –   | n=8          |
| 2   | al-so-w02  | –       | –   | nt | –  | nt | –   | nt  | nt  | –   | n=7          |
| 3   | al-so-w03  | –       | –   | nt | –  | nt | –   | nt  | nt  | –   | n=6          |
| 4   | al-so-w04  | –       | –   | nt | –  | nt | –   | nt  | nt  | –   | n=6          |
| 5   | osk-al-so-w01 | – | – | – | – | nt | – | nt | – | – | – | – | n=8 |

Plus (+) indicates RSA tests were positive, plus-minus (±) indicates RSA tests were suspected positive, and minus (-) RSA tests were negative.

All tested samples from AMD patients were negative in this study. Pre-OPE (pre-operation) and OPE (operation day) indicate data before transplantation.

nt - not tested.
### Table S12. Summary of secondary outcome in this study.

| Case 1: al-so-w01 | Pre-OPE | 52W |
|-------------------|---------|-----|
| Foveal retinal thickness (OCT: µm) | 133 | 89 |
| Subretinal fluid (OCT) | Yes | Yes (Decrease) |
| Retinal edema (OCT) | Yes | No |
| Retinal sensitivity: Multi-focal ERG | 10.9 | 6.9 |
| Retinal sensitivity: Microperimetry (MP3: dB) | 10.97 | 8.3 |
| BCVA | 0.08 (20/250) | 0.06 (20/320) |
| Dye leakage from CNV (FA: µm) | 4.114 | 3.74 |
| Number of anti-VEGF treatment (/year) | 4 | 3 |
| QOL (VFQ-25 scores) | 28.5 | 42.1 |

| Case 2: al-so-w02 | Pre-OPE | 52W |
|-------------------|---------|-----|
| Foveal retinal thickness (OCT: µm) | 123 | 428 |
| Subretinal fluid (OCT) | No | No |
| Retinal edema (OCT) | No | Yes (Increase) |
| Retinal sensitivity: Multi-focal ERG | 7.44 | 6.04 |
| Retinal sensitivity: Microperimetry (MP3: dB) | 16.69 | 13.23 |
| BCVA | 0.1 (10/100) | 0.15 (20/125) |
| Dye leakage from CNV (FA: µm) | 2.332 | 1 |
| Number of anti-VEGF treatment (/year) | 2 | 3 |
| QOL (VFQ-25 scores) | 82.6 | 93.9 |

| Case 3: al-so-w03 | Pre-OPE | 52W |
|-------------------|---------|-----|
| Foveal retinal thickness (OCT: µm) | 688 | 544 |
| Subretinal fluid (OCT) | No | Yes (Decrease) |
| Retinal edema (OCT) | Yes | Yes (Decrease) |
|---------------------|-----|----------------|
| Retinal sensitivity: Multi-focal ERG | 7.52 | 5.85 |
| Retinal sensitivity: Microperimetry (MP3: dB) | 8.86 | 5.43 |
| BCVA | 0.1 (10/100) | 0.15 (20/125) |
| Dye leakage from CNV (FA: µm) | 2.451 | 2.21 |
| Number of anti-VEGF treatment (/year) | 3 | 2 |
| QOL (VFQ-25 scores) | 22.3 | 27.2 |

**Case 4: al-so-w04**

| Pre-OPE | 52W |
|---------|-----|
| Foveal retinal thickness (OCT: µm) | 34 | 21 |
| Subretinal fluid (OCT) | Yes | No |
| Retinal edema (OCT) | No | Yes (Increase) |
| Retinal sensitivity: Multi-focal ERG | nt | nt |
| Retinal sensitivity: Microperimetry (MP3: dB) | 2.4 | 1.3 |
| BCVA | 0.09 (10/100) | 0.1 (10/100) |
| Dye leakage from CNV (FA: µm) | 8.926 | 6.57 |
| Number of anti-VEGF treatment (/year) | 1 | 1 |
| QOL (VFQ-25 scores) | 92.7 | 90.1 |

**Case 5: OSK-al-so-w-01**

| Pre-OPE | 52W |
|---------|-----|
| Foveal retinal thickness (OCT: µm) | 872 | 620 |
| Subretinal fluid (OCT) | Yes | NO |
| Retinal edema (OCT) | Yes | Yes (Decrease) |
| Retinal sensitivity: Multi-focal ERG | 8.97 | 7.94 |
| Retinal sensitivity: Microperimetry (MP3: dB) | 4.4 | 2.4 |
| BCVA | 0.2 (20/100) | 0.15 (20/125) |
|                        | Value 1 | Value 2 |
|------------------------|---------|---------|
| Dye leakage from CNV (FA: µm) | 7.24   | 6.344   |
| Number of anti-VEGF treatment (/year) | 3      | 0       |
| QOL (VFQ-25 scores)     | 95.6    | 95.2    |

Data before transplantation were collected at 0 weeks (2nd screening day: Pre-OPE). Data after the transplantation were collected at 52 weeks (52W) after surgery.

Microperimetry data is shown as the retinal sensitivity (mean: dB) of AMD lesions. Multi-focal ERG data is a mean amplitude of AMD lesions.

Dye leakage from CNV measures the greatest linear diameter (GLD) of CNV by FA examination.

BCVA (best-corrected visual acuity) indicates that 0.1 is equivalent to 10/100 on a Snellen chart.
| Subject ID Code | Drug                                | Administration Route          | Dose          | Administration Start Date | Administration End Date | Reason for Administration                  |
|-----------------|-------------------------------------|-------------------------------|---------------|---------------------------|-------------------------|--------------------------------------------|
| al-so-w01       | Gatifloxacin eyedrops               | Instillation (RE only)        | 4 administrations | March 27, 2017            | Continued through 52W  | Treatment related to this study            |
| al-so-w01       | Betamethasone sodium phosphate eyedrops | Instillation (RE only)      | 8 administrations | March 28, 2017           | April 10, 2017          | Treatment of AE                             |
| al-so-w01       | Cefcapene pivoxil hydrochloride tablets | P.O.                          | 3 tablets     | March 29, 2017            | March 31, 2017          | Treatment related to this study            |
| al-so-w01       | Ofloxacin ophthalmic ointment       | Instillation (RE only)        | 1 administration | March 29, 2017            | April 30, 2017          | Treatment of AE                             |
| al-so-w01       | Alogliptin benzoate tablets         | P.O.                          | 25 mg         | April 01, 2017            | Continued through 52W  | Complication                                |
| al-so-w01       | Purified sodium hyaluronate         | Instillation (RE only)        | 6 administrations | April 05, 2017            | Continued through 52W  | Treatment of AE                             |
| al-so-w01       | d-Chlorpheniramine maleate          | I.V.                          | 5 mg          | June 26, 2017             | June 26, 2017           | Prophylactic administration (prevent contrast media allergy) |
| al-so-w01       | Methylprednisolone sodium succinate | I.V.                          | 40 mg         | June 26, 2017             | June 26, 2017           | Prophylactic administration (prevent contrast media allergy) |
| al-so-w01       | Methylprednisolone sodium succinate | I.V.                          | 40 mg         | September 11, 2017        | September 11, 2017      | Prophylactic administration (prevent contrast media allergy) |

**Table S13. Concomitant drugs in all cases.**

AE - adverse event, RE – right eye.
### Concomitant drugs (continued)

| Subject ID Code | Drug                          | Administration Route | Dose | Administration Start Date | Administration End Date | Reason for Administration |
|-----------------|-------------------------------|----------------------|------|---------------------------|-------------------------|---------------------------|
| al-so-w01       | d-chlorpheniramine maleate salt | I.V.                 | 5 mg | September 11, 2017        | September 11, 2017      | Prophylactic administration (prevent contrast media allergy) |
| al-so-w01       | Prednisolone                  | P.O.                 | 10 mg| April 24, 2017            | April 25, 2017          | Treatment of AE           |
| al-so-w01       | Dexamethasone sodium phosphate| I.V.                 | 3.3 mg| April 24, 2017            | April 24, 2017          | Treatment of AE           |
| al-so-w01       | d-chlorpheniramine maleate    | I.V.                 | 5 mg | April 24, 2017            | April 24, 2017          | Treatment of AE           |
| al-so-w01       | d-chlorpheniramine maleate    | I.V.                 | 5 mg | September 11, 2017        | September 11, 2017      | Treatment of AE           |
| al-so-w01       | Fexofenadine hydrochloride    | P.O.                 | 120 mg| April 24, 2017            | April 25, 2017          | Treatment of AE           |
| al-so-w01       | Fexofenadine hydrochloride    | P.O.                 | 120 mg| June 26, 2017             | June 27, 2017           | Treatment of AE           |
| al-so-w01       | Prednisolone                  | P.O.                 | 10 mg| June 26, 2017             | June 27, 2017           | Treatment of AE           |
| al-so-w01       | Dexamethasone sodium phosphate| I.V.                 | 3.3 mg| September 11, 2017        | September 11, 2017      | Treatment of AE           |
| al-so-w01       | Fexofenadine hydrochloride    | P.O.                 | 120 mg| September 11, 2017        | September 12, 2017      | Treatment of AE           |
| al-so-w01       | Prednisolone                  | P.O.                 | 10 mg| September 11, 2017        | September 12, 2017      | Treatment of AE           |
| al-so-w01       | Tranexamic acid capsule 250 mg| P.O.                 | 750 mg| November 04, 2017         | November 08, 2017       | Treatment of AE           |

*AE - adverse event.*
**Concomitant drugs (continued)**

| Subject ID Code | Drug                                      | Administration Route | Dose   | Administration Start Date | Administration End Date | Reason for Administration                           |
|-----------------|-------------------------------------------|----------------------|--------|---------------------------|-------------------------|------------------------------------------------------|
| al-so-w01       | Fexofenadine hydrochloride 60 mg          | P.O.                 | 120 mg | November 04, 2017         | November 08, 2017       | Treatment of AE                                      |
| al-so-w01       | Metformin hydrochloride                   | P.O.                 | 500 mg | January 06, 2018          | Continued through 52W after transplantation            | Complication                                         |
| al-so-w01       | Methylprednisolone sodium succinate       | I.V.                 | 125 mg | March 14, 2018            | March 14, 2018          | Prophylactic administration (allergy)                |
| al-so-w01       | d-chlorpheniramine maleate                | I.V.                 | 5 mg   | March 14, 2018            | March 14, 2018          | Treatment of AE                                      |
| al-so-w01       | Dexamethasone sodium phosphate            | I.V.                 | 3.3 mg | March 14, 2018            | March 14, 2018          | Treatment of AE                                      |
| al-so-w01       | Dexamethasone sodium phosphate            | I.V.                 | 3.3 mg | March 14, 2018            | March 14, 2018          | Prophylactic administration (allergy prevention)     |
| al-so-w01       | d-chlorpheniramine maleate                | I.V.                 | 5 mg   | March 14, 2018            | March 14, 2018          | Prophylactic administration (allergy)                |
| al-so-w01       | Betamethasone sodium phosphate eyedrops   | Instillation (RE only) | 4 administrations | April 11, 2017 | Continued through 52W | Treatment related to this study                     |
| al-so-w02       | Cefcapene pivoxil hydrochloride hydrate   | P.O.                 | 200 mg | June 28, 2017             | June 30, 2017           | Treatment related to this study                     |
| al-so-w02       | KREMEZIN Fine Granules                    | P.O.                 | 6 g    | Administration began before ENR | Continued through 52W | Complication                                         |

*ENR – enrollment, AE - adverse event, RE – right eye.*
## Concomitant drugs (continued)

| Subject ID Code | Drug                             | Administration Route | Dose   | Administration Start Date | Administration End Date | Reason for Administration |
|-----------------|----------------------------------|----------------------|--------|---------------------------|--------------------------|----------------------------|
| al-so-w02       | Cilostazol                       | P.O.                 | 200 mg | Administration began before ENR | Continued through 52W | Prophylactic administration (prevention of cerebral infarction) |
| al-so-w02       | Doxazosin mesylate               | P.O.                 | 3 mg   | Administration began before ENR | December 15, 2017       | Complication               |
| al-so-w02       | Tamsulosin hydrochloride         | P.O.                 | 0.2 mg | Administration began before ENR | December 15, 2017       | Complication               |
| al-so-w02       | Candesartan cilexetil            | P.O.                 | 8 mg   | Administration began before ENR | Continued through 52W | Complication               |
| al-so-w02       | Febuxostat                       | P.O.                 | 10 mg  | Administration began before ENR | Continued through 52W | Complication               |
| al-so-w02       | Amlodipine besylate              | P.O.                 | 5 mg   | Administration began before ENR | Continued through 52W | Complication               |
| al-so-w02       | Esomeprazole magnesium hydrate   | P.O.                 | 20 mg  | Administration began before ENR | Continued through 52W | Other (gastric mucosa protection) |
| al-so-w02       | Epinastine hydrochloride         | P.O.                 | 20 mg  | Administration began before ENR | Continued through 52W | Complication               |
| al-so-w02       | Gatifloxacin hydrate             | Instillation (LE only) | 4 administrations | June 26, 2017 | Continued through 52W | Treatment related to this study |
| al-so-w02       | Betamethasone sodium phosphate   | Instillation (LE only) | 4 administrations | June 26, 2017 | March 28, 2018 | Treatment related to this study |

ENR – enrollment, LE – left eye.
| Subject ID Code | Drug                          | Administration Route       | Dose         | Administration Start Date | Administration End Date | Reason for Administration |
|-----------------|-------------------------------|----------------------------|--------------|---------------------------|-------------------------|---------------------------|
| al-so-w02       | Latanoprost                   | Instillation (LE only)      | 1 administration | August 14, 2017           | August 28, 2017          | Treatment of AE           |
| al-so-w02       | Latanoprost                   | Instillation LE only        | 1 administration | September 04, 2017        | September 20, 2017       | Treatment of AE           |
| al-so-w02       | Brinzolamide                  | Instillation (LE only)      | 2 administrations | August 29, 2017           | March 28, 2018           | Treatment of AE           |
| al-so-w02       | Rinderon-V ointment 0.12%     | Topical                    | Sufficient quantity | December 21, 2017        | Continued through 52W    | Complication              |
| al-so-w02       | Keratinamin kowa cream 20%    | Topical                    | Sufficient quantity | December 21, 2017        | Continued through 52W    | Complication              |
| al-so-w02       | Patell Tape 40                | Topical                    | Sufficient quantity | December 21, 2017        | Continued through 52W    | Complication              |
| al-so-w02       | Sulprotin ointment 1%         | Topical                    | Sufficient quantity | December 21, 2017        | Continued through 52W    | Complication              |
| al-so-w02       | Dermosol G lotion             | Topical                    | Sufficient quantity | January 26, 2018          | Continued through 52W    | Complication              |
| al-so-w02       | Kindalone ointment 0.05%      | Topical                    | Sufficient quantity | February 22, 2018         | Continued through 52W    | Complication              |
| al-so-w02       | Latanoprost                   | Instillation (LE only)      | 1 administration | November 22, 2017         | Continued through 52W    | Treatment of AE           |
| al-so-w02       | Brinzolamide                  | Instillation (LE only)      | 2 administrations | April 04, 2018            | Continued through 52W    | Treatment of AE           |

AE - adverse event, LE – left eye.
### Concomitant drugs (continued)

| Subject ID Code | Drug                          | Administration Route | Dose  | Administration Start Date | Administration End Date | Reason for Administration                      |
|-----------------|-------------------------------|----------------------|-------|---------------------------|-------------------------|-----------------------------------------------|
| al-so-w02       | COSOPT ophthalmic solution    | Instillation (LE only) | 2     | March 28, 2018            | April 03, 2018          | Treatment of AE                               |
| al-so-w02       | Fluorometholone               | Instillation LE only  | 4     | March 29, 2018            | Continued through 52W   | Treatment related to this study               |
| al-so-w02       | Diamox tablets                | P.O.                 | 500 mg| March 28, 2018            | March 29, 2018          | Treatment of AE                               |
| al-so-w02       | Gluconsan K tablets           | P.O.                 | 10 mEq| March 28, 2018            | March 29, 2018          | Treatment of AE                               |
| al-so-w03       | Aliskiren fumarate tablets    | P.O.                 | 150 mg| Administration began before ENR | Continued through 52W | Complication                                  |
| al-so-w03       | Naftopidil OD tablets         | P.O.                 | 25 mg | Administration began before ENR | Continued through 52W | Complication                                  |
| al-so-w03       | Allopurinol                   | P.O.                 | 100 mg| Administration began before ENR | October 25, 2017       | Complication                                  |
| al-so-w03       | Pitavastatin calcium tablets  | P.O.                 | 1 mg  | Administration began before ENR | October 25, 2017       | Complication                                  |
| al-so-w03       | Zolpidem tartrate tablets     | P.O.                 | 10 mg | Administration began before ENR | Continued through 52W | Complication                                  |
| al-so-w03       | Etodolac tablets              | P.O.                 | 200 mg| Administration began before ENR | Continued through 52W | Complication                                  |
| al-so-w03       | Limaprost alfadex tablets     | P.O.                 | 10 µg | Administration began before ENR | Continued through 52W | Complication                                  |

ENR – enrollment, AE - adverse event, LE – left eye.
## Concomitant drugs (continued)

| Subject ID Code | Drug                          | Administration Route | Dose | Administration Start Date | Administration End Date | Reason for Administration               |
|----------------|-------------------------------|----------------------|------|---------------------------|-------------------------|------------------------------------------|
| al-so-w03      | Hachimijiogan                 | P.O.                 | 7.5 g| Administration began before ENR | Continued through 52W   | Complication                             |
| al-so-w03      | Dorzolamide hydrochloride     | Instillation (RE only) | 3 administrations | October 04, 2017 | June 19, 2018 | Treatment of AE                          |
| al-so-w03      | Latanoprost                   | Instillation RE only | 1 administration | October 25, 2017 | November 13, 2017 | Treatment of AE                          |
| al-so-w03      | Influenza HA vaccine          | Other (S.C.)         | Sufficient quantity | November 02, 2017 | November 02, 2017 | Prophylactic administration (influenza prevention) |
| al-so-w03      | Latanoprost                   | Instillation (RE only) | 1 administration | February 21, 2018 | Continued through 52W | Treatment of AE                          |
| al-so-w03      | Gatifloxacin hydrate          | Instillation (RE only) | 4 administrations | July 24, 2017 | Continued through 52W | Treatment related to this study          |
| al-so-w03      | Betamethasone sodium phosphate | Instillation (RE only) | 4 administrations | July 24, 2017 | May 30, 2018 | Treatment related to this study          |
| al-so-w03      | Acetaminophen                 | P.O.                 | 400 mg | November 20, 2017 | November 20, 2017 | Prophylactic administration (pain after intravitreal injection) |
| al-so-w03      | Fluorometholone               | Instillation (RE only) | 4 administrations | May 30, 2018 | Continued through 52W | Treatment related to this study          |
| al-so-w03      | Acetaminophen                 | P.O.                 | 400 mg | June 14, 2018 | June 14, 2018 | Prophylactic administration (pain after intravitreal injection) |

ENR – enrollment, AE - adverse event, RE – right eye.
### Concomitant drugs (continued)

| Subject ID Code | Drug                          | Administration Route                      | Dose     | Administration Start Date | Administration End Date | Reason for Administration                  |
|-----------------|-------------------------------|--------------------------------------------|----------|---------------------------|-------------------------|---------------------------------------------|
| al-so-w03       | Brinzolamide                  | Instillation (RE only)                     | 2 administrations | June 20, 2018             | Continued through 52W   | Treatment of AE                            |
| al-so-w04       | Olmesartan medoxomil          | P.O.                                       | 20 mg    | Administration began before ENR | Continued through 52W   | Complication                               |
| al-so-w04       | Atorvastatin calcium hydrate  | P.O.                                       | 10 mg    | Administration began before ENR | Continued through 52W   | Complication                               |
| al-so-w04       | Zolpidem tartrate             | P.O.                                       | 5 mg     | Administration began before ENR | Continued through 52W   | Complication                               |
| al-so-w04       | Vonoprazan fumarate           | P.O.                                       | 20 mg    | Administration began before ENR | Continued through 5W    | Complication                               |
| al-so-w04       | Magnesium oxide               | P.O.                                       | 250 mg   | Administration began before ENR | Continued through 52W   | Complication                               |
| al-so-w04       | Latanoprost                   | Instillation (RE only)                     | 1 administration | August 16, 2017       | September 11, 2017      | Complication                               |
| al-so-w04       | Moxifloxacin hydrochloride    | Instillation (RE only)                     | 4 administrations | September 26, 2017   | Continued through 52W   | Treatment related to this study             |
| al-so-w04       | Betamethasone sodium phosphate| Instillation (RE only)                     | 4 administrations | September 13, 2017    | May 23, 2018            | Treatment related to this study             |
| al-so-w04       | Cefcapene pivoxil hydrochloride| P.O.                                     | 300 mg   | September 13, 2017        | September 15, 2017      | Prophylactic administration (postoperative infection) |

ENR – enrollment, AE - adverse event, RE – right eye.
### Concomitant drugs (continued)

| Subject ID Code | Drug                              | Administration Route          | Dose   | Administration Start Date | Administration End Date | Reason for Administration |
|-----------------|-----------------------------------|--------------------------------|--------|---------------------------|-------------------------|---------------------------|
| al-so-w04       | Gatifloxacin hydrate              | Instillation (RE only)         | 4      | September 13, 2017        | September 25, 2017      | Treatment related to this study |
| al-so-w04       | VONOSAP Pack 400                  | P.O.                           | 2      | November 06, 2017         | November 12, 2017       | Complication               |
| al-so-w04       | Miya BM fine granules             | P.O.                           | 80 mg  | November 06, 2017         | November 12, 2017       | Complication               |
| al-so-w04       | Azelnidipine                      | P.O.                           | 16 mg  | Administration began before ENR | Continued through 52W   | Complication               |
| al-so-w04       | Brinzolamide                      | Instillation (RE only)         | 2      | October 23, 2017          | July 11, 2018           | Treatment of AE            |
| al-so-w04       | Latanoprost                       | Instillation (RE only)         | 1      | October 16, 2017          | Continued through 52W   | Treatment of AE            |
| al-so-w04       | Aiphagan ophthalmic solution      | Instillation (RE only)         | 2      | May 23, 2018              | Continued through 52W   | Treatment of AE            |
| al-so-w04       | Betamethasone sodium phosphate    | Instillation (RE only)         | 2      | May 23, 2018              | Continued through 52W   | Treatment of AE            |
| al-so-w04       | Fluorometholone solution 0.1%     | Instillation (RE only)         | 4      | June 02, 2018             | Continued through 52W   | Treatment of underlying disease |
| al-so-w04       | COSOPT ophthalmic solution        | Instillation (RE only)         | 2      | July 12, 2018             | Continued through 52W   | Treatment of AE            |

AE - adverse event, RE – right eye.
| Subject ID Code | Drug                                | Administration Route | Dose  | Administration Start Date | Administration End Date | Reason for Administration                                   |
|----------------|-------------------------------------|----------------------|-------|---------------------------|-------------------------|------------------------------------------------------------|
| OSK-al-so-w-01 | Cefcapene pivoxil hydrochloride     | P.O.                 | 300 mg| September 22, 2017        | September 25, 2017      | Prophylactic administration (infection prevention)          |
| OSK-al-so-w-01 | Teprenone                           | P.O.                 | 150 mg| September 22, 2017        | September 25, 2017      | Prophylactic administration (gastritis prevention)          |
| OSK-al-so-w-01 | Moxifloxacin hydrochloride          | Instillation (RE only)| 3 drops| September 22, 2017        | December 15, 2017       | Prophylactic administration (infection prevention)          |
| OSK-al-so-w-01 | Betamethasone sodium phosphate      | Instillation (RE only)| 3 drops| September 22, 2017        | September 22, 2017      | Treatment of AE                                            |
| OSK-al-so-w-01 | Betamethasone sodium phosphate      | Instillation (RE only)| 15 drops| September 23, 2017        | September 25, 2017      | Treatment of AE                                            |
| OSK-al-so-w-01 | Betamethasone sodium phosphate      | Instillation (RE only)| 4 drops| September 26, 2017        | October 24, 2017        | Treatment of AE                                            |
| OSK-al-so-w-01 | Methylprednisolone sodium succinate | I.V.                 | 1000 mg| September 27, 2017        | September 29, 2017      | Prophylactic administration (rejection prevention)          |
| OSK-al-so-w-01 | Sodium rabeprazole                  | P.O.                 | 10 mg | September 27, 2017        | September 29, 2017      | Prophylactic administration (gastritis prevention)          |
| OSK-al-so-w-01 | Esomeprazole magnesium hydrate      | P.O.                 | 20 mg | September 30, 2017        | October 27, 2017        | Prophylactic administration (gastritis prevention)          |
| OSK-al-so-w-01 | Prednisolone                         | P.O.                 | 20 mg | September 30, 2017        | October 06, 2017        | Prophylactic administration (rejection prevention)          |
| OSK-al-so-w-01 | Prednisolone                         | P.O.                 | 15 mg | October 07, 2017          | October 13, 2017        | Prophylactic administration (rejection prevention)          |

AE - adverse event, RE – right eye.
Concomitant drugs (continued)

| Subject ID Code | Drug                                    | Administration Route | Dose | Administration Start Date | Administration End Date | Reason for Administration                          |
|-----------------|-----------------------------------------|----------------------|------|---------------------------|-------------------------|---------------------------------------------------|
| OSK-al-so-w-01  | Prednisolone                            | P.O.                 | 10 mg| October 14, 2017          | October 20, 2017        | Prophylactic administration (rejection prevention) |
| OSK-al-so-w-01  | Prednisolone                            | P.O.                 | 5 mg | October 21, 2017          | October 27, 2017        | Prophylactic administration (rejection prevention) |
| OSK-al-so-w-01  | Alendronate sodium hydrate (weekly)      | P.O.                 | 35 mg| September 30, 2017        | October 21, 2017        | Prophylactic administration (osteoporosis prevention) |
| OSK-al-so-w-01  | Betamethasone sodium phosphate (RE only) | Instillation (RE only) | 4 drops | October 25, 2017          | December 15, 2017        | Prophylactic administration (inflammation prevention) |

RE – right eye.
Table S14. Concomitant therapies in all cases.

| Subject ID Code | Concomitant Therapy                                      | Start Date   | End Date     | Reason for Therapy                      |
|-----------------|----------------------------------------------------------|--------------|--------------|-----------------------------------------|
| al-so-w01       | Eylea intravitreal injection, RE                         | May 08, 2017 | May 08, 2017 | Treatment of underlying disease         |
| al-so-w01       | sub-Tenon conjunctival injection of triamcinolone, RE    | May 08, 2017 | May 08, 2017 | Treatment of AE                         |
| al-so-w01       | sub-Tenon conjunctival injection of triamcinolone, RE    | June 12, 2017| June 12, 2017| Treatment of AE                         |
| al-so-w01       | sub-Tenon conjunctival injection of triamcinolone, RE    | August 21, 2017| August 21, 2017| Treatment of AE                        |
| al-so-w01       | Eylea intravitreal injection, RE                         | October 16, 2017| October 16, 2017| Treatment of underlying disease        |
| al-so-w01       | Eylea intravitreal injection, LE                         | January 17, 2018| January 17, 2018| Complication                           |
| al-so-w01       | Eylea intravitreal injection, LE                         | March 07, 2018| March 07, 2018| Complication                           |
| al-so-w01       | Eylea intravitreal injection, LE                         | June 19, 2017| June 19, 2017| Complication                           |
| al-so-w02       | Eylea intravitreal injection, LE                         | November 29, 2017| November 29, 2017| Treatment of underlying disease        |
| al-so-w02       | Vitrectomy, LE                                           | January 15, 2018| January 15, 2018| Treatment of AE                        |
| al-so-w02       | Eylea intravitreal injection, LE                         | September 20, 2017| September 20, 2017| Treatment of underlying disease        |
| al-so-w02       | sub-Tenon conjunctival injection of triamcinolone, LE    | October 16, 2017| October 16, 2017| Treatment of AE                        |
| al-so-w02       | Eylea intravitreal injection, LE                         | January 15, 2018| January 15, 2018| Treatment of underlying disease        |
| al-so-w03       | Eylea intravitreal injection, RE                         | November 20, 2017| November 20, 2017| Treatment of underlying disease        |
| al-so-w03       | Eylea intravitreal injection, RE                         | June 14, 2018| June 14, 2018| Treatment of underlying disease        |
| al-so-w04       | Eylea intravitreal injection, LE                         | September 19, 2017| September 19, 2017| Complication                           |
| al-so-w04       | Eylea intravitreal injection, LE                         | December 13, 2017| December 13, 2017| Complication                           |
| al-so-w04       | Eylea intravitreal injection, LE                         | March 06, 2018| March 06, 2018| Complication                           |
| al-so-w04       | Eylea intravitreal injection, RE                         | August 16, 2018| August 16, 2018| Treatment of underlying disease        |

AE - adverse event, RE – right eye, LE – left eye.
| Subject ID Code | Adverse Event (AE)                      | Serious/Non-serious | Date Occurred | Severity       | Treated | Outcome               | Causality                                      | Continued Participation in Study | AE Associated with Transplantation Surgery | AE Caused by iPS Cell-derived RPE Cells |
|----------------|----------------------------------------|---------------------|---------------|----------------|---------|-----------------------|-----------------------------------------------|-------------------------------------|------------------------------------------|-----------------------------------|
| al-so-w01      | Corneal epithelial detachment          | Non-serious         | March 28, 2017| Grade 2 (moderate) | Yes     | Resolved (April 11, 2017) | Related (directly, transplantation surgery procedure) | Continued                           | N/A                                      | N/A                                 |
| al-so-w01      | Increased postoperative inflammation   | Non-serious         | March 30, 2017| Grade 2 (moderate) | No      | Resolved (April 4, 2017)  | Related (directly, transplantation surgery procedure) | Continued                           | N/A                                      | N/A                                 |
| al-so-w01      | Allergic reaction                      | Non-serious         | April 24, 2017| Grade 2 (moderate) | Yes     | Resolved (April 25, 2017)  | Not related (contrast media allergy; caused by patient predisposition) | Continued                           | N/A                                      | Other                               |
| al-so-w01      | Suspected mild rejection               | Non-serious         | April 24, 2017| Grade 2 (moderate) | Yes     | Resolved (December 4, 2017) | Related (directly, transplanted RPE cells) | Continued                           | N/A                                      | Other                               |
| al-so-w01      | Allergic reaction                      | Non-serious         | June 26, 2017 | Grade 2 (moderate) | Yes     | Resolved (June 27, 2017)   | Not related (contrast media allergy; caused by patient predisposition) | Continued                           | N/A                                      | N/A                                 |
| Subject ID Code | Adverse Event (AE)                     | Serious/Non-serious | Date Occurred | Severity         | Treated | Outcome                  | Causality                                                                 | Continued Participation in Study | Associated with Transplantation Surgery | AE Caused by iPS Cell-derived RPE Cells |
|----------------|---------------------------------------|---------------------|---------------|------------------|---------|-------------------------|---------------------------------------------------------------------------|----------------------------------|------------------------------------------|------------------------------------------|
| al-so-w01      | Allergic reaction                     | Non-serious         | September 11, 2017 | Grade 2 (moderate) | Yes     | Resolved (September 12, 2017) | Not related (contrast media allergy; caused by patient predisposition)    | Continued                         | N/A                                      | N/A                                      |
| al-so-w01      | Allergic reaction                     | Non-serious         | November 4, 2017  | Grade 2 (moderate) | Yes     | Resolved (November 8, 2017) | Not related (caused by patient predisposition)                            | Continued                         | N/A                                      | N/A                                      |
| al-so-w01      | Allergic reaction                     | Non-serious         | March 14, 2018    | Grade 2 (moderate) | Yes     | Resolved (March 14, 2018)  | Not related (contrast media allergy, caused by patient predisposition)    | Continued                         | N/A                                      | N/A                                      |
| al-so-w01      | Subretinal hemorrhage                 | Non-serious         | March 14, 2018    | Grade 1 (Mild)    | No      | Remitted (September 18, 2018) | Not related (worsening of underlying disease)                            | Continued                         | N/A                                      | N/A                                      |
| al-so-w02      | Increased intraocular pressure, left   | Non-serious         | August 10, 2017   | Grade 2 (moderate) | Yes     | No change (July 5, 2018)   | Related (weak relationship, medical intervention other than that described above) | Continued                         | N/A                                      | N/A                                      |
| Subject ID Code | Adverse Event (AE)                                      | Serious/Non-serious | Date Occurred         | Severity                          | Treated | Outcome       | Causality                                      | Continued Participation in Study | AE Associated with Transplantation Surgery | AE Caused by iPS Cell-derived RPE Cells |
|-----------------|---------------------------------------------------------|---------------------|-----------------------|-----------------------------------|---------|---------------|-----------------------------------------------|--------------------------------------|------------------------------------------|------------------------------------------|
| al-so-w02       | Mild rejection                                          | Non-serious         | October 4, 2017       | Grade 2 (moderate)                | Yes     | Resolved      | Related (directly, transplanted RPE cells)    | N/A                                  | Other                                    | Other                                    |
|                 | Retinal edema associated with epiretinal membrane      | Serious             | October 27, 2017      | Grade 2 (moderate)                | Yes     | Resolved      | Related (strong relationship, transplantation surgery procedure) | N/A                                  | Other                                    | Other                                    |
| al-so-w02       | Neurally mediated syncope                              | Non-serious         | December 15, 2017     | Grade 1 (Mild)                    | No      | Resolved      | Not related [due to patient predisposition or concomitant drug (alpha-blocker)] | N/A                                  | N/A                                      | N/A                                      |
| al-so-w02       | Cystoid macular edema                                  | Non-serious         | March 28, 2018        | Grade 1 (Mild)                    | No      | No change     | Not related (worsening of underlying disease) | N/A                                  | N/A                                      | N/A                                      |
| al-so-w03       | Increased intraocular pressure, right                   | Non-serious         | October 4, 2017       | Grade 1 (Mild)                    | Yes     | -             | Related (weak relationship, medical intervention other than that described above) | N/A                                  | N/A                                      | N/A                                      |
| Subject ID Code | Adverse Event (AE) | Serious/Non-serious | Date Occurred | Severity | Treated | Outcome | Causality | Continued Participation in Study | AE Associated with Transplantation Surgery | AE Caused by iPS Cell-derived RPE Cells |
|-----------------|--------------------|---------------------|---------------|----------|---------|---------|-----------|---------------------------------|---------------------------------|---------------------------------|
| al-so-w03       | Hyperglycemia      | Non-serious         | August 21, 2017 | Grade 1 (Mild) | No      | Resolved (October 16, 2017) | Not related (because increase was transient and considered to be in the range of physiological change) | Continued | N/A | N/A |
| al-so-w04       | Cystoid macular edema | Non-serious         | October 30, 2017 | Grade 1 (Mild) | No      | Remitted (September 12, 2018) | Not related (worsening of underlying disease) | Continued | N/A | N/A |
| al-so-w04       | Superficial punctate keratopathy | Non-serious         | November 6, 2017 | Grade 1 (Mild) | No      | Remitted (September 12, 2018) | Not related [effect of concomitant drug (hypotensive drug)] | Continued | N/A | N/A |
| al-so-w04       | Macular hole (Macular pseudohole) | Non-serious         | May 23, 2018    | Grade 2 (moderate) | Yes | No change (September 12, 2018) | Not related (due to underlying disease) | Continued | N/A | N/A |
| al-so-w04       | Increased intraocular pressure | Non-serious         | October 16, 2017 | Grade 2 (moderate) | Yes | Remitted (September 12, 2018) | Related (strong relationship; in addition: effect of concomitant medication and glaucoma, a complication) | Continued | N/A | N/A |
### Adverse Events (continued)

| Subject ID Code | Adverse Event                      | Serious/Non-serious | Date Occurred      | Severity          | Treated | Outcome          | Causality                                         | Continued Participation in Study | AE Associated with Transplantation Surgery | AE Caused by iPS Cell-derived RPE Cells |
|-----------------|-----------------------------------|---------------------|-------------------|------------------|---------|------------------|---------------------------------------------------|----------------------------------------|------------------------------------------|------------------------------------------|
| OSK-al-so-w01   | Aseptic endophthalmitis           | Serious             | September 22, 2017| Grade 2 (moderate)| Yes     | Resolved (October 24, 2017) | Related (weak relationship, transplantation surgery procedure) | Continued                             | Other                                    | N/A                                      |

al-so-w01 is Case 1, al-so-w02 is Case 2, al-so-w03 is Case 3, al-so-w04 is Case 4, and OSK-al-so-w01 is Case 5. Other in AE associated with transplantation surgery indicates the adverse events with exception of retinal/choroidal/vitreous hemorrhage or retinal detachment caused by transplantation surgery. Other in AE caused by iPSC-derived RPE cells indicates the adverse events with exception of poor engraftment of transplanted cells, immune rejection, excessive cell proliferation, and tumorigenicity (Suspected immune rejection is “other”).

N/A – Not Applicable.
Table S16. Inflammatory factors for primers and probes in qRT-PCR.

| No. | Molecule                                         | Left primer               | Right primer               | Probe* |
|-----|--------------------------------------------------|---------------------------|---------------------------|--------|
| 1   | Actin, beta (β-actin)                            | ccaaccgccagaagatga        | ecagagctacaggatga         | #64    |
| 2   | Pigment epithelium derived factor (PEDF)         | gtgtaggtcgcagctat         | ccaagagcatgcagtagca       | #57    |
| 3   | Transforming growth factor, beta 2 (TGFβ2)       | ccaaggctgatgctgagac      | cagatgctctggtagtattgtcttgatt | #67    |
| 4   | CD3ε molecule, epsilon (CD3ε)                    | caaggcccaagctgtgac        | tcatagctctggtagtcttgatt   | #49    |
| 5   | Allograft inflammatory factor 1 (AIF1/Iba1)      | ccaaccaggattgtagcagagca  | cgtctgagtctgtggtagtcttgatt | #4     |
| 6   | Interferon, gamma (IFN-γ)                        | ggcattttgaagaattgagaag   | tttgctgggtctgtcatctt      | #21    |

In quantitative RT-PCR, we extracted RNA from the epiretinal membrane tissue in Case 2, cultured iPS-RPE cells, human primary RPE cells, and peripheral blood cells. *Probe - The probe in the Roche Universal Probe Library was used for our qRT-PCR assay.
Supplementary References

1. Wang, K.; Li, M.; Hadley, D.; Liu, R.; Glessner, J.; Grant, S. F.; Hakonarson, H.; Bucan, M.; PennCNV: an integrated hidden Markov model designed for high-resolution copy number variation detection in whole-genome SNP genotyping data. *Genome research* **2007**, *17*, (11), 1665-74.

2. Gonzalez, J. R.; Rodriguez-Santiago, B.; Caceres, A.; Pique-Regi, R.; Rothman, N.; Chanock, S. J.; Armengol, L.; Perez-Jurado, L. A., A fast and accurate method to detect allelic genomic imbalances underlying mosaic rearrangements using SNP array data. *BMC bioinformatics* **2011**, *12*, 166.

3. Koboldt, D. C.; Zhang, Q.; Larson, D. E.; Shen, D.; McLellan, M. D.; Lin, L.; Miller, C. A.; Mardis, E. R.; Ding, L.; Wilson, R. K., VarScan 2: somatic mutation and copy number alteration discovery by exome sequencing. *Genome Res* **2012**, *22*, (3), 568-76.

4. Otsu, N., A Threshold Selection Method from Gray-Level Histograms. *IEEE Trans. Systems, Man and Cybernetics* **1979**, *9*, 62-66.

5. Rausch, T.; Zichner, T.; Schlattl, A.; Stutz, A. M.; Benes, V.; Korbel, J. O., DELLY: structural variant discovery by integrated paired-end and split-read analysis. *Bioinformatics* **2012**, *28*, (18), i333-i339.

6. Teschendorff, A. E.; Marabita, F.; Lechner, M.; Bartlett, T.; Tegner, J.; Gomez-Cabrero, D.; Beck, S., A beta-mixture quantile normalization method for correcting probe design bias in Illumina Infinium 450 k DNA methylation data. *Bioinformatics* **2013**, *29*, (2), 189-96.

7. Kim, J. G.; Takeshima, H.; Niwa, T.; Rehnberg, E.; Shigematsu, Y.; Yoda, Y.; Yamashita, S.; Kushima, R.; Maekita, T.; Ichinose, M.; Kaitai, H.; Park, W. S.; Hong, Y. S.; Park, C. H.; Ushijima, T., Comprehensive DNA methylation and extensive mutation analyses reveal an association between the CpG island methylator phenotype and oncogenic mutations in gastric cancers. *Cancer Lett* **2013**, *330*, (1), 33-40.

8. Mandai, M.; Watanabe, A.; Kurimoto, Y.; Hirami, Y.; Morinaga, C.; Daimon, T.; Fujihara, M.; Akimaru, H.; Sakai, N.; Shibata, Y.; Terada, M.; Nomiya, Y.; Tanishima, S.; Nakamura, M.; Kamao, H.; Sugita, S.; Onishi, A.; Ito, T.; Fujita, K.; Kawamata, S.; Go, M. J.; Shimohara, C.; Hata, K. I.; Sawada, M.; Yamamoto, M.; Ohta, S.; Ohara, Y.; Yoshida, K.; Kuwahara, J.; Kitano, Y.; Amano, N.; Umekage, M.; Kitaoka, F.; Tanaka, A.; Okada, C.; Takasu, N.; Ogawa, S.; Yamanaka, S.; Takahashi, M., Autologous Induced Stem Cells for Macular Degeneration. *N Engl J Med* **2017**, *376*, (11), 1038-1046.

9. Sugita, S.; Ogawa, M.; Shimizu, N.; Morio, T.; Ohguro, N.; Nakai, K.; Maruyama, K.; Nagata, K.; Takeda, A.; Usui, Y.; Sonoda, K. H.; Takeuchi, M.; Mochizuki, M., Use of a comprehensive polymerase chain reaction system for diagnosis of ocular infectious diseases. *Ophthalmology* **2013**, *130*, (9), 1761-8.

10. Sugita, S.; Shimizu, N.; Watanabe, K.; Mizukami, M.; Morio, T.; Sugamoto, Y.; Mochizuki, M., Use of multiplex PCR and real-time PCR to detect human herpes virus genome in ocular fluids of patients with uveitis. *The British journal of ophthalmology* **2008**, *92*, (7), 928-32.

11. Sugita, S.; Iwasaki, Y.; Makabe, K.; Kimura, T.; Futagami, T.; Suegami, S.; Takekishi, M., Lack of T Cell Response to iPSC-Derived Retinal Pigment Epithelial Cells fromHLA Homozygous Donors. *Stem Cell Reports* **2016**, *7*, (4), 619-34.

12. Cense, B.; Chen, T. C.; Park, B. H.; Pierce, M. C.; de Boer, J. F., Invivo depth-resolved birefringence measurements of the human retina nerve fiber layer by polarization-sensitive optical coherence tomography. *Optics letters* **2002**, *27*, (18), 1610-2.

13. Gotzinger, E.; Pircher, M.; Hitzenberger, C. K., High speed spectral domain polarization sensitive optical coherence tomography of the human retina. *Optics express* **2005**, *13*, (25), 10217-29.

14. Yamanari, M.; Lim, Y.; Makita, S.; Yasuno, Y., Visualization of phase retardation of deep posterior eye by polarization-sensitive swept-source optical coherence tomography with 1-microm probe. *Optics express* **2009**, *17*, (15), 12385-96.

15. Pircher, M.; Gotzinger, E.; Findl, O.; Michels, S.; Geitzenauer, W.; Leydolt, C.; Schmidt-Erfurth, U.; Hitzenberger, C. K., Human macula investigated in vivo with polarization-sensitive optical coherence tomography. *Invest Ophthalmo Vis Sc* **2006**, *47*, (12), 5487-94.

16. Baumann, B.; Baumann, S. O.; Konegger, T.; Pircher, M.; Gotzinger, E.; Schlantz, F.; Schutze, C.; Sattmann, H.; Litschauer, M.; Schmidt-Erfurth, U.; Hitzenberger, C. K., Polarization sensitive optical coherence tomography of melanin provides intrinsic contrast based on depolarization. *Biomedical optics express* **2012**, *3*, (7), 1670-83.

17. Gotzinger, E.; Pircher, M.; Geitzenauer, W.; Ahlers, C.; Baumann, B.; Michels, S.; Schmidt-Erfurth, U.; Hitzenberger, C. K., Retinal pigment epithelium segmentation by polarization sensitive optical coherence tomography. *Optics express* **2008**, *16*, (21), 16410-22.

18. Yamanari, M.; Tsuda, S.; Kobukum, T.; Shiga, Y.; Omokada, K.; Aizawa, N.; Yokoyama, Y.; Himori, N.; Kunimatsu-Sanuki, S.; Maruyama, K.; Kunikata, H.; Nakazawa, T., Estimation of Jones matrix, birefringence and entropy using Cloude-Pottier decomposition in polarization-sensitive optical coherence tomography. *Biomedical optics express* **2016**, *7*, (9), 3551-3573.

19. Yamanari, M.; Tsuda, S.; Kobukum, T.; Shiga, Y.; Omokada, K.; Yokoyama, Y.; Himori, N.; Ryu, M.; Kunimatsu-Sanuki, S.; Takahashi, H.; Maruyama, K.; Kunikata, H.; Nakazawa, T., Fiber-based polarization-sensitive OCT for birefringence imaging of the anterior eye segment. *Biomedical optics express* **2015**, *6*, (2), 369-89.