Figure S1. Characterization of hiPSCs. Representative light and confocal microscopy images showing an undifferentiated iPSC colony and robust expression of pluripotency markers, OCT4 and NANOG in a hiPSC colony derived from the fifth hiPSC line used in this study. Scale bar = 50 μm.

Figure S2. Schematic representation of hiPSC-RPE plating/culture on different substrates. (A) A diagram representing the organization and layout of ECM and/or membrane on non-permeable support that was used for hiPSC-RPE plating and cultures under different conditions, BMSF, COL1-BMSF and LAM-TCP. (B) Schematic demonstrating the organization and layout of ECM and/or membrane utilized for culturing of hiPSC-RPE cultures in custom-made chambers (BMSF and COL1-BMSF) and PET-transwells (LAM-TCP).
Figure S3. Morphological characterization of hiPSC-RPE cultures on BMSF, COL1-BMSF and LAM-TCP. (A) Light microscopy images of hiPSC-RPE (plated as spherical aggregates) grown on BMSF membrane, COL1-BMSF membrane and LAM-TCP at D0-2, D14 and D40 displayed attachment, growth, and subsequently characteristic cobblestone morphology. Of note, images of hiPSC-RPE on BMSF and BMSF-COL1, for D0-D2, were taken on Day 1.
while images of hiPSC-RPE on LAM-TCP were taken on Day 2. Also, data from one single line, hiPSC-RPE Line 4, is presented in this panel. Furthermore, RPE monolayers that spread outward from the plated hiPSC-RPE spheres on BMSF unlike COL1-BMSF and LAM-TCP began to selectively retract by Day 40. Scale bar = 250 µm. (B) Light microscopy images of hiPSC-RPE (dissociated and plated) plated on either COL1-BMSF and LAM-TCP remained adherent and showed similar cobblestone morphology for > D60 in culture. Note: hiPSC-RPE line 5 is represented in this panel. Scale bar = 50 µm.
Figure S4. Phagocytosis/degradation of POS by hiPSC-RPE grown on COL1-BMSF vs. LAM-TCP. (A) Cumulative summary of quantitative Western blot analyses showing RHO levels in hiPSC-RPE cultures on COL1-BMSF and LAM-TCP at the 0h and 24h time points. (B-D) Quantitative analysis of RHO from three individual experiments showing i) POS uptake at 0h ((B) 968 %, (C) 92.9%, (D) 62.9% in COL1-BMSF relative to 100% in LAM-TCP) and ii) similar or better POS degradation at 24h ((B) 30.4% in COL1-BMSF vs. 49.9% in LAM-TCP, (C) 98.1% COL1-BMSF vs. 44.5% in LAM-TCP (D) 66.9% COL1-BMSF vs. 4.7% in LAM-TCP relative to the 0h uptake) in POS-fed hiPSC-RPE cultures grown on COL1-BMSF compared to LAM-TCP. hiPSC lines represented are (B) line 1, (C) line 2 and (D) line 5 demonstrating variability between lines in uptake and degradation of POS. ACTN served as loading control in these experiments.