

SUPPLEMENTARY FIGURE S1. Profiling of hiPSC-RPE cells. A) RNA

expression profiling was done for mature RPE markers RPE65, BEST1, RLBP1, and ITGB8, the melanogenesis marker TYR and stem cell markers OCT4 and SOX2 in total RNA derived from hiPSCs (lane 1) and hiPSC-RPE (lane 2). No RNA was added to the negative control (lane 3). RT-PCR was performed with gene-specific primers as given in Supplemental Table S1 and electrophoretically separated in a 2 % agarose gel. The housekeeping gene GUSB was used to control for RNA integrity. B) Relative VEGF secretion to apical and basal sides, followed by enzyme-linked immunosorbent assay. Data represent mean + SD of four independent replicates, calibrated against apically secreted VEGF. The asterisk marks a statistically significant (* = P < 0.05) difference. C) Immunofluorescence staining against lateral/basolateral markers Bestrophin-1 (BEST1, green) and zonula occludens 1 (ZO-1, red). Scale bars 20 µm. D) Vertical z-projection after immunofluorescence staining against BEST1 (green) and ZO-1 (red). Nuclei were visualized with Dapi (blue). E) Vertical z-projection after immunfluorescence stainings against apical markers Sodium/potassium-transporting ATPase subunit alpha-1 (ATP1A1, red) and Sodium/potassium-transporting ATPase subunit beta-1 (ATP1B1, red). Nuclei were visualized with Dapi (blue).



SUPPLEMENTARY FIGURE S2. Representative image of vitronectin detection in Western Blot analysis after SDS-PAGE. HEK293 cells were transfected with expression vectors for VTN rs704:C or VTN rs704:T, or with an empty expression vector (pcDNA3.1, control), 72 hours after transfection, cell pellets and supernatants of transfected cells were subjected to western blot analysis with antibodies against vitronectin. Only the full length 75 kDa isoform as well as the 65 kDa subfragment of the cleaved isoform were detected, no other protein (including the 10 kDa subfragment of cleaved vitronectin) was visible. For densitometric evaluation of vitronectin signals, protein bands between 100 kDa and 55 kDa were measured. This region is also shown in the vitronectin Western Blot images presented in the figures. The 10 kDa subfragment of the cleaved isoform was consequently not included in our measurement. However, the 10 kDa subfragment represents only 13.3 % of the amount of the cleaved isoform while the observed difference between VTN rs704:C and VTN rs704:T protein levels was about 400 % (see Fig. 2). Moreover, cell pellets almost exclusively revealed the uncleaved vitronectin isoform (see Fig. 2 and Supplementary Fig. S2). Exclusion of the 10 kDa subfragment of the cleaved isoform from the densitometric evaluation should therefore not significantly affect the observed difference in protein expression between VTN rs704:C and VTN rs704:T.



SUPPLEMENTARY FIGURE S3. Purification of Streptagged vitronectin isoforms. Purified vitronectin isoforms were subjected to SDS-PAGE and analyzed via (A) silver staining, (B) Coomassie Blue staining and (C) immunoblot using antibodies against vitronectin. Control: protein from supernatant of empty expression vector transfected cells.



SUPPLEMENTARY FIGURE S4. Genomic sequencing of variant rs704 in hiPSC-RPE cells (A) or human retinal tissues (B) of different donors.

0 hours



SUPLLEMENTARY FIGURE S5. Representative micrographs of HUVECs subjected to the scratch assay in the presence of recombinant VTN_rs704:C, VTN_rs704:T, or control eluate. 14 hours after the scratch was set, HUVEC migration was followed microscopically (upper panels). The area closed was measured *via* ImageJ (National Institute of Health) (lower panels, processed pictures).