

Supporting information

LC-MS/MS Based Quantitation of ABC and SLC transporter proteins in plasma membranes of cultured primary human retinal pigment epithelium cells and immortalized ARPE19 cell line

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Characterization of human fetal retinal pigment epithelial (hfRPE) cells

In this study, retinal pigment epithelial (RPE) cell-specific characteristics of human fetal primary RPE (hfRPE) cells (HRPEpiC, 6540, lot 12612, ScienCell Research Laboratories, San Diego, CA, USA) were investigated. After 30 days of culture, pigmentation, cell morphology and photoreceptor outer segment (POS) phagocytosis activity were analyzed. In addition, expression of differentiation markers such as retinal pigment epithelium-specific 65 kDa protein (RPE65), tyrosinase-related protein 1 (TYRP1), microphthalmia-associated transcription factor isoform A (MITF-A) as well as markers for tight junctions (occludin and zonula occludens 1, ZO-1), apical microvilli (ezrin) and plasma membrane proteins monocarboxylate transporter 1 (MCT1), multidrug resistance-associated protein 1 (MRP1) and bestrophin 1 (BEST1) were studied.

METHODS

Cell culture optimization, immunoblotting and qRT-PCR. Preliminary study regarding the requirement of extracellular matrix (fibronectin or laminin) for differentiation of the cells was performed. At passage 3, hfRPE cells were seeded at high density (200 000 cells/cm²) on laminin or fibronectin coated (5 µg/cm², 0.5 µg/cm² and 0.05 µg/cm²) and on non-coated culture dishes and cultured for 30 days. After a month in culture, the protein levels of TYRP1 (ab83774, Abcam, Cambridge, UK) and BEST1 (NB300-164, Novus Biologicals, Abingdon, UK) were studied with immunoblotting. In addition, specific PCR primers and probes were used for quantitation of RPE65 (Hs00165642, Applied Biosystems), TYRP1 (forward 5'-gaccagagggtctcatagtgcagg-3 and reverse 5'-tgacaaataaagggtgagttgtgc-3) and MITF-A (Hs01115553_m1, Applied Biosystems), mRNA levels. RNA was isolated using RNeasy Micro Kit (74004, Qiagen, Hilden, Germany) according to manufacturer's instructions. Mean normalized mRNA expression was calculated using Q-GENE program with beta-actin expression.

Immunofluorescence staining. After culture of 30 days the hfRPE cells were immunostained with primary antibodies for occludin (71-1500, Thermo Fisher Scientific Inc. Rockford, IL, USA), ZO-1 (AB0054-200, SICGEN, Coimbra, Portugal), ezrin (sc-58758, Santa Cruz Biotechnology Inc.),

MCT1 (ab90582, Abcam, Cambridge, UK), MRP1 (ab3368, Abcam, Cambridge, UK) and BEST1 (NB300-164, Novus Biologicals, Abingdon, UK).

Shortly, cells cultured on Ibidi μ -Slides (80826, Ibidi GmbH, Martinsried, Germany) were fixed with 4% paraformaldehyde for 15 min and permeabilized and blocked with 0.1% Triton X-100, 1% BSA in PBS for 45 min (tight-junction proteins occludin and ZO-1 were exceptionally fixed with methanol at -20 °C for 4 hours). After permeabilization, cells were incubated with primary antibodies at dilution 1:100 for 1h at room temperature. Incubation with specific Alexa Fluor® (Thermo Fisher Scientific Inc.) secondary antibodies (dilution 1:500) was carried out at room temperature for 1 h. Cell nuclei were stained with DAPI (P36931, Thermo Fisher Scientific Inc. Bleiswijk, Netherlands). Samples were visualized with Zeiss LSM 800 Airyscan confocal microscope (Carl Zeiss) using 40x or 63x oil immersion objectives.

Photoreceptor outer segment (POS) phagocytosis assay. Fresh porcine eye balls for POS isolation were obtained from the local slaughterhouse. After removal of anterior segment of the eye and vitreous, neural retina was collected for POS isolation. Ten retinas were suspended in 10 ml of 8% Optiprep (Axis Shield, Oslo, Norway) in 0.18M sodium bicarbonate buffer (pH 8.3) and vortexed at maximum speed for 1 min. Homogenate was centrifuged at 720 g for 3 min, and the supernatant was removed and collected in a new tube (centrifugation step was repeated five times). Finally, the supernatant was diluted with 3 volumes of 0.18M sodium bicarbonate buffer and centrifuged at 4400g for 30 min. After centrifugation, pellet was dissolved in 500 μ l of 0.18M sodium bicarbonate buffer and laid carefully on top of the discontinuous gradient formed from 10% and 20% Optiprep. The gradient was centrifuged at 4400 g for 30 min. The interface layer of two Optiprep layers was collected, diluted with 4 volumes of sodium bicarbonate buffer and centrifuged at 14 000g for 30 min. The pellet was washed with 1 ml of sodium bicarbonate buffer and finally, after centrifugation, resuspended in 300 μ l of sodium bicarbonate buffer.

POS labeling with fluorescein isothiocyanate (FITC) was carried out overnight according to manufacturer's protocol (F7250, Sigma, MO, USA) with minor modifications. Shortly, 2 mg of POS was incubated overnight with 0.05 mg of FITC at +4°C, in the dark. After labeling, unbound FITC was removed by 5x centrifugation-washing cycle (14000 g for 5 min, at +4°C combined with 1xPBS washing). For phagocytosis assay, cells cultured on Ibidi μ -Slides were incubated with 10 μ g of labeled FITC-POS/cm² of culture area for 20 hours. Before fixing and immunofluorescence staining with MCT1 or rhodopsin (RET-P1, NeoMarkers, Fremont, CA, USA) antibody, cells were washed four times with 1x PBS to verify removal of not internalized FITC-POS. Slides were visualized with Zeiss LSM 800 Airyscan confocal microscope (Carl Zeiss) using 63x oil immersion objective.

RESULTS

hfRPE cells cultured on non-coated cell culture surfaces display characteristics of RPE cells. BEST1 and TYRP1 protein expression levels were similar whether the cells were cultured on non-coated culture dishes or in the presence of extracellular matrix (data not shown). Furthermore, the mRNA levels were highest in the cells cultured without extracellular matrix (Figure S1). Therefore, for the further investigations and for the actual experiments described in the manuscript, the cells were cultured on regular culture dishes without any extracellular matrix.

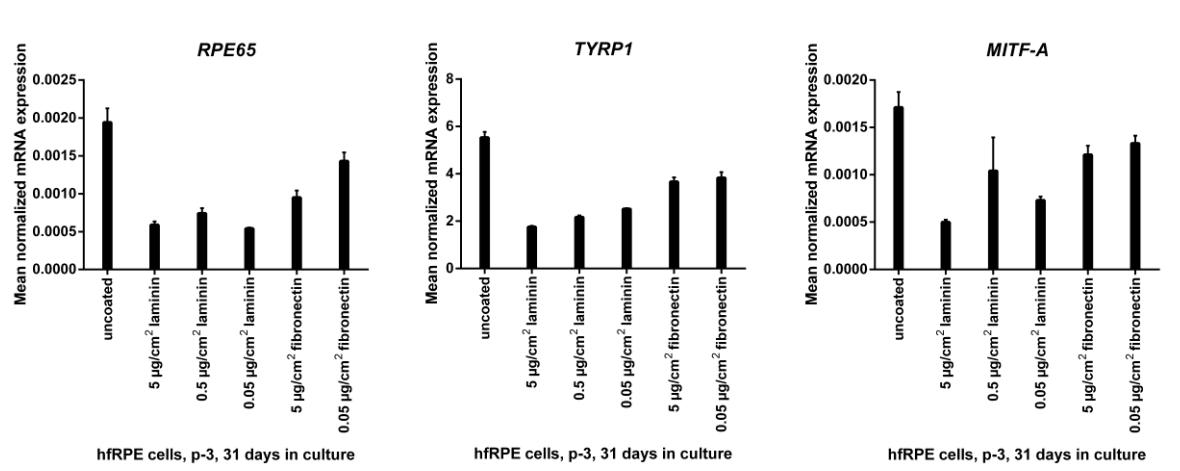


Figure S1. Extracellular matrix did not induce expression of RPE-specific marker genes. mRNA expression of RPE65, MITF-A and TYRP1 was the highest in the hfRPE cells cultured on culture dishes without laminin or fibronectin coating.

hfRPE cells are capable for melanin synthesis (Figure S2). In hfRPE cultures, patchy pigmentation was observed after 2 weeks of cultivation and it was more evident at day 30. Furthermore, the cells started to form fluid filled domes after 2 weeks in culture indicating tight junction formation and apical-basolateral polarity (Figure S3).

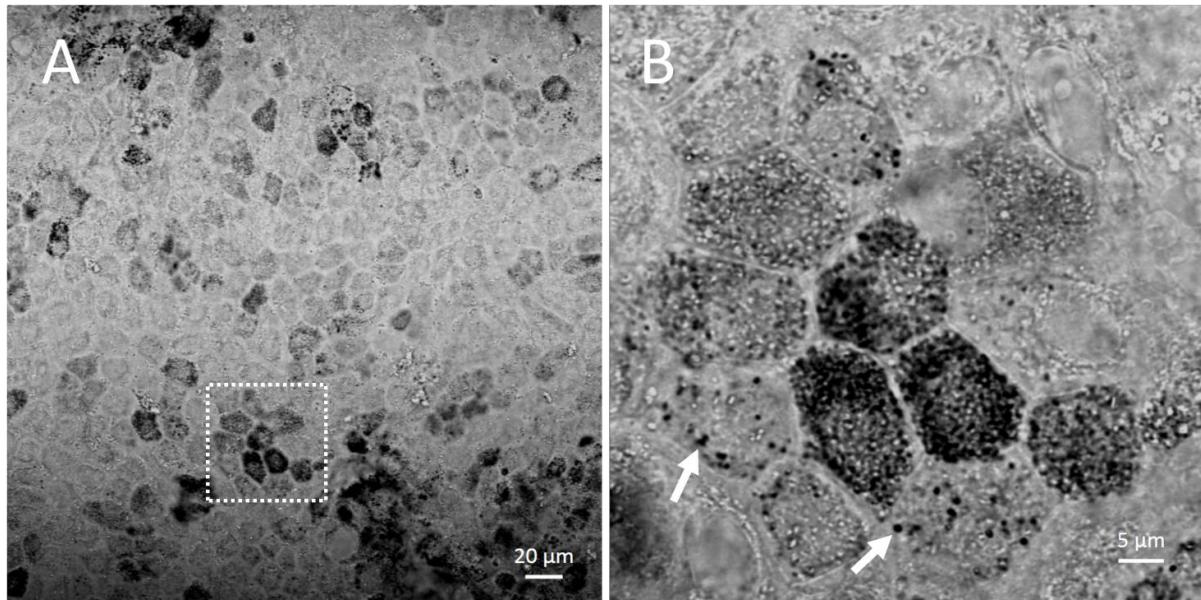


Figure S2. hfRPE cells display typical RPE cell morphology and pigmentation. After 30 days of culture, typical hexagonal RPE cells with pigmentation were observed. In Figure S1B (inset of boxed area in figure A), individual pigmented cell organelles, melanosomes, are indicated by arrows. Cells were visualized by using Zeiss LSM 800 Airyscan confocal microscope (Carl Zeiss) with electronically switchable illumination and detection module (ESID).

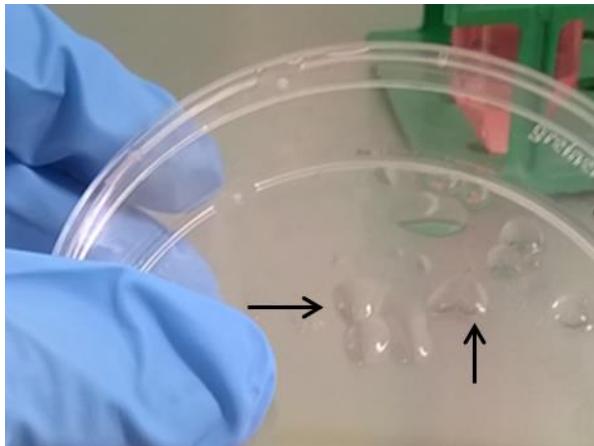


Figure S3. Fluid filled domes were formed in hRPE cell cultures indicating differentiated and polarized cell population after 30 days in culture. After approximately 2 weeks in culture, domes filled with growth medium started to appear in the cell culture. After 30 days in culture, high number of domes were observed in the culture dishes indicating proper apical-basolateral polarity and the presence of tight junctions.

In addition, hRPE cells express specific markers essential for RPE function (Figure S4). Immunofluorescence staining shows apparent expression of tight junction proteins occludin and ZO-1 as well as apical microvilli-specific protein ezrin and transmembrane proteins MCT1, MRP1 and BEST1 in hRPE cells. MCT1 was clearly localized at the apical plasma membrane already after 2 weeks of culture indicating RPE polarization. Whereas, Na⁺/K⁺ATPase, generally suggested as an apical marker, was localized in both, apical and basolateral membrane (data not shown).

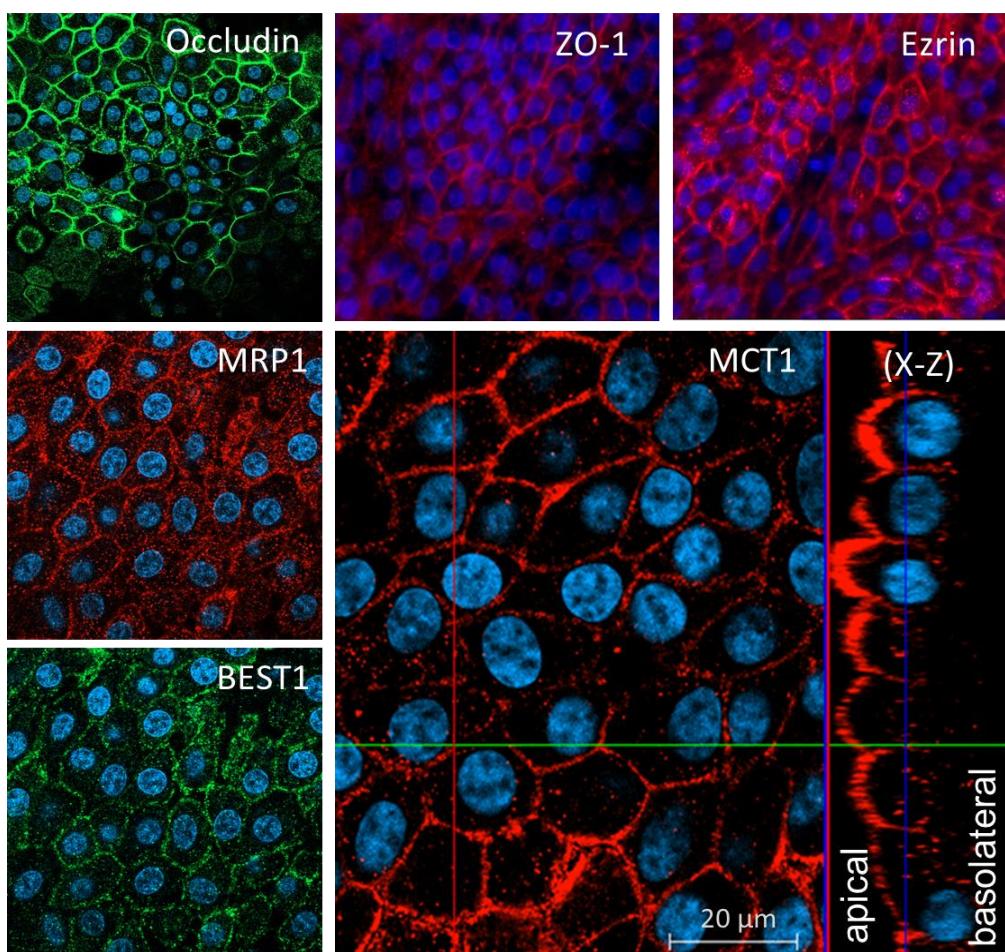


Figure S4. Several RPE-differentiation markers are expressed in hRPE cells. After 30 days of culture, degree of RPE cell differentiation was studied by using immunofluorescence staining with specific antibodies for tight junction proteins occludin (green) and zonula occludens 1 (ZO-1, red) as well as for microvilli-specific protein, ezrin (red) and plasma membrane proteins multi-drug resistance associated protein 1 (MRP1, red) and bestrophin 1 (BEST1, green). Moreover, already after 2 weeks of culture, apical localization of plasma membrane protein monocarboxylate transporter 1 (MCT1, red) was observed (vertical X-Z section image) indicating cell polarization. DAPI stained cell nuclei are in blue.

hfRPE cells display POS phagocytosis activity. In the retina, RPE cells are substantial for renewal of photoreceptors by phagocytosing the shed POS. In phagocytosis assay, after 20 hours of FITC-POS incubation, internalized FITC-POS were clearly observed in hfRPE cells. Internalization of FITC-POS was studied by counterstaining cells with apically localized plasma membrane protein MCT1 (Figure S5A). Immunofluorescence staining with rhodopsin-specific antibody showed colocalization with FITC-POS (Figure S5B).

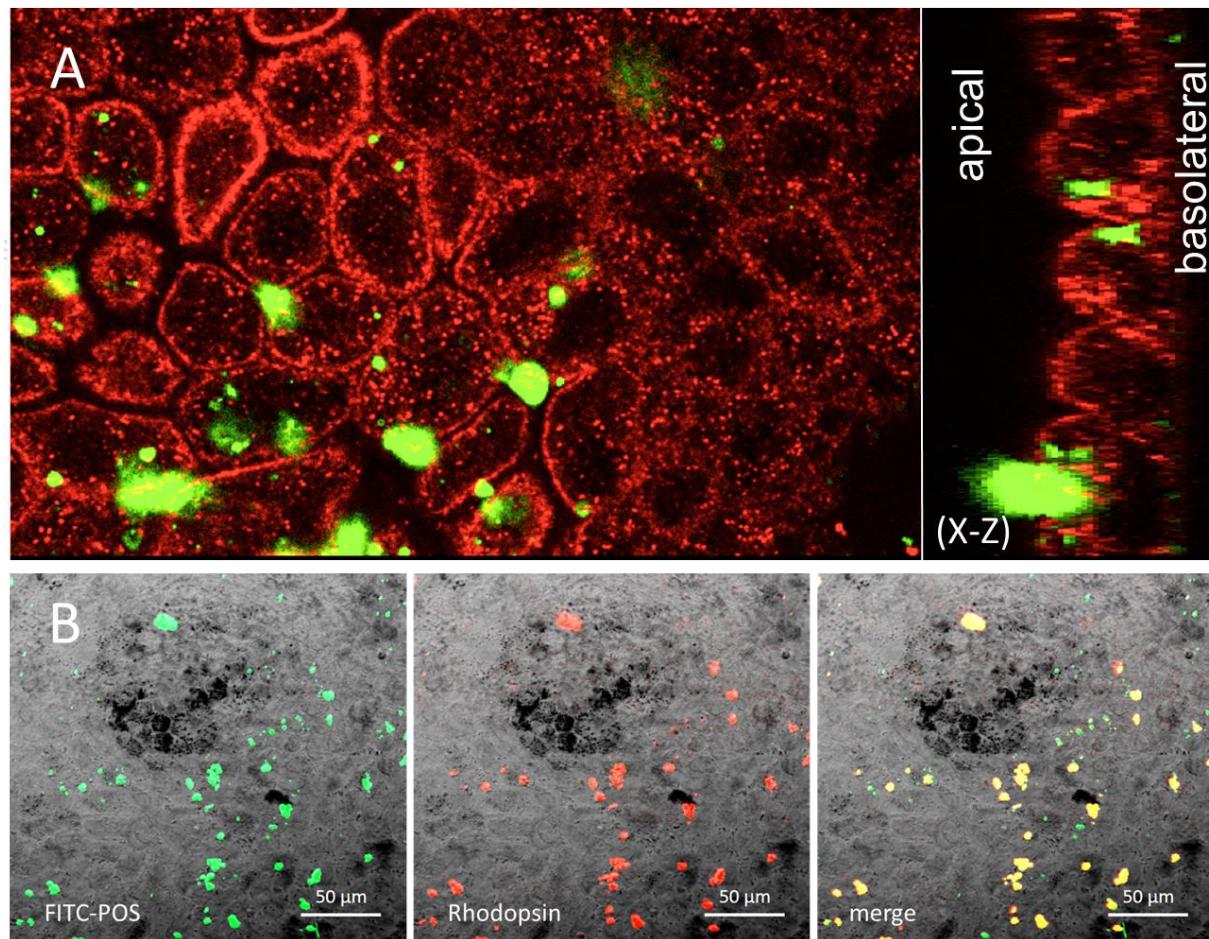


Figure S5. hfRPE cells display phagocytic activity. Confocal microscope image of hfRPE cells cultured on Ibidi slides for 30 days. Cells were exposed to FITC labeled photoreceptor outer segments (FITC-POS, green) for 20 hours. **(A)** After FITC-POS incubation, cells were washed and counterstained with MCT1 (red) localized in plasma membrane. The vertical (X-Z) section image (right panel) shows internalized FITC-POS in hfRPE cells. **(B)** The merged image (yellow) shows colocalization of immunofluorescence stained rhodopsin (red) with phagocytosed FITC-POS (green).

Characterization of ARPE19 cells

Tight junction formation was studied in ARPE19, an immortalized human retinal pigment epithelial cell line by studying the expression of occludin and zonula occludens 1 (ZO-1) with immunofluorescence staining and confocal microscopy. In addition, the expression and localization of MRP1 in ARPE19 cells was investigated.

METHODS

Immunofluorescence staining. ARPE19 cells were cultured for 31 days on ibidi slides (80826, Ibidi GmbH, Martinsried, Germany). Immunostaining and confocal microscopy was carried out as with hfRPE cells using occludin (71-1500, Thermo Fisher Scientific Inc. Rockford, IL, USA), ZO-1 (AB0054-200, SICGEN, Coimbra, Portugal) and MRP1 (ab3368, Abcam, Cambridge, UK) primary antibodies and specific Alexa Fluor® (Thermo Fisher Scientific Inc.) secondary antibodies and nuclei stain DAPI (P36931, Thermo Fisher Scientific Inc. Bleiswijk, Netherlands). Visualization was conducted with Zeiss LSM 800 Airyscan confocal microscope (Carl Zeiss) using 40x or 63x oil immersion objectives.

RESULTS

Tight junction formation. ARPE19 cells represented the expression of tight junction proteins ZO-1 and occludin (Fig. S6 A-C). The expression was mainly localized on the plasma membrane and the co-localization was confirmed (Fig. S6 C). The x-z plane shows, that tight junctional proteins were expressed on the lateral plasma membranes (Fig. S6 C). ARPE19 cells represented clear MRP1 expression on the apical plasma membrane.

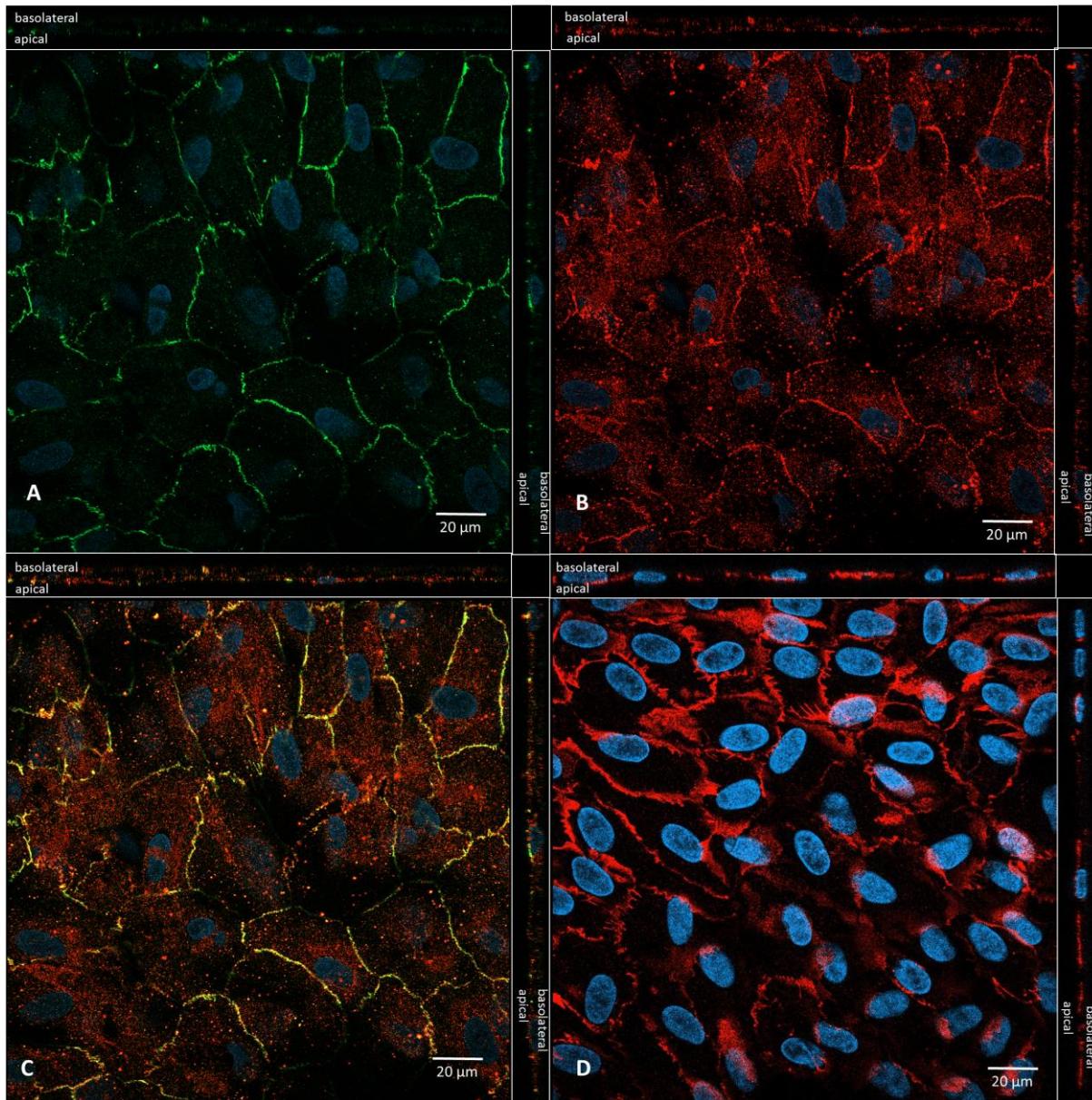


Figure S6. ARPE19 cells represent tight junction proteins occludin (green) and ZO-1 (red) and polarized expression of Multi-drug resistance associated protein 1 (MRP1, red) after 31 days in culture. Occludin (A, C) and zonula occludens 1 (ZO-1; B, C) expression were detected in ARPE19 cells cultured on ibidi slides for 31 days using immunofluorescence staining. Multi-drug resistance associated protein 1 (MRP1) localized on the apical plasma membrane in ARPE19 cells (D).

Table S1. Target peptide transitions in LC-MS/MS analysis

Uni-Prot Accession No.	Gene symbol	Alias	St/Is	Probe Sequence	SRM/MRM transition (<i>m/z</i>)				
					Q1	Q3-1	Q3-2	Q3-3	Q3-4
<i>ABC transporters</i>									
P78363	ABCA4	ABCR	St	VLPULLDSR	507.3	801.4	603.3	704.4	914.5
			Is	VLPULL*DSR	510.8	808.4	610.3	711.4	921.5
O94911	ABCA8	ABCA8	St	GILPQEVDK	499.8	414.9	358.2	828.4	715.4
			Is	GILPQEVE*DK	502.8	417.9	361.2	834.4	721.4
P08183	ABCB1	P-gp, MDR1	St	NTTGALTR	467.8	618.4	719.4	490.3	561.3
			Is	NTTGAL*TR	471.3	625.4	726.4	497.3	568.3
P21439	ABCB4	MDR3	St	IATEAIENIR	565.3	531.3	715.4	644.4	844.5
			Is	IATEA*IENIR	567.3	531.3	719.4	644.4	848.5
Q2M3G0	ABCB5	ABCB5	St	YNTQVGLK	461.8	759.4	645.4	416.3	317.2
			Is	YNTQVGL*K	465.3	766.4	652.4	423.3	324.2
O95342	ABCB11	BSEP	St	STALQLIQR	515.3	529.3	657.4	841.5	770.5
			Is	STALQL*IQR	518.8	536.3	664.4	848.5	777.5
P33527	ABCC1	MRP1	St	TPSGNLVNR	479.3	759.4	672.4	501.3	615.4
			Is	TPSGNL*VNR	482.8	766.4	679.4	508.3	622.4
Q92887	ABCC2	MRP2	St	QLLNNILR	492.3	742.5	629.4	515.3	401.3
			Is	QLLNNIL*R	495.8	749.5	636.4	522.3	408.3
O15438	ABCC3	MRP3	St	AEGEISDPFR	560.8	621.3	734.4	920.4	534.3
			Is	AEGEISDPF*R	565.8	631.3	744.4	930.4	544.3
O15439	ABCC4	MRP4	St	APVLLFFDR	482.8	584.3	697.4	796.4	893.5
			Is	APVL*FFDR	486.3	584.3	704.4	803.4	900.5
O15440	ABCC5	MRP5	St	SLSEASAVAVDR	567.3	646.4	717.4	933.5	559.3
			Is	SL*SEASAVAVDR	570.8	646.4	717.4	933.5	559.3
O95255	ABCC6	MRP6	St	APETEPFLR	530.3	532.3	762.4	891.5	661.4
			Is	APETEPFL*R	533.8	539.3	769.4	898.5	668.4
Q5T3U5	ABCC10	MRP7	St	VFTALALVR	495.3	743.5	571.4	458.3	642.4
			Is	VFTALAL*VR	498.8	750.5	578.4	465.3	649.4
Q96J66	ABCC11	MRP8	St	FNLDPFDR	512.2	534.3	762.4	649.3	437.2
			Is	FNLDPF*DR	517.2	544.3	772.4	659.3	447.2
Q9UNQ0	ABCG2	BCRP	St	SLLSDVLAAR	522.8	644.4	757.5	529.3	430.3
			Is	SLLSDVLR*AAR	526.3	651.4	764.5	536.3	437.3
<i>SLC transporters</i>									
P11166	SLC2A1	GLUT1	St	TFDEIASGFR	571.7	537.3	894.4	779.4	650.4
			Is	TFDEIA*SGFR	573.7	541.3	898.4	783.4	654.4
P08195	SLC3A2	4F2hc	St	ADLLLSTQPGR	585.8	645.3	871.5	758.4	558.3
			Is	ADLLLSTQP*GR	588.8	651.3	877.5	764.4	564.3
P31641	SLC6A6	TAUT	St	FYLYPDITR	594.3	601.3	877.5	764.4	504.3
			Is	FYLYPDI*TR	597.8	608.3	884.5	771.4	511.3
P30825	SLC7A1	CAT1	St	FLANVNDR	474.8	617.3	688.3	503.3	801.4
			Is	FLANVN*DR	477.8	623.3	694.3	509.3	807.4
Q01650	SLC7A5	LAT1	St	VQDAFAAAK	460.7	693.4	360.2	578.3	821.4
			Is	VQDAFAA*A	462.7	697.4	364.2	582.3	825.4
P46059	SLC15A1	PEPT1	St	TLPVFPK	401.2	587.4	244.2	215.1	391.2
			Is	TLPVFP*K	404.2	593.4	250.2	215.1	397.2
P53985	SLC16A1	MCT1	St	SITVFK	421.2	641.4	294.2	441.3	540.3
			Is	SITVFP*K	426.2	651.4	304.2	451.3	550.3
O15427	SLC16A3	MCT4	St	LLDLSVFR	481.8	849.5	736.4	621.4	508.3
			Is	LLDLSVF*R	486.8	859.5	746.4	631.4	518.3
O95907	SLC16A8	MCT3	St	AVSVFVR	413.2	655.4	469.3	568.3	754.4
			Is	AVSVFVR	418.2	665.4	479.3	578.3	764.4
P41440	SLC19A1	RFC1	St	QPPAQGLR	433.7	641.4	345.2	473.3	544.3
			Is	QPPAQGL*R	437.2	648.4	352.2	480.3	551.3
Q9Y6L6	SLCO1B1	OATP1B1	St	NVTGFFQSFK	587.8	961.5	381.2	860.4	656.3
			Is	NVTGFFQSFK*	591.8	969.5	389.2	868.4	664.3
Q9NPD5	SLCO1B3	OATP1B3	St	NVTGFFQSLK	570.8	214.1	927.5	622.4	315.2
			Is	NVTGFFQSLK*	574.8	214.1	935.5	630.4	315.2
O15245	SLC22A1	OCT1	St	LSPSFADLFR	576.8	476.7	768.4	855.4	621.3
			Is	LSPSFADL*FR	580.3	480.2	775.4	862.4	628.3
O15244	SLC22A2	OCT2	St	SLPASLQR	436.2	336.2	671.4	503.3	574.3
			Is	SLPASL*QR	439.7	339.7	678.4	510.3	581.3
O75751	SLC22A3	OCT3	St	FLQGVFGK	448.2	635.4	507.3	351.2	748.4
			Is	FLQGVF*GK	453.2	645.4	517.3	361.2	758.4
O76082	SLC22A5	OCTN2	St	TWNIR	345.2	402.2	260.1	288.2	588.3
			Is	TWNIR*	348.7	409.2	260.1	295.2	595.3
Q4U2R8	SLC22A6	OAT1	St	TSLAVLGK	394.7	600.4	487.3	317.2	416.3
			Is	TSLAVL*GK	398.2	607.4	494.3	324.2	423.3

The optimized SRM/MRM transitions were selected from MS/MS spectra measured with the infusion of each standard peptide into the mass spectrometer. Doubly charged precursor ions were selected as Q1 and four transitions (Q3-1, -2, -3 and -4), determined from high intensity spectra, were selected. St and Is mean respectively standard peptides and internal standard peptides. The stable isotope labeled amino acids were indicated with *.

Table S1. Target peptide transitions in LC-MS/MS analysis (Continued)

Uni-Prot Accession No.	Gene symbol	Alias	St/Is	Probe Sequence	SRM/MRM transition (<i>m/z</i>)				
					Q1	Q3-1	Q3-2	Q3-3	Q3-4
<i>SLC transporters</i>									
Q9Y694	SLC22A7	OAT2	St	NVALLALPR	483.8	753.5	569.4	456.3	682.5
			Is	NVALLAL*PR	487.3	760.5	576.4	463.3	689.5
Q8TCC7	SLC22A8	OAT3	St	YTASDLFR	486.7	708.4	435.3	637.3	809.4
			Is	YTASDL*FR	490.2	715.4	442.3	644.3	816.4
Q9NSA0	SLC22A11	OAT4	St	VVFAVLGK	416.8	634.4	487.3	416.3	733.5
			Is	VVFAVL*GK	420.3	641.4	494.3	423.3	740.5
Q96NT5	SLC46A1	PCFT	St	SIVQLYVAPAPEK	707.9	541.3	874.5	612.3	711.4
			Is	SIVQLYVAPAP*EK	710.9	547.3	880.5	618.3	717.4
Q96FL8	SLC47A1	MATE1	St	GGPEATLEVR	514.8	457.8	617.4	688.4	817.4
			Is	GGPEATLEV*R	517.8	460.8	623.4	694.4	823.4
Q86VL8	SLC47A2	MATE2	St	YLQNQGWLK	575.3	873.5	745.4	631.4	986.5
			Is	YLQNQGWL*K	578.8	880.5	752.4	638.4	993.5
Q86VL8-3	SLC47A2	MATE2k	St	YLQNQK	397.2	630.4	517.3	389.2	275.2
			Is	YL*QNQK	400.7	637.4	517.3	389.2	275.2
<i>Marker protein and other</i>									
P05023, Q5RCD8, P13637	ATP1A1, ATP1A2, ATP1A3	Na ⁺ /K ⁺ ATPase (α1, α2, α3 subunits)	St	AAVPDAVGK	414.2	685.4	586.3	489.3	374.2
			Is	AAVPDAV*GK	417.2	691.4	592.3	495.3	380.2
P09327	VIL1	Villin1	St	DPETPIIVVK	555.8	668.5	769.5	246.2	345.3
			Is	DPETPIIVVK*	559.8	676.5	777.5	254.2	353.3

The optimized SRM/MRM transitions were selected from MS/MS spectra measured with the infusion of each standard peptide into the mass spectrometer. Doubly charged precursor ions were selected as Q1 and four transitions (Q3-1, -2, -3 and -4), determined from high intensity spectra, were selected. St and Is mean respectively standard peptides and internal standard peptides. The stable isotope labeled amino acids were indicated with *.

Table S2. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of hfRPE and ARPE19 cells^a

	Protein expression levels (fmol/µg protein)							
	hfRPE			ARPE19				
	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions		
ABCC1/MRP1	1.16 ± 0.06	0.592 ± 0.204	1.36 ± 0.41	1.28 ± 0.32	1.80 ± 0.76	4.00 ± 2.68		
ABCC4/MRP4	0.0660 ± 0.0055	0.0488 ^b	0.0995 ^b	0.454 ± 0.204	0.591 ± 0.223	1.59 ± 0.53		
ABCC5/MRP5	0.451 ± 0.012	0.369 ^b	0.789 ± 0.004	U.L.Q.(<0.0821)	U.L.Q.(<0.148)	1.10 ^b		
ABCC10/MRP7	U.L.Q.(<0.166)	0.562 ^b	0.782 ^b	U.L.Q.(<0.136)	U.L.Q.(<0.165)	U.L.Q.(<0.113)		
SLC2A1/GLUT1	169 ± 8	142 ± 39	337 ± 44	54.1 ± 12.4	90.9 ± 32.2	205 ± 85		
SLC3A2/4F2hc	1.68 ± 0.16	1.39 ± 0.57	3.81 ± 0.56	2.48 ± 1.08	4.06 ± 1.51	12.5 ± 2.9		
SLC6A6/TAUT	0.374 ± 0.007	0.343 ± 0.088	0.499 ± 0.046	U.L.Q.(<0.0135)	0.169 ± 0.050	0.441 ± 0.175		
SLC7A1/CAT1	0.856 ± 0.055	1.15 ± 0.56	2.26 ± 0.07	0.653 ± 0.218	0.992 ± 0.527	1.65 ± 0.63		
SLC7A5/LAT1	U.L.Q.(<0.257)	U.L.Q.(<0.220)	0.721 ± 0.540	U.L.Q.(<0.194)	U.L.Q.(<0.177)	2.34 ± 0.51		
SLC16A1/MCT1	1.13 ± 0.12	0.977 ± 0.422	3.14 ± 0.96	3.61 ± 1.62	5.90 ± 1.85	15.1 ± 5.3		
SLC16A3/MCT4	5.89 ± 2.73	3.24 ± 2.61	6.91 ± 0.61	6.59 ± 4.49	9.39 ± 5.83	35.2 ± 13.7		
SLC19A1/RFC1	U.L.Q.(<0.333)	1.04 ^c	1.20 ± 0.46	U.L.Q.(<0.365)	U.L.Q.(<0.265)	U.L.Q.(<0.650)		
SLC22A7/OAT2	U.L.Q.(<0.0186)	U.L.Q.(<0.0152)	0.207 ^b	U.L.Q.(<0.251)	U.L.Q.(<0.195)	U.L.Q.(<0.205)		
SLC46A1/PCFT	0.497 ± 0.315	1.58 ± 0.35	4.91 ± 1.20	U.L.Q.(<0.113)	U.L.Q.(<0.105)	0.588 ^c		
SLC47A1/MATE1	0.270 ± 0.045	0.433 ± 0.152	0.851 ± 0.092	U.L.Q.(<0.215)	U.L.Q.(<0.162)	1.58 ± 0.46		
Na ⁺ /K ⁺ ATPase	5.87 ± 1.11	6.08 ± 2.26	12.2 ± 3.1	13.4 ± 1.8	24.8 ± 8.1	59.9 ± 26.5		
ABCA4/ABCR	U.L.Q.(<0.111)	U.L.Q.(<0.104)	U.L.Q.(<0.114)	U.L.Q.(<0.0469)	U.L.Q.(<0.0421)	U.L.Q.(<0.0379)		
ABCA8/ABCA8	U.L.Q.(<0.0163)	U.L.Q.(<0.0204)	U.L.Q.(<0.0210)	U.L.Q.(<0.0633)	U.L.Q.(<0.0605)	U.L.Q.(<0.0509)		
ABCB1/P-gp/MDR1	U.L.Q.(<0.143)	U.L.Q.(<0.138)	U.L.Q.(<0.175)	U.L.Q.(<0.0505)	U.L.Q.(<0.0756)	U.L.Q.(<0.0927)		
ABCB4/MDR3	U.L.Q.(<0.0173)	U.L.Q.(<0.0166)	U.L.Q.(<0.0200)	U.L.Q.(<0.146)	U.L.Q.(<0.132)	U.L.Q.(<0.116)		
ABCB5/ABCB5	U.L.Q.(<0.0619)	U.L.Q.(<0.172)	U.L.Q.(<0.0558)	U.L.Q.(<0.192)	U.L.Q.(<0.169)	U.L.Q.(<0.158)		
ABCB11/BSEP	U.L.Q.(<0.00629)	U.L.Q.(<0.00740)	U.L.Q.(<0.0170)	U.L.Q.(<0.132)	U.L.Q.(<0.116)	U.L.Q.(<0.115)		
ABCC2/MRP2	U.L.Q.(<0.215)	U.L.Q.(<0.203)	U.L.Q.(<0.218)	U.L.Q.(<0.116)	U.L.Q.(<0.128)	U.L.Q.(<0.116)		
ABCC3/MRP3	U.L.Q.(<0.118)	U.L.Q.(<0.121)	U.L.Q.(<0.0911)	U.L.Q.(<0.0960)	U.L.Q.(<0.0625)	U.L.Q.(<0.0709)		
ABCC6/MRP6	U.L.Q.(<0.0140)	U.L.Q.(<0.0185)	U.L.Q.(<0.0213)	U.L.Q.(<0.0548)	U.L.Q.(<0.0516)	U.L.Q.(<0.0460)		
ABCC11/MRP8	U.L.Q.(<0.393)	U.L.Q.(<0.390)	U.L.Q.(<0.395)	U.L.Q.(<0.0887)	U.L.Q.(<0.0567)	U.L.Q.(<0.0592)		
ABCG2/BCRP	U.L.Q.(<0.294)	U.L.Q.(<0.294)	U.L.Q.(<0.297)	U.L.Q.(<0.0672)	U.L.Q.(<0.0688)	U.L.Q.(<0.0633)		

^a The expression levels were described as mean ± S.D. determined from the average values of hfRPE and ARPE19 cells. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The expression levels were calculated as the average values obtained from two samples.

^c The expression level was obtained from one sample. U.L.Q.: under the limit of quantification; a value in brackets following "U.L.Q." represents the values of the quantification limit (fmol/µg protein).

Table S2. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of hfRPE and ARPE19^a (Continued)

	Protein expression levels (fmol/µg protein)					
	hfRPE			ARPE19		
	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions
SLC15A1/PEPT1	U.L.Q.(<0.0182)	U.L.Q.(<0.00897)	U.L.Q.(<0.0194)	U.L.Q.(<0.0397)	U.L.Q.(<0.0386)	U.L.Q.(<0.0364)
SLC16A8/MCT3	U.L.Q.(<0.264)	U.L.Q.(<0.258)	U.L.Q.(<0.260)	U.L.Q.(<0.102)	U.L.Q.(<0.104)	U.L.Q.(<0.0983)
SLC21A6/OATP1B1	U.L.Q.(<1.13)	U.L.Q.(<1.15)	U.L.Q.(<1.13)	U.L.Q.(<0.146)	U.L.Q.(<0.0938)	U.L.Q.(<0.103)
SLC21A8/OATP1B3	U.L.Q.(<0.301)	U.L.Q.(<0.272)	U.L.Q.(<0.209)	U.L.Q.(<0.152)	U.L.Q.(<0.138)	U.L.Q.(<0.132)
SLC22A1/OCT1	U.L.Q.(<1.67)	U.L.Q.(<1.68)	U.L.Q.(<1.69)	U.L.Q.(<0.0391)	U.L.Q.(<0.0195)	U.L.Q.(<0.0301)
SLC22A2/OCT2	U.L.Q.(<0.0734)	U.L.Q.(<0.0768)	U.L.Q.(<0.0750)	U.L.Q.(<0.0852)	U.L.Q.(<0.0761)	U.L.Q.(<0.0709)
SLC22A3/OCT3	U.L.Q.(<0.124)	U.L.Q.(<0.119)	U.L.Q.(<0.106)	U.L.Q.(<0.0653)	U.L.Q.(<0.0442)	U.L.Q.(<0.0581)
SLC22A5/OCTN2	U.L.Q.(<0.127)	U.L.Q.(<0.121)	U.L.Q.(<0.132)	U.L.Q.(<0.119)	U.L.Q.(<0.0954)	U.L.Q.(<0.0927)
SLC22A6/OAT1	U.L.Q.(<0.0641)	U.L.Q.(<0.0623)	U.L.Q.(<0.0639)	U.L.Q.(<0.0230)	U.L.Q.(<0.0224)	U.L.Q.(<0.0226)
SLC22A8/OAT3	U.L.Q.(<0.291)	U.L.Q.(<0.0785)	U.L.Q.(<0.220)	U.L.Q.(<0.123)	U.L.Q.(<0.0628)	U.L.Q.(<0.0723)
SLC22A11/OAT4	U.L.Q.(<0.00950)	U.L.Q.(<0.00640)	U.L.Q.(<0.0130)	U.L.Q.(<0.152)	U.L.Q.(<0.0955)	U.L.Q.(<0.111)
SLC47A2/MATE2	U.L.Q.(<0.236)	U.L.Q.(<0.237)	U.L.Q.(<0.294)	U.L.Q.(<0.410)	U.L.Q.(<0.218)	U.L.Q.(<0.176)
SLC47A2/MATE2k	U.L.Q.(<0.118)	U.L.Q.(<0.427)	U.L.Q.(<0.134)	U.L.Q.(<2.35)	U.L.Q.(<2.15)	U.L.Q.(<1.90)
Villin1	U.L.Q.(<0.171)	U.L.Q.(<0.178)	U.L.Q.(<0.188)	U.L.Q.(<0.110)	U.L.Q.(<0.103)	U.L.Q.(<0.0969)

^a The expression levels were described as mean ± S.D. determined from the average values of hfRPE and ARPE19 cells. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The expression levels were calculated as the average values obtained from two samples.

^c The expression level was obtained from one sample. U.L.Q.: under the limit of quantification; a value in brackets following "U.L.Q." represents the values of the quantification limit (fmol/µg protein).

Table S3. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of three hfRPE samples

	Protein expression levels (fmol/µg protein)					
	1 ^a			2 ^a		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction
ABCC1/MRP1	1.22 ± 0.17	0.821 ± 0.151	1.78 ± 0.21	1.11 ± 0.23	0.528 ^c	1.34 ± 0.12
ABCC4/MRP4	U.L.Q.(<1.37)	U.L.Q.(<0.811)	U.L.Q.(<0.261)	0.0621 ± 0.0263	0.0406 ± 0.0170	0.124 ^c
ABCC5/MRP5	0.445 ^c	0.423 ^c	0.787 ± 0.139	0.444 ^c	U.L.Q.(<0.243)	0.794 ± 0.175
ABCC10/MRP7	U.L.Q.(<0.436)	0.593 ± 0.070	0.866 ± 0.050	U.L.Q.(<0.166)	0.532 ^c	0.698 ± 0.049
SLC2A1/GLUT1	159 ± 6	187 ± 5	387 ± 9	173 ± 3	124 ± 2	319 ± 16
SLC3A2/4F2hc	1.53 ± 0.01	1.62 ± 0.14	4.46 ± 0.13	1.66 ± 0.13	1.82 ± 0.16	3.45 ± 0.15
SLC6A6/TAUT	0.380 ± 0.036	0.431 ± 0.025	0.487 ± 0.017	0.366 ± 0.024	0.342 ± 0.032	0.550 ± 0.036
SLC7A1/CAT1	0.793 ± 0.083	1.71 ± 0.23	2.19 ± 0.05	0.889 ± 0.108	1.16 ± 0.14	2.28 ± 0.18
SLC7A5/LAT1	U.L.Q.(<0.264)	U.L.Q.(<0.227)	1.34 ^c	U.L.Q.(<0.257)	U.L.Q.(<0.344)	0.388 ^d
SLC16A1/MCT1	1.00 ± 0.21	1.40 ± 0.08	4.25 ± 0.25	1.18 ± 0.11	0.981 ± 0.043	2.50 ± 0.15
SLC16A3/MCT4	8.99 ± 0.89	6.09 ± 0.60	6.20 ± 0.52	3.81 ± 0.34	2.67 ± 0.24	7.30 ± 0.65
SLC19A1/RFC1	U.L.Q.(<0.333)	1.04 ^c	1.72 ± 0.13	U.L.Q.(<0.667)	U.L.Q.(<0.646)	1.00 ^c
SLC22A7/OAT2	U.L.Q.(<0.864)	U.L.Q.(<0.537)	U.L.Q.(<0.281)	U.L.Q.(<0.0196)	U.L.Q.(<0.0167)	0.261 ± 0.015
SLC46A1/PCFT	0.145 ^c	1.23 ± 0.10	3.54 ± 0.16	0.754 ± 0.138	1.93 ± 0.38	5.80 ± 0.63
SLC47A1/MATE1	0.293 ± 0.075	0.608 ± 0.081	0.899 ± 0.096	0.298 ^c	0.345 ± 0.092	0.909 ± 0.106
Na ⁺ /K ⁺ ATPase	7.08 ± 0.66	8.66 ± 0.48	15.5 ± 0.7	5.61 ± 0.76	5.08 ± 0.22	11.5 ± 0.7
ABCA4/ABCR	U.L.Q.(<0.337)	U.L.Q.(<0.291)	U.L.Q.(<0.200)	U.L.Q.(<0.111)	U.L.Q.(<0.112)	U.L.Q.(<0.118)
ABCA8/ABCA8	U.L.Q.(<0.0705)	U.L.Q.(<0.0644)	U.L.Q.(<0.0660)	U.L.Q.(<0.0182)	U.L.Q.(<0.0233)	U.L.Q.(<0.0226)
ABCB1/P-gp/MDR1	U.L.Q.(<0.379)	U.L.Q.(<0.410)	U.L.Q.(<0.442)	U.L.Q.(<0.143)	U.L.Q.(<0.141)	U.L.Q.(<0.175)
ABCB4/MDR3	U.L.Q.(<0.0173)	U.L.Q.(<0.0166)	U.L.Q.(<0.0200)	U.L.Q.(<0.166)	U.L.Q.(<0.103)	U.L.Q.(<0.114)
ABCB5/ABCB5	U.L.Q.(<0.0619)	U.L.Q.(<0.172)	U.L.Q.(<0.0558)	U.L.Q.(<0.231)	U.L.Q.(<0.187)	U.L.Q.(<0.235)
ABCB11/BSEP	U.L.Q.(<0.317)	U.L.Q.(<0.331)	U.L.Q.(<0.277)	U.L.Q.(<0.00629)	U.L.Q.(<0.00740)	U.L.Q.(<0.0174)
ABCC2/MRP2	U.L.Q.(<1.04)	U.L.Q.(<0.583)	U.L.Q.(<0.471)	U.L.Q.(<0.215)	U.L.Q.(<0.217)	U.L.Q.(<0.218)
ABCC3/MRP3	U.L.Q.(<0.148)	U.L.Q.(<0.124)	U.L.Q.(<0.0911)	U.L.Q.(<0.238)	U.L.Q.(<0.242)	U.L.Q.(<0.122)
ABCC6/MRP6	U.L.Q.(<0.109)	U.L.Q.(<0.106)	U.L.Q.(<0.103)	U.L.Q.(<0.0140)	U.L.Q.(<0.0200)	U.L.Q.(<0.0213)
ABCC11/MRP8	U.L.Q.(<0.393)	U.L.Q.(<0.400)	U.L.Q.(<0.395)	U.L.Q.(<0.395)	U.L.Q.(<0.390)	U.L.Q.(<0.400)

^a The expression levels were described as mean ± S.E.M obtained from three or four MRM/SRM transitions in each hfRPE sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of hfRPE samples (n=3).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated from only a single SRM/MRM transition due to high noise levels at the other transitions.

^e The expression levels were calculated as the average of two samples.

^f The expression level was represented from the value obtained in one sample.

Table S3. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of three hfRPE samples (Continued)

	Protein expression levels (fmol/µg protein)					
	1 ^a			2 ^a		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction
ABCG2/BCRP	U.L.Q.(<0.294)	U.L.Q.(<0.299)	U.L.Q.(<0.297)	U.L.Q.(<0.294)	U.L.Q.(<0.294)	U.L.Q.(<0.299)
SLC15A1/PEPT1	U.L.Q.(<0.0182)	U.L.Q.(<0.00897)	U.L.Q.(<0.0194)	U.L.Q.(<0.0584)	U.L.Q.(<0.0568)	U.L.Q.(<0.0610)
SLC16A8/MCT3	U.L.Q.(<0.939)	U.L.Q.(<0.914)	U.L.Q.(<0.548)	U.L.Q.(<0.264)	U.L.Q.(<0.258)	U.L.Q.(<0.266)
SLC21A6/OATP1B1	U.L.Q.(<1.13)	U.L.Q.(<1.15)	U.L.Q.(<1.13)	U.L.Q.(<1.17)	U.L.Q.(<1.16)	U.L.Q.(<1.15)
SLC21A8/OATP1B3	U.L.Q.(<6.44)	U.L.Q.(<5.78)	U.L.Q.(<2.54)	U.L.Q.(<0.301)	U.L.Q.(<0.272)	U.L.Q.(<0.356)
SLC22A1/OCT1	U.L.Q.(<1.67)	U.L.Q.(<1.69)	U.L.Q.(<1.69)	U.L.Q.(<1.69)	U.L.Q.(<1.68)	U.L.Q.(<1.69)
SLC22A2/OCT2	U.L.Q.(<0.225)	U.L.Q.(<0.158)	U.L.Q.(<0.210)	U.L.Q.(<0.0778)	U.L.Q.(<0.0891)	U.L.Q.(<0.0809)
SLC22A3/OCT3	U.L.Q.(<0.258)	U.L.Q.(<0.181)	U.L.Q.(<0.106)	U.L.Q.(<0.124)	U.L.Q.(<0.119)	U.L.Q.(<0.121)
SLC22A5/OCTN2	U.L.Q.(<0.203)	U.L.Q.(<0.190)	U.L.Q.(<0.203)	U.L.Q.(<0.127)	U.L.Q.(<0.121)	U.L.Q.(<0.132)
SLC22A6/OAT1	U.L.Q.(<0.0641)	U.L.Q.(<0.0623)	U.L.Q.(<0.0639)	U.L.Q.(<0.103)	U.L.Q.(<0.104)	U.L.Q.(<0.106)
SLC22A8/OAT3	U.L.Q.(<0.354)	U.L.Q.(<0.313)	U.L.Q.(<0.220)	U.L.Q.(<0.291)	U.L.Q.(<0.0785)	U.L.Q.(<0.286)
SLC22A11/OAT4	U.L.Q.(<0.489)	U.L.Q.(<0.329)	U.L.Q.(<0.168)	U.L.Q.(<0.0145)	U.L.Q.(<0.00950)	U.L.Q.(<0.0130)
SLC47A2/MATE2	U.L.Q.(<1.45)	U.L.Q.(<1.72)	U.L.Q.(<1.34)	U.L.Q.(<0.256)	U.L.Q.(<0.302)	U.L.Q.(<0.294)
SLC47A2/MATE2k	U.L.Q.(<0.118)	U.L.Q.(<0.427)	U.L.Q.(<0.134)	U.L.Q.(<0.922)	U.L.Q.(<0.969)	U.L.Q.(<1.15)
Villin1	U.L.Q.(<0.171)	U.L.Q.(<0.362)	U.L.Q.(<0.245)	U.L.Q.(<0.206)	U.L.Q.(<0.192)	U.L.Q.(<0.188)

^a The expression levels were described as mean ± S.E.M obtained from three or four MRM/SRM transitions in each hfRPE sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of hfRPE samples (n=3).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated from only a single SRM/MRM transition due to high noise levels at the other transitions.

^e The expression levels were calculated as the average of two samples.

^f The expression level was represented from the value obtained in one sample.

Table S3. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of three hfRPE samples (Continued)

	Protein expression levels (fmol/µg protein)					
	3 ^a			Average ^b		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions
ABCC1/MRP1	1.15 ± 0.14	0.428 ^c	0.957 ± 0.119	1.16 ± 0.06	0.592 ± 0.204	1.36 ± 0.41
ABCC4/MRP4	0.0699 ^c	0.0570 ^c	0.0746 ± 0.0274	0.0660 ± 0.0055	0.0488 ^e	0.0995 ^e
ABCC5/MRP5	0.466 ^c	0.315 ^c	0.787 ± 0.124	0.451 ± 0.012	0.369 ^e	0.789 ± 0.004
ABCC10/MRP7	U.L.Q.(<0.450)	U.L.Q.(<0.167)	U.L.Q.(<0.184)	U.L.Q.(<0.166)	0.562 ^e	0.782 ^e
SLC2A1/GLUT1	174 ± 4	114 ± 2	304 ± 8	169 ± 8	142 ± 39	337 ± 44
SLC3A2/4F2hc	1.85 ± 0.17	0.742 ± 0.147	3.53 ± 0.25	1.68 ± 0.16	1.39 ± 0.57	3.81 ± 0.56
SLC6A6/TAUT	0.375 ± 0.034	0.256 ^c	0.461 ± 0.032	0.374 ± 0.007	0.343 ± 0.088	0.499 ± 0.046
SLC7A1/CAT1	0.886 ± 0.080	0.590 ± 0.091	2.32 ± 0.24	0.856 ± 0.055	1.15 ± 0.56	2.26 ± 0.07
SLC7A5/LAT1	U.L.Q.(<0.284)	U.L.Q.(<0.220)	0.430 ^d	U.L.Q.(<0.257)	U.L.Q.(<0.220)	0.721 ± 0.540
SLC16A1/MCT1	1.22 ± 0.08	0.553 ± 0.031	2.68 ± 0.14	1.13 ± 0.12	0.977 ± 0.422	3.14 ± 0.96
SLC16A3/MCT4	4.86 ± 0.50	0.962 ± 0.080	7.23 ± 0.51	5.89 ± 2.73	3.24 ± 2.61	6.91 ± 0.61
SLC19A1/RFC1	U.L.Q.(<0.840)	U.L.Q.(<0.579)	0.876 ^c	U.L.Q.(<0.333)	1.04 ^f	1.20 ± 0.46
SLC22A7/OAT2	U.L.Q.(<0.0186)	U.L.Q.(<0.0152)	0.153 ^c	U.L.Q.(<0.0186)	U.L.Q.(<0.0152)	0.207 ^e
SLC46A1/PCFT	0.590 ^c	1.59 ± 0.18	5.38 ± 0.13	0.497 ± 0.315	1.58 ± 0.35	4.91 ± 1.20
SLC47A1/MATE1	0.218 ± 0.037	0.344 ± 0.055	0.746 ± 0.156	0.270 ± 0.045	0.433 ± 0.152	0.851 ± 0.092
Na ⁺ /K ⁺ ATPase	4.90 ± 0.30	4.49 ± 0.49	9.48 ± 0.27	5.87 ± 1.11	6.08 ± 2.26	12.2 ± 3.1
ABCA4/ABCR	U.L.Q.(<0.119)	U.L.Q.(<0.104)	U.L.Q.(<0.114)	U.L.Q.(<0.111)	U.L.Q.(<0.104)	U.L.Q.(<0.114)
ABCA8/ABCA8	U.L.Q.(<0.0163)	U.L.Q.(<0.0204)	U.L.Q.(<0.0210)	U.L.Q.(<0.0163)	U.L.Q.(<0.0204)	U.L.Q.(<0.0210)
ABCB1/P-gp/MDR1	U.L.Q.(<0.152)	U.L.Q.(<0.138)	U.L.Q.(<0.195)	U.L.Q.(<0.143)	U.L.Q.(<0.138)	U.L.Q.(<0.175)
ABCB4/MDR3	U.L.Q.(<0.165)	U.L.Q.(<0.102)	U.L.Q.(<0.178)	U.L.Q.(<0.0173)	U.L.Q.(<0.0166)	U.L.Q.(<0.0200)
ABCB5/ABCB5	U.L.Q.(<0.247)	U.L.Q.(<0.186)	U.L.Q.(<0.237)	U.L.Q.(<0.0619)	U.L.Q.(<0.172)	U.L.Q.(<0.0558)
ABCB11/BSEP	U.L.Q.(<0.0129)	U.L.Q.(<0.0110)	U.L.Q.(<0.0170)	U.L.Q.(<0.00629)	U.L.Q.(<0.00740)	U.L.Q.(<0.0170)
ABCC2/MRP2	U.L.Q.(<0.226)	U.L.Q.(<0.203)	U.L.Q.(<0.228)	U.L.Q.(<0.215)	U.L.Q.(<0.203)	U.L.Q.(<0.218)
ABCC3/MRP3	U.L.Q.(<0.118)	U.L.Q.(<0.121)	U.L.Q.(<0.122)	U.L.Q.(<0.118)	U.L.Q.(<0.121)	U.L.Q.(<0.0911)
ABCC6/MRP6	U.L.Q.(<0.0178)	U.L.Q.(<0.0185)	U.L.Q.(<0.0229)	U.L.Q.(<0.0140)	U.L.Q.(<0.0185)	U.L.Q.(<0.0213)
ABCC11/MRP8	U.L.Q.(<0.401)	U.L.Q.(<0.396)	U.L.Q.(<0.405)	U.L.Q.(<0.393)	U.L.Q.(<0.390)	U.L.Q.(<0.395)

^a The expression levels were described as mean ± S.E.M obtained from three or four MRM/SRM transitions in each hfRPE sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of hfRPE samples (n=3).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated from only a single SRM/MRM transition due to high noise levels at the other transitions.

^e The expression levels were calculated as the average of two samples.

^f The expression level was represented from the value obtained in one sample.

Table S3. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of three hfRPE samples (Continued)

	Protein expression levels (fmol/µg protein)					
	3 ^a			Average ^b		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions
ABCG2/BCRP	U.L.Q.(<0.301)	U.L.Q.(<0.298)	U.L.Q.(<0.311)	U.L.Q.(<0.294)	U.L.Q.(<0.294)	U.L.Q.(<0.297)
SLC15A1/PEPT1	U.L.Q.(<0.0580)	U.L.Q.(<0.0575)	U.L.Q.(<0.0599)	U.L.Q.(<0.0182)	U.L.Q.(<0.00897)	U.L.Q.(<0.0194)
SLC16A8/MCT3	U.L.Q.(<0.297)	U.L.Q.(<0.262)	U.L.Q.(<0.260)	U.L.Q.(<0.264)	U.L.Q.(<0.258)	U.L.Q.(<0.260)
SLC21A6/OATP1B1	U.L.Q.(<1.17)	U.L.Q.(<1.15)	U.L.Q.(<1.17)	U.L.Q.(<1.13)	U.L.Q.(<1.15)	U.L.Q.(<1.13)
SLC21A8/OATP1B3	U.L.Q.(<0.305)	U.L.Q.(<0.323)	U.L.Q.(<0.311)	U.L.Q.(<0.301)	U.L.Q.(<0.272)	U.L.Q.(<0.209)
SLC22A1/OCT1	U.L.Q.(<1.68)	U.L.Q.(<1.69)	U.L.Q.(<1.70)	U.L.Q.(<1.67)	U.L.Q.(<1.68)	U.L.Q.(<1.69)
SLC22A2/OCT2	U.L.Q.(<0.0734)	U.L.Q.(<0.0768)	U.L.Q.(<0.0750)	U.L.Q.(<0.0734)	U.L.Q.(<0.0768)	U.L.Q.(<0.0750)
SLC22A3/OCT3	U.L.Q.(<0.131)	U.L.Q.(<0.120)	U.L.Q.(<0.121)	U.L.Q.(<0.124)	U.L.Q.(<0.119)	U.L.Q.(<0.106)
SLC22A5/OCTN2	U.L.Q.(<0.131)	U.L.Q.(<0.131)	U.L.Q.(<0.133)	U.L.Q.(<0.127)	U.L.Q.(<0.121)	U.L.Q.(<0.132)
SLC22A6/OAT1	U.L.Q.(<0.104)	U.L.Q.(<0.106)	U.L.Q.(<0.100)	U.L.Q.(<0.0641)	U.L.Q.(<0.0623)	U.L.Q.(<0.0639)
SLC22A8/OAT3	U.L.Q.(<0.296)	U.L.Q.(<0.288)	U.L.Q.(<0.290)	U.L.Q.(<0.291)	U.L.Q.(<0.0785)	U.L.Q.(<0.220)
SLC22A11/OAT4	U.L.Q.(<0.00950)	U.L.Q.(<0.00640)	U.L.Q.(<0.0314)	U.L.Q.(<0.00950)	U.L.Q.(<0.00640)	U.L.Q.(<0.0130)
SLC47A2/MATE2	U.L.Q.(<0.236)	U.L.Q.(<0.237)	U.L.Q.(<0.324)	U.L.Q.(<0.236)	U.L.Q.(<0.237)	U.L.Q.(<0.294)
SLC47A2/MATE2k	U.L.Q.(<1.07)	U.L.Q.(<1.07)	U.L.Q.(<1.06)	U.L.Q.(<0.118)	U.L.Q.(<0.427)	U.L.Q.(<0.134)
Villin1	U.L.Q.(<0.194)	U.L.Q.(<0.178)	U.L.Q.(<0.205)	U.L.Q.(<0.171)	U.L.Q.(<0.178)	U.L.Q.(<0.188)

^a The expression levels were described as mean ± S.E.M obtained from three or four MRM/SRM transitions in each hfRPE sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of hfRPE samples (n=3).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated from only a single SRM/MRM transition due to high noise levels at the other transitions.

^e The expression levels were calculated as the average of two samples.

^f The expression level was represented from the value obtained in one sample.

Table S4. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of five ARPE19 samples

	Protein expression levels (fmol/µg protein)					
	1 ^a			2 ^a		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction
ABCC1/MRP1	1.25 ± 0.08	1.67 ± 0.14	5.20 ± 0.92	1.31 ^c	U.L.Q.(<1.05)	1.92 ± 0.17
ABCC4/MRP4	0.242 ± 0.037	0.417 ± 0.017	1.61 ± 0.21	0.644 ± 0.056	0.589 ± 0.035	1.45 ± 0.04
ABCC5/MRP5	U.L.Q.(<0.0821)	U.L.Q.(<0.182)	0.836 ± 0.157	U.L.Q.(<0.192)	U.L.Q.(<0.262)	1.37 ± 0.08
ABCC10/MRP7	U.L.Q.(<0.136)	U.L.Q.(<0.165)	U.L.Q.(<0.113)	U.L.Q.(<0.377)	U.L.Q.(<0.487)	U.L.Q.(<0.492)
SLC2A1/GLUT1	39.4 ± 2.3	90.1 ± 4.0	187 ± 9	68.7 ± 3.1	67.2 ± 0.9	158 ± 4
SLC3A2/4F2hc	1.35 ± 0.23	2.72 ± 0.14	12.7 ± 0.3	3.44 ± 0.21	5.37 ± 0.19	11.3 ± 0.5
SLC6A6/TAUT	U.L.Q.(<0.0553)	U.L.Q.(<0.0429)	0.297 ± 0.042	U.L.Q.(<0.0135)	0.117 ± 0.022	0.473 ± 0.045
SLC7A1/CAT1	0.761 ^c	1.90 ± 0.37	2.57 ± 0.26	0.766 ± 0.128	0.611 ^c	1.32 ± 0.22
SLC7A5/LAT1	U.L.Q.(<0.282)	U.L.Q.(<0.241)	2.79 ^c	U.L.Q.(<0.492)	U.L.Q.(<0.413)	U.L.Q.(<0.338)
SLC16A1/MCT1	2.02 ^c	4.28 ± 0.37	14.7 ± 0.6	5.58 ± 0.59	5.03 ± 0.34	12.0 ± 1.0
SLC16A3/MCT4	2.59 ± 0.14	6.10 ± 0.19	39.0 ± 1.5	8.99 ± 0.20	11.6 ± 0.4	31.8 ± 0.6
SLC19A1/RFC1	U.L.Q.(<0.365)	U.L.Q.(<0.349)	U.L.Q.(<0.650)	U.L.Q.(<3.06)	U.L.Q.(<3.16)	U.L.Q.(<3.19)
SLC22A7/OAT2	U.L.Q.(<0.251)	U.L.Q.(<0.254)	U.L.Q.(<0.261)	U.L.Q.(<0.311)	U.L.Q.(<0.302)	U.L.Q.(<0.298)
SLC46A1/PCFT	U.L.Q.(<0.123)	U.L.Q.(<0.234)	0.588 ± 0.099	U.L.Q.(<0.113)	U.L.Q.(<0.196)	U.L.Q.(<0.188)
SLC47A1/MATE1	U.L.Q.(<0.224)	U.L.Q.(<0.223)	1.95 ± 0.18	U.L.Q.(<0.244)	U.L.Q.(<0.277)	1.87 ± 0.19
Na ⁺ /K ⁺ ATPase	12.0 ± 1.1	26.4 ± 1.43	69.0 ± 5.9	14.4 ± 2.3	17.2 ± 1.6	40.8 ± 4.0
ABCA4/ABCR	U.L.Q.(<0.0469)	U.L.Q.(<0.0421)	U.L.Q.(<0.0379)	U.L.Q.(<0.0995)	U.L.Q.(<0.0921)	U.L.Q.(<0.0857)
ABCA8/ABCA8	U.L.Q.(<0.0633)	U.L.Q.(<0.0605)	U.L.Q.(<0.0509)	U.L.Q.(<0.138)	U.L.Q.(<0.137)	U.L.Q.(<0.142)
ABCB1/P-gp/MDR1	U.L.Q.(<0.0990)	U.L.Q.(<0.0982)	U.L.Q.(<0.0927)	U.L.Q.(<0.0895)	U.L.Q.(<0.306)	U.L.Q.(<0.407)
ABCB4/MDR3	U.L.Q.(<0.146)	U.L.Q.(<0.132)	U.L.Q.(<0.116)	U.L.Q.(<0.234)	U.L.Q.(<0.234)	U.L.Q.(<0.236)
ABCB5/ABCB5	U.L.Q.(<0.192)	U.L.Q.(<0.169)	U.L.Q.(<0.158)	U.L.Q.(<0.270)	U.L.Q.(<0.273)	U.L.Q.(<0.261)
ABCB11/BSEP	U.L.Q.(<0.132)	U.L.Q.(<0.124)	U.L.Q.(<0.115)	U.L.Q.(<0.199)	U.L.Q.(<0.190)	U.L.Q.(<0.192)
ABCC2/MRP2	U.L.Q.(<0.116)	U.L.Q.(<0.128)	U.L.Q.(<0.116)	U.L.Q.(<0.223)	U.L.Q.(<0.281)	U.L.Q.(<0.375)
ABCC3/MRP3	U.L.Q.(<0.152)	U.L.Q.(<0.146)	U.L.Q.(<0.131)	U.L.Q.(<0.179)	U.L.Q.(<0.109)	U.L.Q.(<0.114)
ABCC6/MRP6	U.L.Q.(<0.0548)	U.L.Q.(<0.0516)	U.L.Q.(<0.0460)	U.L.Q.(<0.133)	U.L.Q.(<0.121)	U.L.Q.(<0.129)
ABCC11/MRP8	U.L.Q.(<0.107)	U.L.Q.(<0.103)	U.L.Q.(<0.0892)	U.L.Q.(<0.105)	U.L.Q.(<0.102)	U.L.Q.(<0.0786)

^a The expression levels were described as mean ± S.E.M obtained from three to four MRM/SRM transitions in each ARPE19 sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of ARPE19 samples (n=5).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated as the average of two samples.

^e The expression level was represented from the value obtained in one sample.

Table S4. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of five ARPE19 samples (Continued)

	Protein expression levels (fmol/µg protein)					
	1 ^a			2 ^a		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction
ABCG2/BCRP	U.L.Q.(<0.0672)	U.L.Q.(<0.0688)	U.L.Q.(<0.0633)	U.L.Q.(<0.194)	U.L.Q.(<0.183)	U.L.Q.(<0.175)
SLC15A1/PEPT1	U.L.Q.(<0.0397)	U.L.Q.(<0.0386)	U.L.Q.(<0.0364)	U.L.Q.(<0.0877)	U.L.Q.(<0.0827)	U.L.Q.(<0.0832)
SLC16A8/MCT3	U.L.Q.(<0.102)	U.L.Q.(<0.104)	U.L.Q.(<0.104)	U.L.Q.(<0.161)	U.L.Q.(<0.240)	U.L.Q.(<0.180)
SLC21A6/OATP1B1	U.L.Q.(<0.203)	U.L.Q.(<0.195)	U.L.Q.(<0.172)	U.L.Q.(<0.152)	U.L.Q.(<0.185)	U.L.Q.(<0.157)
SLC21A8/OATP1B3	U.L.Q.(<0.152)	U.L.Q.(<0.138)	U.L.Q.(<0.132)	U.L.Q.(<0.697)	U.L.Q.(<0.679)	U.L.Q.(<0.661)
SLC22A1/OCT1	U.L.Q.(<0.0557)	U.L.Q.(<0.0550)	U.L.Q.(<0.0520)	U.L.Q.(<0.0640)	U.L.Q.(<0.0454)	U.L.Q.(<0.0414)
SLC22A2/OCT2	U.L.Q.(<0.0852)	U.L.Q.(<0.0761)	U.L.Q.(<0.0709)	U.L.Q.(<0.185)	U.L.Q.(<0.176)	U.L.Q.(<0.171)
SLC22A3/OCT3	U.L.Q.(<0.0653)	U.L.Q.(<0.0442)	U.L.Q.(<0.0581)	U.L.Q.(<0.163)	U.L.Q.(<0.162)	U.L.Q.(<0.160)
SLC22A5/OCTN2	U.L.Q.(<0.119)	U.L.Q.(<0.0954)	U.L.Q.(<0.0927)	U.L.Q.(<0.246)	U.L.Q.(<0.238)	U.L.Q.(<0.229)
SLC22A6/OAT1	U.L.Q.(<0.0230)	U.L.Q.(<0.0224)	U.L.Q.(<0.0226)	U.L.Q.(<0.0899)	U.L.Q.(<0.0460)	U.L.Q.(<0.0466)
SLC22A8/OAT3	U.L.Q.(<0.167)	U.L.Q.(<0.154)	U.L.Q.(<0.135)	U.L.Q.(<0.316)	U.L.Q.(<0.108)	U.L.Q.(<0.0949)
SLC22A11/OAT4	U.L.Q.(<0.166)	U.L.Q.(<0.145)	U.L.Q.(<0.130)	U.L.Q.(<0.182)	U.L.Q.(<0.169)	U.L.Q.(<0.157)
SLC47A2/MATE2	U.L.Q.(<0.495)	U.L.Q.(<0.450)	U.L.Q.(<0.176)	U.L.Q.(<0.410)	U.L.Q.(<1.03)	U.L.Q.(<0.506)
SLC47A2/MATE2k	U.L.Q.(<2.35)	U.L.Q.(<2.15)	U.L.Q.(<1.92)	U.L.Q.(<2.92)	U.L.Q.(<2.83)	U.L.Q.(<2.76)
Villin1	U.L.Q.(<0.110)	U.L.Q.(<0.103)	U.L.Q.(<0.0969)	U.L.Q.(<0.164)	U.L.Q.(<0.179)	U.L.Q.(<0.187)

^a The expression levels were described as mean ± S.E.M obtained from three to four MRM/SRM transitions in each ARPE19 sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of ARPE19 samples (n=5).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated as the average of two samples.

^e The expression level was represented from the value obtained in one sample.

Table S4. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of five ARPE19 samples (Continued)

	Protein expression levels (fmol/µg protein)					
	3 ^a			4 ^a		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction
ABCC1/MRP1	1.77 ^c	1.86 ± 0.22	2.91 ± 0.29	1.19 ^c	0.916 ^c	1.83 ± 0.13
ABCC4/MRP4	0.554 ± 0.056	0.802 ± 0.045	1.63 ± 0.04	0.606 ± 0.009	0.327 ± 0.030	0.893 ± 0.129
ABCC5/MRP5	U.L.Q.(<0.210)	U.L.Q.(<0.256)	U.L.Q.(<0.254)	U.L.Q.(<0.285)	U.L.Q.(<0.267)	U.L.Q.(<0.241)
ABCC10/MRP7	U.L.Q.(<0.465)	U.L.Q.(<0.476)	U.L.Q.(<0.377)	U.L.Q.(<0.478)	U.L.Q.(<0.368)	U.L.Q.(<0.347)
SLC2A1/GLUT1	62.1 ± 2.9	89.7 ± 3.1	189 ± 10	56.8 ± 1.0	63.4 ± 2.3	139 ± 5
SLC3A2/4F2hc	3.07 ± 0.22	5.76 ± 0.13	13.9 ± 0.4	3.28 ± 0.25	2.42 ± 0.23	8.35 ± 0.22
SLC6A6/TAUT	U.L.Q.(<0.0300)	0.173 ± 0.027	0.441 ± 0.034	U.L.Q.(<0.0368)	U.L.Q.(<0.0329)	0.282 ± 0.023
SLC7A1/CAT1	0.610 ^c	0.929 ± 0.042	1.73 ± 0.10	0.836 ± 0.331	0.624 ^c	0.859 ± 0.065
SLC7A5/LAT1	U.L.Q.(<0.534)	U.L.Q.(<0.223)	1.78 ^c	U.L.Q.(<0.861)	U.L.Q.(<0.658)	U.L.Q.(<0.539)
SLC16A1/MCT1	3.94 ± 0.53	7.48 ± 0.79	15.8 ± 0.2	4.62 ± 0.61	4.43 ± 0.49	9.47 ± 0.49
SLC16A3/MCT4	7.03 ± 0.18	17.7 ± 0.7	40.6 ± 1.7	12.6 ± 0.5	2.20 ± 0.10	13.8 ± 0.3
SLC19A1/RFC1	U.L.Q.(<3.29)	U.L.Q.(<0.547)	U.L.Q.(<3.19)	U.L.Q.(<3.19)	U.L.Q.(<0.468)	U.L.Q.(<3.15)
SLC22A7/OAT2	U.L.Q.(<0.309)	U.L.Q.(<0.302)	U.L.Q.(<0.300)	U.L.Q.(<0.311)	U.L.Q.(<0.298)	U.L.Q.(<0.295)
SLC46A1/PCFT	U.L.Q.(<0.202)	U.L.Q.(<0.186)	U.L.Q.(<0.206)	U.L.Q.(<0.162)	U.L.Q.(<0.186)	U.L.Q.(<0.201)
SLC47A1/MATE1	U.L.Q.(<0.257)	U.L.Q.(<0.244)	0.937 ^c	U.L.Q.(<0.267)	U.L.Q.(<0.236)	U.L.Q.(<0.247)
Na ⁺ /K ⁺ ATPase	14.5 ± 1.1	25.9 ± 1.0	53.5 ± 3.8	14.9 ± 1.5	17.5 ± 0.2	35.0 ± 4.2
ABCA4/ABCR	U.L.Q.(<0.0945)	U.L.Q.(<0.0861)	U.L.Q.(<0.0823)	U.L.Q.(<0.103)	U.L.Q.(<0.0891)	U.L.Q.(<0.0915)
ABCA8/ABCA8	U.L.Q.(<0.133)	U.L.Q.(<0.136)	U.L.Q.(<0.142)	U.L.Q.(<0.140)	U.L.Q.(<0.138)	U.L.Q.(<0.128)
ABCB1/P-gp/MDR1	U.L.Q.(<0.0711)	U.L.Q.(<0.240)	U.L.Q.(<0.233)	U.L.Q.(<0.0505)	U.L.Q.(<0.279)	U.L.Q.(<0.317)
ABCB4/MDR3	U.L.Q.(<0.221)	U.L.Q.(<0.217)	U.L.Q.(<0.229)	U.L.Q.(<0.234)	U.L.Q.(<0.225)	U.L.Q.(<0.237)
ABCB5/ABCB5	U.L.Q.(<0.305)	U.L.Q.(<0.301)	U.L.Q.(<0.258)	U.L.Q.(<0.314)	U.L.Q.(<0.311)	U.L.Q.(<0.315)
ABCB11/BSEP	U.L.Q.(<0.201)	U.L.Q.(<0.193)	U.L.Q.(<0.190)	U.L.Q.(<0.203)	U.L.Q.(<0.187)	U.L.Q.(<0.183)
ABCC2/MRP2	U.L.Q.(<0.211)	U.L.Q.(<0.281)	U.L.Q.(<0.427)	U.L.Q.(<0.174)	U.L.Q.(<0.258)	U.L.Q.(<0.407)
ABCC3/MRP3	U.L.Q.(<0.0974)	U.L.Q.(<0.104)	U.L.Q.(<0.116)	U.L.Q.(<0.0960)	U.L.Q.(<0.0967)	U.L.Q.(<0.108)
ABCC6/MRP6	U.L.Q.(<0.146)	U.L.Q.(<0.129)	U.L.Q.(<0.128)	U.L.Q.(<0.127)	U.L.Q.(<0.128)	U.L.Q.(<0.129)
ABCC11/MRP8	U.L.Q.(<0.107)	U.L.Q.(<0.0802)	U.L.Q.(<0.112)	U.L.Q.(<0.0887)	U.L.Q.(<0.0893)	U.L.Q.(<0.0967)

^a The expression levels were described as mean ± S.E.M obtained from three to four MRM/SRM transitions in each ARPE19 sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of ARPE19 samples (n=5).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated as the average of two samples.

^e The expression level was represented from the value obtained in one sample.

Table S4. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of five ARPE19 samples (Continued)

	Protein expression levels (fmol/µg protein)					
	3 ^a			4 ^a		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction
ABCG2/BCRP	U.L.Q.(<0.178)	U.L.Q.(<0.191)	U.L.Q.(<0.176)	U.L.Q.(<0.178)	U.L.Q.(<0.165)	U.L.Q.(<0.160)
SLC15A1/PEPT1	U.L.Q.(<0.0843)	U.L.Q.(<0.0857)	U.L.Q.(<0.0816)	U.L.Q.(<0.0852)	U.L.Q.(<0.0839)	U.L.Q.(<0.0849)
SLC16A8/MCT3	U.L.Q.(<0.127)	U.L.Q.(<0.144)	U.L.Q.(<0.194)	U.L.Q.(<0.150)	U.L.Q.(<0.148)	U.L.Q.(<0.100)
SLC21A6/OATP1B1	U.L.Q.(<0.146)	U.L.Q.(<0.205)	U.L.Q.(<0.200)	U.L.Q.(<0.156)	U.L.Q.(<0.157)	U.L.Q.(<0.167)
SLC21A8/OATP1B3	U.L.Q.(<0.634)	U.L.Q.(<0.641)	U.L.Q.(<0.480)	U.L.Q.(<0.723)	U.L.Q.(<0.691)	U.L.Q.(<0.701)
SLC22A1/OCT1	U.L.Q.(<0.0476)	U.L.Q.(<0.0482)	U.L.Q.(<0.0517)	U.L.Q.(<0.0521)	U.L.Q.(<0.0563)	U.L.Q.(<0.0424)
SLC22A2/OCT2	U.L.Q.(<0.190)	U.L.Q.(<0.182)	U.L.Q.(<0.185)	U.L.Q.(<0.193)	U.L.Q.(<0.214)	U.L.Q.(<0.190)
SLC22A3/OCT3	U.L.Q.(<0.167)	U.L.Q.(<0.166)	U.L.Q.(<0.158)	U.L.Q.(<0.319)	U.L.Q.(<0.159)	U.L.Q.(<0.159)
SLC22A5/OCTN2	U.L.Q.(<0.254)	U.L.Q.(<0.257)	U.L.Q.(<0.248)	U.L.Q.(<0.262)	U.L.Q.(<0.236)	U.L.Q.(<0.250)
SLC22A6/OAT1	U.L.Q.(<0.0937)	U.L.Q.(<0.0880)	U.L.Q.(<0.0402)	U.L.Q.(<0.0853)	U.L.Q.(<0.0391)	U.L.Q.(<0.0405)
SLC22A8/OAT3	U.L.Q.(<0.298)	U.L.Q.(<0.0881)	U.L.Q.(<0.0937)	U.L.Q.(<0.123)	U.L.Q.(<0.108)	U.L.Q.(<0.0996)
SLC22A11/OAT4	U.L.Q.(<0.184)	U.L.Q.(<0.156)	U.L.Q.(<0.156)	U.L.Q.(<0.184)	U.L.Q.(<0.166)	U.L.Q.(<0.147)
SLC47A2/MATE2	U.L.Q.(<0.440)	U.L.Q.(<0.421)	U.L.Q.(<0.429)	U.L.Q.(<0.430)	U.L.Q.(<0.380)	U.L.Q.(<0.481)
SLC47A2/MATE2k	U.L.Q.(<3.72)	U.L.Q.(<3.01)	U.L.Q.(<2.32)	U.L.Q.(<3.04)	U.L.Q.(<3.30)	U.L.Q.(<3.14)
Villin1	U.L.Q.(<0.194)	U.L.Q.(<0.189)	U.L.Q.(<0.188)	U.L.Q.(<0.179)	U.L.Q.(<0.206)	U.L.Q.(<0.178)

^a The expression levels were described as mean ± S.E.M obtained from three to four MRM/SRM transitions in each ARPE19 sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of ARPE19 samples (n=5).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated as the average of two samples.

^e The expression level was represented from the value obtained in one sample.

Table S4. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of five ARPE19 samples (Continued)

	Protein expression levels (fmol/µg protein)					
	5 ^a			Average ^b		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions
ABCC1/MRP1	0.872 ^c	2.76 ± 0.28	8.12 ± 0.97	1.28 ± 0.32	1.80 ± 0.76	4.00 ± 2.68
ABCC4/MRP4	0.225 ± 0.021	0.823 ± 0.046	2.37 ± 0.19	0.454 ± 0.204	0.591 ± 0.223	1.59 ± 0.53
ABCC5/MRP5	U.L.Q.(<0.246)	U.L.Q.(<0.148)	U.L.Q.(<0.192)	U.L.Q.(<0.0821)	U.L.Q.(<0.148)	1.10 ^d
ABCC10/MRP7	U.L.Q.(<0.342)	U.L.Q.(<0.288)	U.L.Q.(<0.253)	U.L.Q.(<0.136)	U.L.Q.(<0.165)	U.L.Q.(<0.113)
SLC2A1/GLUT1	43.4 ± 2.3	144 ± 2	354 ± 12	54.1 ± 12.4	90.9 ± 32.2	205 ± 85
SLC3A2/4F2hc	1.24 ± 0.21	4.02 ± 0.14	16.1 ± 0.2	2.48 ± 1.08	4.06 ± 1.51	12.5 ± 2.9
SLC6A6/TAUT	U.L.Q.(<0.303)	0.218 ± 0.011	0.715 ± 0.078	U.L.Q.(<0.0135)	0.169 ± 0.050	0.441 ± 0.175
SLC7A1/CAT1	0.291 ^c	0.902 ± 0.058	1.76 ± 0.12	0.653 ± 0.218	0.992 ± 0.527	1.65 ± 0.63
SLC7A5/LAT1	U.L.Q.(<0.194)	U.L.Q.(<0.177)	2.44 ^c	U.L.Q.(<0.194)	U.L.Q.(<0.177)	2.34 ± 0.51
SLC16A1/MCT1	1.88 ± 0.22	8.28 ± 0.52	23.5 ± 0.7	3.61 ± 1.62	5.90 ± 1.85	15.1 ± 5.3
SLC16A3/MCT4	1.78 ± 0.10	9.42 ± 0.34	50.6 ± 1.3	6.59 ± 4.49	9.39 ± 5.83	35.2 ± 13.7
SLC19A1/RFC1	U.L.Q.(<0.388)	U.L.Q.(<0.265)	U.L.Q.(<2.13)	U.L.Q.(<0.365)	U.L.Q.(<0.265)	U.L.Q.(<0.650)
SLC22A7/OAT2	U.L.Q.(<0.299)	U.L.Q.(<0.195)	U.L.Q.(<0.205)	U.L.Q.(<0.251)	U.L.Q.(<0.195)	U.L.Q.(<0.205)
SLC46A1/PCFT	U.L.Q.(<0.138)	U.L.Q.(<0.105)	U.L.Q.(<0.0997)	U.L.Q.(<0.113)	U.L.Q.(<0.105)	0.588 ^e
SLC47A1/MATE1	U.L.Q.(<0.215)	U.L.Q.(<0.162)	1.58 ^c	U.L.Q.(<0.215)	U.L.Q.(<0.162)	1.58 ± 0.46
Na ⁺ /K ⁺ ATPase	10.9 ± 1.1	37.1 ± 5.9	101 ± 13	13.4 ± 1.8	24.8 ± 8.1	59.9 ± 26.5
ABCA4/ABCR	U.L.Q.(<0.0754)	U.L.Q.(<0.0550)	U.L.Q.(<0.0667)	U.L.Q.(<0.0469)	U.L.Q.(<0.0421)	U.L.Q.(<0.0379)
ABCA8/ABCA8	U.L.Q.(<0.138)	U.L.Q.(<0.0872)	U.L.Q.(<0.0862)	U.L.Q.(<0.0633)	U.L.Q.(<0.0605)	U.L.Q.(<0.0509)
ABCB1/P-gp/MDR1	U.L.Q.(<0.0608)	U.L.Q.(<0.0756)	U.L.Q.(<0.103)	U.L.Q.(<0.0505)	U.L.Q.(<0.0756)	U.L.Q.(<0.0927)
ABCB4/MDR3	U.L.Q.(<0.222)	U.L.Q.(<0.142)	U.L.Q.(<0.157)	U.L.Q.(<0.146)	U.L.Q.(<0.132)	U.L.Q.(<0.116)
ABCB5/ABCB5	U.L.Q.(<0.279)	U.L.Q.(<0.194)	U.L.Q.(<0.255)	U.L.Q.(<0.192)	U.L.Q.(<0.169)	U.L.Q.(<0.158)
ABCB11/BSEP	U.L.Q.(<0.175)	U.L.Q.(<0.116)	U.L.Q.(<0.134)	U.L.Q.(<0.132)	U.L.Q.(<0.116)	U.L.Q.(<0.115)
ABCC2/MRP2	U.L.Q.(<0.243)	U.L.Q.(<0.156)	U.L.Q.(<0.152)	U.L.Q.(<0.116)	U.L.Q.(<0.128)	U.L.Q.(<0.116)
ABCC3/MRP3	U.L.Q.(<0.100)	U.L.Q.(<0.0625)	U.L.Q.(<0.0709)	U.L.Q.(<0.0960)	U.L.Q.(<0.0625)	U.L.Q.(<0.0709)
ABCC6/MRP6	U.L.Q.(<0.127)	U.L.Q.(<0.0842)	U.L.Q.(<0.0861)	U.L.Q.(<0.0548)	U.L.Q.(<0.0516)	U.L.Q.(<0.0460)
ABCC11/MRP8	U.L.Q.(<0.0924)	U.L.Q.(<0.0567)	U.L.Q.(<0.0592)	U.L.Q.(<0.0887)	U.L.Q.(<0.0567)	U.L.Q.(<0.0592)

^a The expression levels were described as mean ± S.E.M obtained from three to four MRM/SRM transitions in each ARPE19 sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of ARPE19 samples (n=5).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated as the average of two samples.

^e The expression level was represented from the value obtained in one sample.

Table S4. Transporter expression levels in whole cell lysate, crude membrane fraction and plasma membrane fraction of five ARPE19 samples (Continued)

	Protein expression levels (fmol/µg protein)					
	5 ^a			Average ^b		
	Whole cell lysate	Crude membrane fraction	Plasma membrane fraction	Whole cell lysates	Crude membrane fractions	Plasma membrane fractions
ABCG2/BCRP	U.L.Q.(<0.147)	U.L.Q.(<0.102)	U.L.Q.(<0.106)	U.L.Q.(<0.0672)	U.L.Q.(<0.0688)	U.L.Q.(<0.0633)
SLC15A1/PEPT1	U.L.Q.(<0.0410)	U.L.Q.(<0.0549)	U.L.Q.(<0.0571)	U.L.Q.(<0.0397)	U.L.Q.(<0.0386)	U.L.Q.(<0.0364)
SLC16A8/MCT3	U.L.Q.(<0.113)	U.L.Q.(<0.111)	U.L.Q.(<0.0983)	U.L.Q.(<0.102)	U.L.Q.(<0.104)	U.L.Q.(<0.0983)
SLC21A6/OATP1B1	U.L.Q.(<0.160)	U.L.Q.(<0.0938)	U.L.Q.(<0.103)	U.L.Q.(<0.146)	U.L.Q.(<0.0938)	U.L.Q.(<0.103)
SLC21A8/OATP1B3	U.L.Q.(<0.685)	U.L.Q.(<0.415)	U.L.Q.(<0.443)	U.L.Q.(<0.152)	U.L.Q.(<0.138)	U.L.Q.(<0.132)
SLC22A1/OCT1	U.L.Q.(<0.0391)	U.L.Q.(<0.0195)	U.L.Q.(<0.0301)	U.L.Q.(<0.0391)	U.L.Q.(<0.0195)	U.L.Q.(<0.0301)
SLC22A2/OCT2	U.L.Q.(<0.183)	U.L.Q.(<0.141)	U.L.Q.(<0.128)	U.L.Q.(<0.0852)	U.L.Q.(<0.0761)	U.L.Q.(<0.0709)
SLC22A3/OCT3	U.L.Q.(<0.154)	U.L.Q.(<0.101)	U.L.Q.(<0.103)	U.L.Q.(<0.0653)	U.L.Q.(<0.0442)	U.L.Q.(<0.0581)
SLC22A5/OCTN2	U.L.Q.(<0.244)	U.L.Q.(<0.154)	U.L.Q.(<0.181)	U.L.Q.(<0.119)	U.L.Q.(<0.0954)	U.L.Q.(<0.0927)
SLC22A6/OAT1	U.L.Q.(<0.0442)	U.L.Q.(<0.0549)	U.L.Q.(<0.0256)	U.L.Q.(<0.0230)	U.L.Q.(<0.0224)	U.L.Q.(<0.0226)
SLC22A8/OAT3	U.L.Q.(<0.298)	U.L.Q.(<0.0628)	U.L.Q.(<0.0723)	U.L.Q.(<0.123)	U.L.Q.(<0.0628)	U.L.Q.(<0.0723)
SLC22A11/OAT4	U.L.Q.(<0.152)	U.L.Q.(<0.0955)	U.L.Q.(<0.111)	U.L.Q.(<0.152)	U.L.Q.(<0.0955)	U.L.Q.(<0.111)
SLC47A2/MATE2	U.L.Q.(<0.460)	U.L.Q.(<0.218)	U.L.Q.(<0.320)	U.L.Q.(<0.410)	U.L.Q.(<0.218)	U.L.Q.(<0.176)
SLC47A2/MATE2k	U.L.Q.(<4.22)	U.L.Q.(<2.31)	U.L.Q.(<1.90)	U.L.Q.(<2.35)	U.L.Q.(<2.15)	U.L.Q.(<1.90)
Villin1	U.L.Q.(<0.172)	U.L.Q.(<0.117)	U.L.Q.(<0.128)	U.L.Q.(<0.110)	U.L.Q.(<0.103)	U.L.Q.(<0.0969)

^a The expression levels were described as mean ± S.E.M obtained from three to four MRM/SRM transitions in each ARPE19 sample. U.L.Q.: represents the values of the quantification limit (fmol/µg protein).

^b The average values (mean ± S.D.) were calculated as the average of ARPE19 samples (n=5).

^c The expression levels were calculated as an average of 2 quantitative values obtained from two SRM/MRM transitions.

^d The expression levels were calculated as the average of two samples.

^e The expression level was represented from the value obtained in one sample.