Title: *Gene expression analysis of membrane transporters and drug metabolizing enzymes in the lung of healthy and COPD subjects.*

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SUPPLEMENTARY INFORMATION (SI)

SI. Figure 1. Individual expression pattern of differential expressed genes encoding membrane transporters. Graphs show expression levels of individual genes encoding membrane transporters regarding differential expression between central airways and peripheral tissue. Black circles denote COPD patients and unfilled circles denote healthy subjects.

SI. Figure 2. Individual expression pattern of differential expressed genes encoding drug metabolizing enzymes. Graphs show expression levels of individual genes encoding drug metabolizing enzymes regarding differential expression between central airways and peripheral tissue. Black circles denote COPD patients and unfilled circles denote healthy subjects.

SI. Table 1. TLDA probes and median Ct-values for membrane transporters and housekeeping genes in healthy and COPD lung.

Gene	Applied Biosystems ID	Healthy		COPD	
		Central	Peripheral	Central	Peripheral
ABC Transporters					
ABCA1	Hs00194045_m1	28.73	27.97	28.09	28.07
ABCA2	Hs00242232_m1	30.40	31.22	29.83	29.84
ABCA3	Hs00184543_m1	27.21	27.15	26.97	25.55
ABCA4	Hs00184367_m1	33.21	-	33.42	34.88
ABCA5	Hs00363322_m1	28.87	30.75	28.36	28.88
ABCA6	Hs00365329_m1	29.25	30.51	28.41	28.41
ABCA7	Hs00185303_m1	30.15	32.82	29.85	31.10
ABCA9	Hs00329320_m1	30.11	30.83	28.46	28.97
ABCA10	Hs00365268_m1	31.12	33.11	29.92	30.99
ABCA12	Hs00292421_m1	34.44	-	32.44	-
ABCB1	Hs00184491_m1	33.33	33.41	32.02	31.82
ABCB4	Hs00240956_m1	-	-	34.51	34.39
ABCB5	Hs00698751_m1	-	-	-	-
ABCB6	Hs00180568_m1	28.77	31.84	28.97	29.68
ABCB7	Hs00188776_m1	29.51	30.09	28.17	28.28
ABCB8	Hs00185159_m1	29.01	29.84	28.84	29.06
ABCB9	Hs00608640_m1	31.65	33.88	31.90	31.82
ABCB10	Hs00429240_m1	30.38	31.23	29.51	29.89
ABCC1	Hs00219905_m1	29.43	30.89	28.93	29.45
ABCC2	Hs00166123_m1	34.77	34.74	34.50	34.34
ABCC3	Hs00358656_m1	31.01	30.80	29.80	30.25
ABCC4	Hs00195260_m1	30.72	31.08	29.69	29.03
ABCC5	Hs00194701_m1	30.46	31.83	30.45	31.19

ABCC6	Hs01077866_m1	29.59	31.99	29.45	29.25
ABCC7	Hs00357011_m1	32.72	-	-	-
ABCC8	Hs00165861_m1	29.16	30.85	28.94	28.32
ABCC9	Hs00245832_m1	29.43	30.89	28.93	29.45
ABCC10	Hs00375716_m1	29.58	30.49	29.00	29.82
ABCC11	Hs00261546_m1	-	-	-	-
ABCC12	Hs00264354_m1	-	-	-	-
ABCG1	Hs01555193_m1	28.36	29.23	27.94	27.77
ABCG2	Hs01053790_m1	33.70	34.37	32.50	31.23
ABCG4	Hs00967540_m1	-	-	-	-
ABCG5	Hs03037375_m1	-	-	-	-
ABCG8	Hs02880035_m1	-	-	-	-
Solute Carriers					
SLC47A1	Hs00217320_m1	31.31	31.75	30.48	29.07
SLC47A2	Hs00945650_m1	-	-	-	-
SLC15A1	Hs00192639_m1	-	-	34.94	-
SLC15A2	Hs01113665_m1	28.91	31.19	28.78	29.50
SLC16A1	Hs00161826_m1	31.20	33.41	30.58	30.66
SLC16A3	Hs01108070_m1	32.50	32.91	31.68	31.85
SLC16A4	Hs00190794_m1	29.91	31.55	29.39	28.60
SLC16A7	Hs00190974_m1	-	-	-	-
SLC19A1	Hs00953345_m1	31.13	31.75	30.74	29.46
SLC19A2	Hs00294767_m1	30.25	30.49	29.05	28.45
SLC19A3	Hs00228858_m1	31.38	31.82	30.28	28.65
SLC22A1	Hs00427554_m1	33.62	34.09	33.08	33.18
SLC22A11	Hs00945829_m1	-	-	-	-
SLC22A2	Hs00161893_m1	-	-	-	-

SLC22A3	Hs01009568_m1	30.55	30.07	29.10	28.09
SLC22A4	Hs00268200_m1	30.02	33.66	29.64	32.26
SLC22A5	Hs00161895_m1	30.78	32.91	30.04	30.87
SLC22A6	Hs00191220_m1	-	-	-	-
SLC22A7	Hs00198527_m1	-	-	-	-
SLC22A8	Hs00188599_m1	-	-	-	-
SLC22A9	Hs00971064_m1	-	-	-	-
SLC28A1	Hs00188418_m1	34.85	-	-	-
SLC28A2	Hs00188407_m1	33.86	-	34.29	-
SLC28A3	Hs00910439_m1	31.25	34.42	30.58	32.49
SLC29A1	Hs00191940_m1	27.80	28.41	27.43	27.03
SLC29A2	Hs00155426_m1	31.53	32.11	30.72	30.95
SLC29A3	Hs00983219_m1	30.54	30.57	29.54	29.65
SLC29A4	Hs00542001_m1	31.23	34.31	32.04	32.05
SLC2A1	Hs00892681_m1	28.17	32.32	27.64	29.91
SLC31A1	Hs00741015_m1	29.56	32.67	28.74	28.88
SLC31A2	Hs00156984_m1	28.63	28.77	27.52	26.77
SLC36A4	Hs00403119_m1	29.16	30.41	28.87	28.64
SLC3A2	Hs00374243_m1	28.82	30.67	28.04	27.70
SLC51A	Hs00380895_m1	30.26	33.20	28.96	33.60
SLC51B	Hs00418306_m1	32.49	33.10	30.69	31.16
SLC6A2	Hs01567442_m1	-	-	-	-
SLC6A3	Hs00168988_m1	-	34.11	-	-
SLC6A4	Hs00169010_m1	28.06	28.28	34.98	27.27
SLC7A1	Hs00931450_m1	29.10	31.97	27.76	29.30
SLC7A5	Hs00185826_m1	31.36	32.45	30.08	31.15
SLC7A6	Hs00187757_m1	29.25	31.05	28.84	28.89

SLC7A8	Hs00794796_m1	30.51	30.47	29.73	29.06
SLC7A11	Hs00204928_m1	32.51	-	32.28	31.91
Solute Carrier Organic Anion Transporters					
SLCO1A2	Hs00366488_m1	32.63	34.30	33.05	32.65
SLCO1B1	Hs00272374_m1	-	-	-	-
SLCO1B3	Hs00251986_m1	34.70	-	33.68	-
SLCO1C1	Hs00213714_m1	-	-	-	-
SLCO2B1	Hs00200670_m1	28.75	29.62	27.33	26.03
SLCO3A1	Hs00203184_m1	30.96	31.01	30.26	29.90
SLCO4A1	Hs00249583_m1	28.65	27.97	31.43	29.87
SLCO4C1	Hs00698884_m1	31.20	31.65	30.01	29.10
SLCO5A1	Hs00229597_m1	32.74	32.73	32.68	32.34
SLCO6A1	Hs00542846_m1	-	-	-	-
Copper-Transporting ATPases					
ATP7A	Hs00921963_m1	31.65	32.67	30.38	30.35
ATP7B	Hs00163739_m1	29.33	31.39	28.80	30.33
Housekeeping genes					
18S	Hs99999901_s1	15.19	16.08	15.03	14.81
ACTB	Hs99999903_m1	22.30	23.64	21.87	20.99
B2M	Hs00984230_m1	23.30	23.81	22.23	21.55
RPLP0	Hs99999902_m1	23.29	26.46	23.07	23.25
UBC	Hs00824723_m1	25.13	26.39	25.07	24.65

Table listing gene, Applied Biosystem assay ID, and median Ct-values for mRNA of membrane transporters and housekeeping genes in healthy and COPD lung. Median Ct-value of ≥35 is arbitrary set as cut off value.

SI. Table 2. TLDA probes and median Ct-values for drug metabolizing enzymes, transcription factors, and cell specific markers in healthy and COPD lung.

		Healthy		COPD	
Gene	Applied Biosystems ID	Central	Peripheral	Central	Peripheral
Cytochrome P450 enzymes					
CYP1A1	Hs00153120_m1	-	-	-	-
CYP1A2	Hs00167927_m1	-	-	-	-
CYP1B1	Hs00164383_m1	28.62	29.24	28.75	28.52
CYP2A6	Hs00868409_s1*	31.17	32.19	33.31	32.53
CYP2A13	Hs00426372_m1	31.70	32.77	-	34.23
CYP2B6	Hs03044634_m1	27.91	28.38	28.19	29.07
CYP2C19	Hs00426380_m1	34.09	33.22	-	-
CYP2C9	Hs00426397_m1	32.94	32.66	-	-
CYP2D6	Hs02576167_m1	34.38	-	-	-
CYP2E1	Hs00559368_m1	32.43	32.16	32.54	32.38
CYP2F1	Hs00167949_m1	28.72	28.44	32.56	31.37
CYP2J2	Hs00951113_m1	31.50	31.37	33.05	32.42
CYP2S1	Hs00258076_m1	28.86	28.49	30.63	30.24
CYP3A4	Hs00604506_m1	-	-	-	-
CYP3A5	Hs01070905_m1	34.10	34.80	33.30	33.46
CYP4B1	Hs00167970_m1	25.84	24.53	26.36	24.91
CYP4F2	Hs00426608_m1	-	-	-	-
Epoxide hydrolases					
EPHX1	Hs01116806_m1	26.46	26.07	27.07	25.76

EPHX2	Hs00157403_m1	29.90	30.06	31.37	30.55
EPHX3	Hs00227184_m1	33.17	32.59	33.71	32.92
EPHX4	Hs00543140_m1	33.23	32.91	33.47	33.54
Flavin monooxygenases					
FMO1	Hs00266654_m1	33.73	34.18	34.38	34.48
FMO2	Hs00155158_m1	27.77	26.57	27.61	26.31
FMO3	Hs00199368_m1	29.78	30.11	30.74	30.49
FMO4	Hs00157614_m1	31.80	30.98	32.95	31.44
FMO5	Hs00356233_m1	26.52	27.29	27.56	28.03
Glutathione S-Transferases					
GSTA1	Hs00275575_m1	26.30	26.85	31.30	28.32
GSTA2	Hs00747232_mH	29.19	29.82	33.31	31.61
GSTA3	Hs00374175_m1	32.23	33.08	34.43	33.94
GSTA4	Hs00155308_m1	29.45	28.70	29.14	28.47
GSTA5	Hs00604085_m1	-	-	-	-
GSTK1	Hs00210861_m1	26.02	25.60	25.87	25.79
GSTM1	Hs02341469_m1	-	-	-	-
GSTM2	Hs00265266_g1*	29.09	28.18	28.94	28.45
GSTM3	Hs00356079_m1	29.71	29.38	29.84	29.03
GSTM4	Hs00426432_m1	31.01	30.95	31.38	31.25
GSTM5	Hs00757076_m1	32.21	31.95	32.62	30.71
GSTO1	Hs00818731_m1	28.49	27.62	27.24	26.49
GSTO2	Hs00826661_m1	33.18	32.23	33.08	33.16
GSTP1	Hs00168310_m1	22.88	22.16	22.96	22.82
GSTT1	Hs01091674_m1	-	34.06	32.72	-
GSTZ1	Hs01041668_m1	30.89	30.15	30.66	30.81
Arylamine N-acetyltransferase					

NAT1	Hs00377717_m1	-	34.72	-	-
NAT2	Hs00605099_m1	-	-	-	-
SULFO-Transferases					
SULT1A1	Hs00738644_m1	-	-	-	-
SULT1A2	Hs02340929_g1*	32.69	32.86	31.74	31.45
SULT1C2	Hs00602560_m1	-	34.02	33.73	33.77
SULT1C4	Hs00198159_m1	31.73	32.35	31.28	30.80
SULT2B1	Hs00190268_m1	29.21	28.85	29.44	28.86
SULT4A1	Hs00205005_m1	-	-	-	-
SULT6B1	Hs01376028_m1	-	-	-	-
UDP- Glycosyl-Transferases					
UGT1A1	Hs02511055_s1*	33.07	31.88	33.42	33.71
UGT1A3	Hs04194492_g1*	34.47	33.40	34.96	-
UGT1A4	Hs01655285_s1*	34.26	33.33	-	-
UGT1A6	Hs01592477_m1	33.60	33.06	-	-
UGT1A7	Hs02517015_s1*	32.24	32.64	32.64	33.72
UGT1A8	Hs01592482_m1	-	34.54	-	-
UGT1A9	Hs02516855_sH*	33.94	34.14	34.11	-
UGT1A10	Hs02516990_s1*	33.12	32.98	34.16	34.78
UGT2A1	Hs00792016_m1	31.35	33.57	-	-
UGT2B4	Hs02383831_s1*	-	34.24	-	34.83
UGT2B7	Hs00426592_m1	-	-	-	-
UGT2B10	Hs02556282_s1*	-	-	-	-
UGT2B15	Hs00870076_s1*	-	-	-	-
Carboxyl esterase					
CES1	Hs00275607_m1	27.66	27.19	27.44	26.69
CES2	Hs00187279_m1	29.80	29.75	30.30	30.17

CES3	Hs00227775_m1	30.64	29.89	33.26	32.28
CES4A	Hs00545143_m1	28.79	28.70	30.44	29.51
CES5A	Hs00326937_m1	-	-	-	-
Transcription factors					
NR1H4	Hs00231968_m1	-	-	-	-
NR1I2	Hs00243666_m1	33.31	33.86	-	-
NR1I3	Hs00901571_m1	-	-	-	-
AHR	Hs00907322_m1	28.39	27.95	27.66	27.31
AHRR	Hs00324967_m1	34.86	-	-	-
ARNT	Hs00231048_m1	28.38	27.66	28.17	27.42
AIP	Hs00610222_m1	27.71	26.98	27.17	26.74
NR3C1	Hs00353740_m1	28.76	27.84	27.57	27.29
CEBPA	Hs00269972_s1*	29.69	28.80	28.38	28.54
CEBPB	Hs00942496_s1*	26.67	25.60	25.52	24.55
CEBPD	Hs00270931_s1*	27.59	26.61	26.28	25.61
Cell specific markers					
AQP5	Hs00387048_m1	25.38	25.08	30.19	29.06
CD68	Hs00154355_m1	26.11	26.19	24.52	24.62
CDH1	Hs01023894_m1	25.90	24.86	26.26	25.14
CEACAM8	Hs00266198_m1	-	-	34.91	33.67
IVL	Hs00902520_m1	30.89	30.15	30.66	30.81
LCK	Hs00178427_m1	31.75	31.26	30.36	30.10
MUC5AC	Hs01365601_m1	26.78	27.02	34.42	34.91
P4HB	Hs00168586_m1	26.18	25.87	25.93	26.20
PECAM1	Hs00169777_m1	25.39	26.11	24.87	24.30
PTPRC	Hs00894734_m1	32.94	31.80	30.77	30.69
SFTPC	Hs00161628_m1	21.51	21.13	20.10	19.12

Housekeeping genes					
18S	Hs99999901_s1	16.29	16.92	16.71	15.89
ACTB	Hs99999903_m1	22.74	22.44	21.74	22.33
B2M	Hs00984230_m1	22.12	21.44	20.85	20.51
RPLP0	Hs99999902_m1	23.57	23.52	23.48	23.62
UBC	Hs00824723_m1	24.66	24.77	25.24	24.11

Table listing gene, Applied Biosystem assay ID, and median Ct-values for mRNA of drug metabolizing enzymes, transcription factors, cell specific markers, and housekeeping genes in healthy and COPD lung. Median Ct-value of ≥35 is arbitrary set as cut off value.

SI. Table 3. Gene expression of membrane transporter from healthy and COPD lung in % of expression of Housekeeping genes.

		Healthy		COPD	
Gene	Protein	Central	Peripheral	Central	Peripheral
ABC-transporters					
ABCA1	ABCA1	-	-	0.10	-
ABCA2	ABCA2	3.76	7.47	1.82	2.22
ABCA3	ABCA3	1.00	0.83	0.76	0.48
ABCA4	ABCA4	8.26	21.36	3.06	10.26
ABCA5	ABCA5	0.06	-	0.07	-
ABCA6	ABCA6	2.63	1.43	2.46	0.99
ABCA7	ABCA7	3.83	4.01	1.75	2.18
ABCA9	ABCA9	0.99	0.86	0.66	0.25
ABCA10	ABCA10	0.61	0.39	0.52	0.40
ABCA12	ABCA12	-	-	0.10	-
ABCB1	MDR1	0.17	0.16	0.12	0.16
ABCB4	MDR3	-	-	-	-
ABCB5	ABCB5	-	-	-	-
ABCB6	ABCB6	2.72	1.64	1.55	0.56
ABCB7	ABCB7	2.16	3.11	1.70	1.57
ABCB8	ABCB8	1.87	2.11	1.37	0.75
ABCB9	ABCB9	0.29	0.18	0.16	0.10
ABCB10	ABCB10	1.06	0.89	1.35	0.51
ABCC1	MRP1	1.41	1.35	1.11	0.61
ABCC2	MRP2	-	0.08	-	-
ABCC3	MRP3	0.70	0.98	0.49	0.48
ABCC4	MRP4	0.95	1.21	0.67	0.92
ABCC5	MRP5	0.84	0.64	0.48	0.21
ABCC6	MRP6	1.43	1.62	0.83	0.86
ABCC7	CFTR	0.17	1.39	-	-
ABCC8	ABCC8	1.75	2.00	0.99	1.55
ABCC9	ABCC9	1.41	1.35	1.11	0.61
ABCC10	MRP7	1.28	1.30	1.25	0.43
ABCC11	MRP8	-	-	-	-
ABCC12	MRP9	-	-	-	-

ABCG1	ABCG1	3.49	5.47	2.05	2.13
ABCG2	BCRP	0.14	0.09	0.08	0.15
ABCG4	ABCG4	-	-	-	-
ABCG5	ABCG5	-	-	-	-
ABCG8	ABCG8	-	-	-	-
Solute Carriers					
SLC47A1	MATE1	0.40	0.85	0.31	0.92
SLC47A2	MATE2	-	-	-	-
SLC15A1	PepT1	-	-	-	-
SLC15A2	PepT2	1.96	1.08	1.43	0.75
SLC16A1	MCT1	0.42	0.28	0.36	0.26
SLC16A3	MCT3	0.24	0.35	0.21	0.12
SLC16A4	MCT4	0.88	1.04	0.75	1.09
SLC16A7	MCT2	-	-	-	-
SLC19A1	RFP1	0.64	1.26	0.30	0.75
SLC19A2	THT2	2.05	1.77	0.95	1.59
SLC19A3	THTR2	0.53	1.07	0.34	1.33
SLC22A1	OCT1	0.06	0.11	0.05	0.05
SLC22A11	OAT4	-	-	-	-
SLC22A2	OCT2	-	-	-	-
SLC22A3	OCT3	1.06	2.43	1.01	1.84
SLC22A4	OCTN1	1.17	0.18	1.16	0.18
SLC22A5	OCTN2	0.53	0.39	0.48	0.27
SLC22A6	OAT1	-	-	-	-
SLC22A7	OAT2	-	-	-	-
SLC22A8	OAT3	-	-	-	-
SLC22A9	UST3H	-	-	-	-
SLC28A1	CNT1	-	-	-	-
SLC28A2	CNT2	-	-	-	-
SLC28A3	CNT3	0.35	0.09	0.38	0.08
SLC29A1	ENT1	5.49	5.93	2.98	3.79
SLC29A2	ENT2	0.39	0.44	0.30	0.26
SLC29A3	ENT3	0.95	1.18	0.65	0.69
SLC29A4	ENT4	0.29	0.11	0.18	0.07
SLC2A1	GLUT1	3.09	0.55	3.89	0.55
SLC31A1	Ctr1	1.48	0.62	1.52	1.01
SLC31A2	Ctr2	3.40	5.44	2.57	4.24
SLC36A4	PAT4	2.09	2.12	1.17	1.16

SLC3A2	4F2HC	3.27	4.44	1.98	2.11
SLC51A	OSTalpha	0.87	0.14	1.21	0.09
SLC51B	OSTBETA	0.27	0.18	0.27	0.18
SLC6A14	ATB(0+)	1.70	0.96	1.49	1.59
SLC7A1	CAT1	2.00	1.54	2.66	0.77
SLC7A5	LAT1	0.31	0.57	0.58	0.25
SLC7A6	LAT-2, LAT3, y+LAT-2	2.41	2.17	1.28	0.95
SLC7A8	LAT2, LPI-PC1	1.02	1.21	0.66	0.65
SLC7A11	SLC7A11	0.12	0.06	0.11	0.15
SLC6A2	NAT	-	-	-	-
SLC6A3	DAT	-	-	-	-
SLC6A4	SERT	3.76	8.08	0.87	3.38
Solute Carrier Organic Anion Transporters					
SLCO1A2	OATP1A2	0.16	0.05	0.10	0.13
SLCO1B1	OATP1B1	-	-	-	-
SLCO1B3	OATP1B3	-	-	-	-
SLCO1C1	OATP1C1	-	-	-	-
SLCO2B1	OATP2B1	3.23	7.76	2.49	7.19
SLCO3A1	OATP3A1	0.68	0.99	0.41	0.54
SLCO4A1	OATP4A1	2.64	6.96	0.28	0.47
SLCO4C1	OATP4C1	0.60	0.97	0.44	0.76
SLCO5A1	OATP5A1	0.20	0.28	0.12	0.06
SLCO6A1	OATP6A1	-	-	-	-
Copper Transporters					
ATP7A	ATP7A	0.49	0.48	0.35	0.35
ATP7B	ATP7B	1.41	0.84	1.29	0.43

Gene expression of membrane transporter from healthy and COPD lung in % of expression of Housekeeping genes. Expression levels correspond to average ΔCt within each group expressed in % of the expression of the mean of the three housekeeping genes *4* (avg HKGs). Expression is calculates as (% avg HKGs) = $2^{-(Ct(\text{Gene of interest})-Ct(\text{avg HKGs}))} \times 100$. Non detectable (-) $\% < 0.05$; very low (+/-) $0.05 \leq \% < 0.1$, low (+) $0.1 \leq \% < 1$, moderate (++) $1 \leq \% < 10$, high (+++) $10 \leq \% < 100$, very high (++++) $100 \leq \%$.

SI.Table 4. Inter-individual variability of expressed genes encoding membrane transporters in healthy or COPD human lung in central or peripheral airways.

	Healthy						**COPD**					
	Central			**Peripheral**			**Central**			**Peripheral**		
Gene	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**
ABC-transporters												
ABCA1	**4.3**	29.0	26.8	**3.2**	29.4	27.7	**3.5**	30.0	27.4	**3.5**	29.5	26.8
ABCA2	**3.3**	30.7	28.9	**3.1**	32.7	30.9	**2.8**	30.5	28.7	**2.9**	31.8	29.3
ABCA3	**3.4**	28.7	27.0	**3.0**	27.6	26.1	**8.2**	31.6	26.3	**4.0**	27.7	24.7
ABCA4	**4.6**	35.0	32.0				**2.8**	33.9	32.0			
ABCA5	**4.2**	29.5	27.2	**1.7**	31.5	30.4	**2.8**	28.7	27.1	**2.4**	30.6	28.7
ABCA6	**6.5**	29.3	26.1	**6.3**	32.6	28.7	**2.4**	29.4	27.7	**2.5**	29.0	26.9
ABCA7	**0.6**	30.4	30.0	**3.5**	33.0	31.0	**3.2**	31.1	28.6	**1.5**	31.9	30.6
ABCA9	**7.1**	30.3	26.6	**2.4**	31.2	29.8	**1.9**	29.7	28.4	**3.7**	29.9	26.8
ABCA10	**5.4**	32.1	28.9	**2.6**	34.1	32.4	**2.1**	31.0	29.4	**3.4**	32.3	28.9
ABCA12	**1.1**	35.0	34.2				**3.2**	34.0	31.8			
ABCB1	**4.1**	33.4	31.1	**4.9**	34.8	31.6	**1.9**	33.2	31.7	**3.5**	33.4	30.1
ABCB6	**4.1**	29.5	27.2	**2.6**	32.1	30.5	**2.1**	29.1	27.8	**2.3**	31.1	28.9
ABCB7	**4.5**	29.7	27.4	**4.6**	32.2	29.6	**1.9**	29.3	27.8	**1.9**	29.4	27.8
ABCB8	**1.4**	29.6	28.8	**4.6**	31.8	29.2	**2.2**	29.5	27.9	**3.2**	31.3	28.7
ABCB9	**2.0**	32.4	31.2	**2.8**	34.7	32.8	**1.4**	32.4	31.2	**3.2**	34.3	31.4
ABCB10	**2.8**	30.5	29.0	**4.5**	32.2	29.5	**2.0**	30.7	29.2	**2.6**	31.4	29.0
ABCC1	**2.5**	30.2	28.7	**4.3**	32.0	29.4	**1.7**	29.8	28.4	**3.8**	31.9	28.4
ABCC2				**1.4**	35.0	34.0						
ABCC3	**3.9**	31.6	29.3	**5.6**	32.8	29.3	**3.6**	32.0	29.3	**2.1**	31.1	29.4

ABCC4	**4.3**	30.9	28.6	**5.1**	31.5	28.7	**2.9**	31.0	28.8	**2.8**	30.4	28.1
ABCC5	**0.2**	30.6	30.4	**2.2**	32.5	31.0	**2.4**	31.1	29.3	**2.8**	32.6	30.1
ABCC6	**2.4**	30.8	29.4	**3.9**	32.5	30.2	**3.5**	31.2	28.4	**2.1**	30.2	28.6
ABCC7	**5.4**	35.0	31.5	**9.0**	35.0	29.8	**0.0**	35.0	35.0	**0.7**	35.0	34.4
ABCC8	**3.5**	30.1	28.1	**3.6**	32.4	30.2	**2.3**	30.3	28.6	**2.4**	29.5	27.4
ABCC9	**2.5**	30.2	28.7	**4.3**	32.0	29.4	**1.7**	29.8	28.4	**3.8**	31.9	28.4
ABCC10	**2.9**	30.4	28.7	**3.6**	32.2	30.1	**2.4**	29.6	27.9	**3.6**	32.4	29.2
ABCG1	**1.9**	29.1	28.1	**2.3**	29.8	28.5	**2.0**	29.1	27.6	**3.5**	29.7	26.9
ABCG2	**4.8**	34.0	31.1	**5.1**	35.0	31.8	**3.5**	34.9	32.0	**4.4**	34.5	30.2
Solute Carriers												
SLC47A1	**3.2**	32.2	30.2	**6.2**	32.5	28.9	**4.0**	32.9	29.9	**3.8**	31.2	27.6
SLC15A2	**3.2**	29.9	28.0	**4.1**	31.9	29.5	**3.1**	30.0	27.9	**3.1**	31.1	28.5
SLC16A1	**2.6**	32.0	30.4	**7.9**	34.2	29.5	**1.5**	31.2	29.9	**3.2**	32.6	29.6
SLC16A3	**2.4**	32.6	31.2	**5.8**	33.5	30.0	**3.4**	33.1	30.5	**3.3**	33.7	30.9
SLC16A4	**4.0**	31.3	28.9	**2.1**	32.7	31.4	**1.8**	30.3	29.0	**3.7**	30.9	27.8
SLC19A1	**1.5**	31.6	30.7	**2.9**	32.6	30.8	**4.7**	33.3	29.8	**2.2**	30.4	28.8
SLC19A2	**6.8**	30.4	26.9	**2.3**	30.7	29.4	**3.0**	30.7	28.5	**3.5**	30.0	27.4
SLC19A3	**3.0**	31.8	30.0	**2.6**	32.7	31.0	**7.5**	35.3	29.3	**2.5**	30.1	28.0
SLC22A1	**3.9**	34.7	32.0	**1.7**	35.0	33.9	**1.6**	33.9	32.8	**1.8**	34.3	32.4
SLC22A3	**3.9**	30.7	28.6	**5.1**	32.6	29.5	**1.5**	29.8	28.7	**2.8**	29.5	27.3
SLC22A4	**4.1**	30.7	28.4	**1.1**	34.3	33.7	**3.7**	30.2	27.9	**6.2**	34.3	29.5
SLC22A5	**2.6**	31.7	30.1	**0.6**	33.3	32.9	**2.6**	31.2	29.3	**2.7**	32.3	29.6
SLC28A3				**4.5**	34.7	32.0				**3.8**	34.3	30.5
SLC29A1	**1.7**	28.2	27.3	**2.8**	29.7	28.3	**2.2**	28.6	27.0	**2.6**	28.4	26.1
SLC29A2	**2.2**	31.9	30.6	**8.7**	34.1	28.7	**2.5**	32.1	30.1	**2.3**	32.0	30.2
SLC29A3	**3.8**	30.9	28.7	**4.7**	32.5	29.6	**1.9**	30.7	29.3	**3.4**	31.2	27.9
SLC29A4	**3.3**	32.9	30.9	**6.0**	34.8	31.1	**1.8**	32.2	30.9	**3.6**	35.0	31.9

SLC2A1	**4.5**	29.6	27.0	**6.6**	33.0	29.1	**2.3**	27.9	26.5	**4.4**	32.3	28.0
SLC31A1	**7.1**	31.5	27.3	**1.2**	32.9	32.1	**1.6**	29.1	28.1	**3.0**	30.5	28.0
SLC31A2	**3.7**	29.3	27.3	**2.4**	29.7	28.4	**2.6**	28.8	27.2	**2.8**	28.4	26.0
SLC36A4	**3.8**	29.8	27.7	**3.7**	32.4	30.4	**2.2**	29.9	28.2	**2.4**	30.0	28.1
SLC3A2	**4.4**	29.1	26.8	**3.7**	31.3	29.1	**0.9**	28.6	27.9	**4.0**	30.2	26.8
SLC51A	**3.9**	31.2	28.8	**2.5**	34.2	32.6	**1.9**	29.6	28.2	**5.3**	35.0	30.6
SLC51B	**3.9**	32.7	30.4	**6.4**	34.9	30.7	**3.1**	32.4	30.1	**3.4**	33.4	30.2
SLC6A14	**6.5**	31.1	27.3	**3.3**	31.8	29.8	**1.8**	29.4	28.1	**2.9**	29.7	27.6
SLC7A1	**3.9**	29.9	27.7	**2.5**	32.0	30.6	**1.6**	28.7	27.5	**3.0**	31.0	28.5
SLC7A5	**4.8**	33.1	30.2	**0.7**	32.8	32.4	**2.9**	31.4	29.3	**3.5**	32.9	29.8
SLC7A6	**3.6**	29.6	27.6	**3.4**	32.1	30.0	**2.5**	29.9	28.0	**2.6**	30.6	28.3
SLC7A8	**5.8**	31.4	28.0	**8.8**	33.0	27.7	**1.1**	30.3	29.4	**4.0**	32.0	28.4
SLC7A11	**4.6**	34.5	31.6	**4.4**	35.0	32.4	**1.8**	33.2	31.9	**0.9**	32.4	31.7
SLC6A4	**8.0**	32.1	27.9	**6.8**	31.3	27.5	**11.3**	35.0	27.0	**8.4**	32.1	25.1
Solute Carrier Organic Anion Transporters												
SLCO1A2	**3.7**	34.7	32.6	**4.1**	34.8	32.2	**2.6**	33.9	31.9	**3.6**	35.0	31.9
SLCO2B1	**4.9**	29.3	26.7	**5.8**	31.4	28.0	**6.0**	30.7	26.7	**3.9**	28.0	25.0
SLCO3A1	**2.6**	31.1	29.6	**8.7**	32.2	27.2	**3.4**	32.2	29.4	**2.3**	31.2	29.1
SLCO4A1	**6.4**	31.6	28.2	**14.0**	29.4	22.4	**2.6**	32.2	30.0	**3.2**	31.7	29.2
SLCO4C1	**3.2**	31.6	29.7	**11.6**	31.7	25.7	**3.2**	32.0	29.4	**3.1**	31.0	28.5
SLCO5A1	**2.0**	32.8	31.7	**10.9**	34.0	27.5	**3.2**	33.7	31.3	**3.9**	35.0	31.8
Copper-Transporting ATPases												
ATP7A	**3.7**	31.8	29.7	**0.4**	32.8	32.5	**1.8**	31.4	30.2	**2.5**	31.8	29.6
ATP7B	**3.7**	30.5	28.3	**2.2**	32.0	30.6	**1.4**	29.3	28.4	**2.7**	31.5	28.8

The inter-individual Variability (CV) among genes encoding membrane transporters in healthy or COPD human lung from both central airways and peripheral tissue. The inter individual variability in gene expression is evaluated by calculation of the coefficient of variation using the CT values (CV = 100x(ΔCt standard deviation/mean ΔCt)).

SI. Table 5. Gene expression of drug metabolizing enzymes from healthy and COPD lung in % of expression of Housekeeping genes.

		Healthy		**COPD**	
Genes	***Protein***	**Central**	**Peripheral**	**Central**	**Peripheral**
Cytochrome P450 enzymes					
CYP1A1	CYP1A1	-	-	-	-
CYP1A2	CYP1A2	-	-	-	-
CYP1B1	CYP1B1	1.12	0.84	1.06	1.10
CYP2A6	CYP2A6	1.00	0.36	0.15	0.06
CYP2A13	CYP2A13	0.29	0.15	-	-
CYP2B6	CYP2B6	4.26	12.26	7.61	1.49
CYP2C19	CYP2C19	0.07	0.06	-	-
CYP2C9	CYP2C9	0.11	0.09	-	-
CYP2D6	CYP2D6	-	-	-	-
CYP2E1	CYP2E1	0.24	0.16	0.25	0.13
CYP2F1	CYP2F1	3.28	1.56	0.23	0.18
CYP2J2	CYP2J2	0.66	0.32	0.17	0.07
CYP2S1	CYP2S1	1.55	1.87	0.76	0.40
CYP3A4	CYP3A4	-	-	-	-
CYP3A5	CYP3A5	0.08	-	0.14	0.05
CYP4B1	CYP4B1	63.00	32.77	20.06	24.69
CYP4F2	CYP4F2	-	-	-	-
Epoxide hydrolases					
EPHX1	EPHX1	11.14	8.71	6.19	7.51

EPHX2	EPHX2	0.80	0.59	0.40	0.35
EPHX3	EPHX3	0.13	0.10	0.09	0.08
EPHX4	EPHX4	0.08	0.08	-	-
Flavin monooxygenases					
FMO1	FMO1	0.09	0.06	-	-
FMO2	FMO2	5.91	4.98	8.05	6.43
FMO3	FMO3	0.84	0.51	0.51	0.40
FMO4	FMO4	0.28	0.23	0.13	0.15
FMO5	FMO5	11.28	5.48	11.50	4.19
Glutathione S-Transferases					
GSTA1	GSTA1	10.02	7.78	0.69	2.15
GSTA2	GSTA2	3.52	1.70	0.15	0.37
GSTA3	GSTA3	0.27	0.11	0.06	-
GSTA4	GSTA4	1.76	1.52	2.51	1.62
GSTA5	GSTA5	-	-	-	-
GSTK1	GSTK1	12.01	11.57	8.91	8.69
GSTM1	GSTM1	-	-	-	-
GSTM2	GSTM2	2.42	2.22	3.01	1.94
GSTM3	GSTM3	1.26	0.77	1.04	0.90
GSTM4	GSTM4	0.41	0.28	0.28	0.24
GSTM5	GSTM5	0.27	0.13	0.20	0.24
GSTO1	GSTO1	3.45	3.46	4.22	5.02
GSTO2	GSTO2	0.13	0.12	0.05	0.07
GSTP1	GSTP1	152.80	140.59	101.93	66.64
GSTT1	GSTT1	0.12	0.05	0.25	0.05
GSTZ1	GSTZ1	0.49	0.49	0.29	0.27
N-Acetyl-Transferases					

NAT1	NAT1	-	-	-	-
NAT2	NAT2	-	-	-	-
SULFO-Transferases					
SULT1A1	SULT1A1	-	-	-	-
SULT1A2	SULT1A2	0.16	0.09	0.38	0.18
SULT1C2	SULT1C2	0.01	0.06	0.02	0.05
SULT1C4	SULT1C4	0.37	0.16	0.41	0.25
SULT2B1	SULT2B1	2.38	1.27	2.32	1.29
SULT4A1	SULT4A1	-	-	-	-
SULT6B1	SULT6B1	-	-	-	-
UDP- Glycosyl-Transferases					
UGT1A1	UGT1A1	0.15	0.45	0.13	0.03
UGT1A3	UGT1A3	-	0.11	-	-
UGT1A4	UGT1A4	-	0.11	-	-
UGT1A6	UGT1A6	-	0.07	-	-
UGT1A7	UGT1A7	0.16	0.53	0.28	-
UGT1A8	UGT1A8	-	-	-	-
UGT1A9	UGT1A9	0.06	0.19	0.08	-
UGT1A10	UGT1A10	0.09	0.24	0.08	-
UGT2A1	UGT2A1	0.17	0.10	-	-
UGT2B4	UGT2B4	-	-	-	-
UGT2B7	UGT2B7	-	-	-	-
UGT2B10	UGT2B10	-	-	-	-
UGT2B15	UGT2B15	-	-	-	-
Carboxylesterases					
CES1	Carboxyl esterase 1	7.19	3.84	5.66	4.35
CES2	Carboxyl esterase 2	0.85	0.77	0.88	0.39

CES3	Carboxyl esterase 3	0.54	0.53	0.09	0.24
CES4A	Carboxyl esterase 4A	3.56	2.03	1.00	0.57
CES5A	Carboxyl esterase 5	-	-	-	-

Gene expression of drug metabolizing enzymes from healthy and COPD lung in % of expression of housekeeping genes. Expression levels correspond to average ΔCt within each group expressed in % of the expression of the mean of the three housekeeping genes *ACTB, B2M, and RPLP0* (avg HKGs). Expression is calculates as (% avg HKGs) = $2^{-(\mathrm{Ct(Gene\ of\ interest)}-\mathrm{Ct(avg\ HKGs)})} \times 100$. Non detectable (-) % < 0.05; very low (+/-) 0.05 ≤ % < 0.1, low (+) 0.1 ≤ %< 1, moderate (++) 1 ≤ % < 10, high (+++) 10 ≤ % < 100, very high (++++) 100 ≤ %.

SI. Table 6. The inter-individual variability among genes encoding metabolizing enzymes with in healthy or COPD human lung from both central airways and peripheral tissue.

	Healthy						**COPD**					
	Central			**Peripheral**			**Central**			**Peripheral**		
Gene	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**
Cytochrome P450 enzymes												
CYP1B1	**8.4**	32.5	28.3	**4.9**	32.1	28.5	**6.9**	31.8	28.2	**7.2**	32.8	28.0
CYP2A13	**5.0**	33.0	30.0	**5.9**	35.0	30.2						
CYP2A6	**9.2**	35.0	29.7	**2.7**	33.1	31.1	**4.7**	35.0	32.0	**5.7**	35.8	31.8
CYP2B6	**3.4**	29.3	27.5	**3.6**	29.4	27.1	**5.1**	29.8	27.0	**2.9**	30.2	28.0
CYP2C9	**4.4**	34.3	31.5									
CYP2C19	**3.7**	34.5	32.3	**2.8**	35.0	32.3	**1.1**	35.0	34.3	**0.0**	35.0	35.0
CYP2E1	**2.7**	32.6	31.1	**2.7**	33.9	31.4	**0.6**	32.7	32.3	**3.1**	33.9	31.5
CYP2F1	**7.2**	29.8	26.1	**10.4**	35.0	27.1	**4.8**	35.0	32.1	**8.6**	35.0	29.6
CYP2J2	**7.4**	32.2	28.3	**5.2**	34.0	29.6	**2.6**	34.5	32.9	**4.2**	35.0	32.2
CYP2S1	**2.5**	30.0	28.7	**7.0**	32.4	27.3	**3.5**	31.3	29.3	**5.7**	33.3	28.9
CYP3A5	**5.0**	35.0	31.9				**2.4**	34.4	32.9	**4.8**	34.8	31.4
CYP4B1	**5.1**	25.9	23.8	**5.8**	26.6	23.0	**7.8**	27.1	23.6	**3.9**	26.0	23.5
Epoxide hydrolases												
EPHX1	**5.8**	27.6	24.8	**6.2**	29.2	25.1	**6.2**	28.8	25.6	**5.4**	28.7	25.4
EPHX2	**4.3**	31.4	28.9	**6.0**	33.6	28.9	**4.2**	32.4	29.9	**5.5**	33.5	29.3
EPHX3	**5.2**	34.1	31.0	**3.6**	34.9	31.5	**4.5**	34.7	31.8	**3.0**	34.3	31.7
EPHX4	**5.2**	34.8	31.5	**3.2**	35.0	32.0						
Flavin monooxygenases												
FMO1	**5.8**	35.0	31.4				**4.1**	35.0	32.5			

FMO2	**3.9**	28.3	26.3	**4.6**	29.2	26.3	**4.6**	27.9	25.7	**4.8**	28.2	25.0
FMO3	**6.1**	31.9	28.4	**4.5**	32.5	29.1	**4.3**	32.1	29.6	**3.4**	32.0	29.4
FMO4	**4.1**	32.8	30.3	**5.2**	34.7	30.5	**4.3**	34.1	31.4	**4.8**	34.4	30.7
FMO5	**5.8**	28.6	25.8	**3.2**	29.1	26.8	**3.6**	28.8	26.8	**3.1**	28.3	26.3
Glutathione S-Transferases												
GSTA1	**5.9**	27.9	25.0	**10.2**	31.7	24.7	**4.6**	31.5	29.1	**13.2**	33.2	25.9
GSTA2	**7.7**	29.6	25.9	**11.8**	35.0	26.1	**5.0**	35.0	31.8	**12.7**	36.7	28.2
GSTA3	**6.7**	33.5	29.6	**5.7**	35.0	30.5	**1.0**	34.9	34.3	**2.5**	35.0	33.1
GSTA4	**4.2**	29.9	27.7	**2.9**	30.2	28.3	**2.9**	29.4	27.9	**4.3**	30.6	27.6
GSTK1	**2.4**	27.0	25.8	**6.0**	28.9	25.0	**6.0**	28.3	25.4	**3.5**	27.7	25.5
GSTM2	**4.4**	31.0	28.7	**5.7**	31.3	27.0	**4.4**	30.4	28.0	**1.8**	29.2	28.0
GSTM3	**6.0**	31.0	27.7	**3.8**	32.1	29.2	**5.2**	31.2	28.3	**4.5**	31.4	28.1
GSTM4	**4.2**	32.3	29.8	**4.2**	33.8	30.5	**2.7**	32.7	31.1	**3.8**	33.1	30.0
GSTM5	**10.0**	35.2	29.3	**3.9**	34.5	31.4	**5.5**	33.7	30.4	**4.6**	33.5	29.9
GSTO1	**7.4**	29.8	26.0	**3.7**	29.1	26.5	**6.8**	29.6	26.1	**4.6**	28.7	25.7
GSTO2	**5.5**	34.2	30.9	**4.3**	34.9	30.9	**3.9**	35.0	32.6	**3.5**	34.8	31.9
GSTP1	**6.5**	23.7	21.0	**7.5**	25.4	21.2	**5.2**	24.4	22.1	**7.6**	25.9	21.6
GSTT1	**9.6**	35.3	30.2				**2.7**	32.7	31.3	**3.4**	35.0	32.5
GSTZ1	**4.5**	32.1	29.4	**5.6**	34.0	29.4	**5.0**	33.3	30.6	**4.3**	33.3	30.0
SULFO-Transferases												
SULT1A2	**1.5**	33.5	32.6	**3.6**	34.7	31.9	**2.4**	32.2	30.7	**3.8**	33.6	30.7
SULT1C2				**2.5**	35.0	32.8				**2.5**	34.6	32.6
SULT1C4	**4.2**	32.7	30.2	**2.8**	33.3	30.9	**2.7**	32.1	30.4	**5.3**	33.6	29.6
SULT2B1	**4.7**	29.8	27.3	**5.2**	31.9	28.0	**3.4**	29.5	27.8	**5.0**	30.9	27.1
UDP- Glycosyl-Transferases												
UGT1A10	**4.4**	34.7	31.9	**2.5**	33.6	31.6	**1.5**	35.0	34.1			
UGT1A1	**3.7**	33.4	31.3	**1.9**	32.3	30.7	**2.8**	34.8	33.0			

UGT1A3				**1.4**	34.0	32.9						
UGT1A4				**1.4**	34.0	32.9						
UGT1A6				**3.3**	35.0	31.8						
UGT1A7	**4.5**	33.8	31.0	**3.5**	33.0	30.2	**2.7**	33.9	32.3			
UGT1A9	**4.1**	34.7	32.1	**3.3**	34.5	31.7	**1.6**	35.0	34.0			
UGT2A1	**5.8**	34.5	31.3				**0.0**	35.0	35.0			
Carboxylesterases												
CES1	**5.0**	28.1	25.7	**5.0**	29.6	26.5	**4.7**	28.6	26.1	**5.0**	29.2	25.7
CES2	**3.1**	31.0	29.2	**5.5**	32.8	28.4	**2.4**	30.9	29.5	**4.6**	32.9	29.4
CES3	**2.8**	31.6	30.0	**7.3**	35.0	29.3	**3.3**	34.3	32.1	**3.2**	33.0	30.7
CES4A	**4.8**	28.8	26.6	**7.6**	32.5	26.6	**4.2**	32.5	30.2	**5.3**	32.4	28.6

The inter individual-variability (CV) among genes encoding metabolizing enzymes in healthy or COPD human from both central airways and peripheral tissue. The inter-individual variability in gene expression is evaluated by calculation of the coefficient of variation using the CT values (CV = 100x (ΔCt standard deviation/mean ΔCt)).

SI. Table 7. Expression of genes encoding transcription factors from healthy and COPD lung in % of expression of Housekeeping genes.

		Healthy		**COPD**	
Gene	**Protein**	**Central**	**Peripheral**	**Central**	**Peripheral**
NR1H4	FXR	-	-	-	-
NR1I2	PXR	0.10	-	-	-
NR1I3	CAR	-	-	-	-
AHR	AHR	2.50	2.49	2.38	3.02
AHRR	AHRR	-	-	-	-
ARNT	ARNT	4.07	2.83	4.64	2.87
AIP	AIP	5.28	3.98	5.60	4.56
NR3C1	GR	3.15	2.55	3.92	3.43
CEBPA	C/EBPα	1.27	1.79	2.75	1.41
CEBPB	C/EBPβ	13.90	21.51	22.53	19.41
CEBPD	C/EBPδ	8.40	9.05	16.56	13.73

SI. Table 7. Expression of genes encoding transcription factors from healthy and COPD lung in % of expression of Housekeeping genes. Expression levels correspond to average ΔCt within each group expressed in % of the expression of the mean of the three housekeeping genes *ACTB, B2M, and RPLP0* (avg HKGs). Expression is calculates as (% avg HKGs) = $2^{-(\mathrm{Ct(Gene\ of\ interest)}-\mathrm{Ct(avg\ HKGs)})} \times 100$. Non detectable (-) % < 0.05; very low (+/-) 0.05 ≤ % < 0.1, low (+) 0.1 ≤ %< 1, moderate (++) 1 ≤ % < 10, high (+++) 10 ≤ % < 100, very high (++++) 100 ≤ %.

SI. Table 8. Expression of genes encoding transcription factors from healthy and COPD lung in % of expression of Housekeeping genes.

		Healthy		**COPD**	
Gene	**Protein**	**Central**	**Peripheral**	**Central**	**Peripheral**
NR1H4	FXR	-	-	-	-
NR1I2	PXR	+	-	-	-
NR1I3	CAR	-	-	-	-
AHR	AHR	++	++	++	++
AHRR	AHRR	-	-	-	-
ARNT	ARNT	++	++	++	++
AIP	AIP	++	++	++	++
NR3C1	GR	++	++	++	++
CEBPA	C/EBPα	++	++	++	++
CEBPB	C/EBPβ	+++	+++	+++	+++
CEBPD	C/EBPδ	++	++	+++	+++

Expression of genes encoding transcription factors from healthy and COPD lung in % of expression of Housekeeping genes. Expression levels correspond to average ΔCt within each group expressed in % of the expression of the mean of the three housekeeping genes *ACTB, B2M, and RPLP0* (avg HKGs). Expression is calculates as (% avg HKGs) = $2^{-(Ct(Gene\ of\ interest)-Ct(avg\ HKGs))} \times 100$. Non detectable (-) % < 0.05; very low (+/-) 0.05 ≤ % < 0.1, low (+) 0.1 ≤ %< 1, moderate (++) 1 ≤ % < 10, high (+++) 10 ≤ % < 100, very high (++++) 100 ≤ %.

SI. Table 9. Differential expressed genes encoding metabolizing enzymes between central aiorways and peripheral tissue.

	Central >Peripheral	p-Value
1	*GSTZ1*	0.0006
2	*GST02*	0.0007
3	*CYP2F1*	0.0010
4	*AQP5*	0.0013
5	*CYP2J2*	0.0019
6	*CYP2S1*	0.0027
7	*CES4A*	0.0029
8	*MUC5AC*	0.0033
9	*GSTA3*	0.0038
10	*FMO4*	0.0039
11	*CES3*	0.0039
12	*GSTP1*	0.0047
13	*GSTA1*	0.0052
14	*CYP2C9*	0.0062
15	*GSTA2*	0.0099
	Peripheral > Central	p-Value
1	*CEBPD*	0.0016
2	*PTPRC/CD45*	0.0028
3	*CEBPA*	0.0071
4	*CEBPB*	0.0090

SI. Table 10. Inter-individual variability of genes encoding transcription factors in healthy or COPD human lung in both central airways or peripheral tissue.

	Healthy						**COPD**					
	Central			**Peripheral**			**Central**			**Peripheral**		
Gene	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**
Transcription factors												
AHR	**5.2**	29.8	27.0	**4.4**	30.0	27.1	**5.6**	30.2	27.4	**3.9**	29.2	26.7
ARNT	**4.1**	28.7	26.7	**3.0**	29.3	27.4	**2.5**	28.5	27.2	**3.2**	29.2	27.0
AIP	**4.6**	28.4	26.1	**3.8**	29.3	26.8	**4.7**	28.6	26.2	**4.6**	29.0	25.7
NR3C1	**4.3**	29.0	26.9	**3.4**	29.6	27.3	**4.4**	29.1	26.8	**3.8**	29.1	26.4
CEBPA	**2.5**	30.2	28.7	**3.6**	31.1	28.3	**4.2**	29.6	27.3	**4.9**	30.9	27.4
CEBPB	**6.9**	27.4	24.2	**3.0**	27.0	24.9	**3.4**	26.3	24.6	**4.7**	26.6	23.9
CEBPD	**5.7**	27.8	25.2	**3.9**	28.4	25.6	**3.6**	26.8	25.0	**4.3**	27.2	24.4
NR1H4	**0.0**	35.0	35.0	**0.0**	35.0	35.0	**0.0**	35.0	35.0	**0.4**	35.0	34.7
NR1I2	**3.1**	34.0	32.0	**3.6**	35.0	32.0	**0.0**	35.0	35.0	**2.6**	35.0	33.1

The inter-individual variability (CV) of genes encoding transcription factors. The inter individual variability in gene expression is evaluated by calculation of the coefficient of variation using the CT values (CV = 100x(ΔCt standard deviation/mean ΔCt)).

SI. Table 11. Expression of genes encoding cell specific markers in % of expression of Housekeeping genes.

			Healthy		**COPD**	
Marker	***Gene***	**Protein**	**Central**	**Peripheral**	**Central**	**Peripheral**
Epithelial cells	*CDH1*	*E-Cadherin*	20.60	22.54	18.13	13.00
Type I cells	*AQP5*	Aquaporin 5	15.28	15.15	1.46	1.00
Type II cells	*SFTPC*	surfactant protein C	352.85	360.85	1121.72	942.96
Goblet cells	*MUC5AC*	mucin 5AC. oligomeric mucus/gel-forming	10.17	7.03	0.10	0.48
Squamous cells	*IVL*	*Involucrine*	-	-	-	-
Hematolymphoid cells	*PTPRC*	Protein tyrosine phosphatase. receptor type. C (CD45)	0.14	0.22	0.41	0.37
Granulocytes	*CEACAM8*	Carcinoembryonic antigen-related cell adhesion molecule 8 (CD66b)	-	-	-	0.06
Lymphocytes	*LCK*	Tyrosine-protein kinase Lck	0.23	0.32	0.32	0.31
Monocytes/ macrophages	*CD68*	Cluster of Differentiation 68	10.09	11.14	28.54	21.71
Endothelial cells	*PECAM1*	platelet/endothelial cell adhesion molecule (CD31)	28.61	14.97	49.67	30.93
fibroblasts	*P4HB*	prolyl 4-hydroxylase. beta polypeptide	11.04	9.79	7.73	6.43

Expression of genes encoding cell specific markers in % of expression of Housekeeping genes. Expression levels correspond to average ΔCt within each group expressed in % of the expression of the mean of the three housekeeping genes *ACTB. B2M. and RPLP0* (avg HKGs). Expression is calculates as (% avg HKGs) = $2^{-(\mathrm{Ct(Gene\ of\ interest)}-\mathrm{Ct(avg\ HKGs)})} \times 100$. Non detectable (-) % < 0.05; very low (+/-) 0.05 ≤ % < 0.1. low (+) 0.1 ≤ %< 1. moderate (++) 1 ≤ % < 10. high (+++) 10 ≤ % < 100. very high (++++) 100 ≤ %.

SI. Table 12. Expression of genes encoding cell specific markers in % of expression of Housekeeping genes.

			Healthy		**COPD**	
Marker	***Gene***	**Protein**	**Central**	**Peripheral**	**Central**	**Peripheral**
Epithelial cells	*CDH1*	*E-Cadherin*	+++	+++	+++	+++
Type I cells	*AQP5*	Aquaporin 5	+++	+++	++	+
Type II cells	*SFTPC*	surfactant protein C	++++	++++	+++++	+++
Goblet cells	*MUC5AC*	mucin 5AC. oligomeric mucus/gel-forming	+++	++	+/-	+
Squamous cells	*IVL*	*Involucrine*	-	-	-	-
Hematolymphoid cells	*PTPRC*	Protein tyrosine phosphatase. receptor type. C (CD45)	+	+	+	+
Granulocytes	*CEACAM8*	Carcinoembryonic antigen-related cell adhesion molecule 8 (CD66b)	-	-	-	+/-
Lymphocytes	*LCK*	Tyrosine-protein kinase Lck	+	+	+	+
Monocytes/ macrophages	*CD68*	Cluster of Differentiation 68	+++	+++	+++	+++
Endothelial cells	*PECAM1*	platelet/endothelial cell adhesion molecule (CD31)	+++	+++	+++	+++
fibroblasts	*P4HB*	prolyl 4-hydroxylase. beta polypeptide	+++	++	++	++

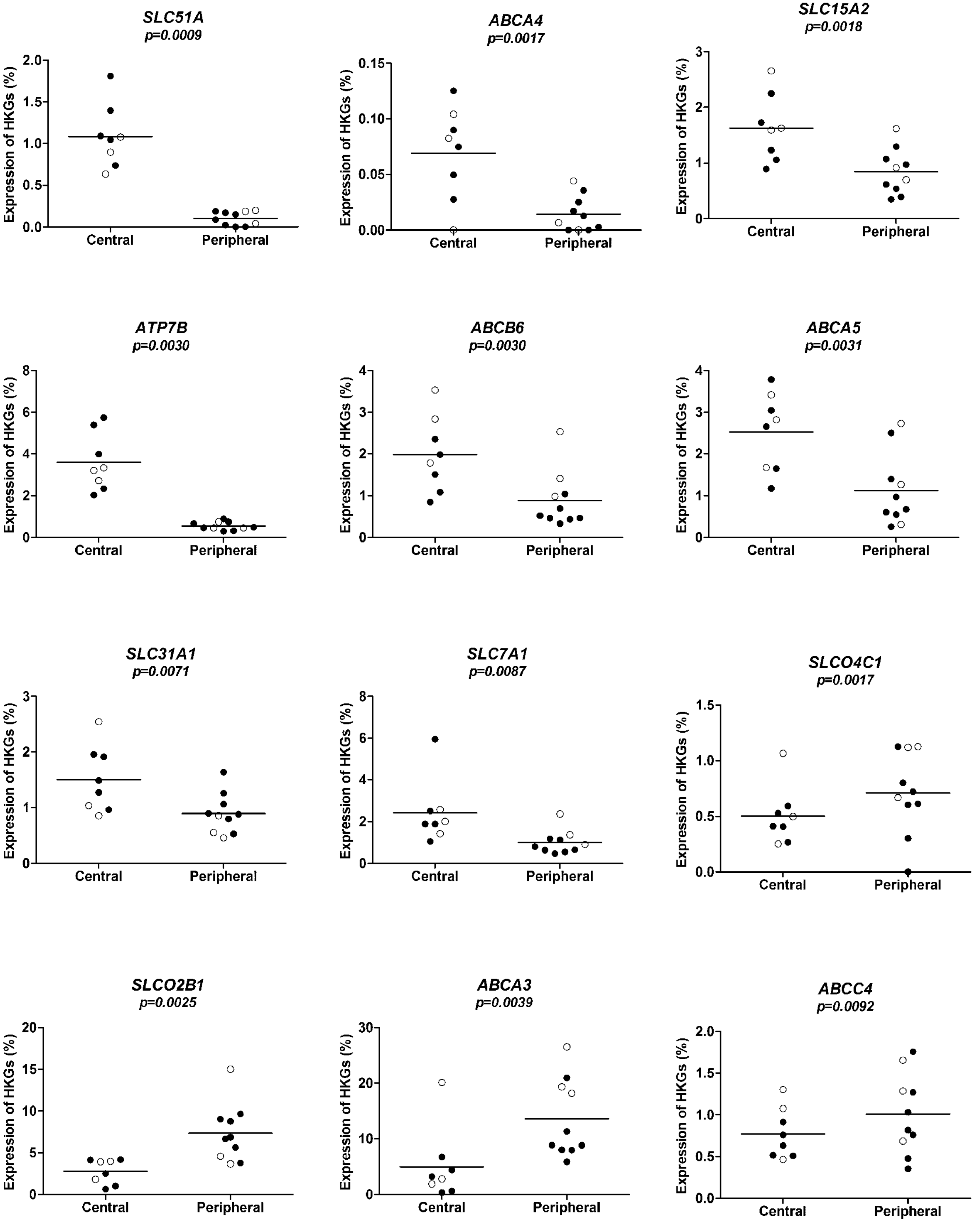
Expression of genes encoding cell specific markers in % of expression of Housekeeping genes. Expression levels correspond to average ΔCt within each group expressed in % of the expression of the mean of the three housekeeping genes *ACTB. B2M. and RPLP0* (avg HKGs). Expression is calculates as (% avg HKGs) = $2^{-(\mathrm{Ct(Gene\ of\ interest)} - \mathrm{Ct(avg\ HKGs)})} \times 100$. Non detectable (-) % < 0.05;

very low (+/-) 0.05 ≤ % < 0.1. low (+) 0.1 ≤ %< 1. moderate (++) 1 ≤ % < 10. high (+++) 10 ≤ % < 100. very high (++++) 100 ≤ %.

SI. Table 13. Inter-individual variability among genes encoding cell specific markers within healthy or COPD human lung in both central airways and peripheral tissue.

	Healthy						**COPD**					
	Central			**Peripheral**			**Central**			**Peripheral**		
Gene	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**	**CV (%)**	**High**	**Low**
Cell specific markers												
AQP5	**7.2**	27.8	24.3	**8.8**	30.4	24.8	**5.5**	31.4	28.3	**11.7**	35.0	27.0
CD68	**3.8**	27.5	25.6	**7.9**	28.8	24.4	**5.4**	26.3	23.9	**4.8**	26.6	23.6
CDH1	**3.7**	26.1	24.4	**4.3**	27.0	24.1	**4.0**	26.6	24.8	**3.9**	27.1	24.7
CEACAM8	**0.0**	35.0	35.0	**3.4**	35.0	32.7	**0.6**	35.0	34.6	**5.5**	35.0	30.9
IVL												
LCK	**3.1**	32.9	30.9	**2.9**	32.3	30.1	**6.2**	33.4	30.1	**6.6**	34.1	29.1
MUC5AC	**3.2**	27.2	25.6	**19.5**	37.8	24.9	**7.3**	36.1	31.6	**13.1**	35.0	27.6
P4HB	**5.9**	27.8	24.8	**4.9**	28.8	25.4	**5.5**	28.4	25.9	**5.3**	28.7	25.2
PECAM1	**5.6**	26.7	24.0	**3.9**	27.2	24.6	**1.4**	24.9	24.3	**6.5**	27.1	23.3
PTPRC	**4.9**	34.0	31.0	**5.2**	34.1	30.2	**4.3**	32.5	29.9	**4.7**	32.7	29.0
SFTPC	**7.5**	23.9	20.9	**26.6**	31.5	19.9	**7.7**	21.0	18.3	**6.7**	21.5	18.3

Inter-individual variability (CV) of genes encoding cell specific markers in healthy or COPD human lung both central airways and peripheral tissue. The inter-individual variability in gene expression is evaluated by calculation of the coefficient of variation using the CT values (CV = 100x (ΔCt standard deviation/mean ΔCt)).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ABCA4
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SLC15A2
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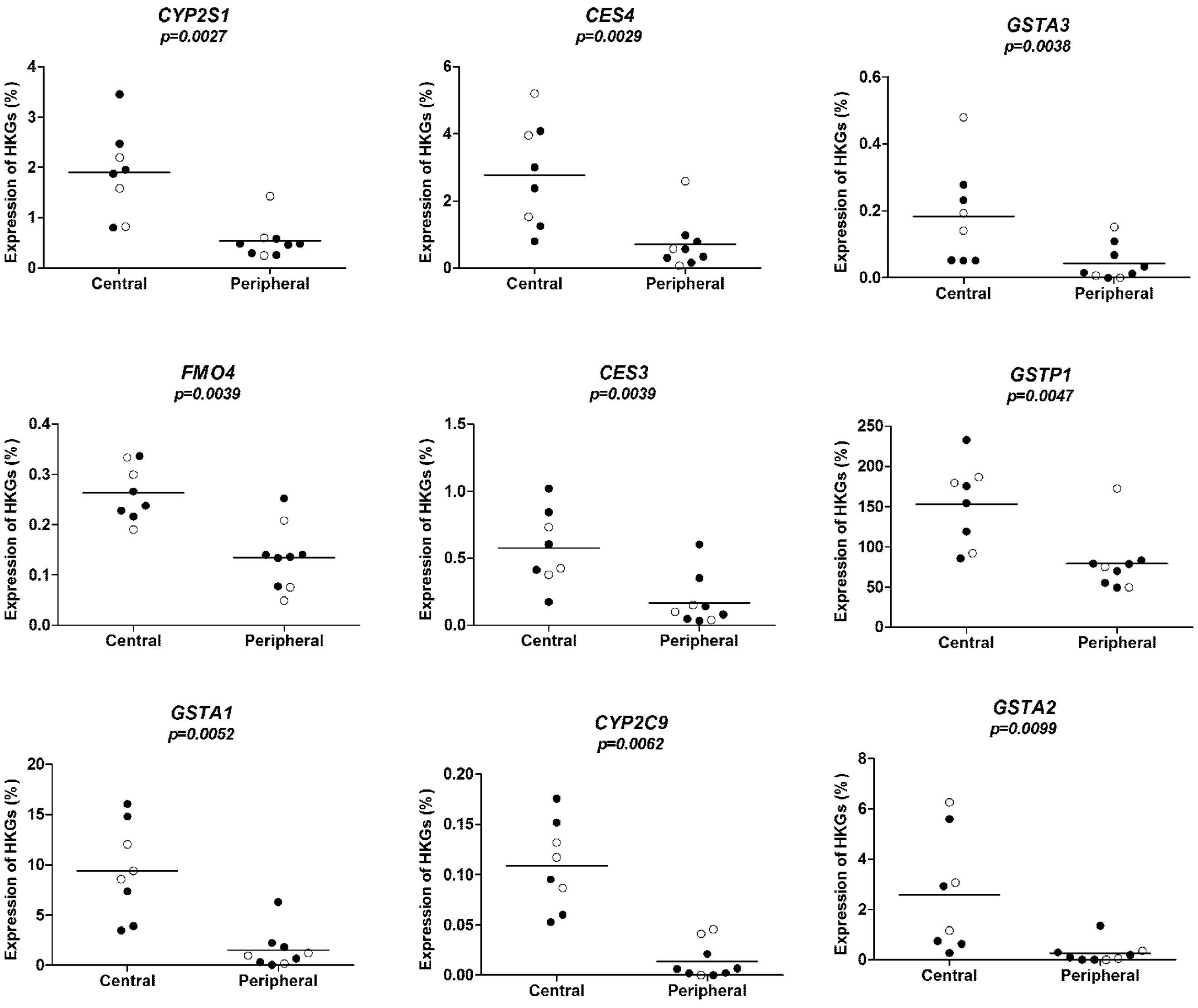
ATP7B
p=0.0030
ABCB6
p=0.0030
ABCA5
p=0.0031
SLC31A1
p=0.0071
SLC7A1
p=0.0087
SLCO4C1
p=0.0017
SLCO2B1
p=0.0025
ABCA3
p=0.0039
ABCC4
p=0.0092
Expression of HKGs (%)
Central
Peripheral



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CES4
p=0.0029
GSTA3
p=0.0038
FMO4
p=0.0039
CES3
p=0.0039
GSTP1
p=0.0047
GSTA1
p=0.0052
CYP2C9
p=0.0062
GSTA2
p=0.0099
Expression of HKGs (%)
Central
Peripheral
0
1
2
3
4
6
0.0
0.2
0.4
0.6
0.1
0.3
0.5
1.0
1.5
50
100
150
200
250
5
10
15
20
0.00
0.05
0.10
0.15
0.20
8