

## SUPPLEMENTARY INFORMATION

**Table S1.** Overview of the 58 selected candidate genes from phase I regarding the fold change, gender and the TaqMan assay used for performing qRT-PCR.

**Table S2.** Overview of all genes that were predictive for discriminating survival status based on gene expression differences. Data are presented separately for male (left side) and female (right side) rhesus macaques and ordered starting with untreated, treated, and untreated and treated groups combined. The number of measurements and the mean gene expression values (Ct values) are provided by survival status as well as the fold-change difference (delog of inverse log<sub>2</sub> transformed Ct values). The *P* value of this group comparison originates from a parametric *t* test or a non-parametric Kruskal-Wallis test, where applicable. Data are presented in black for the gender showing significant differences and in gray for the gender where significance was not achieved. Genes are ordered per treatment group starting with genes that were significantly associated with survival in both genders followed by genes with increasing *P* value.

**Table S3.** Based on the probability function of the receiver operating characteristic (ROC) curves reflecting true positives (surviving), true negatives (not-surviving), false positives (not-surviving identified as surviving) and false negatives (surviving identified as not-surviving) for each measurement, a quantification of the correct/incorrect allocation of gene expression measurements/comparisons was made. The following test characteristics are shown for most predictive genes and gene combinations (*EPX* and *SLC22A*) in males and (*MBOAT4*) in females: sensitivity, 1-specificity, positive predictive value (PPV), negative predictive value (NPV). Rows with bold numbers represent the best prediction per category.

**Fig. S1.** Network of predicted associations for *MBOAT4* and *SLC22A4* and potential target genes, respective proteins, with additional aggregation of their coding function using their gene ontology data in the table.

**Fig. S2.** NGS-based fold changes recalculated by only taking reads from the area, covered by the TaqMan assay and the qRT-PCR-based fold changes. Data are shown for four of the most predictive candidate genes (from Table 2) in which differential gene expression values are of comparable magnitude (*MBOAT4*, *LCN2*, *DYSF* and *SLC22A4*). Additionally, the coverage of the TaqMan assay is rated by providing the percentage of

total reads in the assay area for the specific genes. Furthermore, the total exon reads per gene and the exon reads in the probe area are shown, as well as the number of exons per gene.

## SUPPLEMENTARY INFORMATION

**Table S1.** Overview of the 58 selected candidate genes from phase I regarding the fold-change, gender and the TaqMan assay used for performing qRT-PCR.

**Table S2.** Overview of all genes that were predictive for discriminating survival status based on gene expression differences. Data are presented separately for male (left side) and female (right side) rhesus macaques and ordered starting with untreated, treated, and untreated and treated groups combined. The number of measurements and the mean gene expression values (Ct-values) are provided by survival status as well as the fold-change difference (delog of inverse log<sub>2</sub> transformed Ct-values). The *P* value of this group comparison originates from a parametric *t* test or a non-parametric Kruskal-Wallis test, where applicable. Data are presented in black for the gender showing significant differences and in gray for the gender where significance was not achieved. Genes are ordered per treatment group starting with genes that were significantly associated with survival in both genders followed by genes with increasing *P* value.

**Table S3.** Based on the probability function of the receiver operating characteristic (ROC) curves reflecting true positives (surviving), true negatives (not-surviving), false positives (not-surviving identified as surviving) and false negatives (surviving identified as not-surviving) for each measurement, a quantification of the correct/incorrect allocation of gene expression measurements/comparisons was made. The following test characteristics are shown for most predictive genes and gene combinations (*EPX* and *SLC22A*) in males and (*MBOAT4*) in females: sensitivity, 1-specificity, positive predictive value (PPV), negative predictive value (NPV). Rows with bold numbers represent the best prediction per category.

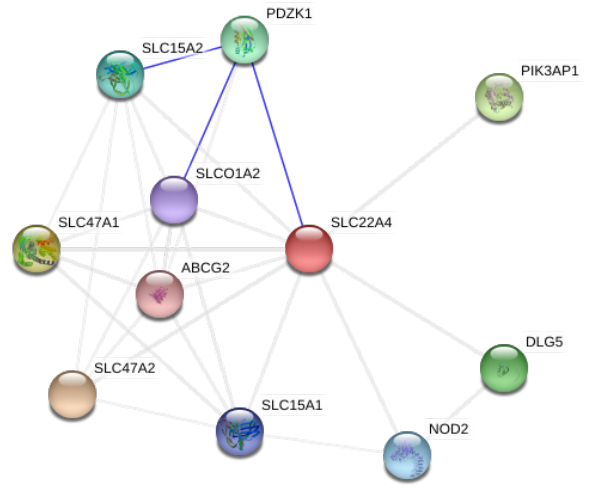
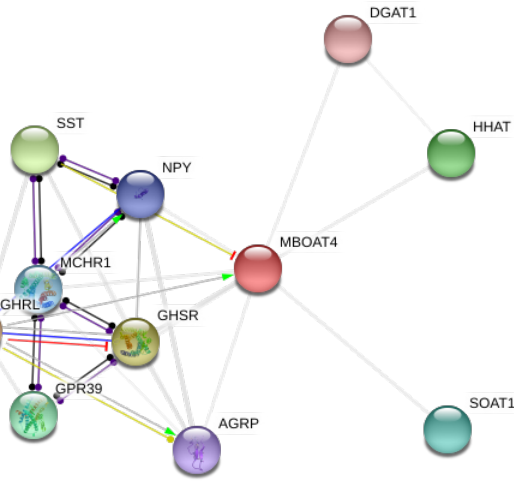
**Fig. S1.** Network of predicted associations for *MBOAT4* and *SLC22A4* and potential target genes, respective proteins, with additional aggregation of their coding function using their gene ontology data in the table.

**Fig. S2.** NGS-based fold changes recalculated by only taking reads from the area, covered by the TaqMan assay and the qRT-PCR-based fold changes. Data are shown for four of the most predictive candidate genes (from Table 2) in which differential gene expression values are of comparable magnitude (*MBOAT4*, *LCN2*, *DYSF* and *SLC22A4*). Additionally, the coverage of the TaqMan assay is rated by providing the percentage of

total reads in the assay area for the specific genes. Furthermore, the total exon reads per gene and the exon reads in the probe area are shown, as well as the number of exons per gene.

# Supplemental Figure S1

Ostheim et al.



### Functional enrichments in your network

Biological Process (GO)			
GO-term	description	count in gene set	false discovery rate
GO:0008343	adult feeding behavior	4 of 10	3.74e-08
GO:0007631	feeding behavior	5 of 94	4.68e-07
GO:0032100	positive regulation of appetite	3 of 4	1.07e-06
GO:2000253	positive regulation of feeding behavior	3 of 10	3.74e-06
GO:0007186	G protein-coupled receptor signaling pathway	7 of 1247	5.30e-05

Molecular Function (GO)			
GO-term	description	count in gene set	false discovery rate
GO:0008374	O-acyltransferase activity	4 of 49	1.23e-06
GO:0005179	hormone activity	4 of 123	2.13e-05
GO:0005184	neuropeptide hormone activity	2 of 29	0.0015
GO:0005102	signaling receptor binding	5 of 1513	0.0082
GO:0004930	G protein-coupled receptor activity	4 of 824	0.0082

Cellular Component (GO)			
GO-term	description	count in gene set	false discovery rate
GO:0044432	endoplasmic reticulum part	5 of 1294	0.0345

publication	(year) title	count in gene set	false discovery rate
PMID:21428875	(2011) Interaction between gastric and upper small intestin...	8 of 27	4.07e-16
PMID:23103610	(2013) Obesity pharmacotherapy: what is next?	7 of 32	4.35e-13
PMID:22523723	(2012) Yin and Yang - the Gastric XA-like Cell as Possible D...	7 of 30	4.35e-13
PMID:23621300	(2013) New advances in models and strategies for developi...	7 of 37	8.09e-13
PMID:23659638	(2013) Changes in ghrelin-related factors in gastroesophag...	6 of 12	1.23e-12

KEGG Pathways			
pathway	description	count in gene set	false discovery rate
hsa04024	cAMP signaling pathway	3 of 195	0.0019
hsa04920	Adipocytokine signaling pathway	2 of 69	0.0042
hsa04080	Neuroactive ligand-receptor interaction	2 of 272	0.0395

Reactome Pathways			
pathway	description	count in gene set	false discovery rate
HSA-373076	Class A/1 (Rhodopsin-like receptors)	5 of 311	1.86e-05
HSA-375276	Peptide ligand-binding receptors	4 of 183	5.18e-05
HSA-416476	G alpha (q) signalling events	3 of 205	0.0019
HSA-388396	GPCR downstream signalling	5 of 1082	0.0019
HSA-418594	G alpha (i) signalling events	3 of 387	0.0067

### Functional enrichments in your network

Biological Process (GO)			
GO-term	description	count in gene set	false discovery rate
GO:0015893	drug transport	5 of 155	9.34e-06
GO:0006811	ion transport	8 of 1292	1.57e-05
GO:0006812	cation transport	7 of 866	1.98e-05
GO:1902600	proton transmembrane transport	4 of 137	0.00013
GO:0055085	transmembrane transport	7 of 1235	0.00013

Molecular Function (GO)			
GO-term	description	count in gene set	false discovery rate
GO:0022804	active transmembrane transporter activity	7 of 354	2.33e-08
GO:0015291	secondary active transmembrane transporter activity	6 of 235	7.89e-08
GO:0005215	transporter activity	8 of 1223	1.22e-06
GO:0015078	proton transmembrane transporter activity	4 of 120	1.08e-05
GO:0015298	solute:cation antiporter activity	3 of 33	1.71e-05

Cellular Component (GO)			
GO-term	description	count in gene set	false discovery rate
GO:0005886	plasma membrane	11 of 5159	3.42e-05
GO:0098590	plasma membrane region	5 of 1061	0.0026
GO:0044459	plasma membrane part	7 of 2651	0.0026
GO:0044425	membrane part	10 of 6517	0.0026
GO:0016324	apical plasma membrane	3 of 307	0.0067

publication	(year) title	count in gene set	false discovery rate
PMID:28375174	(2017) Protein Kinases C-Mediated Regulations of Drug Tra...	7 of 41	1.27e-12
PMID:26056583	(2014) Role of solute carriers in response to anticancer dru...	7 of 38	1.27e-12
PMID:27843352	(2016) Profile of once-daily darunavircobiscistat fixed-dose ...	6 of 20	8.43e-12
PMID:24856391	(2014) Ocular cytochrome P450s and transporters: roles in ...	7 of 64	9.26e-12
PMID:28401035	(2017) Development and Application of Human Renal Proxi...	6 of 25	1.62e-11

KEGG Pathways			
pathway	description	count in gene set	false discovery rate
hsa04976	Bile secretion	2 of 71	0.0089

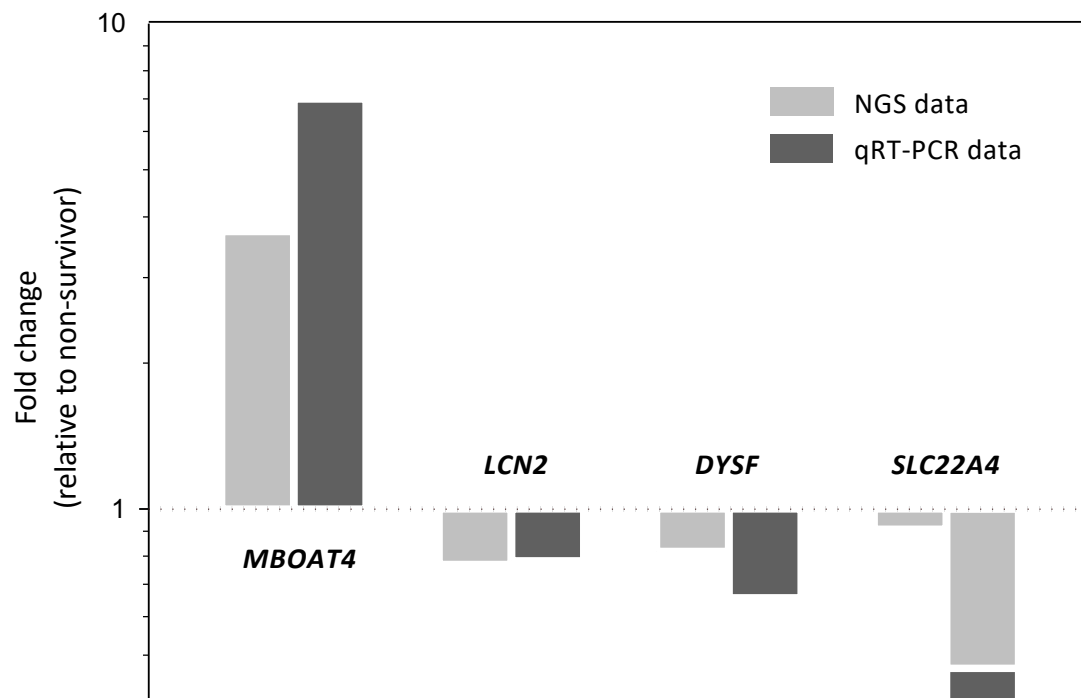
  

Reactome Pathways			
pathway	description	count in gene set	false discovery rate
HSA-425407	SLC-mediated transmembrane transport	6 of 241	1.03e-07
HSA-382551	Transport of small molecules	7 of 706	7.43e-07
HSA-427975	Proton/oligopeptide cotransporters	2 of 4	8.89e-05
HSA-425366	Transport of bile salts and organic acids, metal ions and a...	3 of 85	0.00022



## Supplemental Figure S2

Ostheim et al.



<b># exons per gene</b>	3	9	60	15
<b>Total exon reads</b>	193	3362	8241	188
<b>Exon reads in PPD area</b>	140	690	407	34
<b>Coverage - % of total reads in PPD area</b>	73	21	5	18