Supplemental Data

Table S1. Protein sequences used to construct phylogeny of the NAT/NCS2 family

Organism	Transporter (mnemonic)	Family (NCBI)	Accession number
BACTERIA			
Escherichia coli			
	XanQ (YgfO)	NAT/NCS2	P67444
	XanP (YicE)	NAT/NCS2	P0AGM9
	UraA	NAT/NCS2	P0AGM7
	UacT (YgfU)	NAT/NCS2	Q46821
	RutG (YcdG)	NAT/NCS2	AAC74091
	YbbY	NAT/NCS2	P77328
	PurP (YieG)	AzgA-like	P31466
	YicO	AzgA-like	P31440
	YgfQ	AzgA-like	Q46817
	YjcD	AzgA-like	P0AF52
Bacillus subtilis			
	PbuX	NAT/NCS2	P42086
	PucJ	NAT/NCS2	O32139
	PucK	NAT/NCS2	O32140
	PyrP	NAT/NCS2	YP_003865951
	PbuO	AzgA-like	O34978
	PbuG	AzgA-like	O34987
Sinorhizobium meliloti			
	SMc02513	NAT/NCS2	CAC47601
	SMc02512	NAT/NCS2	CAC47602
	SMb20289	NAT/NCS2	CAC48679
	SMb20134	NAT/NCS2	CAC48534
	SMb21281	AzgA-like	NP_437325.1
ARCHAEA			
Pyrococcus abyssi			
	P.abyssi NAT	NAT/NCS2	NP_126472.1
	P.abyssi HGAT	AzgA-like	NP_126753.1
Haloferax volcanii			
	H.volcanii NAT1	NAT/NCS2	YP_003533379.1
	H.volcanii NAT2	NAT/NCS2	YP_003536273.1
Halobacterium sp.			
	Halobacterium NAT	NAT/NCS2	ZP_09028835.1
	Halobacterium HGAT	AzgA-like	NP_280776.1
Sulfolobus acidocaldarius			
	Sulfolobus HGAT	AzgA-like	YP_256300.1
Methanococcus maripaludis			
	Methanococcus NAT	NAT/NCS2	NP_987801.1
Methanocaldococcus jannaschii			
	M.jannaschi HGAT	AzgA-like	NP_247298.1
PROTISTA			
Dictyostelium discoideum			
	Dictyostelium NAT1	NAT/NCS2	XP_638319.1
	Dictyostelium NAT2	NAT/NCS2	XP_642632.1
Phaeodactylum tricornutum			
	Phaeodactylum NAT1	NAT/NCS2	XP_002184514.1
	Phaeodactylum NAT2	NAT/NCS2	XP_002177123.1
	Phaeodactylum AzgA	AzgA-like	XP_002176623.1
Chlorella variabilis			
	Chlorella NAT1	NAT/NCS2	EFN55989.1
	Chlorella NAT2	NAT/NCS2	EFN51042.1
	Chlorella AzgA1	AzgA-like	EFN58296.1
	Chlorella AzgA2	AzgA-like	EFN55661.1
	Chlorella AzgA3	AzgA-like	EFN53511.1
	Chlorella AzgA4	AzgA-like	EFN58112.1
Micromonas sp.			

	Micromonas NAT	NAT/NCS2	XP_002507868.1
Chlamydomonas reinhardtii			
	Chlamydomonas NAT1	NAT/NCS2	XP_001690343.1
	Chlamydomonas NAT2	NAT/NCS2	XP_001702660.1
	Chlamydomonas NAT3	NAT/NCS2	XP_001690514.1
	Chlamydomonas AzgA	AzgA-like	XP_001696326.1
Ectocarpus siliculosus			
	Ectocarpus NAT	NAT/NCS2	CBJ33435.1
FUNGI			
Aspergillus nidulans			
	UapA	NAT/NCS2	Q07307
	UapC	NAT/NCS2	P48777
	AzgA	AzgA-like	Q7Z8R3
Aspergillus fumigatus			
	AfUapA	NAT/NCS2	XP748919
	AfAzgA	AzgA-like	XP_753664.1
Candida albicans			
	Xut1	NAT/NCS2	AAX22221.1
Schizosaccharomyces pombe			
	S.pombe NAT	NAT/NCS2	NP_593513.1
	S.pombe AzgA	AzgA-like	NP_596491.1
PLANTAE			
Arabidopsis thaliana			
	AtNAT1	NAT/NCS2	AEC05969
	AtNAT2	NAT/NCS2	AEC08934
	AtNAT3	NAT/NCS2	AEC07849
	AtNAT4	NAT/NCS2	AEE32500
	AtNAT5	NAT/NCS2	AED95881
	AtNAT6	NAT/NCS2	AED97669
	AtNAT7	NAT/NCS2	AEE33651
	AtNAT8	NAT/NCS2	AEE28592
	AtNAT9	NAT/NCS2	AED93439
	AtNAT10	NAT/NCS2	AEE34395
	AtNAT11	NAT/NCS2	AEE86867
	AtNAT12	NAT/NCS2	AEC08049
	AtAzgA1	AzgA-like	AEE74982
	AtAzgA2	AzgA-like	AED95923
Zea mays			
	Lpe1	NAT/NCS2	NP_001150400.1
Oryza sativa			
	OsNAT	NAT/NCS2	NP_001051745.1
	OsAzgA	AzgA-like	EAY97568.1
ANIMALIA			
Caenorhabditis elegans			
	C.elegans C51E3.6	NAT/NCS2	CAB01641
	C.elegans T07G12.5	NAT/NCS2	CAB05270
	C.elegans Y59E9AL.4	NAT/NCS2	CCD74085
	C.elegans R11E3.2	NAT/NCS2	CCD72237
	C.elegans T07G12.2	NAT/NCS2	CAB05274
	C.elegans T07G12.4	NAT/NCS2	NP_501946
Drosophila melanogaster			
	Drosophila NAT	NAT/NCS2	AAF54519
Anopheles gambiae			
	Anopheles NAT	NAT/NCS2	AAM97678
Danio rerio			
	Zebrafish SVCT1	NAT/NCS2	NP_001166970.1
	Zebrafish SVCT2	NAT/NCS2	XP_001339365.2
Mus musculus			
	mSVCT1	NAT/NCS2	Q9Z2J0
	mSVCT2	NAT/NCS2	Q93PR4
	mSlc23a3 (Yspl1)	NAT/NCS2	Q60850.1

Rattus norvegicus			
	rSVCT1	NAT/NCS2	Q9WTW7
	rSVCT2	NAT/NCS2	Q9WTW8
	rSlc23a3	NAT/NCS2	NP_001102476
	rSNBT1	NAT/NCS2	BAI66650
Sus scrofa			
	pSVCT1	NAT/NCS2	XP_003124027
	pSVCT2	NAT/NCS2	NP_999343
	pSlc23a3	NAT/NCS2	XP_1925561
	pSLC23A4	NAT/NCS2	XP_003134705
Homo sapiens			
	hSVCT1	NAT/NCS2	Q9UHI7
	hSVCT2	NAT/NCS2	Q9UGH3
	hSlc23a3	NAT/NCS2	Q6PIS1

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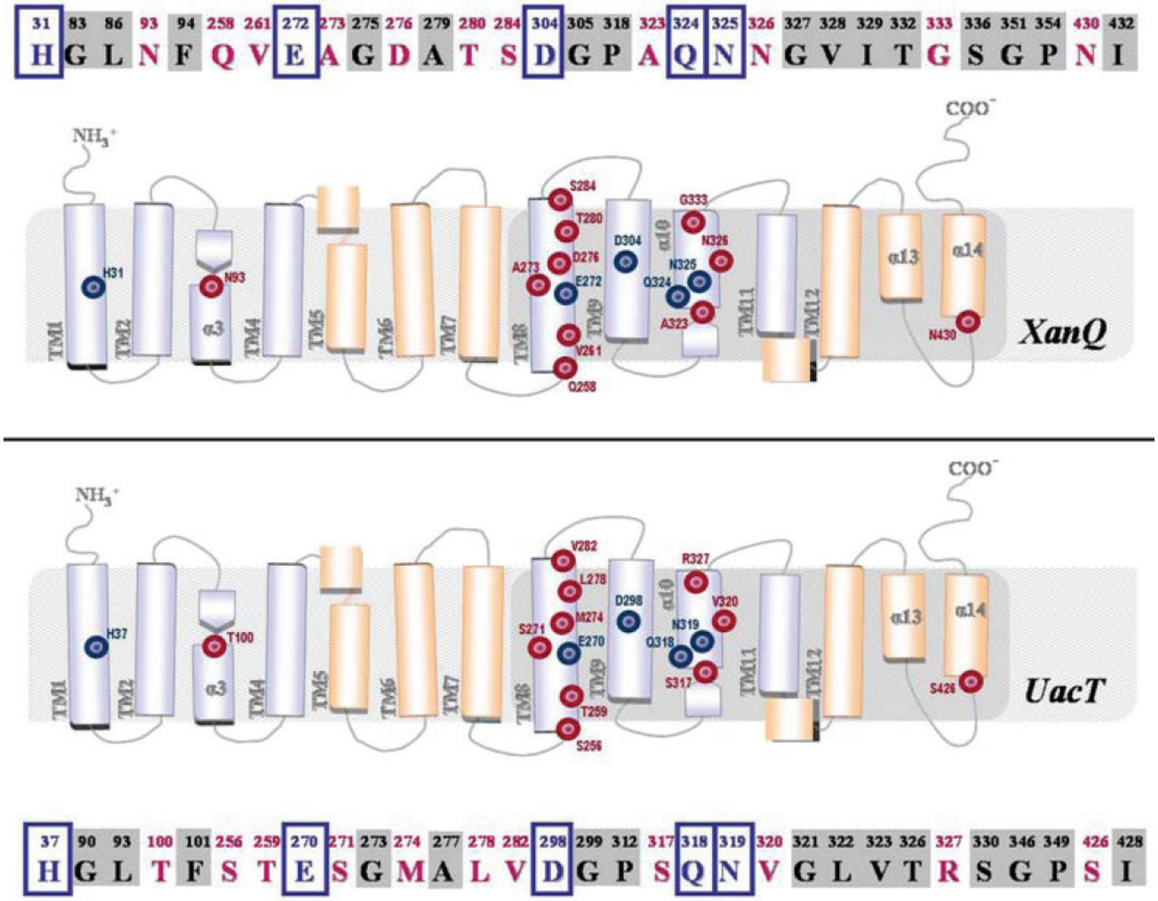

Figure S1. Mutagenesis targets from the set of important residues of permease XanQ. Topology models of permeases XanQ and UacT showing residues subjected to mutagenesis at invariable (*blue*) and variable positions (*red*) [26]. Selection of mutagenesis targets is based on Cys-scanning analysis of XanQ (see text). The corresponding residues of XanQ (*top*) and UacT (*bottom*) are shown in separate rows, highlighting residues subjected to mutagenesis at variable (*red*) and invariable positions (*blue*) and other invariably conserved side chains that were not studied in UacT (*black labels with grey background*). Cylinders of different colors denote transmembrane segments (TMs) of the core domain (*light blue*) and the gate domain (*light orange*). The topology models are based on homology threading on the x-ray structure of UraA [25].