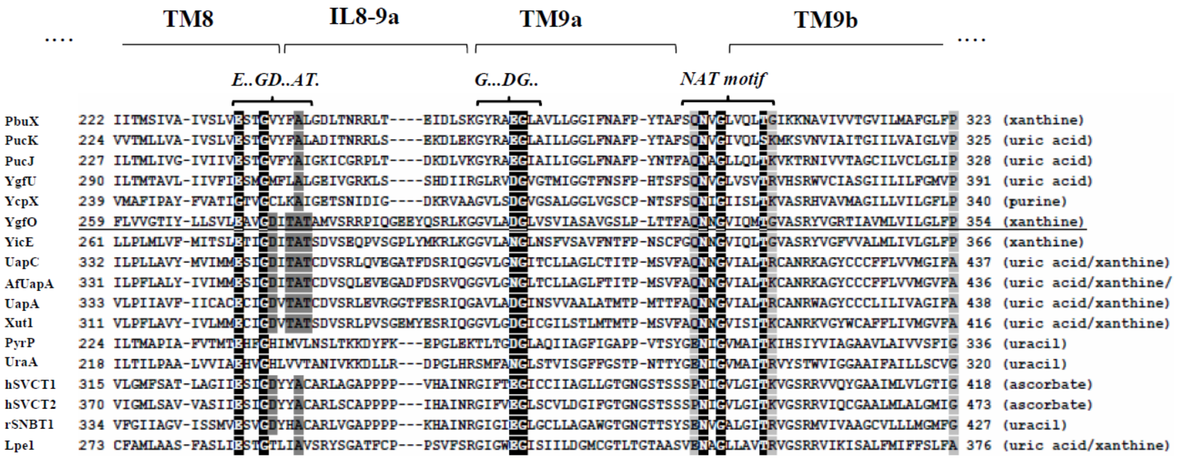
Supplemental Data

Figure S1



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PbuX    222 IITMSIVA-IVSLVESTGVYFALGDLTNRRLT----EIDLSKGYRAEGLAVLLGGIFNAFP-YTAFSQNVGLVQLTGIKKNAVIVVTGVILMAFGLFP 323 (xanthine)
PucK    224 VVTMLLVA-IVSLVESTGVYFALADITNRRLS----EKDLEKGYRAEGLAILLGGLFNAFP-YTAFSQNVGIVQLSKMKSVNVIAITGIILVAIGLVP 325 (uric acid)
PucJ    227 ILTMLIVG-IVIIVESTGVFYAIGKICGRPLT----DKDLVKGYRAEGIAILIGGLFNAFP-YNTFAQNAGLLQLTKVKTRNIVVTAGCILVCLGLIP 328 (uric acid)
YgfU    290 ILTMTAVL-IIVFIESMGMFLALGEIVGRKLS----SHDIIRGLRVDGVGTMIGGTFNSFP-HTSFSQNVGLVSVTRVHSRWVCIASGIILILFGMVP 391 (uric acid)
YcpX    239 VMAFIPAY-FVATIGTVGCLKAIGETSNIDIG----DKRVAAGVLSDGVGSALGGLVGSCP-NTSFSQNIGIISLTKVASRHVAVMAGILLVILGFLP 340 (purine)
YgfO    259 FLVVGTIY-LLSVLEAVGDITATAMVSRRPIQGEEYQSRLKGGVLADGLVSVIASAVGSLP-LTTFAQNNGVIQMTGVASRYVGRTIAVMLVILGLFP 354 (xanthine)
YicE    261 LLPLMLVF-MITSLETIGDITATSDVSEQPVSGPLYMKRLKGGVLANGLNSFVSAVFNTFP-NSCFGQNNGVIQLTGVASRYVGFVVALMLIVLGLFP 366 (xanthine)
UapC    332 ILPLLAVY-MVIMMESIGDITATCDVSRLQVEGATFDSRIQGGVLGNGITCLLAGLCTITP-MSVFAQNNGVIALTRCANRKAGYCCCFFLVVMGIFA 437 (uric acid/xanthine)
AfUapA  331 ILPFLALY-IVIMMESIGDITATCDVSQLEVEGADFDSRVQGGVLGNGLTCLLAGLFTITP-MSVFAQNNGVIALTKCANRKAGYCCCFFLVVMGVFA 436 (uric acid/xanthine/
UapA    333 VLPIIAVF-IICACECIGDVTATCDVSRLEVRGGTFESRIQGAVLADGINSVVAALATMTP-MTTFAQNNGVIALTRCANRWAGYCCCLILIVAGIFA 438 (uric acid/xanthine)
Xut1    311 VLPFLAVY-IVLMMECIGDVTATSDVSRLPVSGEMYESRIQGGVLGDGICGILSTLMTMTP-MSVFAQNNGVISITKCANRKVGYWCAFFLIVMGVFA 416 (uric acid/xanthine)
PyrP    224 ILTMAPIA-FVTMTEHFGHIMVLNSLTKKDYFK---EPGLEKTLTGDGLAQIIAGFIGAPP-VTSYGENIGVMAITKIHSIYVIAGAAVLAIVVSFIG 336 (uracil)
UraA    218 ILTILPAA-LVVIAEHVGHLVVTANIVKKDLLR---DPGLHRSMFANGLSTVISGFFGSTP-NTTYGENIGVMAITRVYSTWVIGGAAIFAILLSCVG 320 (uracil)
hSVCT1  315 VLGMFSAT-LAGIIESIGDYYACARLAGAPPPP---VHAINRGIFTEGICCIIAGLLGTGNGSTSSSPNIGVLGITKVGSRRVVQYGAAIMLVLGTIG 418 (ascorbate)
hSVCT2  370 VIGMLSAV-VASIIESIGDYYACARLSCAPPPP---IHAINRGIFVEGLSCVLDGIFGTGNGSTSSSPNIGVLGITKVGSRRVIQCGAALMLALGMIG 473 (ascorbate)
rSNBT1  334 VFGIIAGV-ISSMVESVGDYHACARLVGAPPPP---KHAINRGIGIEGLGCLLAGAWGTGNGTTSYSENVGALGITRVGSRMVIVAAGCVLLLMGMFG 427 (uracil)
Lpe1    273 CFAMLAAS-FASLIESTGTLIAVSRYSGATFCP---PSVFSRGIGWEGISIILDGMCGTLTGTAASVENAGLLAVTRVGSRRVIKISALFMIFFSLFA 376 (uric acid/xanthine)
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Alignment of functionally characterized members of the NAT/NCS2 family in sequences of amphipathic helices TM8, TM9a and TM9b, and intervening loops. Shown is a consensus of the 17 characterized NAT/NCS2 transporters, including *Escherichia coli* YgfO (XanQ) (P67444), YicE (XanP) (P0AGM9), YgfU (Q46821) (Papakostas and Frillingos, unpublished results), and UraA (P0AGM7), *Bacillus subtilis* PbuX (P42086), PucK (O32140), and PucJ (O32139), *Clostridium perfringens* YcpX (BAB80103), *Lactococcus lactis* PyrP (AAK05701), *Aspergillus nidulans* UapA (Q07307) and UapC (P487777), *A. fumigatus* AfUapA (XP748919), *Candida albicans* Xut1 (AAX2221), *Zea mays* Lpe1 (AAB17501), *Homo sapiens* SVCT1 (SLC23A1) (AAH50261) and SVCT2 (SLC23A2) (Q9UGH3) and *Rattus norvegicus* SNBT1 (AB511909) (Yamamoto et al., 2010). The full-length sequences were aligned using ClustalW and part of this alignment including the residues of interest is presented. Major substrates of each transporter are shown on the right. Positions of high sequence conservation are shown in dark background and conserved sequence motifs, including the NAT-signature motif AQ**N**x**G**xxxx**T**G (loop between TM9a and TM9b) (Georgopoulou et al., 2010), **E**xx**GD**xx**A**T (TM8 and IL8-9a), and Gxxx**DG** (TM9a) are indicated above.

References used in Figure S1

Yamamoto, S., Inoue, K., Murata, T., Kamigaso, S., Yasujima, T., Maeda J., Yoshida, Y., Ohta, K., and Yuasa, H. (2010). *J. Biol. Chem.* **285**, 6522-6531.

Georgopoulou, E., Mermelekas, G., Karena, E., and Frillingos, S. (2010). *J. Biol. Chem.* **285**, 19422-19433.