Supplementary Information

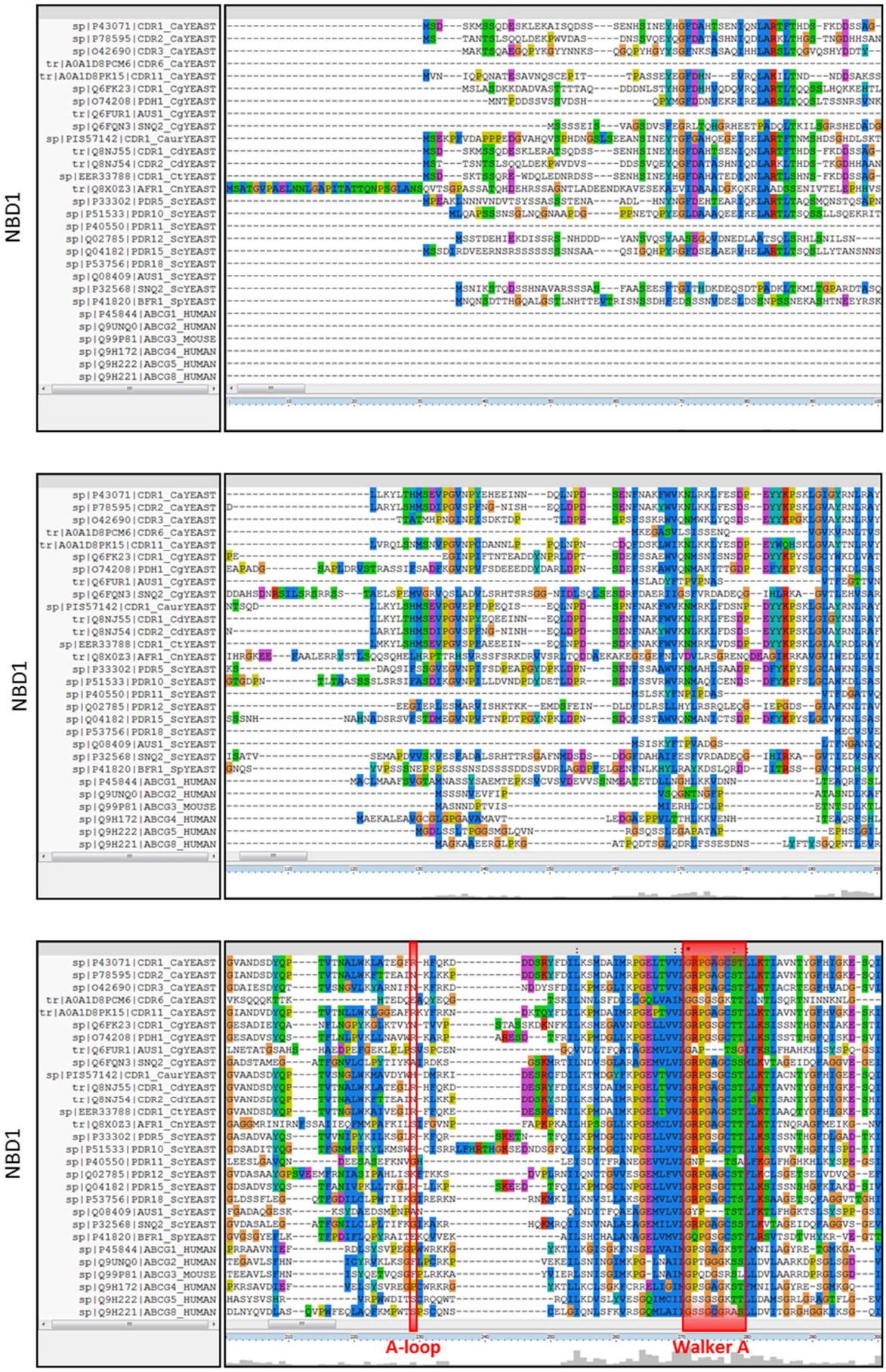
Multidrug Resistance in Mammals and Fungi—From MDR to PDR: A Rocky Road from Atomic Structures to Transport Mechanisms

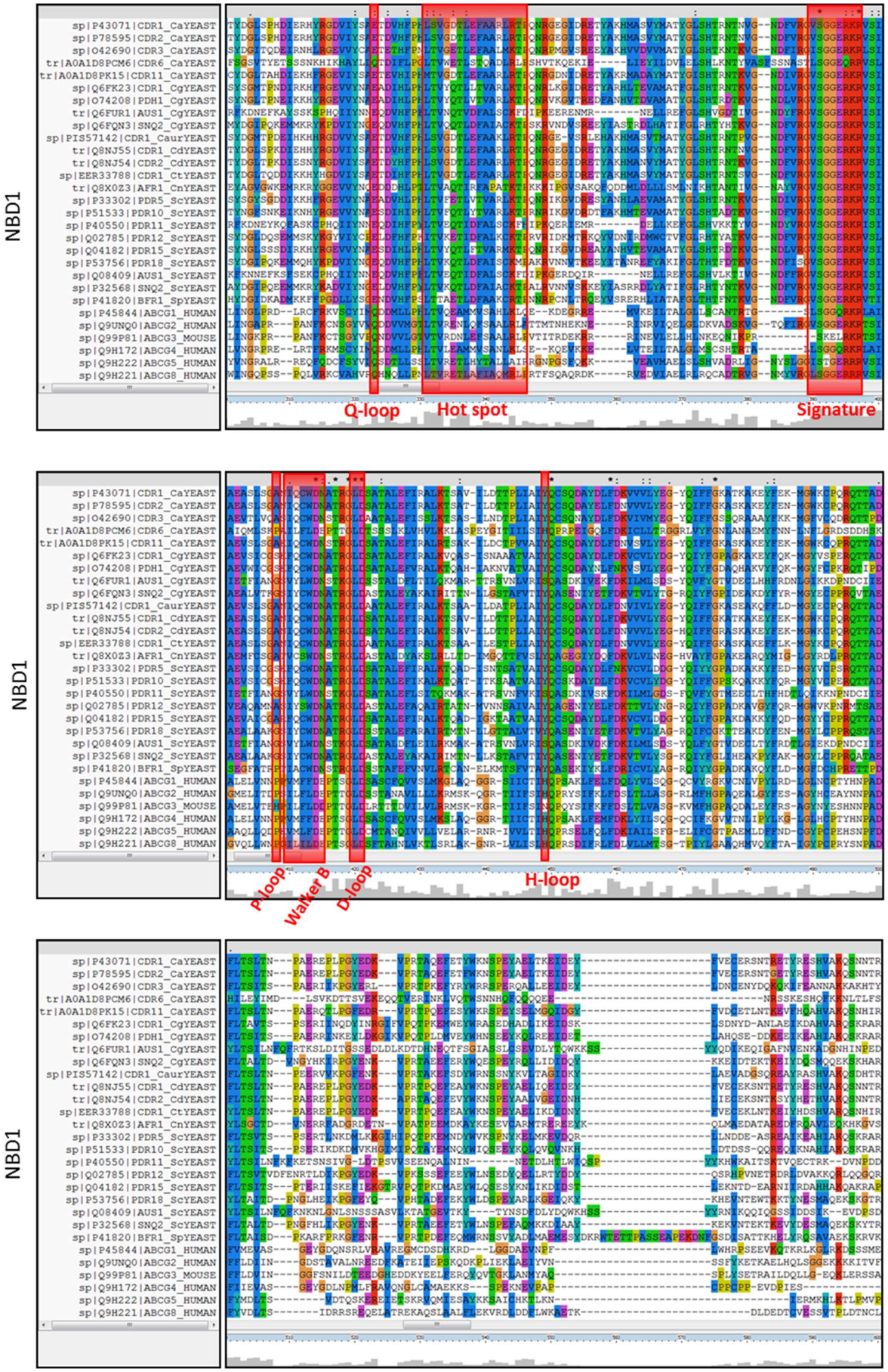
Narakorn Khunweeraphong and Karl Kuchler *

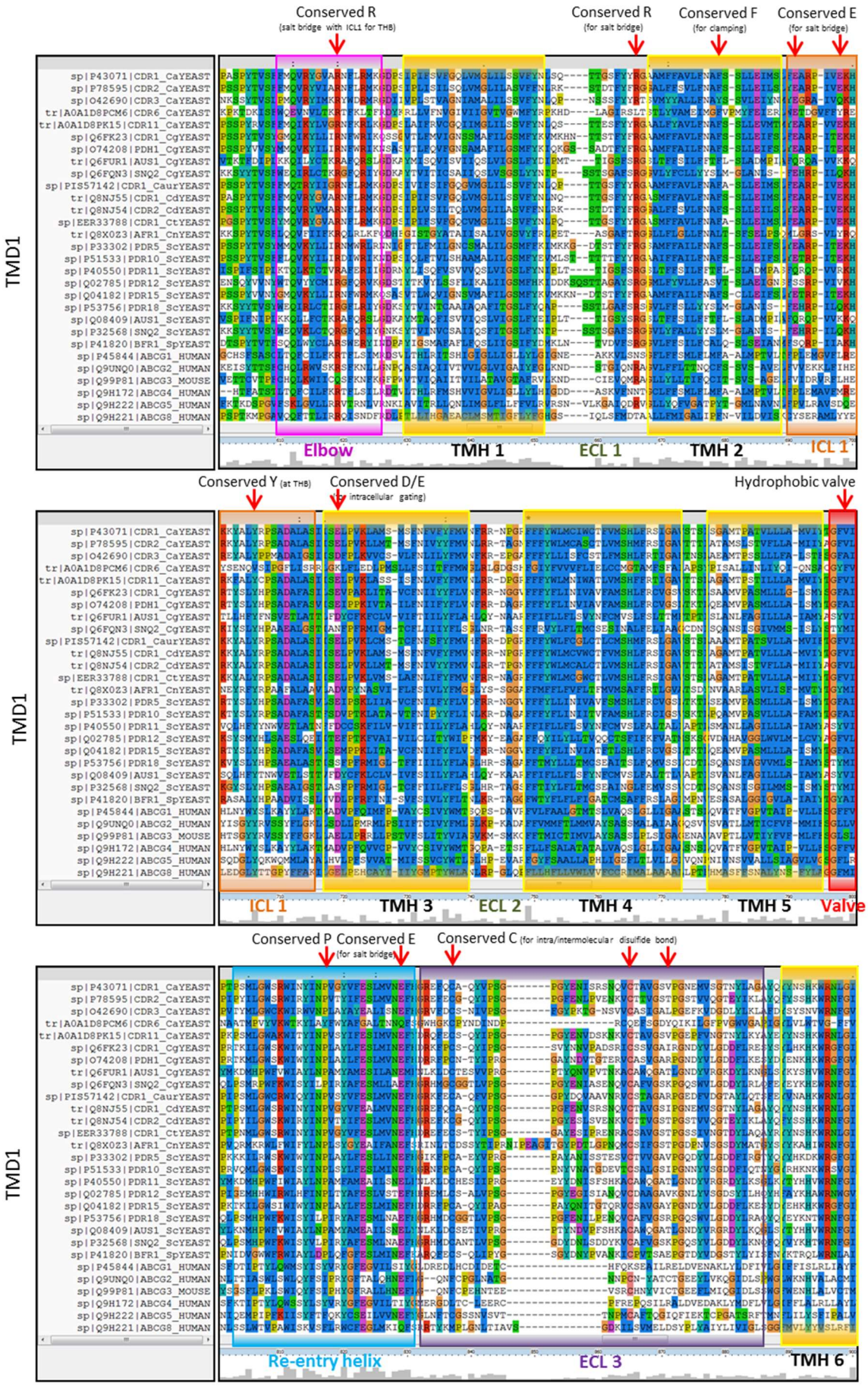
Center for Medical Biochemistry, Max Perutz Labs Vienna, Campus Vienna Biocenter, Medical University of Vienna, Dr. Bohr-Gasse 9/2, A-1030 Vienna, Austria; narakorn.khunweeraphong@meduniwien.ac.at
* Correspondence: karl.kuchler@meduniwien.ac.at; Tel.: +43-1-4277-61807; Fax: +43-1-4277-9618

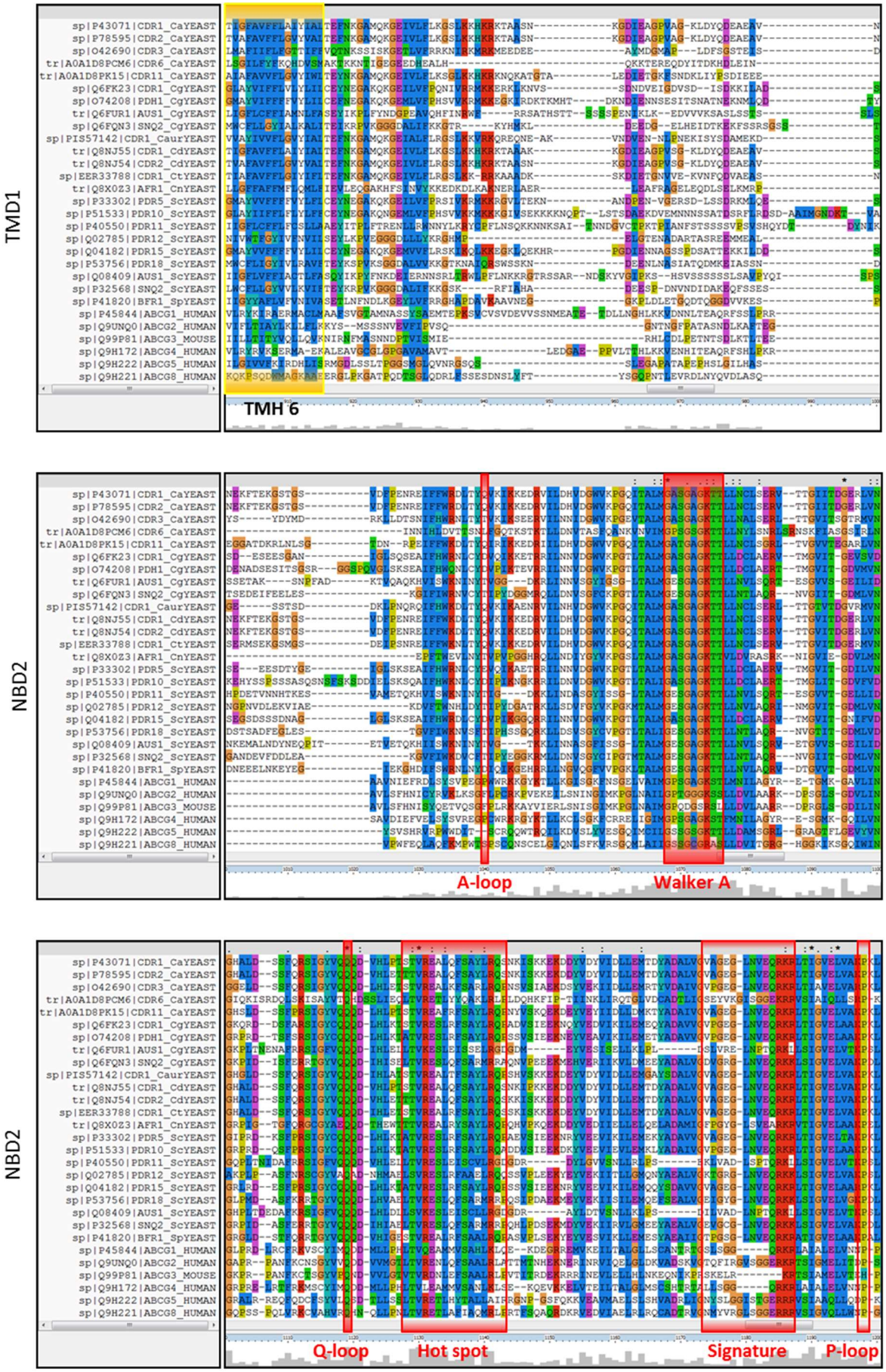
Keywords: yeast; multidrug transporter; anticancer; antifungal resistance; ABC transporters; mechanism

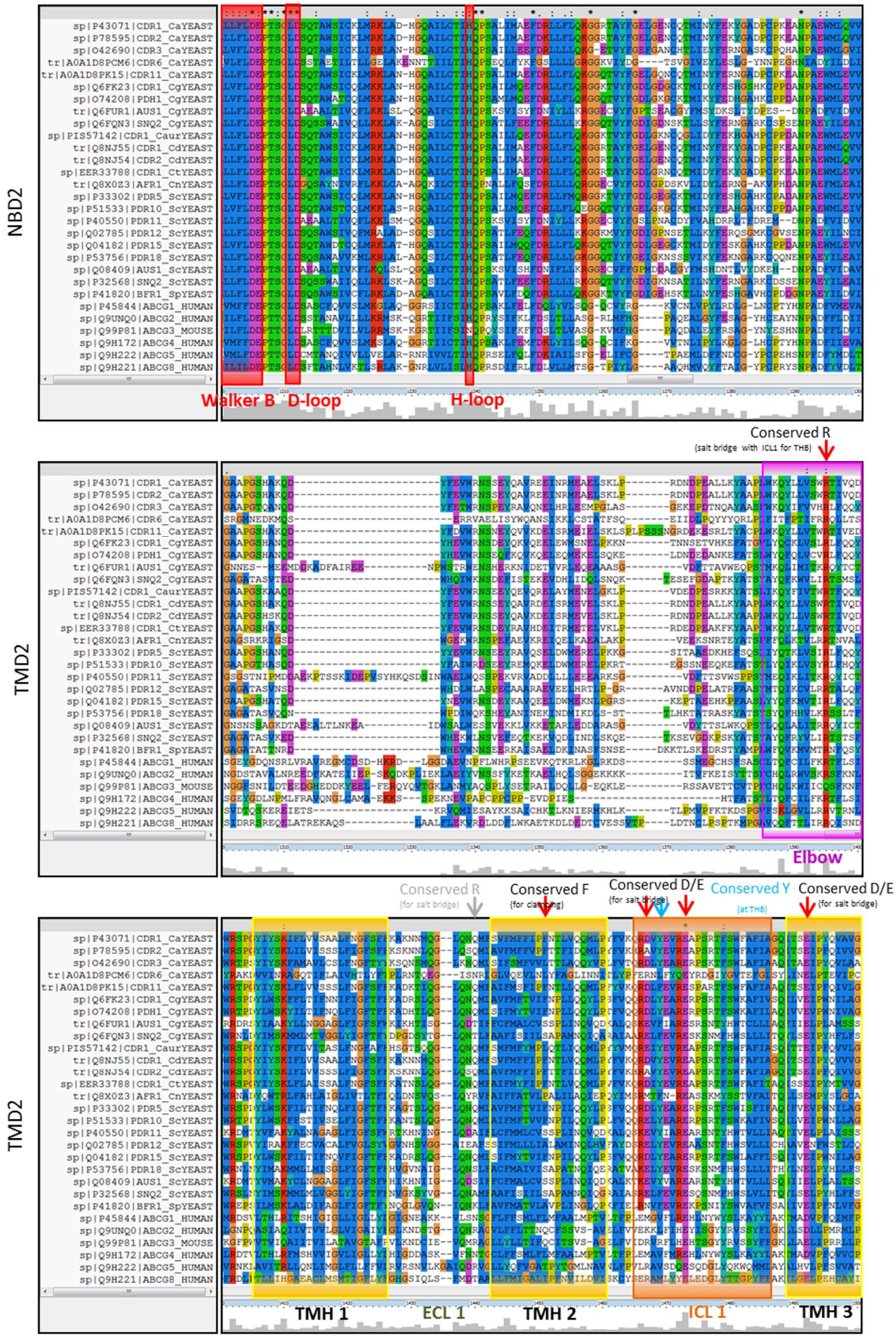
Supplementary Figures and Legends

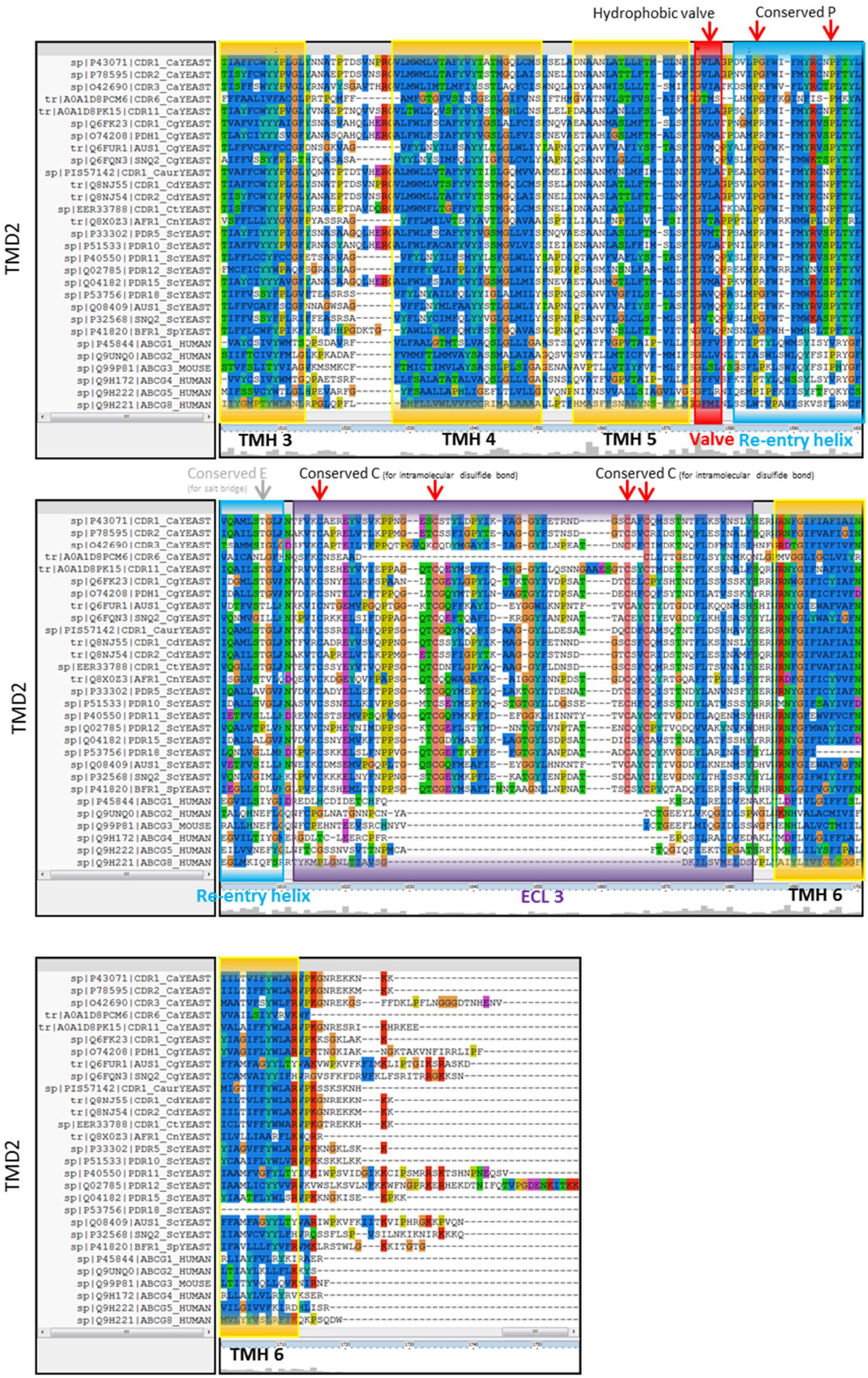



NBD1
Q-loop
Hot spot
Signature
NBD1
P-loop
Walker B
D-loop
H-loop
NBD1


TMD1
Conserved R
(salt bridge with ICL1 for THB)
Conserved R
(for salt bridge)
Conserved F
(for clamping)
Conserved E
(for salt bridge)
Elbow
TMH 1
ECL 1
TMH 2
ICL 1
Conserved Y (at THB)
Conserved D/E
(for intracellular gating)
Hydrophobic valve
ICL 1
TMH 3
ECL 2
TMH 4
TMH 5
Valve
Conserved P
Conserved E
(for salt bridge)
Conserved C (for intra/intermolecular disulfide bond)
Re-entry helix
ECL 3
TMH 6


TMD1
sp|P43071|CDR1_CaYEAST
sp|P78595|CDR2_CaYEAST
sp|O42690|CDR3_CaYEAST
tr|A0A1D8PCM6|CDR6_CaYEAST
tr|A0A1D8PK15|CDR11_CaYEAST
sp|Q6FK23|CDR1_CgYEAST
sp|O74208|PDH1_CgYEAST
tr|Q6FUR1|AUS1_CgYEAST
sp|Q6FQN3|SNQ2_CgYEAST
sp|PIS57142|CDR1_CaurYEAST
tr|Q8NJ55|CDR1_CdYEAST
tr|Q8NJ54|CDR2_CdYEAST
sp|EER33788|CDR1_CtYEAST
tr|Q8X0Z3|AFR1_CnYEAST
sp|P33302|PDR5_ScYEAST
sp|P51533|PDR10_ScYEAST
sp|P40550|PDR11_ScYEAST
sp|Q02785|PDR12_ScYEAST
sp|Q04182|PDR15_ScYEAST
sp|P53756|PDR18_ScYEAST
sp|Q08409|AUS1_ScYEAST
sp|P32568|SNQ2_ScYEAST
sp|P41820|BFR1_SpYEAST
sp|P45844|ABCG1_HUMAN
sp|Q9UNQ0|ABCG2_HUMAN
sp|Q99P81|ABCG3_MOUSE
sp|Q9H172|ABCG4_HUMAN
sp|Q9H222|ABCG5_HUMAN
sp|Q9H221|ABCG8_HUMAN
TMH 6
NBD2
A-loop
Walker A
NBD2
Q-loop
Hot spot
Signature
P-loop


NBD2
Walker B
D-loop
H-loop
Conserved R
(salt bridge with ICL1 for THB)
TMD2
Elbow
Conserved R
(for salt bridge)
Conserved F
(for clamping)
Conserved D/E
(for salt bridge)
Conserved Y
(at THB)
Conserved D/E
(for salt bridge)
TMD2
TMH 1
ECL 1
TMH 2
ICL 1
TMH 3


Hydrophobic valve
Conserved P
TMD2
TMH 3
TMH 4
TMH 5
Valve
Re-entry helix
Conserved E
(for salt bridge)
Conserved C (for intramolecular disulfide bond)
Conserved C (for intramolecular disulfide bond)
TMD2
Re-entry helix
ECL 3
TMH 6
TMD2
TMH 6

Supplementary Figure S1: Amino acid sequence alignment of fungal ABC transporters (PDR subfamily) and mammalian ABCG subfamily.

The multiple sequence alignments (MSA) were conducted using BioEdit and ClustalX2. Conserved residues are highlighted with the conservation scale as the height of gray bars at the bottom. Conserved motifs in the NBDs are highlighted in the red boxes, including A-loop, Walker A, Q-loop, hot spot helix, Signature loop, Pro-loop, Walker B, D-loop and H-loop, respectively. The putative conserved motifs in the TMDs are highlighted in color boxes, the elbow helix (pink), TMH1-TMH6 (yellow), ICL (orange), re-entry helix (blue) and ECL (violet), respectively. Ca: *Candida albicans*, Cg: *Candida glabrata*, Caur: *Candida auris*, Cd: *Candida dubliniensis*, Ct: *Candida tropicalis*, Cn: *Cryptococcus neoformans*, Sc: *Saccharomyces cerevisiae*, Sp: *Schizosaccharomyces pombe*.