

Supplemental Figures:

Supplemental Figure S1: multiple sequence alignment of Rai1 and Dxo1 homologs before and after gene duplication.

Supplemental Figure S2: Sequence logos visualizing different patterns of sequence conservation in Rai1 and Dxo1 paralogs and non-duplicated orthologs.

Supplemental Figure S3: A change in the active site that occurred in Dxo1 after gene duplication is not sufficient to explain functional divergence between Rai1 and Dxo1.

Supplemental Table S1: Plasmids used

Supplemental Figure S1: Alignment of Dxo1 and Rai1 sequences generated by CLUSTAL 2.1. Catalytic motifs I to VI are marked by red boxes. The D and Q motifs that are more conserved in duplicated Rai1 proteins compared to the unduplicated ones are highlighted with filled blue boxes. The R/HH motif in Dxo1 proteins is highlighted with filled green boxes. Residues of Rai1 that interact with Rat1 in the crystal structure of the *S. pombe* proteins (PDB: 3FQD) are highlighted with filled purple boxes. Sequences are named with the first three letters of the genus and species. Full species names are in Figure 5.

CanalbDxo1	-----MERIPLSVFEKFNNQEL-----LSD
CandubDxo1	-----MDRIPLSVFEKLNNQDL-----CSD
CanmetDxo1	-----MLDKLKLSVFEDIVKG-----IQ
CanortDxo1	-----MLNKLKLSLFENIVNG-----VK
CanparDxo1	-----MLDKLRSLSFENIVNG-----SE
SpapasDxo1	-----MIDKIKLSIFEKLNTKYLSLEEP-----SYD
LodeloDxo1	-----MMQQQPLSFFREILKSENTIQN-----SSN
SchstiDxo1	-----MNSIALSIIEKLTTSYLRGLETKDQDSSLKRN
VanpolRai1	-----MAVTSNLFVKQKGNTT-----
TordelRai1	-----MGKTYNLFVKQKGTTT-----
SaccerRai1	-----MGVSANLFVKQRGSTT-----
CanglaRai1	-----MGISANLFVNQKGTTT-----
NaucasRai1	-----MAITANLFVNQKGTTT-----
LackluRai1	-----MGLSANLFVKKKGSTT-----
LacwalRai1	-----MVISNLFVQKRSATN-----
KlulacRai1	-----MVLSSSLFVQKRSTTT-----
HanosmRai1	-----MMIKP-LFIRERSNVT-----
CanalbRai1	-----MAKSLPLNSRSKTT-----
CandubRai1	-----MEKSLPLNSRSKTT-----
SpapasRai1	-----MIKTLPLNSRAKTT-----
CanparRai1	-----MSKTFPITSRAKTT-----
CanortRai1	-----MNKTLPITSRAKTT-----
CanmetRai1	-----MSKTLPITSRAKTT-----
LodeloRai1	-----MSSRKLPLSARAKTT-----
SchstiRai1	-----MMKTLSLQSRAKTT-----
Canlus	-----MLKLLPLSARSDST-----
Metbis	-----MNHTLPLSTRAETT-----
Canaur	-----MIKTFKLNSRSETS-----
Canten	-----MIRTLPLTARAPVA-----
Wiccif	-----MSSSKLLPLNSRAATT-----
Cybjad	-----MSGVKLFPLNSRADTT-----
Ogapol	-----MEFSKVYPLQSQDA-----
Kompha	-----MSKEKILPLAARSKKA-----
Lypsta	-----MAGRPHFQSTPWTNGTPQVSSHGQRQAPALSPLISSARIR-----
Yarlip	-----MSSFSTTERLAAK-----
SaccerDxo1	MSTEQDAVLGLAKDLEGINLLTVPNLERGHQSKLCKEKTTSDDSSSRKPSQQR-----
NaucasDxo1	-----MKKTGQELMPLHTTVQS-----
VanpolDxo1	MDEHIN-----DVQTQLSNLKIG---EDNPSRKVKQNKSRPK-----
TordelDxo1	MSKTSDDSSTASSLEVHLLGNKLNLSLGLQDSPHGSPKQRRKQQS-----
LackluDxo1	-----MTIPTDELTAISKLSLQHGQSNT-----
LacwalDxo1	-----MLPNLQDLQLQDRTEEVH-----
KlulacDxo1	-----MTTVSCDKDENKVDQLGESLSQLRISTRKNNKPS-----
CanglaDxo1	---MEEVVNQLEALSLSNDKRRVKGQRKGKKKHGNSRARDHTTVVIR-----
Hanosmdxo1	-----MSSVDDLLLDVSKLSLTEDGHAKKELHATES-----

CanalbDxo1	VPEDRFISKSLQSPEIFSTPCEECTYFT--KSNNNN-----ILKFDDT-
CandubDxo1	VPEDRFVSKCLRSQETFTSTPCKEWTYFT--KGNN-----ILEFHDT-
CanmetDxo1	IENEKELNESSTRGQAFSRDPEELCHYT--KEDT-----TLKFADI-
CanortDxo1	IANEDELNEILEERQAFACNPEELCYYS--KDEK-----RLKFADI-
CanparDxo1	IVEDEVLNEFLN--VPYNCDPEELCYT--KDES-----TLKFGDI-
SpapasDxo1	DHEDAFIYNTLLKDASTDITPEEWLHFS--KATED-----EPAFDDI-
LodeloDxo1	GSDNISDTPLLTSSSEIFNEEPPEEICHYT--KTSH-----QLKYNDI-
SchstiDxo1	KEDVHLAKYLAKDSVIFDQSPSELLYFSLIKEKEKS-----EILFEDK-
VanpolRail	-----SLKQPKEISFYSRTPEDE-----FNVKDD-
TordelRail	-----ALKQPKEISYYSRTTNEE-----FLVGND-
SaccerRail	-----ALKQPKEIGFYSRTKDEE-----YLISDD-
CanglaRail	-----ALKQPKEIGYYSRNQTEE-----YLVSDD-
NaucasRail	-----SLKQPKEISYYSRTQEDE-----FLVGDD-
LackluRail	-----ALKQPKELGFYSKTQENS-----FLIDDD-
LacwalRail	-----SLKQPKELGFYSKTQEGE-----FLINDK-
KlulacRail	-----ALKQPKELGHYSTRQDNG-----FLVNDD-
HanosmRail	-----ALKQPKEIGRYSRKSYPENVENESXKQNCSTAGYKSKYYINDD-
CanalbRail	-----ALKQPRELFSYARDIDGK-----YVYDDP-
CandubRail	-----ALKQPRELFSYARDIDGR-----YVYDDP-
SpapasRail	-----TLKQPRELFSYARDIDGE-----YVYDDDES
CanparRail	-----ALKQPKELFYTRDIEGE-----YHYNANQ
CanortRail	-----ALKQPKELFYTRDIEGE-----YHYNANQ
CanmetRail	-----ALKQPKELFYTRDIEGE-----YHYNSNQ
LodeloRail	-----ALKQPKEVFTFTRDIEGK-----YHYNAEH
SchstiRail	-----ALKQPKEIFAFARDIDGE-----FVYDQKI
Canlus	-----ALKQPKELFYSYRDESSE-----WNIDEHV
Metbis	-----ALKQPKELFYSYRNADGG-----WQTDDKE
Canaur	-----SLKLPKEVFSFSRDLDE-----WHTDDAK
Canten	-----SLKKPKELTTYRDLNGN-----YIHDDE-
Wiccif	-----ALKQPKEIASFSRTFDGE-----YVNDDS-
Cybjad	-----ALRQPKELYCFSTRFDGE-----YVNGDV-
Ogapol	-----SVKQPKELISYSRDIEGK-----YRVDDS-
Kompha	-----MLRQPKQVAYFSRDLNYK-----THPDRS-
Lypsta	-----GPAMRQPREVTSFSYDNNRS-----LHFDDS-
Yarlip	-----LKKPKEVYSYSITDG-K-----VTMDQS-
SaccerDxo1	-DNYRKRPRKLCIPYTSFLHTGMHNFLTTPPRDIFHESKE-----VALFTNGRA
NaucasDxo1	-----QKQAPITRVPFGEFSHSSISLFPTCT-QPFYESSNQ-----VALYHNHKL
VanpolDxo1	-----KNVINIIPFHRFVHSNARSFPQKT-KDLFLESKT-----VAFFQKDQL
TordelDxo1	-----GKRTVCIPFSKFEHSDLDYFPDDT-ADFFEGCEE-----VATYQNGYL
LackluDxo1	-----ANCKGFVHSNVSHFSPVCKFFQESREI-----GTFTRMVSS
LacwalDxo1	-----ANCKNFQHAQINQFPKNVLPFFDEVQEV-----ATITHLLDT
KlulacDxo1	-----QKKGSLVLSCKKFPHVSVNYVVDKTPKLLTDCKEV-----HNCSYIIND
CanglaDxo1	-----GNKQRLKTSHHKNMPQFYDSAKTLG-----IFHDHKL
Hanosmdxo1	-----LLASFQYDPEKSRTYLESQPVLCCKEMELMG-----SVLKIRKKKKDK

CanalbDxo1	---TGLNTVLVSYTQ-----QSKKRKQKKTNASSKGRPK-----IIGSDLT
CandubDxo1	---TGLNKVLISFTQ-----PAKKRKQKKPNGS-RNQPK-----IIGSDLT
CanmetDxo1	---SGLDQVKIPFG-----PQDKK-KKEK-KRENEPP-----LIGACLS
CanortDxo1	---SGLDEVRI PFG-----AKDKKEKKEKGKKKARPP-----IIGTCLT
CanparDxo1	---SGLHEVKIPFG-----SKGKT--KKKRVSDKGPV-----IIGTCLT
SpapasDxo1	---SGLKKLAIHIPD-----GTKKKHTRKKLKDPECESHS-----IIGSCMT
LodeloDxo1	---SGLSVIKIRIDNNNRTSHSHSTKKNRTRKNRTKKKANANACPNRNEKGPPTIGADLK
SchstiDxo1	---SALKQVNVPLEQSKK---VANKQKQGKKKKNSKNHEKDVS-----QLIGGSLS
VanpolRail	---SRLRYYYLPDA-----ELDMN-----LDLC
TordelRail	---ANLNYYYLPDA-----ELDNR-----LDLS
SaccerRail	---TNLNYYYLPDA-----ELDRK-----LDLS
CanglaRail	---INLRYYYLPDQ-----EIEHG-----IDLS
NaucasRail	---SRLSYYYLPNA-----DLDDK-----LDLS
LackluRail	---SKLNYYYLPDA-----DLDDN-----LDLT
LacwalRail	---SKLSYYYLPDT-----DLDDN-----LDLT
KlulacRail	---SRLAYYYLPDT-----DLDDK-----LDLL
HanosmRail	---IFLNYYYPND-----DLDDRI-----INLS
CanalbRail	--ENSLSYYYLPDS-----TIDTG-----IDLQ
CandubRail	--QDSLSYYYLPDS-----TIDNG-----IDLQ
SpapasRail	V-QSAISYYYLPDS-----AVDSR-----LDLQ
CanparRail	S-HDHLPYYYLPDT-----KVDTR-----IDLQ
CanortRail	S-HDHLPYYYLPDS-----KVDTR-----IDLQ
CanmetRail	S-HDHSYYYLPDS-----KVDTR-----IDLQ
LodeloRail	S-HDGLSYYYLPDS-----KIDTR-----IDLQ
SchstiRail	VKDENVSYYYLPDS-----KIDGS-----IDLQ
Canlus	SKDEALSYYFPPDS-----YVDQH-----MDLQ
Metbis	AKLQGLNYFYFPA-----YVDKN-----ISLQ
Canaur	AKEEALSYYFPPDS-----YIDRN-----YNLG
Canten	----GHSYFYFPPDS-----YVERG-----FDMA
Wiccif	----SLGYYFLPDS-----DIETN-----IDLG
Cybjad	----CLSYFPLPDS-----DVDTN-----IDLG
Ogapol	----QLSYFYLPDSQL-----NVP GG-----IDLA
Kompha	----NLSYFLLPDG-----DIDNS-----IDLS
Lypsta	----SLSYFYLLQDD-----VTASGG-----IDLS
Yarlip	----QLKYYYLPEET-----ILKA-----IDLT
SaccerDxo1	YTI--LRKDLIPNLKE-----SIAELYESSLLEAKKRKVPYLGHDLF
NaucasDxo1	YPA--SQYDIIPHLKN-----DIAQLPKKSASEARTLKRSYLGSDLY
VanpolDxo1	FIN--VEDAALPLLKK-----DIANISGKSVLNSKKYKLPYLGSDLY
TordelDxo1	FMKDSSKKPLYPCLQM-----FAALIAEN---RGPKNKLPYIGCDLY
LackluDxo1	GKYLFDKLGRLPLKD-----DICEYIHNPAKNASKIKTQYLG YDLL
LacwalDxo1	DEFLLDDKLGMP ELVQ-----DLCEFTES-GKLAN KGK--YIGHDLL
KlulacDxo1	ATLLWNEASRKPRLRP-----EVCTYIKDSKWENKAVKDSFIGIDLT
CanglaDxo1	YEMNRMDLFPQLKDP-----IAHIAKSTPAEKTQLVRPFLGISLY
Hanosmdxo1	HCHDYDYQFHLKEGNYEG-----LAVINADLQESFQSDRMKLSKKCLSRYIPSNLE

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CanalbDxo1 QGFS-DFKPE--SLKDIYSLNDIFKSIQYLIQNKNFTP----QDFKIVTARRHLQKLMT-
CandubDxo1 EGFS-EFKPE--SLKDVYSFDDILRSIQYLIHNKKFNL----DDLKIVTIRRHQLQKLMT-
CanmetDxo1 EGFD-GFVSS--NLDIVYSLDDIFKSVQHILIESHTLSR----DKLKVLTTTTRHLMKLMS-
CanortDxo1 EGFD-EFVPP--DLNDVYSLNDFKSLQHILIESNRLSR----DELKVLTMRRHLMKLMLC-
CanparDxo1 EGFD-KFEQP--NLNDVYSLEDLFRSLQYLIQSGELSR----DSLKFLTMRRHLMKLMLC-
SpapasDxo1 LGFD-NYQHP--KLADIYSLKDLFKCVEHLVQEKNHSL----QDFKILTTLRRHLHLLLK-
LodeloDxo1 KGFNSNYTRP--SQMEIYSLDDVLGSIQYSVANKLLSM----TDLKFITTRRHLSKLMG-
SchstiDxo1 YGYE-QFSPP--KQEEIYSLNMLRAIEYLVREKGKPL----EDFKMLSLRNLHLLMT-
VanpolRail GGIKKFKDHY-KNFQDPGTLKGLLKTQAYEEIKQKK-----VKVDIITFRGVIRKLIS-
TordelRail AGVAKMRDTA-KEFKDPGTLRGLLATVQSVEEKKQKR-----TKADIITFRGVIRRLIS-
SacerRail SGFQKFKDYY-KDFEDRCSLRGLLETIESSERHKGKK-----INADIITFRGIARKLIS-
CanglaRail AGASKFRDVA-KDFKDRCSLKGLLDTLMEYEKKKNKK-----SNVDIITFRGIMSKLIR-
NaucaRail SGIKKFKDCS-KNMKDRCTLNGLLDTIMEHEKCKNKK-----IKADIITFRGIIRKLIS-
LackluRail GGIKKFRECNPDPSFDCTLRALLSTIQSYEQRKNNK-----AKADIITFRGIIRKLIS-
LacwalRail AGIKKFKESNNPEVDACTLDGLLKTQAYEERKQSK-----VSADIITFRGIIRKLIS-
KlulacRail SGIKKFKECN-TEEFDSTTLHGLLSTLEEYERRKSKK-----TKVDIITFRGIIRKLIS-
HanosmRail GGFNKFKNAS---PVDDLHLGLLATLIDIESKKNKK-----SKVDVVTMRGIIKSLIML
CanalbRail GGYSKFKKIP--DEQNADFNLSLLKAI IKYETSEGKK-----ISSDIITFREIMTKILS-
CandubRail AGYSKFKKIP--EEQNADFNLSLLKAI IKYETSEGKK-----ISSDIITFRGIMTKILS-
SpapasRail SGYSKFKKIP--EEQNADFTSYLTAIQKHEESSGEK-----VQGDIVTFRGVMTKILA-
CanparRail SGFRNFKKIS--EEANMSDFGPLLDIAIVQYERDENDGK----LGGDVVTFRGIMTRLMS-
CanortRail SGFKNFKKIS--EEANMSDFEPLLNAIMQYERDEFSDR----IGGDVITFRGIMTRLMS-
CanmetRail SGFKNFKKIS--EEANMADFEPLLDIAIMRYERDEIKTK----VAGDIVTFRGIMTRLMS-
LodeloRail SGFKHFQIP--IEENLGDFHPFLEAIMKYEQ-EGSSR----LSGDIVTFRGIMTKILS-
SchstiRail AGYAKFKKIP--EEKNMSDMKCLLTALTKEYEQEHNNGEK---VNVVDIITYRGLMTKLLA-
Canlus AGFKSFRKIP--EEQNKAHFPSLLAALQQHEQKTGKK-----VAVDIITFRGIMTKLLT-
Metbis AGLGSFKKIP--DAQNTADFPLLLRLCLQQHEQTSQKK-----VRADIISFRGMVTRLLT-
Canaur DGFNFKKIP--EAENVPNFASFLLKAIKEHEQQSGKK-----IKVDIVTFRGMVMTKLLT-
Canten AGFSKFNKIP--EAKNLGDFHAILAALVKHEQSVGAR-----VECDVIAFRGIMTKLMT-
Wiccif AGFKKFKKFD--EARD-GEFDGLLGAIKNYEETNKTGK-----VKAHIITWRGIMTKLLT-
Cybjad AGFGKFKKMD--DDKD-GVFDGFIGGLEDYERRTGSK-----VKADIITFRGIMTQLLI-
Ogapol G-FKDFHAN----GEDFGEFTGLLAALSYERKIGAK-----TPANIITWRGLMRSLML-
Kompha VGSKHFLG---DSVELSKLDPILLALKEIEKESGAK-----TKDRIITWRGIMRKLTL-
Lypsta AGYNVFKKRD---DTIDEHLGLLLSLVDLEKNTRKK-----TTGDIITWRGIVTKLLC-
Yarlip KGIENTWTQPN---E-HDTHLDTLLESLSKYERETGSK-----IDAEIITWRGILTKIMT-
SacerDxo1 ANIDEFVPMTISELDSVSPCFSYIENWILDNPGKDFKIG---KKFTVVTTRHHIVDLTMH
NaucaDxo1 DGFETFPMSAKDLDSLEPCMSFIKDWER-KASTKYKPG---RKFNIIVSTRHHIVEMTMK
VanpolDxo1 ASTDKYGPLPEDVLDSPKPCFDFIRHWENEHGEHYGAH---ADYTILSPRHHIVTEIVMS
TordelDxo1 QGHERYKPLPSELDSIACFEYIKKWERRKISKSFNS----GKVTIISPRHHIVVDLVMA
LackluDxo1 NGFEDIYPLSEDELNNMDGILNFIGNWEE-KNGKKYGESE---NKFTIVSNRHHILIDLIMC
LacwalDxo1 DHFDEYVPITPKQLEDMAGVQAFLEWRKQ-LHGRSFCDN---ADFTIVCSRHHILIDLIMM
KlulacDxo1 KGYDDYVPLDRNVLSLVILKEAYQRYEK-TLNP-----EKTTFVSLRHHIIDIIMC
CanglaDxo1 ENHDKYSMTAKELDTTEACSTYLDQYENSHGQKYGED---RDFVIVTARHHIMIDLAIL
Hanosmdxo1 NGFQNYVPISPVELVSARSFVEFLIKYEQHYKTPLNKSASEKNDFLYVTRRHHLTSLAS-

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CanalbDxo1	-----IPIHKQEVQFNVIYWKG---MIFPAYDWKSESTTKVEDP-----
CandubDxo1	-----IPIYKQEVQFNVIYWKG---MIFPAYDWKSESTNNNDNSSSK-----
CanmetDxo1	-----IPLNKQPVSFVDVIYWRG---LIIFAYDWDKELKVVPDNF-----
CanortDxo1	-----IPLNKQPISFVDVYWRD---LVIFAYDWEKELEVASGSH-----
CanparDxo1	-----IPLNKQPVSFNVIYWRG---LIIFAYDWDEELKLIPDDY-----
SpapasDxo1	-----VPIRKQSIQFHVIYWKG---LIIFAYDWEPEAQYKKQNPPNG-----
LodeloDxo1	-----ILLDNQPVAFNVIYWKG---LIFFVYDWRFKDEINAESSHGDDQENDHQN
SchstiDxo1	-----IPISKQTTSFNLIYWNG---LIFLSYDWKSSEKSKETRKENASDKR----
VanpolRail	-----SAFDSPKFNQVNLRIVLFDG---QIFMKEVPRKEEEPKD-----
TordelRail	-----AAFDSPKFNKVDLRVAFDG---QIFIRDVASKDEELRM-----
SaccerRail	-----CAFDSPSFNTVDLRIVSFNG---QLFIKEVPEAVNAAKASSAT-----
CanglaRail	-----ASMEPPNFNKVDLRIVSYDG---QLFIKDVSDYNAATNESNSSGVN-----
NaucasRail	-----SAFETANFPINLRIVSFDG---QLFIKDMADLNDKKVLNAKE-----
LackluRail	-----SAFDNPRYNRVNLRIVSFDG---QLFIKEVGEPFVPP-----
LacwalRail	-----SAFDSPKYNHVNLRVVSFNG---QLFIKEVKTDASETSIN-----
KlulacRail	-----SAFDSSQFNPNFRIVSFDG---QLFIKEVKTDASETSIN-----
HanosmRail	FNSLG--SRNTTASSTDVDLQVVTFDG---QIFIKKAGSLNSQHQETQEKPSTNESLTRP
CanalbRail	-----LPYNLTDPIDLYVVPFDG---QLFIKSDELDMKRRKEQEVRMKQTN----
CandubRail	-----LPYNLTEPIDLYVVPFDG---QLFIKSDELDIKRRKEQDDRMKQTS----
SpapasRail	-----LPFNINEPFDLNIVPFDG---QLFMNVDVNIETNRREQREAELRNNN----
CanparRail	-----IPYYIQDALDLVIVPFDG---QLFMNFNNEIELRRRKEQEDRLRQTS----
CanortRail	-----IPYNLQDALDLVIVPFDG---QLFINFNNEVELKRRKDQDDRRLRQTS----
CanmetRail	-----IPYNLADPLDLVIVPYDG---QLFINFNTAVELKRRKEQDDRIRQTT----
LodeloRail	-----LPYNLTDPDLVIVPFDG---QLFINFDFEIELKRRQEEDRTRQTT----
SchstiRail	-----LPYNLNDPVDLNVLAYDG---QLFINSDEEIELARRKEEDEHKQQSM----
Canlus	-----LPYNNNGFRLHVLAFDG---QLFIRNDDDFDLQARQKEREALSPD----
Metbis	-----LPYDLNSEIHLHVLAYDG---QIFLKNDDLDLKKRAAEQORLGADA----
Canaur	-----LPYDTKTPIHLYVIAFDG---QLFITPDSEYELKQRAAEDEQLKASD----
Canten	-----LPIAR-DDFSLKVLTYGG---HIMIKNNDEFELTRRTANTPT-----
Wiccif	-----LPYNLNDPLDFNVVYFDG---HLFIQEDKALKTARETKPTDE-----
Cybjad	-----LPYEQRNHIDLNVYFDG---HIFIQQDKKAKKLHERAPSVE-----
Ogapol	-----LPFDNRDKIVLNIVVFDG---QLFIQQD--FQNAREAADLEKLTQS-----
Kompha	-----LPYDSEEDFVLDVVSFDG---QLFIQFNVPYLKSKDVQKQGD-----
Lypsta	-----LPYSRNDGFELNAVWFDR---QLFIEEDLPYKLATQRLPDQR-----
Yarlip	-----HPYDQNEPIVLNITYFDG---HYFIEEDWQSKQGGKKAPDEQ-----
SaccerDxo1	LFN-----RRNRQTSLIVTYMG--AGLLSFCRN-VKKDSQMSKEGIYSND-----
NaucasDxo1	LFTGKTNNYNNTKKVQDYVLNVVYTGDETGRLLF TKD--WSNTGNSMNEGIYSKN-----
VanpolDxo1	LFE-----DEKNCSVYLLCTYLK--NGIILLSKDDASSSSNSNTTGLNSSN-----
TordelDxo1	LFH-----DD---EVSIICTNIG--KGKLIFSGD---RSKEERNGLNSKN-----
LackluDxo1	PFS-----LEEANLIVTHLDG--LLIISSDKS-----KPKVDSGIRSKD-----
LacwalDxo1	PFS-----DEDVHLKIQFSNG--YLNLSPPAQ-----YQKTDQGIHSGD-----
KlulacDxo1	PFL-----DEPLSLLMTVQPDKNILISVDKS-----KDKPNGIHETRN-----
CanglaDxo1	P-----FSRQFTNVNLLCAYTPG--NLLEISQDPADNTNDKVGVTNDN-----
Hanosmdxo1	-----SLFLSESTKMDLVLFDG---LLILHEGRPDFGGIHSDDHK-----

CanalbDxo1	-----YNKLIQYTGFKFEEV
CandubDxo1	-----YHKLMQYTGFKFEKV
CanmetDxo1	-----QRMFQYSGFQFERV
CanortDxo1	-----QKMCQYSGFKFEKV
CanparDxo1	-----LKLYQYNGFKFEEV
SpapasDxo1	-----IERLLQYSGMNFENI
LodeloDxo1	NHQNNHQNNHQNNHQNNHQSNHQSVNHSLVETEARSADNIRRLLELQYCGFKFEEI
SchstiDxo1	-----ADNLRLIQYTGFAFERL
VanpolRail	-----GKIAP-PVYSGYKFENL
TordelRail	-----TTESRNAWYTGKFTV
SaccerRail	-----EAGRNINQDLNVFTGYKFETL
CanglaRail	-----SRQQAGTSRQQIDTYTGKFEI
NaucasRail	-----NDHIDLGSYSGYKFETL
LackluRail	-----KTTDSIEHRSYYSGYKFESL
LacwalRail	-----KNTDAMQYRSYYSGYKFESL
KlulacRail	-----KNRESLQARAYYSGYKFEAL
HanosmRail	VGSRF-----SNTTRESQYLKKCEYSGYKFETC
CanalbRail	-----TVERYDYMKRCYVGYKFETI
CandubRail	-----TEERYDYLKRCYIYGYKFETI
SpapasRail	-----PPDKYEYLKKCEFSGYKFETI
CanparRail	-----TKEKYEYVKKCEYSGYKFETV
CanortRail	-----PKEKYEYIKKCEYSGYKFETV
CanmetRail	-----AREKYEYIKKCEYSGYKFETI
LodeloRail	-----TKEKYEHLKKLEYSYGYKFEAI
SchstiRail	-----TPEKYDHMKRCFSGYKFEAI
Canlus	-----RQRYLDLCEYGGYKFEAL
Metbis	-----A--KEKHLRTCEYGGYKFEAV
Canaur	-----PE-KYQYNKTCYTGKFEAL
Canten	-----DLGQRLEYSYGYKFEKL
Wiccif	-----HARIMYSYGYKFESI
Cybjad	-----QQRIMYSYGYKFESV
Ogapol	-----DLNKRQIYSYGYKFEKI
Kompha	-----TEFHKKLQFSYGYKFEKM
Lypsta	-----SELMYWGKFEQI
Yarlip	-----MKKHIIYSYGYKFESV
SaccerDxo1	-----PNMKKICYSGFEFENW
NaucasDxo1	-----IILKRICYSGFALEDL
VanpolDxo1	-----PMTRKICYSGFAFEDL
TordelDxo1	-----SMTRKICYSGFALEDK
LackluDxo1	-----TRVRKICYTGFELENL
LacwalDxo1	-----TKIKKICYTGFELENL
KlulacDxo1	-----SFNKKICYTGFALEDL
CanglaDxo1	-----PILKKICFSGFALEDI
Hanosmdxo1	-----LAHMCYHGFALENL

III

CanalbDxo1	VSE-----GTRD---SNFYTVVQHCVDN-IPVIYTAEVDCSIDK-ETG-
CandubDxo1	LSE-----GIKD---SNFYTVVQHCVDN-IPVIYTAEIDCSIDK-EKG-
CanmetDxo1	VTG-----KSHQETPSSFYTVVQHTVGQ-DNVTYSAEIDCAISL-EPG-
CanortDxo1	VTE-----RGPHDSNSSFHTVVQHTSGK-TSVTYSAEIDCALPG-SPG-
CanparDxo1	VTD-----HAADEPKSSFHSVTQHFAGK-NMITYSAEIDCAISK-MPG-
SpapasDxo1	VCG-----DDSADYKSRYYSVVNHTVNG-VPLLYCAEIDCAIKS-EPG-
LodeloDxo1	ITTS-----QTSTTSSVFSKFYTVVKHKVNG-IPVVYTAEVDCAVDN-VPG-
SchstiDxo1	ITSSP-----ASVSFDDNSITSFYSLVSHKVGE-IPHFYTAEIDACKDITKDG-
VanpolRail	VTVSKPIPYTSRTTIEKRPKKIVSNGDEYISVVRTGVGN-CKLMLGAEVDAIFDFKEEDK
TordelRail	ATLSQPLPYVDRETVEKRPKKLVTNGDEYITVVRTGVGN-SKLILGAEVDCIFDFKEEGK
SaccerRail	ATLSNPLQYTPREVIEKRTRKRVSHGDEYISVVRTGVGN-CKLILGAEVDCIFDFKENGK
CanglaRail	ATLDKPLPYVEREVIEKRPRKILNNGDEYITVVRTGVGE-CKVVLGAEIDCIFDFKEEGK
NaucasRail	ATLSQPVYPVSRATLDKRSKKICNNGDEYVTVVKTGVGS-AKLVLGAEIDCVFDFKEDGK
LackluRail	VTLPKPLGEVSRRTTIEKRPKKIVNNGEQYISVVRTGVGK-SKLILGAEVDCVFDFKEDSG
LacwalRail	ATLSKPLPQTPRSSLEKRSKKICNNGDQFVTVVRSGVGN-CKLVLGAEVDCVFDFAEEDTS
KlulacRail	ATLSLPLPLVPRTTIEKRPKKIINNGDQFISMVRTGIGK-CKILIGAEVDCIFDFKEDSD
HanosmRail	ATLPRPVSEIPREKLDKRYKKIGTNDQYNILVKTGIGN-CKMILGAEVDAVFDFKEESQ
CanalbRail	ATIPKPWSQVSRQIENRNKKVNNYEQYLSVIRTGIGN-VKLVLAGEIDCCWDYLPDE-
CandubRail	ATLKPWSQVSRNQIENRNKKTNNYEQYLSVIRTGIGN-VKLVLAGEIDCCWDYLPDE-
SpapasRail	ATLPRPWADCSRSEIEKRPKKMNNYEQHLSVIKTGIGN-VKLVLAGEIDCVWDYLPDD-
CanparRail	ATIPQPWKDVSRKYIDSRHKKPVNNYEQFLSVIKTGIGP-VKLVLAGEIDCCWDYIPEK-
CanortRail	ATIPHPWKDVSRKCIDSRHKKPVNNYEQFLSVIKTGIGP-VKLVLAGEIDCCWDYIPEK-
CanmetRail	ATIPQPWKDASRKYIDSRHKKPVNNYEQFLSVIKTGIGP-VKLVLAGEIDCCWDYIPEK-
LodeloRail	ATIPDIWANVSRKTIESRHKKHVNNEQFMSVIKTGIGN-QKLILAGEVDCWDYVPEQ-
SchstiRail	ATLKPWADCSRQIDKRGKKMVNNYEQYISVIKTGIGE-AKMLLAGEVDCVWDYIPEK-
Canlus	ATLKPWQAQCNRSSTIEKRKTKTSSYEQYISVVRTGIGK-IKTLLAGEVDCIWDYVPT-
Metbis	ATLPRPWAHTPRAAIEKRHKKVSNYEQYISVVRTGVGR-VKTLLAGEVDCVWDYLPDN-
Canaur	TTLKPWQAQCSRLIEKRAKKTNNYEQYISVVRTGIGK-VKTLLAGEVDCAWDYIPSEE
Canten	VMLPRPWSECSRATIESRPTQEVNNYEQYISVVRTGIGK-TRMVLAGEVDCIWDYKPV-
Wiccif	ATLKPPLAQVSRATIDKNHKKIVSNAEQYCSIVKTGIGK-QRIIGGEVDCVWDYKPED-
Cybjad	ATVPKPLNEVSRATIEKRSKKIVNNEQYCSVVRTGIGK-TRIVLGGEVDCVWDYKPED-
Ogapol	ATLSKPWAQCSRKEIEQRNKLNVNNEQYATVVKTSFGK-TGLVMGAEVDCVFDYKPED-
Kompha	ATLKPWPPECTRKEIDSRASKCNNEQYGAIVRTGISR-IKILIGGEVDCIWDYDEN-
Lypsta	ATIPQWNECSRQEVESRGQKPVSNVAQYCSVVKTLGLD-VRMVIAGEVDCVWDYKPD-
Yarlip	ALLNEPWFKSSREDIESR-FDDIPNGDQFVSVVRTQIGD-NKILIGGEVDCVFD-PCAK
SaccerDxo1	VTENSKVAD-----LTGSKCPIFSLVESKLSEEIGLLIRCEMDAFNP-----
NaucasDxo1	MTETTSELEK-----EGEKLTGGEKAVFAVVENKLDDDICILLRCELDAFNG-----
VanpolDxo1	VLED-----IAENARPIFSVVESKLTESINLLLRNELDGYNN-----
TordelDxo1	LTTS-----HDERMGPFYSIVEGKINERLSLLLRCEMDAYNP-----
LackluDxo1	VTKG-----KVDSPGMHTCFYSIVENKLTEGVSLLLQAEMDSYNP-----
LacwalDxo1	ITA-----TSKPDVRSSFYSLVEGKLGDGIKLLKAEMDCFNS-----
KlulacDxo1	LIESP-----TEGHILEHELYYSIVHGSLNDEIDLLIQAEMDSINT-----
CanglaDxo1	LTES-----ANDEERNPTFLIVENEIAN-TRLLMRCEIDAYNP-----
Hanosmdxo1	LSKD-----TQSDSTGHYYVYNKCTLDNGKEILLQAELDAMLNP-----

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	IV	V	VI
CanalbDxo1	-----LENYIELKTH	TKLADDKISTINKLN	NKKLLSTFIQTKFIDCQHSIIGF
CandubDxo1	-----LENYVELKTH	SKLPDDKISTINKLN	NKKLLSTFIQTKFIDCQHSIVGF
CanmetDxo1	-----LHNYVELKTH	ATLPDDKLKTTNKL	QKLMAMYCQNKFISCKYSAIGF
CanortDxo1	-----LHSYVELKTH	PTLDDKLKTANKL	QWKMALYCQNKFISCNYSIAIGF
CanparDxo1	-----LSNYVELKTH	SSLPDDKLKTANKL	QKLMALYCQNKFISCNYSIAIGF
SpapasDxo1	-----LCNYVELKTH	SKSADDKIKTVNKL	NKKLLEAYCQNKLVGCGHLMVGY
LodeloDxo1	-----LANYVELKTH	SILSDDKAKTINKF	SRKLMALYCQNKFISCKNSVIGF
SchstiDxo1	-----LSNYIELKAR	AIPSGPKGRANSS	FORKLLSAYCQNKLIGSQNLVIGF
VanpolRail	-----DNLKHYVELKT	TNAVLTPS--	DARKFEQKIFKTIWQCFLVGIPRIIYGF
TordelRail	-----DNLKHYAELKC	SAMVSTQA--	DARKFEKKIFKTIWQCFLVGIPRIIYGF
SaccerRail	-----DNLKHYAELKC	QQVANIS--	DTHKFERKLFRTWQCFLVGIPRIIYGF
CanglaRail	-----DNLKHYTELKC	SSQISTTN--	DVRRFEKKMFRAWQCFLVGVPRIIYGF
NaucasRail	-----DNLKHYAELKC	TTQVITAA--	DAHKFERKIFRTWQCFLVGIPRIIYGF
LackluRail	-----DNLKHYTELKC	TGVTTIA--	EARAFERKIFKTIWQCFLVGVPRIIYGF
LacwalRail	-----NNLKHYAELKC	TGVSTFA--	EARSFERKLFKTIWQCFLVGINRIIYGF
KlulacRail	-----DNLKHYAELKC	TTMVNTVS--	DAHKFERKLFKTIWQCFLVGINRIIYGF
HanosmRail	KIG----	EVPENLKHYLELKT	SKMITNAH--QAKTFENKLFNAWLQCFLVGVPRIITYGF
CanalbRail	-----QNKKLNHVELKT	SRI IENNS--	QVVSFEQKLFKAWCQCFLMGVTKIIYGF
CandubRail	-----RNKILNHVELKT	SRI IENNM--	QVVSFEKKLFKTIWQCFLMGVTKIIYGF
SpapasRail	-----NKHTLDHYVELKT	SRI IETNG--	NVVTFEKKLFKTIWQCFLMGVRYIIYGF
CanparRail	-----TAFSLSHYVELKT	SKVIESNS--	QILNFEKKLFKAWCQCFLMGVGKVVYGF
CanortRail	-----TSSSLSHYVELKT	NKVIDSPP--	QILNFEKKLFKTIWQCFLMGVGKVIYGF
CanmetRail	-----ASSSLSHYVELKT	SKVIDSNN--	QILNFEKKLFKTIWQCFLMGVGKVVYGF
LodeloRail	-----PSQILNHVELKT	SRVIETNN--	QVVNFEKKLFKTIWQCFLMGVGKVVYGF
SchstiRail	-----GKDVLSHYMELKT	TRILESNG--	QVVNFEKKLFKTIWQCFLMGIRKVVYGF
Canlus	-----KGDSILSHYELKT	SRVETPQ--	NASAFEKKLFRTWAQCFLLGITRIVYGF
Metbis	-----AAD-VLAHYELKT	SRVETPQ--	QAAQFEKKLFRTWAQCFLLGVPRIIYGF
Canaur	NGA----	SKNDILKHYELKT	SMVVDQPH--KAVNFERKLFKTIWQCFLLGIPRIIYGF
Canten	-----DSNLPHYIELKT	NNLITNEH--	QMKSFEEKLYKTWAQCFLMGIKNIGVGF
Wiccif	-----SNPLPHYVELKT	SKVISEPK--	HSIIFEKKLFRTWAQCFLLGISKVIYGF
Cybjad	-----SNPLPHYVELKT	SSQISEPG--	QSVTFEKKLFKTIWQCFLLGITRIVYGF
Ogapol	-----ADPLAHYVELKT	SRVLDSPQ--	AVFSFENKLLKFWAQCFLVGIPKIIYGF
Kompha	-----DPLSRHYIELKT	TRTINQYK--	DMIAFEKKLFRTWAQCFLLGIPKIIYGF
Lypsta	DNVDNDPKLFDNPLDHYELKT	NRVIQSDR--	DASTFENKLFKVWAQSFLLGVPKAIIGF
Yarlip	G-----TSRYGELKT	SREVHNAK--	DGEILERKMNRAWAQSFLLGVKHIIYGY
SaccerDxo1	-----VSETNTELKC	FAPLSMHN----	SNHRKLLKTWVQTGLLPNSDIMIGI
NaucasDxo1	-----AEKKFTELKC	FSPLKMSN----	FSHRKLLKAWVQTGVLPDSILIGI
VanpolDxo1	-----VTNMFTELKC	FAPLKCMF----	SAK--EVLKTWVQTGLIPESDIVIGI
TordelDxo1	-----IFNRYTELKC	FTKLNVD----	TAHRKLLKTWVQIGLIPDSDLIIGT
LackluDxo1	-----KTDNYVELKC	SVNFQLKN----	SNHRKLLRMWIQTGLVPRTDLLVGF
LacwalDxo1	-----STRSYTEIKC	SSGLKVKS----	TYHRKLLRMWVQTSLPVSTNLLVGI
KlulacDxo1	-----LTDITYTEIKS	SVHFKLGN----	TYHRKLLRMWIQTNLLPKSDLLIGE
CanglaDxo1	-----ITSHYTELKC	YAKYNFGN----	PNHRKLLKSWIQTGVIPPTDIVIGV
Hanosmdxo1	-----TEKVFTELKC	TVPLNPYS----	SFHAMKLLKMWLQTCFLPNTLVLGI

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VI

CanalbDxo1 RST--DLKIASIKKYTQRELAGEINSFPVILS---DKCSINTKSIFQWYKLIMNWIIS--
CandubDxo1 RST--DLKIASIKKYTQRELASVINSFPVFLT---DKCSINTKSIFQWYNLVINWIVS--
CanmetDxo1 RSQ--NFRLVSLKKYTEYELVGLLDTLPIFLT---HSCSIKTKHIFQWYNLVICWLSQ--
CanortDxo1 RST--DFKLVSIIKKYTEFELTGMLDKLPFLT---HPYSIKPKHIFQWYNIVINWLCQ--
CanparDxo1 RTT--DFRLSSIIKKYTQYELVGLLDKLPFLS---NSCFIKTKHIFQWYNLVIGWLCQ--
SpapasDxo1 RTL--DFKLASIKTFKIGEVANIVNNDPIFLK---HGCAINTKGIFRWYQLVIQWLVFQ--
LodeloDxo1 RSA--DCKLASMKTYSERDLVNTLRASPIPGF---NGYSFNTKHIFHWYRHLVHLWSTM--
SchstiDxo1 RSP--ELKVSSIKRYETNELNGIINKEPVYFT---ENSTLNCSKMVKWYKLVISWITEHN--
VanpolRail RDN--NFILKSVIEFSTDEVPLLLKSNPQ-----LGNSCVDAIKWYGVFTEWLLNQ--
TordelRail RDD--NCILKTVIEFAADEVPILKSNNPQ-----MSTACLDIAIKWYGLTVEWLLNT--
SaccerRail KDD--HYVLKTVIEFSTEEVPVLLKNNNPQ-----VGSACLEAIKWYGLLTEWLLKM--
CanglaRail RDD--QYMLKTVIEEFSTEEIPVLIKANNPT-----LGQSCLDIAIKWYGLFTDWLLKI--
NaucasRail RDE--NYVLKTVIEEYSTDEIPILLKNNNTK-----MNSMCLDAIKWYGLFTEWLLKI--
LackluRail RDD--NFILKSVIEFSTQEIPIILKNNNPQ-----MTNACVDAIKWYGAFTEWLLKT--
LacwalRail RDE--HFILRSVIEEYGSHEIPLLLKNNNPQ-----LTNACMDAVRWYGAFTWELLSS--
KlulacRail RDD--NFMLKTVIEEFTTSEVPLILKNNNPQ-----MQTVCVDAIKWYGAFTEWLLTS--
HanosmRail RDD--DFNLVAVIEEFLTNEIPVNLKNNMSL-----VSNHFGDSIKWYGAVVEWLLKN--
CanalbRail RDN--NLILKNVELFNTEEIPILIKNNPLTNAATEK--KINCTNALKWYGAVVDWLNTT--
CandubRail RDD--NLNLRNVELYNTTEEIPVLIKNNPLTNTATEK--KINCTNALKWYGAVVDWLNTT--
SpapasRail RDD--DLCLRNVEVFKTDEVPLLIKNNPLT--AESKN--KVNCVGALKWYGAVLEWLNTE--
CanparRail RDD--QFILRNVEIYQTEEIPLLIKDNPLNNLKQNQASKINCTSAMKWYGAVVEWLNDV--
CanortRail RDD--QFILRNVEIYQTEEIPMLIKDNPLNNLKQNQANKINCTSALKWYGAVVEWLNDV--
CanmetRail RDD--QFILRNVEIYQTEEIPILIKENPLNNLKQNQATKVNCTSALKWYGAVVEWLNES--
LodeloRail RDD--SLILRNVEFYNTTEEIPVMIKNNPLNSTPQGQONKINCTSALKWYGAVVEWLNDS--
SchstiRail RDD--SFFLRDVELYKTEEIPLLIKNNALTENKSGG--KINCTTALKWYGAVIEWLLQE--
Canlus RDD--QHILTDVEVYNTTEEVPVLVKE-----KRIVCVDALKWYGAVLEWLRSN--
Metbis RDD--NYVLRDVEVYRTEEVPMLIKDSAVA---GRSGAPLLCTNALRWYGAVLDWLVT--
Canaur RDQ--KHLLKNVEIYNTTEEIPLLLKNNSEYP---RGGVQKFHCVDIAIKWYGAVLEWITQN--
Canten RDE--SLHLRNVEIYEADEIPAMLDK-----KINCVSSLKFFGALMEWLN--E--
Wiccif RDD--NLILRTVEQYKVDEIPVLIKNNPVN----TNPKRINCIDALKWYGAVVEWIVEN--
Cybjad RDQ--NLTLRAVEEYKTEEIPVLLKSNPVN----TNPRKINCVDALKWYGALVECIKAE--
Ogapol RDD--NLILRTVEEYKTEQIPVMIKNNPLP---NRHPTKNKFMQSLKFFNGLINWINDT--
Kompha RDD--NCILRTVEEFSTNDIPLMVKNNPLN---EQPKKENCYMSSINFYGAFTWELLNES--
Lypsta RTE--QGYLQTFEEFETQKIPGIVKSKYSNP----YTTWDGVDALAFLAACLQWLKTT--
Yarlip RTG--DHKLAADVYFKTEDLP-----MYAGA----SSTWSGTDEINFLNAALTCLKD--
SaccerDxo1 RDSH--SGQLLDIQWYSRDLLCKKFNPGLP--TNKKELNYNAQIAVEWCHYICIEAICKL--
NaucasDxo1 RDSS--FGELEDVEWYSRDRLRSKINNRLP--ESKIDWNFNAQVATQWSQHCIRSICKL--
VanpolDxo1 RDTQ--SGLLEDLVWYNRKDLCRTFNNPSLP--PAPSHFNFNANIAVEWLKFTMESIVSL--
TordelDxo1 RDTQ--VGQLEDLTWYSRGSLYKKFNNPSIA--RNNKYLNFNANIAVEWCFHCIESICDL--
LackluDxo1 RDPY--YNQLDALKPYTRDEIYKKFSTRNLN--ENRKYYNFNSTVAVQWSSHVIAKITEL--
LacwalDxo1 RDPY--YHQLTSFECYTRSOLYRKFNQRLT--VMRKNNYNATISVQWFRHVIQQLCQM--
KlulacDxo1 RNSY--SNELEQLKAYKIQDIYHKINNSSIIG--KPGKFYKFNPNVANDWFQHFQVLKQN--
CanglaDxo1 RDTE--SGCLQDVRCYNRNLLYNKLISKSLP--RCDSELNYDPAISVVWYRSLINTLT--
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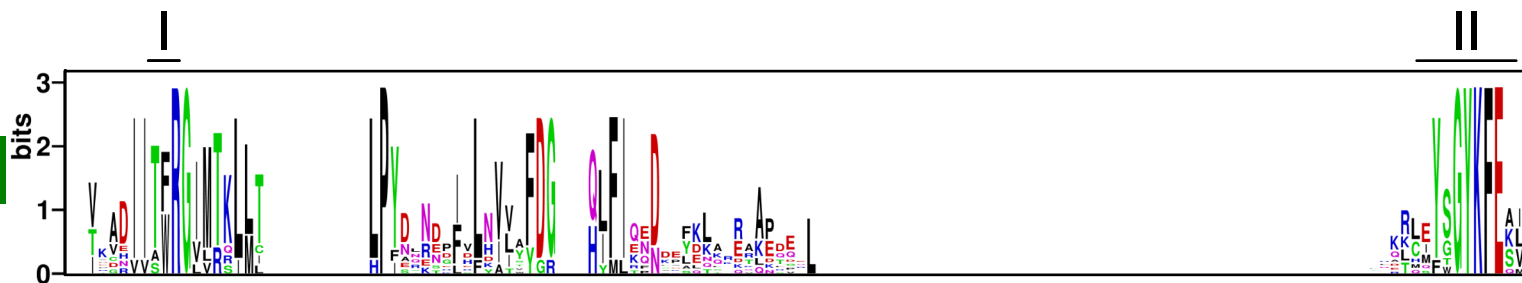
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CanalbDxo1	---KEITDHNTPTQIFRLSFKRDQELMNSYLKLEKILQEDDNDTIFNDLVPEWFQSFIMN-
CandubDxo1	---KEITDPNTPQIFRLSFKRAQELINSYLIMEKIQ---DDTIFNDLIPKWFQSFINT
CanmetDxo1	---RQFDD-DKPHVFKLRFQGEDELMDSHLSMDSVPQEE-EMQIFNKLVPEWFQNFY---
CanortDxo1	---KQFDE-DKPHVFKLYFKREPELMDSHLSMESVTGEE-ELRVFNKLVPEWFQNFY---
CanparDxo1	---KSFND-NQPRVFKLSFEREIELMDSHLSMKSVTGEE-ELRIFNRLVPEWFQNFY---
SpapasDxo1	-E-KNLKNQDEATVYRLSFDREDELMDSYLSLTKVDKEE-SAMIFNSTVPEWFQTFVISQ
LodeloDxo1	-DDDNDNNKDNPRVFKLCFQRTREFVDSSVLKPVSESE-SSTILNTFVPKWFQDFINTT
SchstiDxo1	QITTVDHIDASVPLAYRLEFTLKDKVMESCLEINPVEEQD-VQSLIKELIPWFQKFMNEN
VanpolRail	-IPRDDP--SIKKAYKLVYENNHLR--LTEITEEEGEFNELIN-GETVLTNEFKEWNRSL
TordelRail	-IPRDDV--ANIKPYKLVYENNHLR--LTEMDEIDEEYDAIVN-GEAVITNDFKQWRTSL
SaccerRail	-IPRDEDPHSQIRAFKLVFENNHLR--LSEIEESDEEYSGLID-GEHILSNGFKEWKRS
CanglaRail	-IPREQS--GNIRAYRLVYENNHLR--LSEIEEQDGEYSRYVL-EDGILTPEFKEWRESL
NaucasRail	-IPRDQP--KEIRPYKLVLENNHLK--LSEIESTDEEYDSLNVN-GESVLSKEFQEWRLSL
LackluRail	-IP--HENDGGLRAYKLIYDSNHLK--LNEVEESDPEYEGLVE-GESVLTNEFKEWRTSL
LacwalRail	-IPR-DESVDVMKSYRLIFENNHLK--LSEIEQHDPEYINLVE-GNGILSSEFKEWKRL
KlulacRail	-IPRPEDDIDTIKAYKLIFENNHLK--LTEIESDDEEYKQLVE-GEEILSNSFKQWRKDL
HanosmRail	-VEYKEG---QENYYRLFYQDNYLK--LEKIPDXDTEKVXEYK-NX--ISDEFKRWRLSL
CanalbRail	-VDKKDE----IKSYRLKYDPVRKS--FTLSETDSETNEKLRN--GQLLTPEFTEWRQSL
CandubRail	-IDKKDE----IKSYRLKYDPVRKS--FTLSETDSETNEKLRN--GQLLTSEFLEWRQSL
SpapasRail	-IDKNDT----SKSYRLSYDPGSKS--FSLLELMSDDNQRLRN--GEILTKEFKKWREGL
CanparRail	-IDKTDE----SVSYNLKYDPLRKS--LVLSEASKEENDRLRN--GGLLTEDFKQWRQRM
CanortRail	-IDKNDE----RFSYNLKYDPLKKS--LHLSETSKEVDENLRN--GKLLTEEFKTKWRQGL
CanmetRail	-IDKNDE----SVSYNLKYDPVKKT--LSLSETSTEVDKLRN--GGLLTEFKFKWREEL
LodeloRail	-IDKNDE----SKSYSLKYSPLHKT--FSLDEIKGEKNDQLRN--GGLLSEEFKTKWRVSO
SchstiRail	-IPRDDT----SKAYRVSFDPSTRT--FTLRELMGNENSRLRN--GEMLTSEFKQWRESI
Canlus	-VDPSDE----STTYTVTYDPSGRS--FSLAECIGDDGRVRK--EILTDEFCGWREQL
Metbis	-VDVADE----RSAYKLDYDPSGRS--FMLSECVGDENRRLRH--GGILTPEFTAWRETL
Canaur	-VDANDE----SKAYKIIYDSGSRT--FSLNECMGDENKRLRN--GEILTEEFKSWREQL
Canten	-LDKT-V----TKSYTMSFESGKVM--LMESPLSFES-----EFLTTEEFKRWRLQSL
Wiccif	-VPKD-E----SKAFRISYDNKNKS--FALNELPSDVSDNVLS---TMLTEDFKNWRLQK
Cybjad	-IPRD-E----SKSWRLTFDPQNK--LSLYELPPDISAEVLS---TLLPESFKQWRLQS
Ogapol	-IPRD-E----TKTYRLVFDPAVNPYLNLSENNATVTNQLLDPETGMISKAFRDWRNEL
Kompha	-VKDD-----QVWKLKYAKRNRQ--YLVLKEVTDENEKQQIVD--SAIPAWFKWRSSEL
Lypsta	-IPRAEE----NVVWKIRYLPRSDY--LTASKTDQ-----QSFLHPGFVKWRGEP
Yarlip	-LP-KED----NKLWRLVFDANKK--VDITELDG-----ESFLLKEFVDWR--K
SaccerDxo1	-----VEA-NISDYSSTKP--ESFEIGIDTNNAIVITKLKTTPRNVELFGM---
NaucasDxo1	-----VDE-NLDQKAISNP--QGFQIRIDSRNRIRIKCLSKVPKDILEYL----
VanpolDxo1	-----VSS-SIADSNHPC----SFKLKIDNHKTISIQLSRIPQTVQRQIPKEF
TordelDxo1	-----VMKNSLSSPDDPYPKYESFKVIVDKSHNIIIVKKLTKVPRHVQ--IPRAF
LackluDxo1	-----VDK-NLTDEPLQ-----SFKLTLTRDLQLSLTKLANTPAGLIPEKFLNS
LacwalDxo1	-----IKP-FIEKGSKEEV--NFRLTLRKNLTIKLRKMPETPAPTGTIFKVP
KlulacDxo1	-----LLL-LSQESTST-----TFKVQIDTNLTLSISPASQFVTALG-----
CanglaDxo1	-----IASLLDKFGRDEPQ--LFSIKVDNNCNIRIEHRQNP-----
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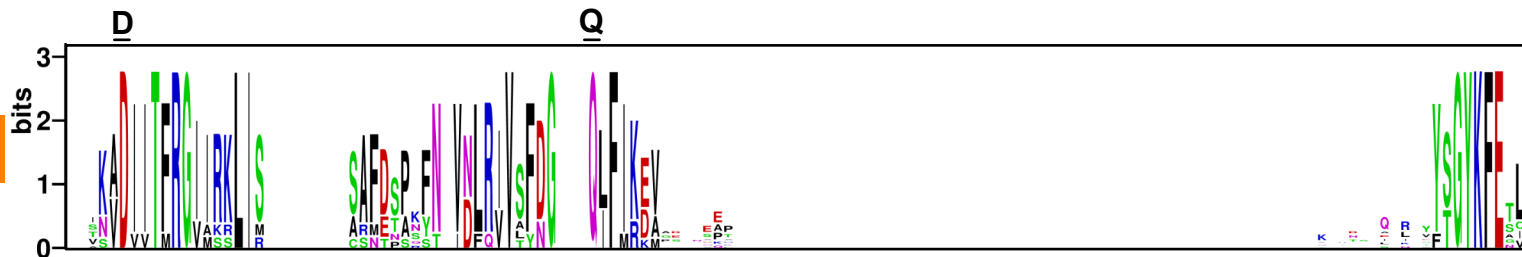
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CandubDxo1	SNNPLYVHD--
CanmetDxo1	-----
CanortDxo1	-----
CanparDxo1	-----
SpapasDxo1	K-----
LodeloDxo1	PS-----
SchstiDxo1	KNKKRNDYR--
VanpolRail	KVPK-----
TordelRail	PQ-----
SaccerRail	K-----
CanglaRail	RVPSEETPKAD
NaucasRail	-----
LackluRail	ASRQT-----
LacwalRail	SQKTEQA----
KlulacRail	RK-----
HanosmRail	QH-----
CanalbRail	KK-----
CandubRail	KK-----
SpapasRail	V-----
CanparRail	KK-----
CanortRail	KK-----
CanmetRail	KNQ-----
LodeloRail	RKNQLS-----
SchstiRail	QK-----
Canlus	RSK-----
Metbis	RGR-----
Canaur	RG-----
Canten	A-----
Wiccif	RNE-----
Cybjad	RSSS-----
Ogapol	RSR-----
Kompha	RNSEGNI----
Lypsta	PMK-----
Yarlip	SM-----
SaccerDxo1	-----
NaucasDxo1	-----
VanpolDxo1	V-----
TordelDxo1	R-----
LackluDxo1	RLAAK-----
LacwalDxo1	KKK-----
KlulacDxo1	-----
CanglaDxo1	-----
Hanosmdxo1	RKTNE-----

Supplemental Figure S2: Sequence logos visualizing different patterns of sequence conservation in Rai1 and Dxo1 paralogs and non-duplicated orthologs. The multiple sequence alignment of Supplemental Figure 1 was split into 5 alignments and each alignment was visualized as a sequence logo. The top panel depicts proteins from species with one gene from lines 26 to 35 of the alignment in Supplemental Figure S1. The second panel depicts duplicated Rai1 genes from clade 1 from lines 9 to 17. The third panel depicts duplicated Rai1 genes from clade 2 from lines 18 to 25. The fourth panel depicts duplicated Dxo1 genes from clade 1 from lines 36 to 44. The fifth panel depicts duplicated Dxo1 genes from clade 2 from lines 1 to 8 of the alignment. Motifs discussed in the text are indicated above the sequence logos.

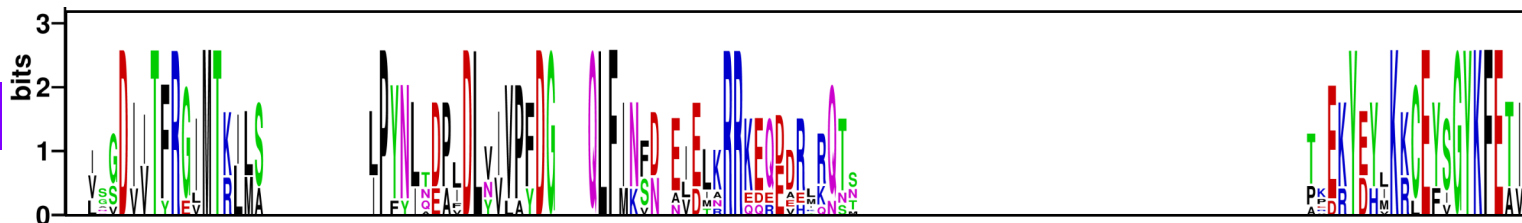
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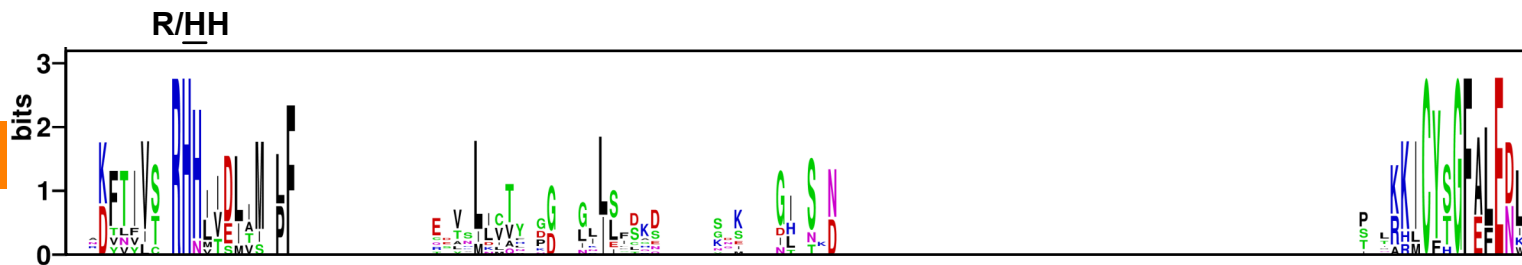
clade 1 Rai1



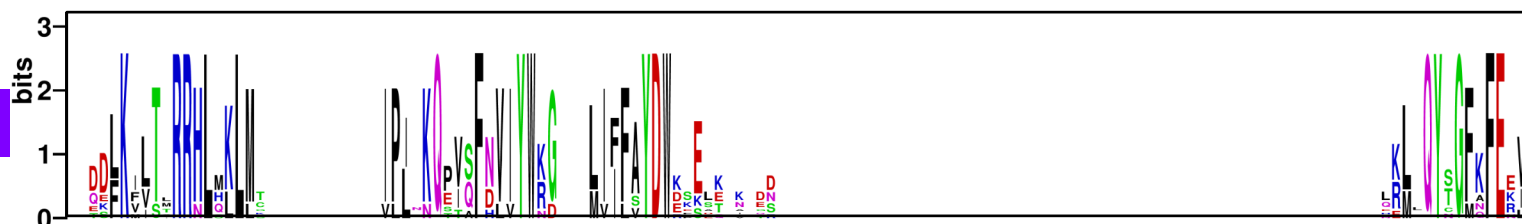
clade 2 Rai1



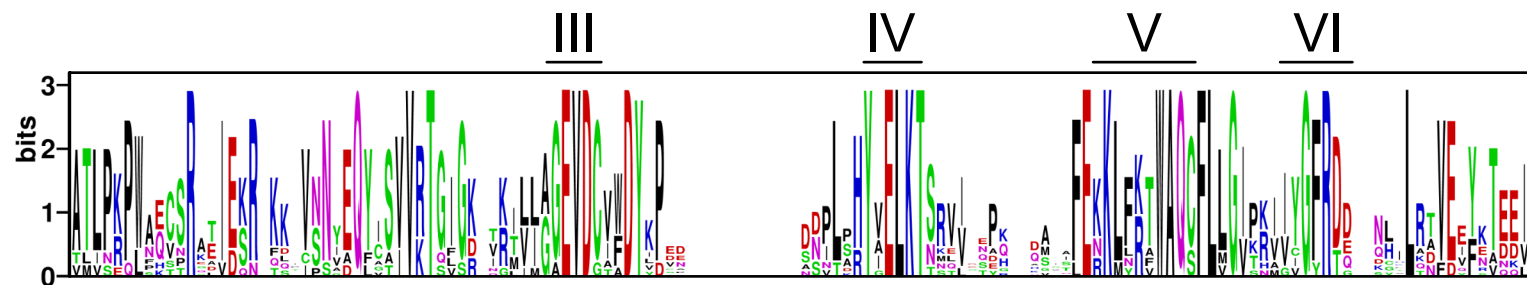
clade 1 Dxo1



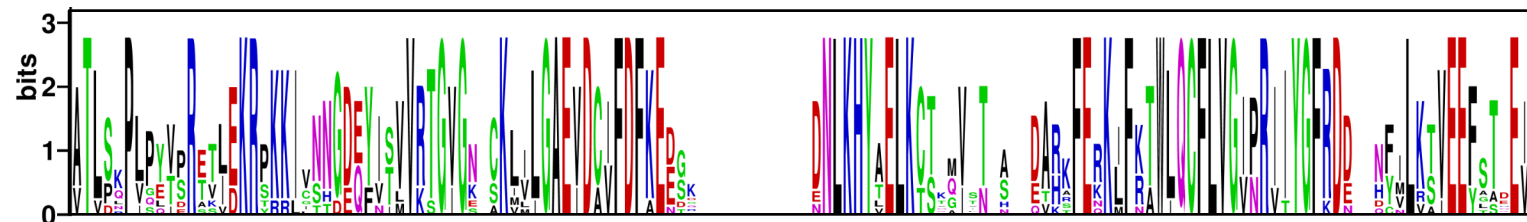
clade 2 Dxo1



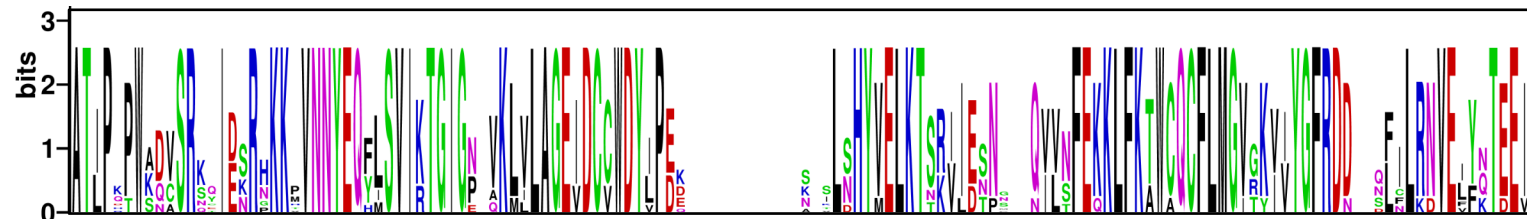
Non duplicated



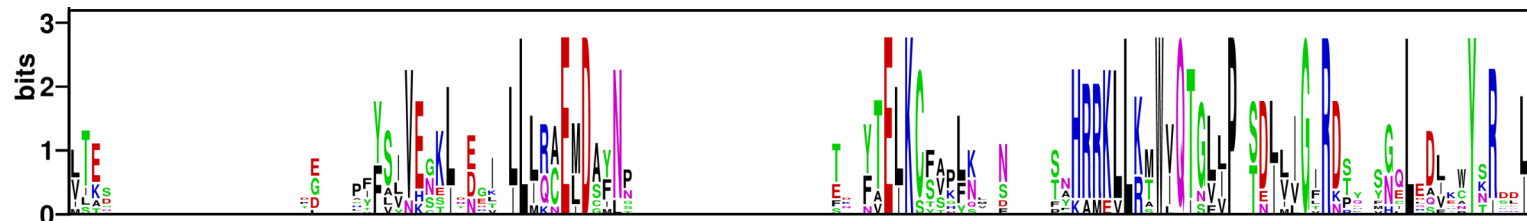
clade 1 Rai1



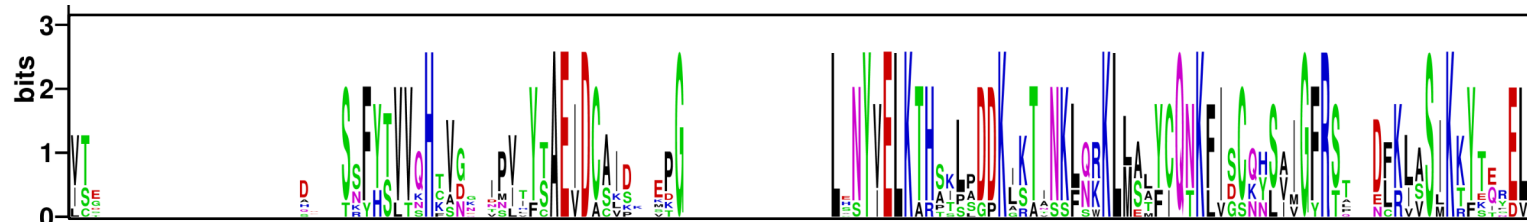
clade 2 Rai1



clade 1 Dxo1

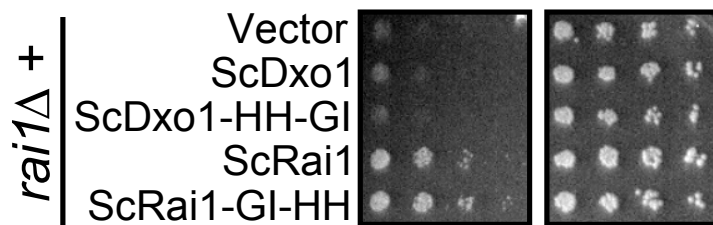


clade 2 Dxo1

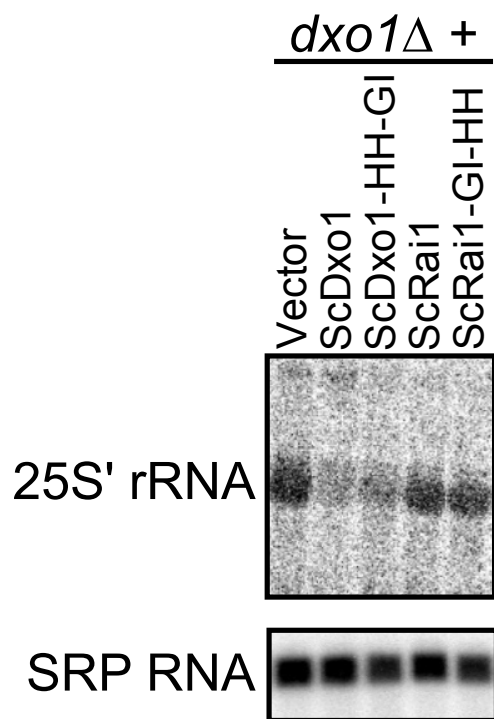


Supplemental Figure S3: Point mutants were generated to change the R/HH motif in Dxo1 to the Rai1-like sequence and to introduce the R/HH motif in Rai1. Functional analyses were performed as in Figure 3 and no effect of the point mutations was observed, indicating that these changes are not sufficient to convert Rai1 into Dxo1 or *vice versa*.

A



B



Supplemental Table 1

Plasmid name	description
pRS416	vector control
pAv1804	<i>S. cerevisiae DXO1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1814	<i>K. lactis RAI1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1815	<i>C. glabrata</i> nonduplicated <i>RAI1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1816	<i>C. albicans DXO1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1817	<i>C. auris</i> nonduplicated coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1818	<i>C. albicans RAI1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1819	<i>K. lactis DXO1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1820	<i>S. cerevisiae RAI1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1821	<i>W. ciferrii</i> nonduplicated <i>RAI1</i> coding region with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1968	<i>S. cerevisiae DXO1</i> coding region with H191G and H192I mutations with <i>S. cerevisiae DXO1</i> promoter and 3'UTR
pAv1969	<i>S. cerevisiae RAI1</i> coding region with G106H and I107H mutations with <i>S. cerevisiae DXO1</i> promoter and 3'UTR