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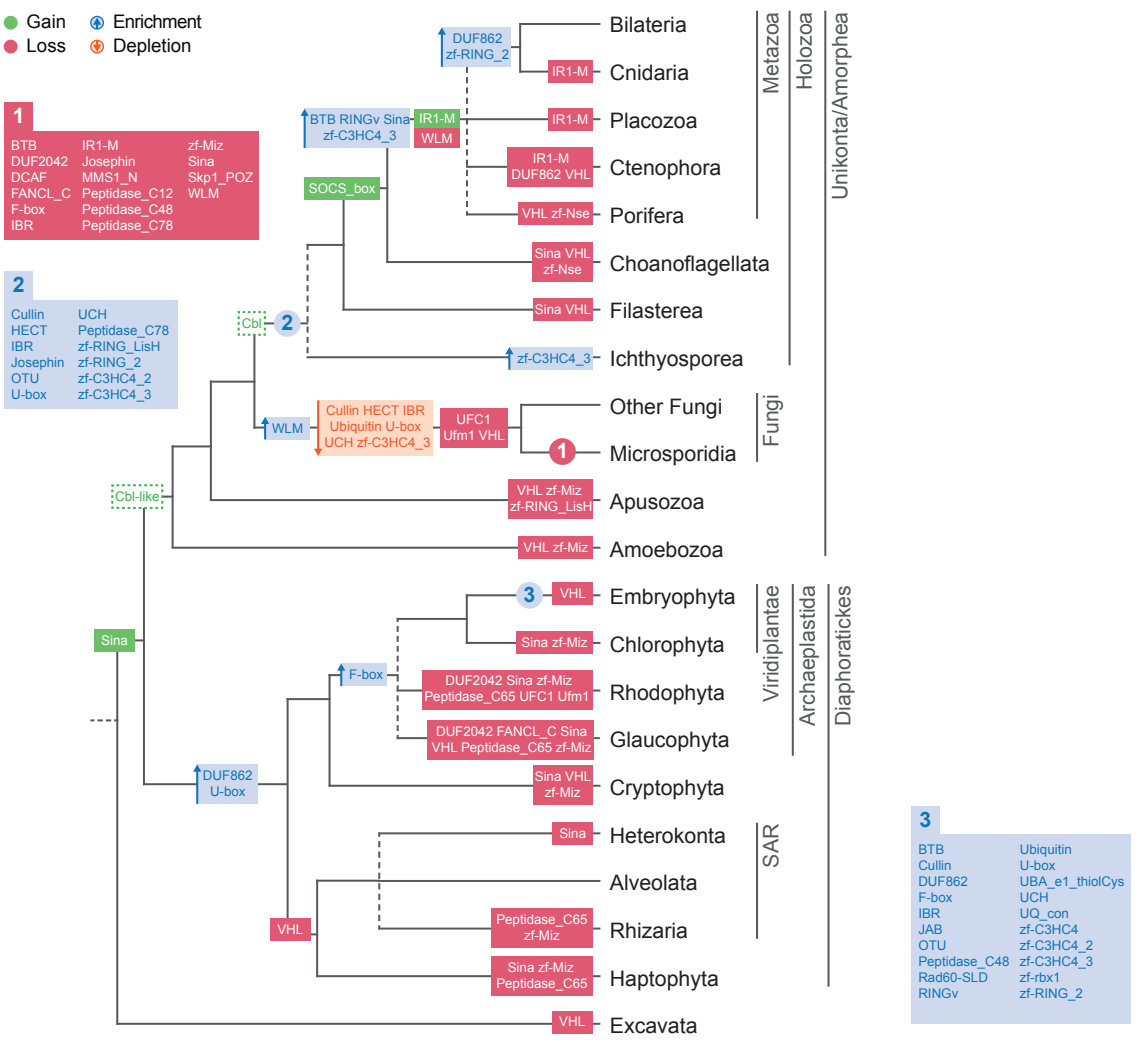

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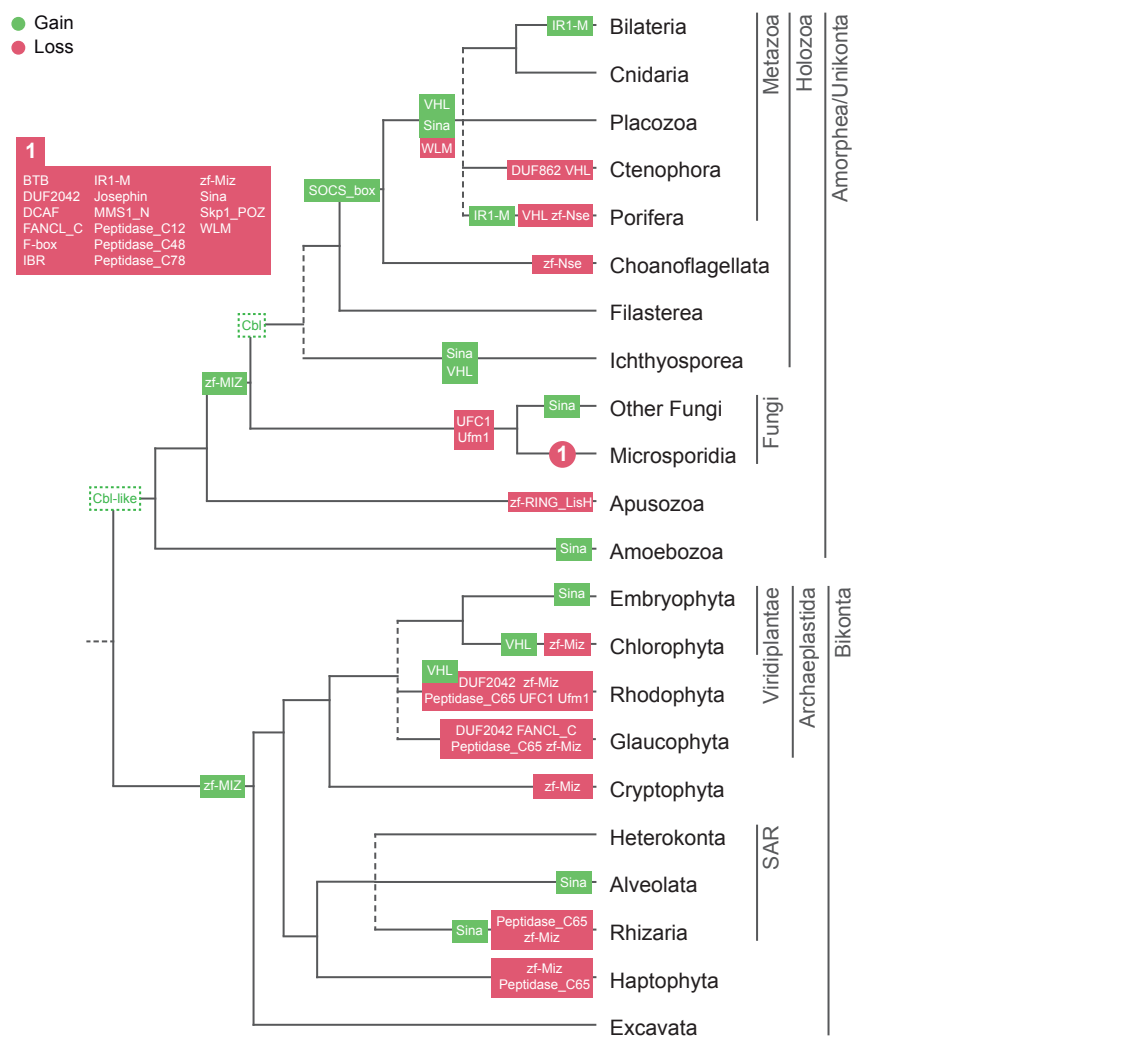

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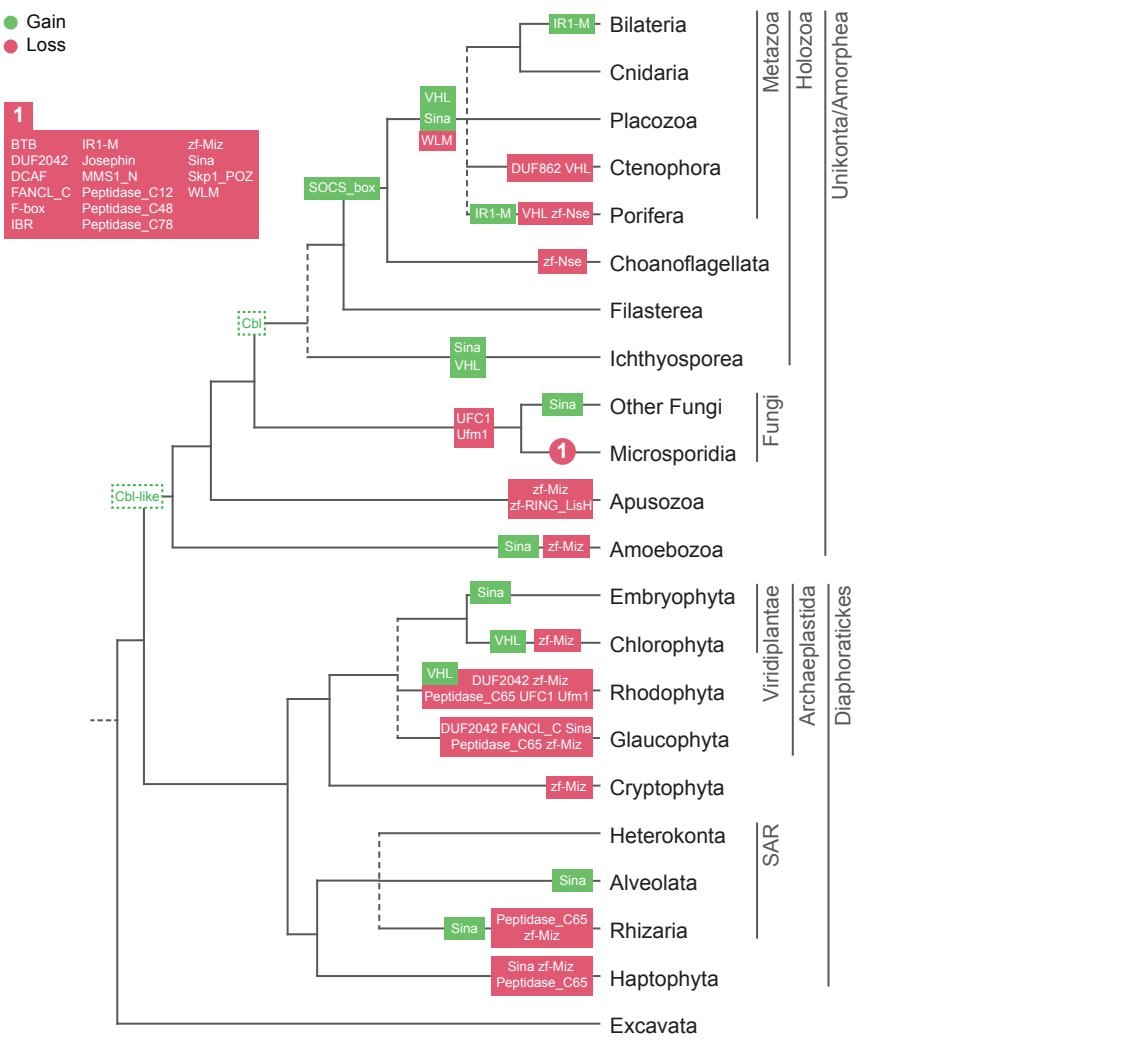

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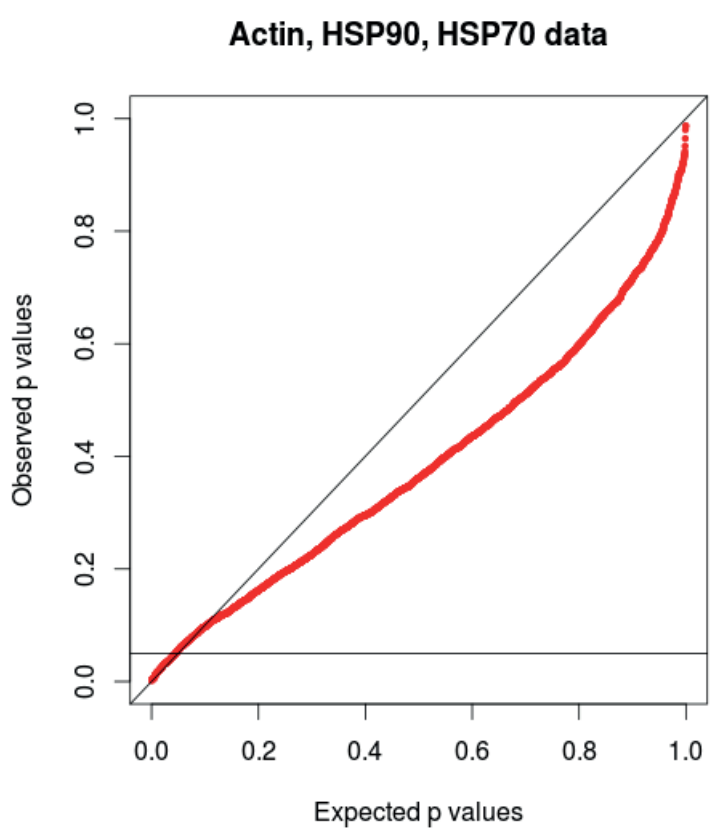

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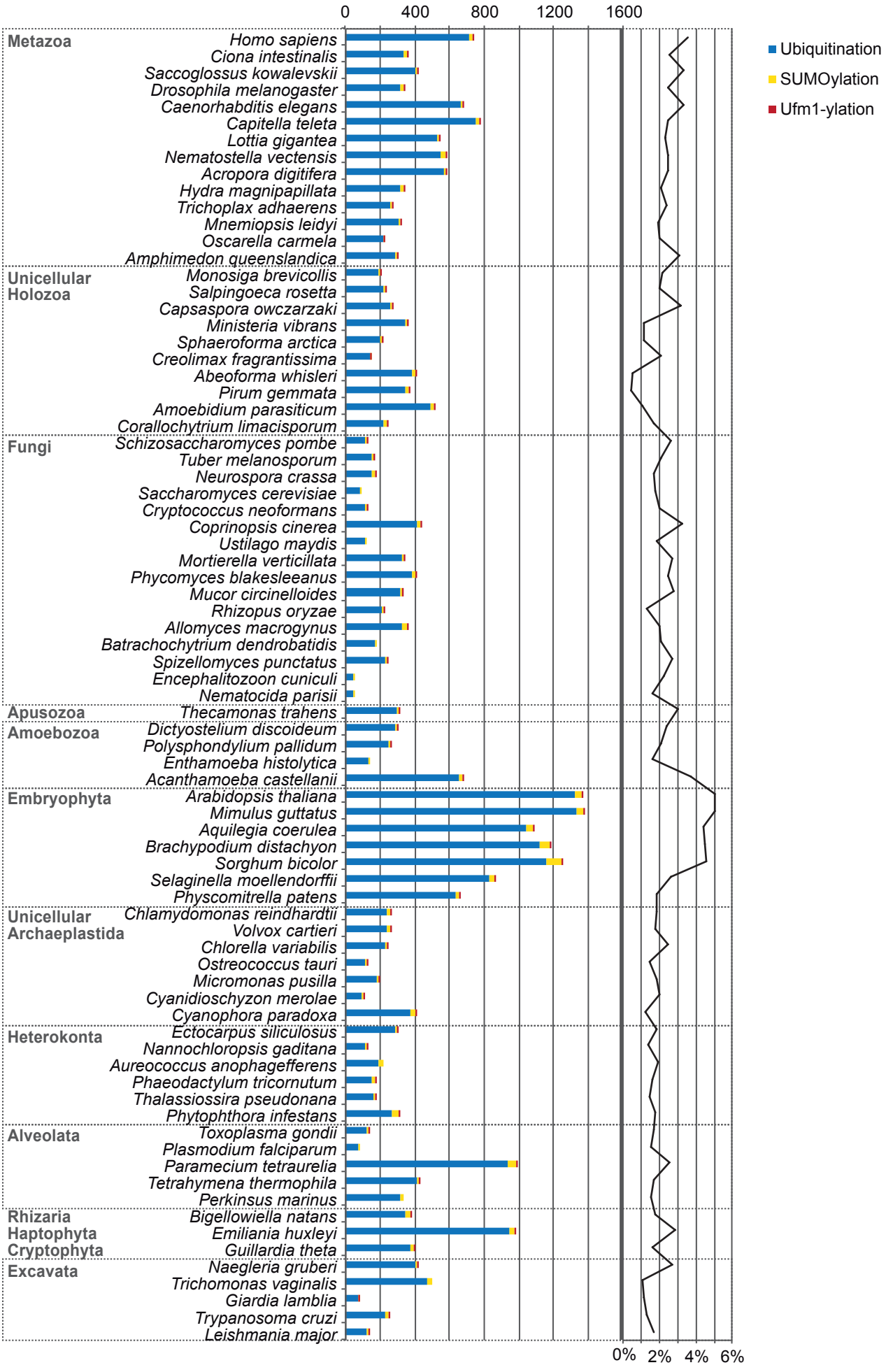
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Drosophila melanogaster
Caenorhabditis elegans
Capitella teleta
Lottia gigantea
Nematostella vectensis
Acropora digitifera
Hydra magnipapillata
Trichoplax adhaerens
Mnemiopsis leidyi
Oscarella carmela
Amphimedon queenslandica
Unicellular Holozoa
Monosiga brevicollis
Salpingoeca rosetta
Capsaspora owczarzaki
Ministeria vibrans
Sphaeroforma arctica
Creolimax fragrantissima
Abeoforma whisleri
Pirum gemmata
Amoebidium parasiticum
Corallochytrium limacisporum
Fungi
Schizosaccharomyces pombe
Tuber melanosporum
Neurospora crassa
Saccharomyces cerevisiae
Cryptococcus neoformans
Coprinopsis cinerea
Ustilago maydis
Mortierella verticillata
Phycomyces blakesleeanus
Mucor circinelloides
Rhizopus oryzae
Allomyces macrogynus
Batrachochytrium dendrobatidis
Spizellomyces punctatus
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Nematocida parisii
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Arabidopsis thaliana
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Physcomitrella patens
Unicellular Archaeplastida
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Volvox cartieri
Chlorella variabilis
Ostreococcus tauri
Micromonas pusilla
Cyanidioschyzon merolae
Cyanophora paradoxa
Heterokonta
Ectocarpus siliculosus
Nannochloropsis gaditana
Aureococcus anophagefferens
Phaeodactylum tricornutum
Thalassiosira pseudonana
Phytophthora infestans
Alveolata
Toxoplasma gondii
Plasmodium falciparum
Paramecium tetraurelia
Tetrahymena thermophila
Perkinsus marinus
Rhizaria
Haptophyta
Cryptophyta
Bigellowiella natans
Emiliania huxleyi
Guillardia theta
Excavata
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Giardia lamblia
Trypanosoma cruzi
Leishmania major
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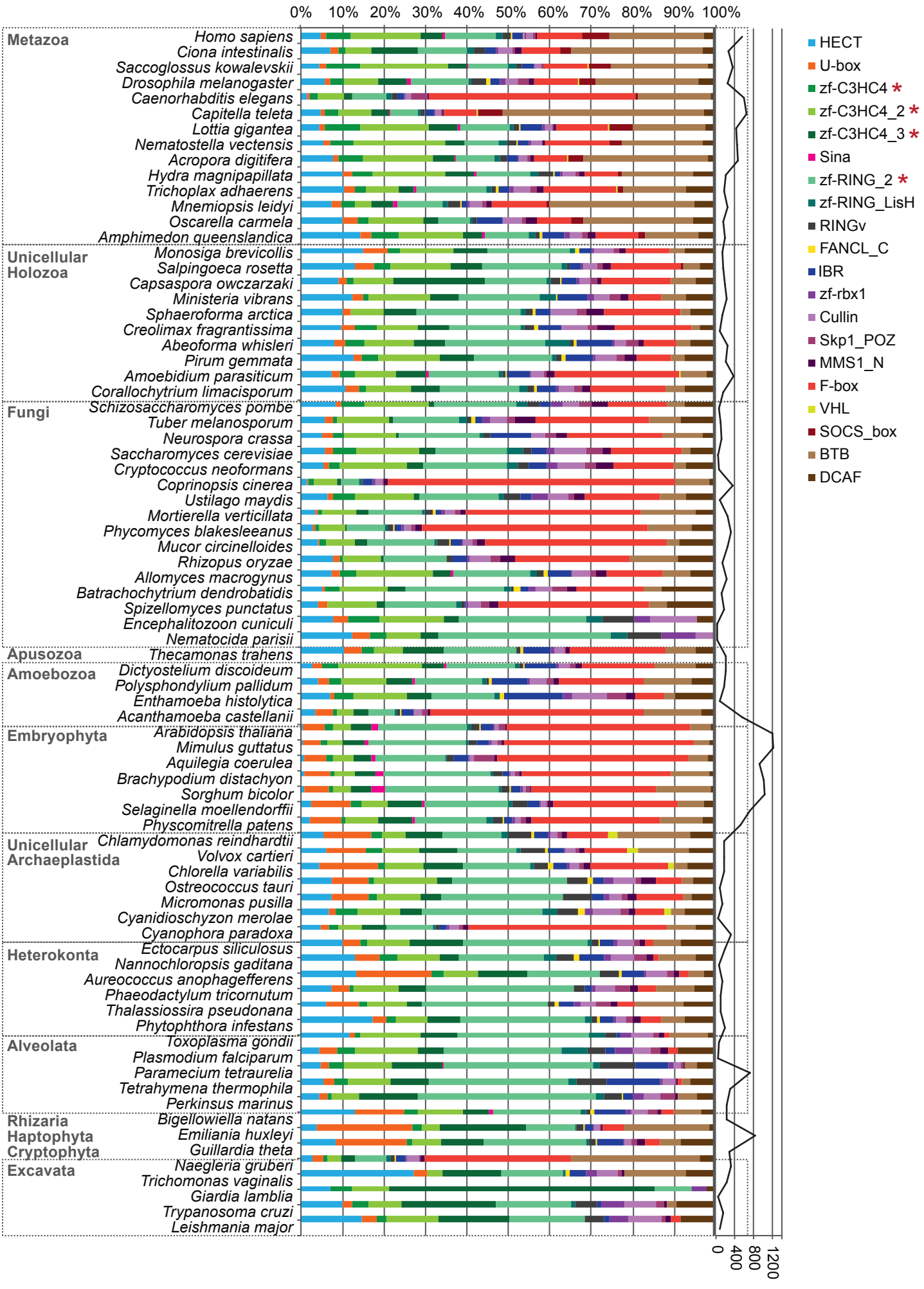
2%
4%
6%

Figure S3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Lottia gigantea
Nematostella vectensis
Acropora digitifera
Hydra magnipapillata
Trichoplax adhaerens
Mnemiopsis leidyi
Oscarella carmela
Amphimedon queenslandica
Unicellular Holozoa
Monosiga brevicollis
Salpingoeca rosetta
Capsaspora owczarzaki
Ministeria vibrans
Sphaeroforma arctica
Creolimax fragrantissima
Abeoforma whisleri
Pirum gemmata
Amoebidium parasiticum
Corallochytrium limacisporum
Fungi
Schizosaccharomyces pombe
Tuber melanosporum
Neurospora crassa
Saccharomyces cerevisiae
Cryptococcus neoformans
Coprinopsis cinerea
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Mortierella verticillata
Phycomyces blakesleeanus
Mucor circinelloides
Rhizopus oryzae
Allomyces macrogynus
Batrachochytrium dendrobatidis
Spizellomyces punctatus
Encephalitozoon cuniculi
Nematocida parisii
Apusozoa
Thecamonas trahens
Amoebozoa
Dictyostelium discoideum
Polysphondylium pallidum
Enthamoeba histolytica
Acanthamoeba castellanii
Embryophyta
Arabidopsis thaliana
Mimulus guttatus
Aquilegia coerulea
Brachypodium distachyon
Sorghum bicolor
Selaginella moellendorffii
Physcomitrella patens
Unicellular Archaeplastida
Chlamydomonas reindhardtii
Volvox cartieri
Chlorella variabilis
Ostreococcus tauri
Micromonas pusilla
Cyanidioschyzon merolae
Cyanophora paradoxa
Heterokonta
Ectocarpus siliculosus
Nannochloropsis gaditana
Aureococcus anophagefferens
Phaeodactylum tricornutum
Thalassiossira pseudonana
Phytophthora infestans
Alveolata
Toxoplasma gondii
Plasmodium falciparum
Paramecium tetraurelia
Tetrahymena thermophila
Perkinsus marinus
Rhizaria
Haptophyta
Cryptophyta
Bigellowiella natans
Emiliania huxleyi
Guillardia theta
Excavata
Naegleria gruberi
Trichomonas vaginalis
Giardia lamblia
Trypanosoma cruzi
Leishmania major
HECT
U-box
zf-C3HC4 *
zf-C3HC4_2 *
zf-C3HC4_3 *
Sina
zf-RING_2 *
zf-RING_LisH
RINGv
FANCL_C
IBR
zf-rbx1
Cullin
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MMS1_N
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BTB
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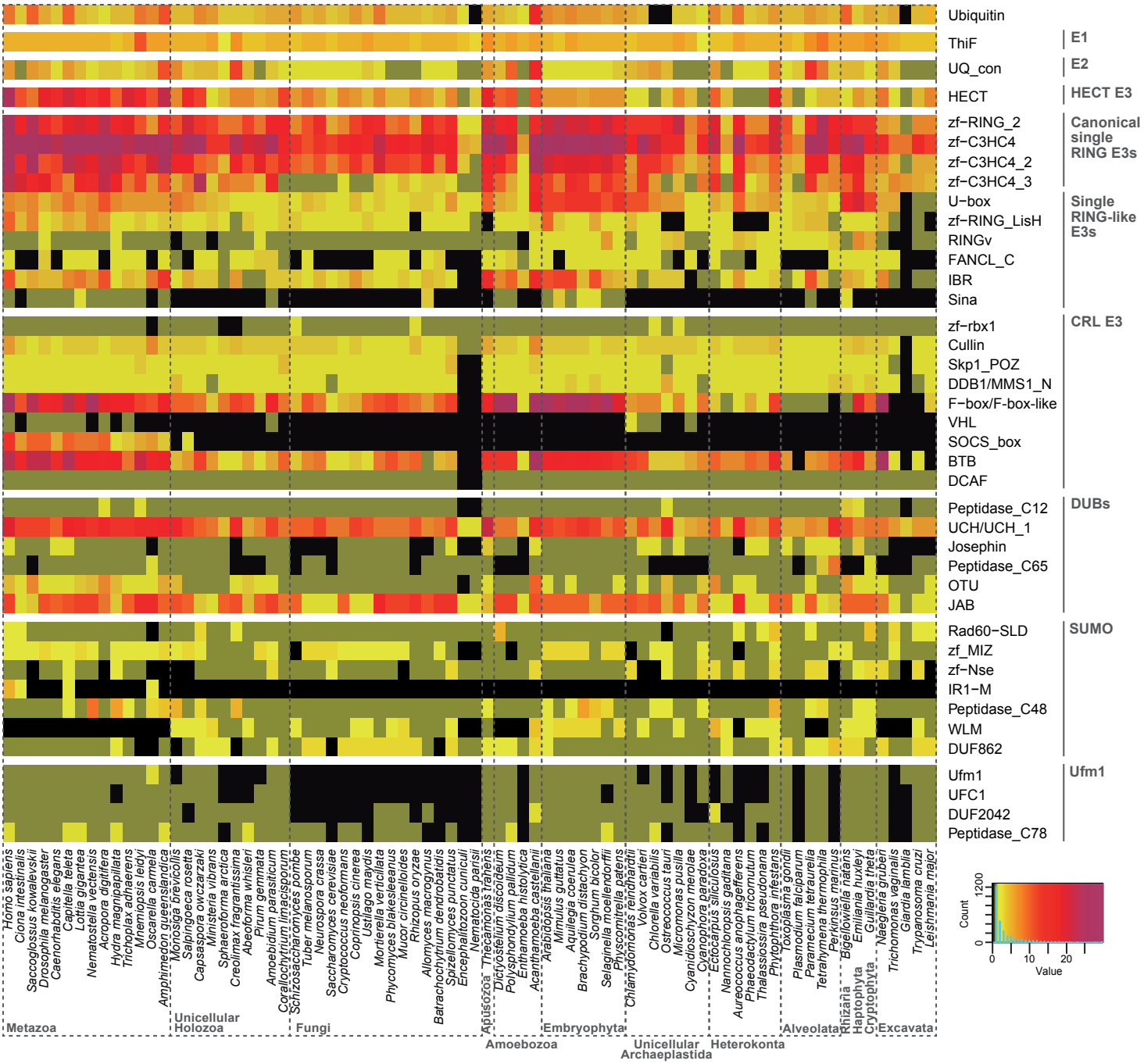
Figure S4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zf−C3HC4_3
U−box
zf−RING_LisH
RINGv
FANCL_C
IBR
Sina
zf−rbx1
Cullin
Skp1_POZ
DDB1/MMS1_N
F−box/F-box-like
VHL
SOCS_box
BTB
DCAF
Peptidase_C12
UCH/UCH_1
Josephin
Peptidase_C65
OTU
JAB
Rad60−SLD
zf_MIZ
zf−Nse
IR1−M
Peptidase_C48
WLM
DUF862
Ufm1
UFC1
DUF2042
Peptidase_C78
E1
E2
HECT E3
Canonical single RING E3s
Single RING-like E3s
CRL E3
DUBs
SUMO
Ufm1
Homo sapiens
Ciona intestinalis
Saccoglossus kowalevskii
Drosophila melanogaster
Caenorhabditis elegans
Capitella teleta
Lottia gigantea
Nematostella vectensis
Acropora digitifera
Hydra magnipapillata
Trichoplax adhaerens
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Oscarella carmela
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Monosiga brevicollis
Salpingoeca rosetta
Capsaspora owczarzaki
Ministeria vibrans
Sphaeroforma arctica
Creolimax fragrantissima
Abeoforma whisleri
Pirum gemmata
Amoebidium parasiticum
Coraliochytrium limacisporum
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Tuber melanosporum
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Saccharomyces cerevisiae
Cryptococcus neoformans
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Mortierella verticillata
Phycomyces blakesleeanus
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Rhizopus oryzae
Allomyces macrogynus
Batrachochytrium dendrobatidis
Spizellomyces punctatus
Encephalitozoon cuniculi
Nematocida parisii
Aphelida
Thecamonas trahens
Dictyostelium discoideum
Polysphondylium pallidum
Entamoeba histolytica
Acanthamoeba castellanii
Arabidopsis thaliana
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Plasmodium falciparum
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Rhizaria
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Haptophyta
Guillardia theta
Cryptophyta
Naegleria gruberi
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Giardia lamblia
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Leishmania major
Excavata
Alveolata
Heterokonta
Unicellular Archaeplastida
Embryophyta
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Metazoa
Count
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1200
0
10
20
Value

Figure S5A – ThiF

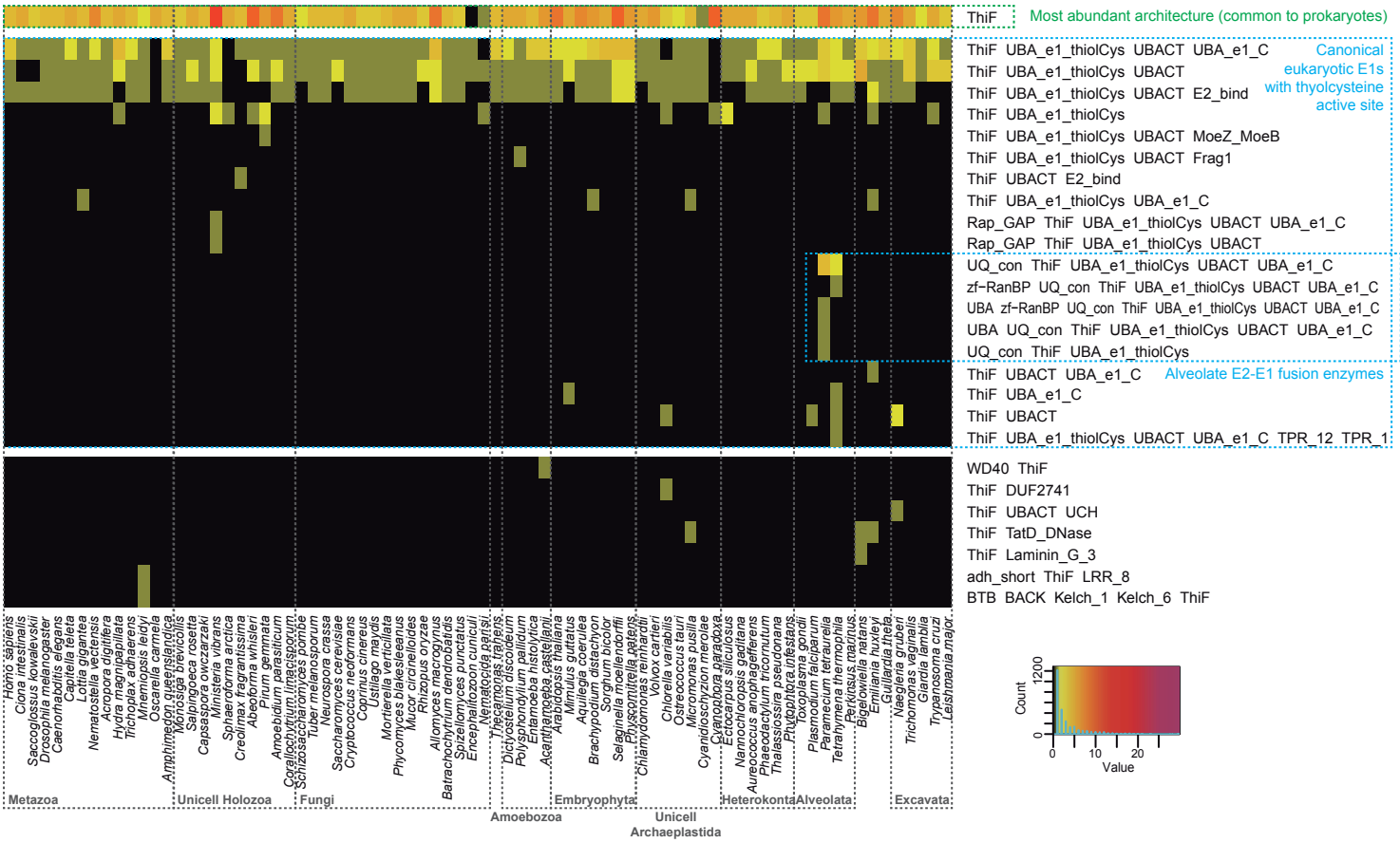


Figure S5B – UQ_con

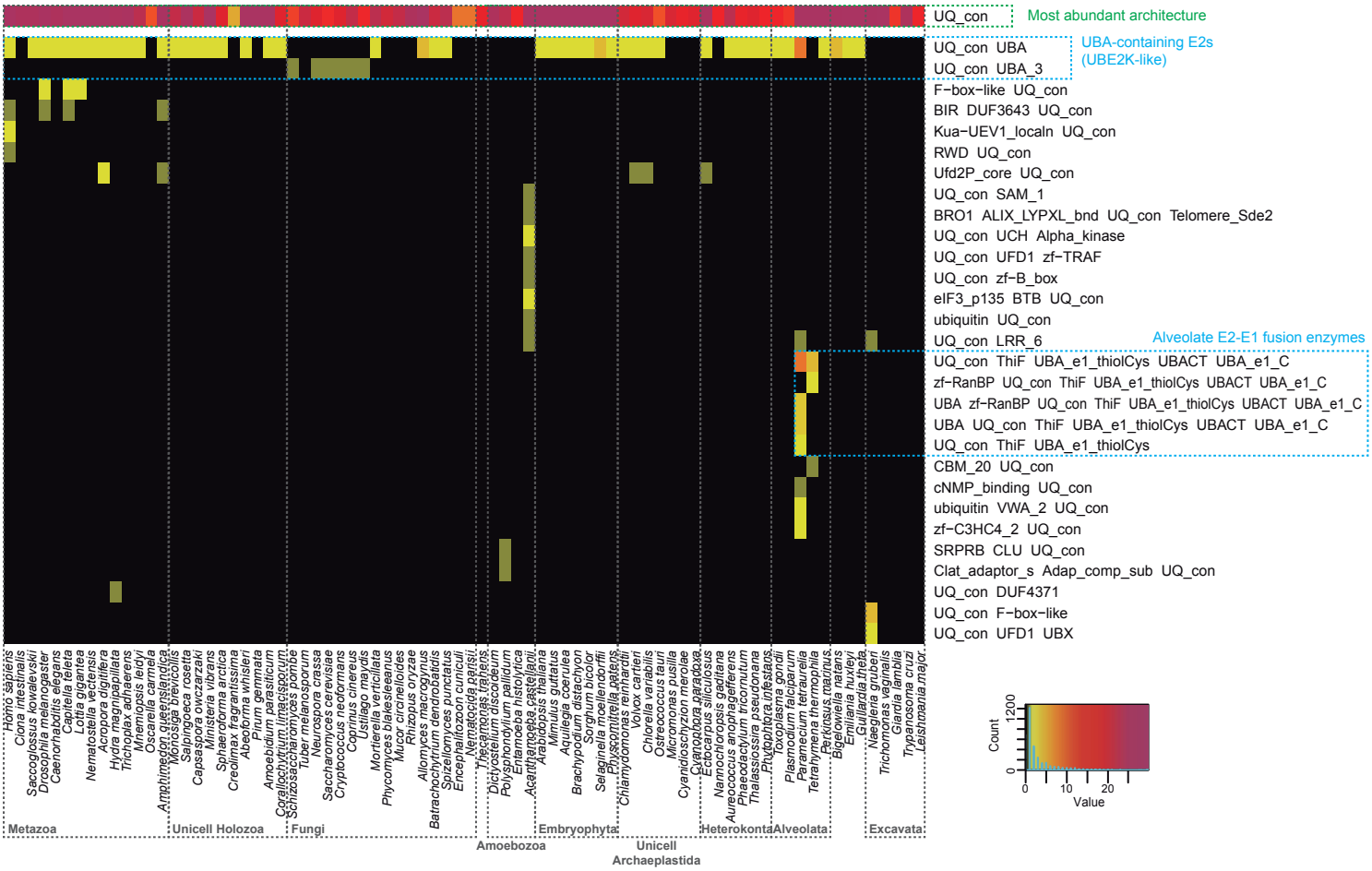


Figure S5C – HECT

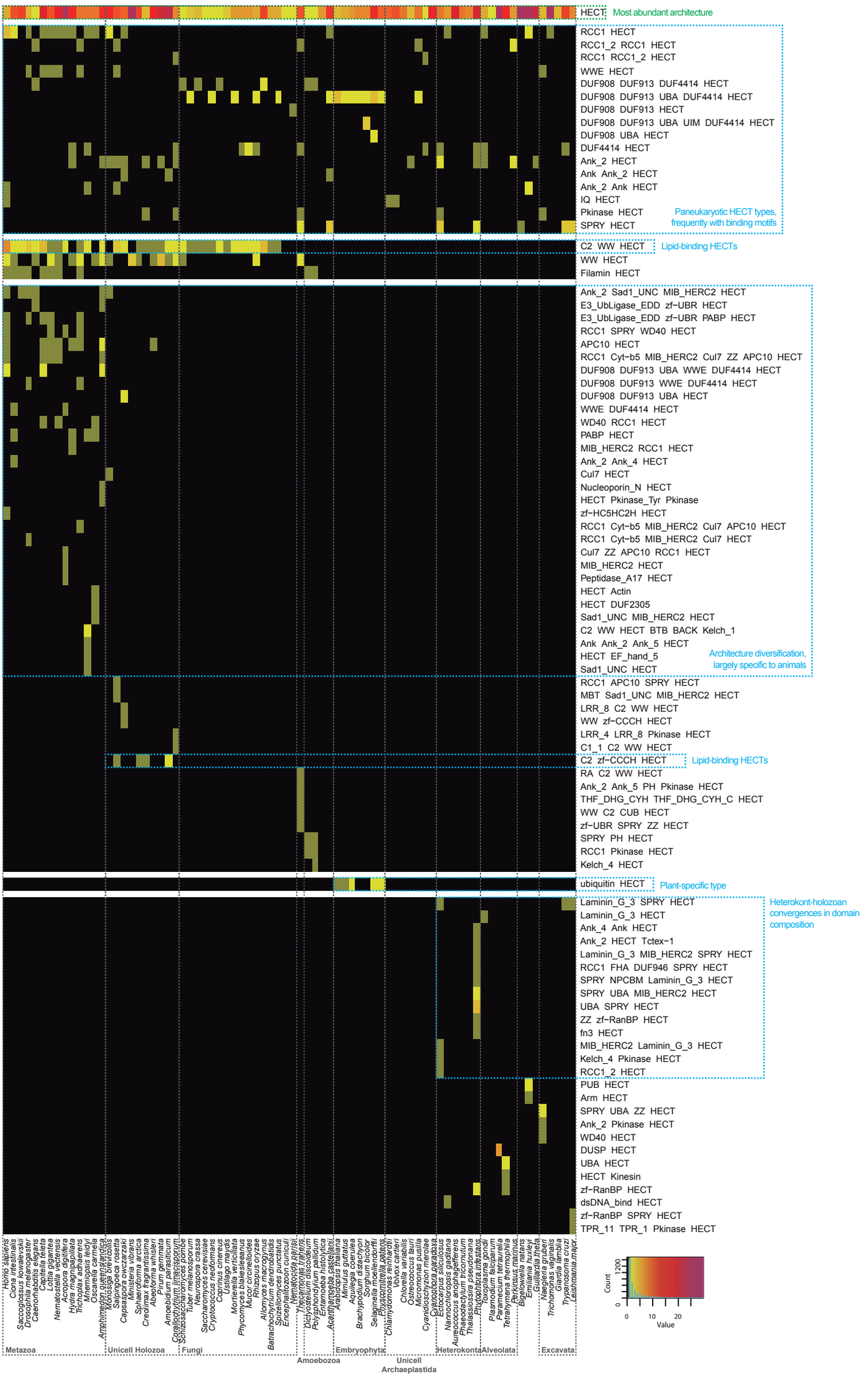


Figure S5D – zf-RING_2

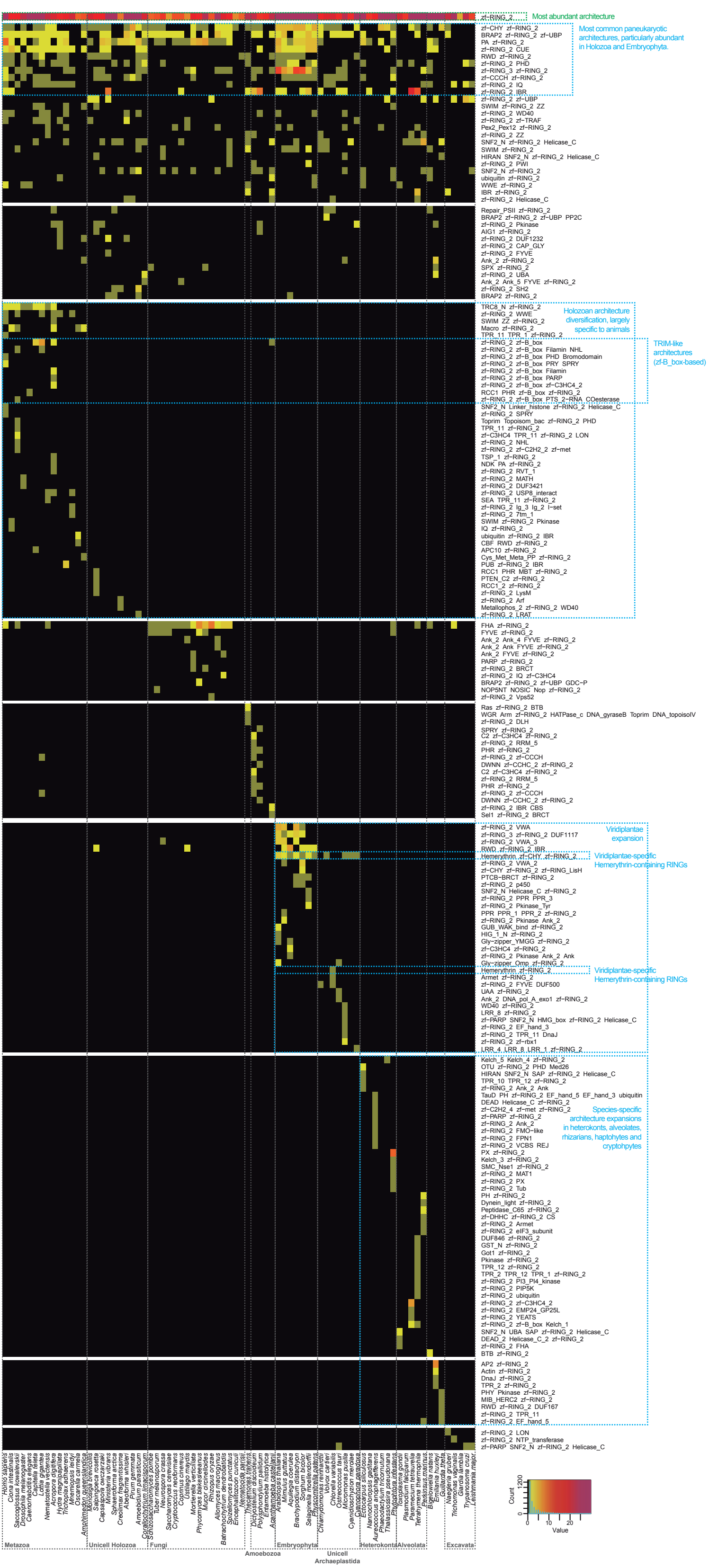


Figure S5E – zf-C3HC4

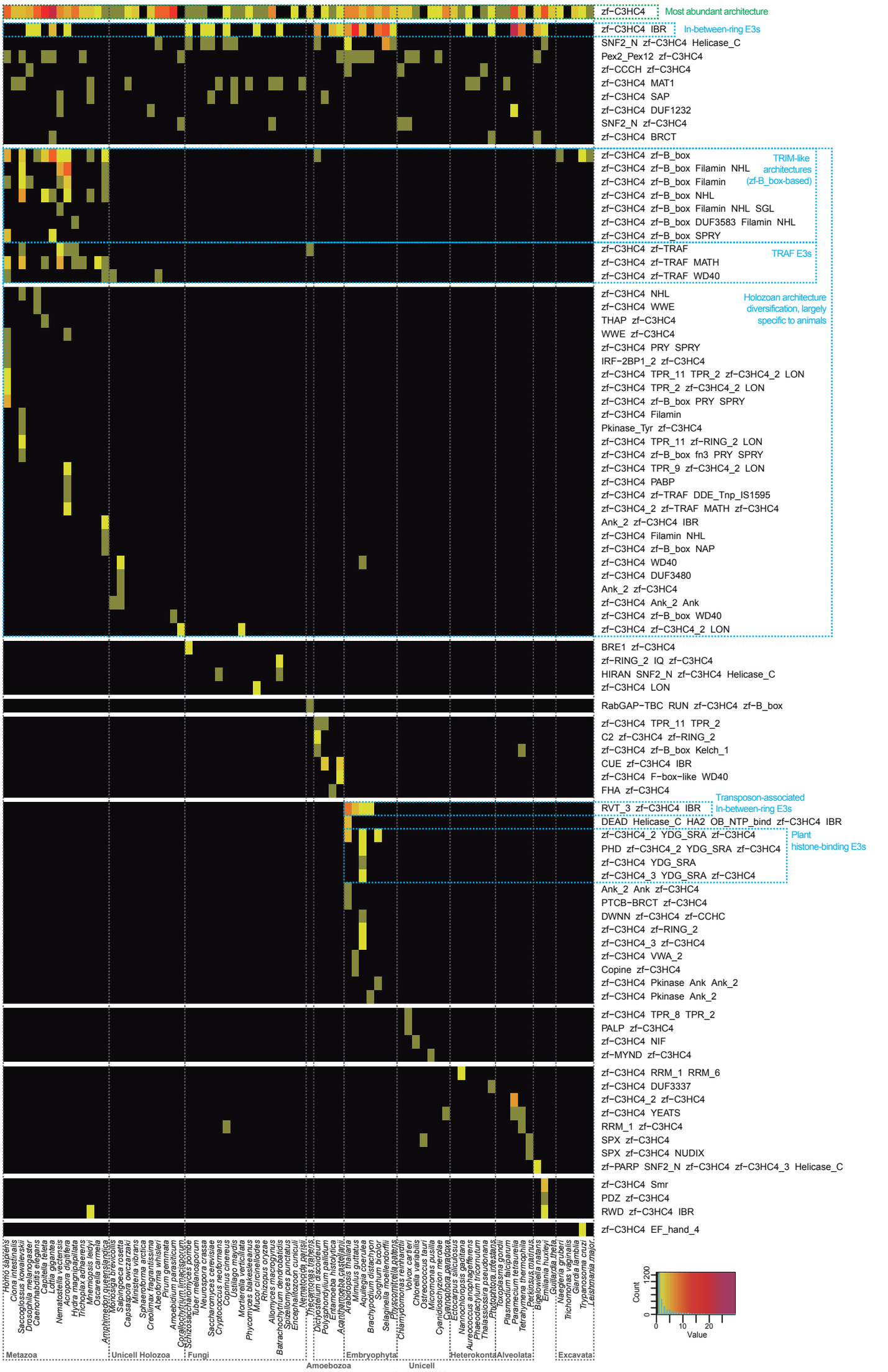


Figure S5F – zf-C3HC4_2

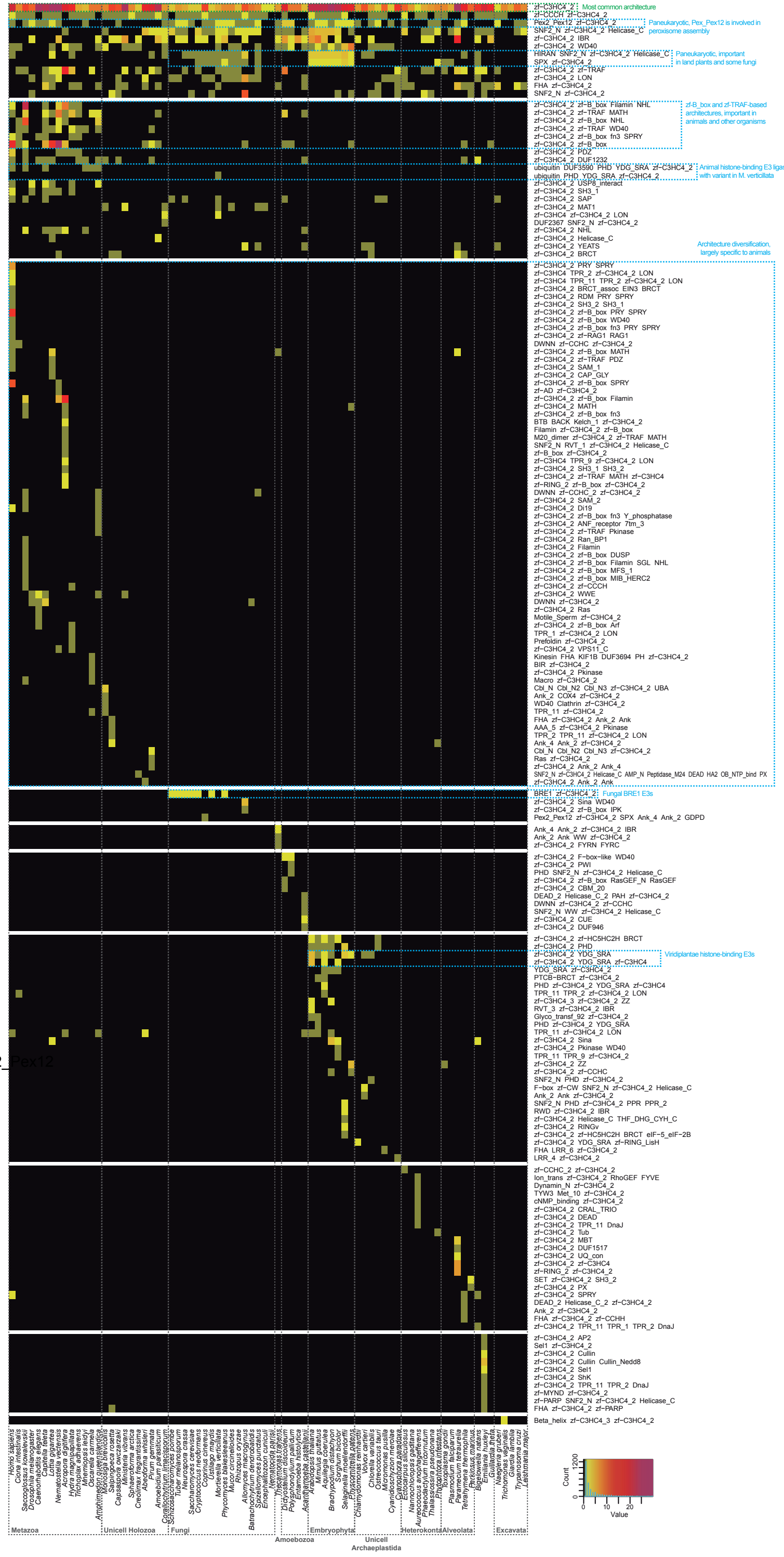


Figure S5G – zf-C3HC4_3

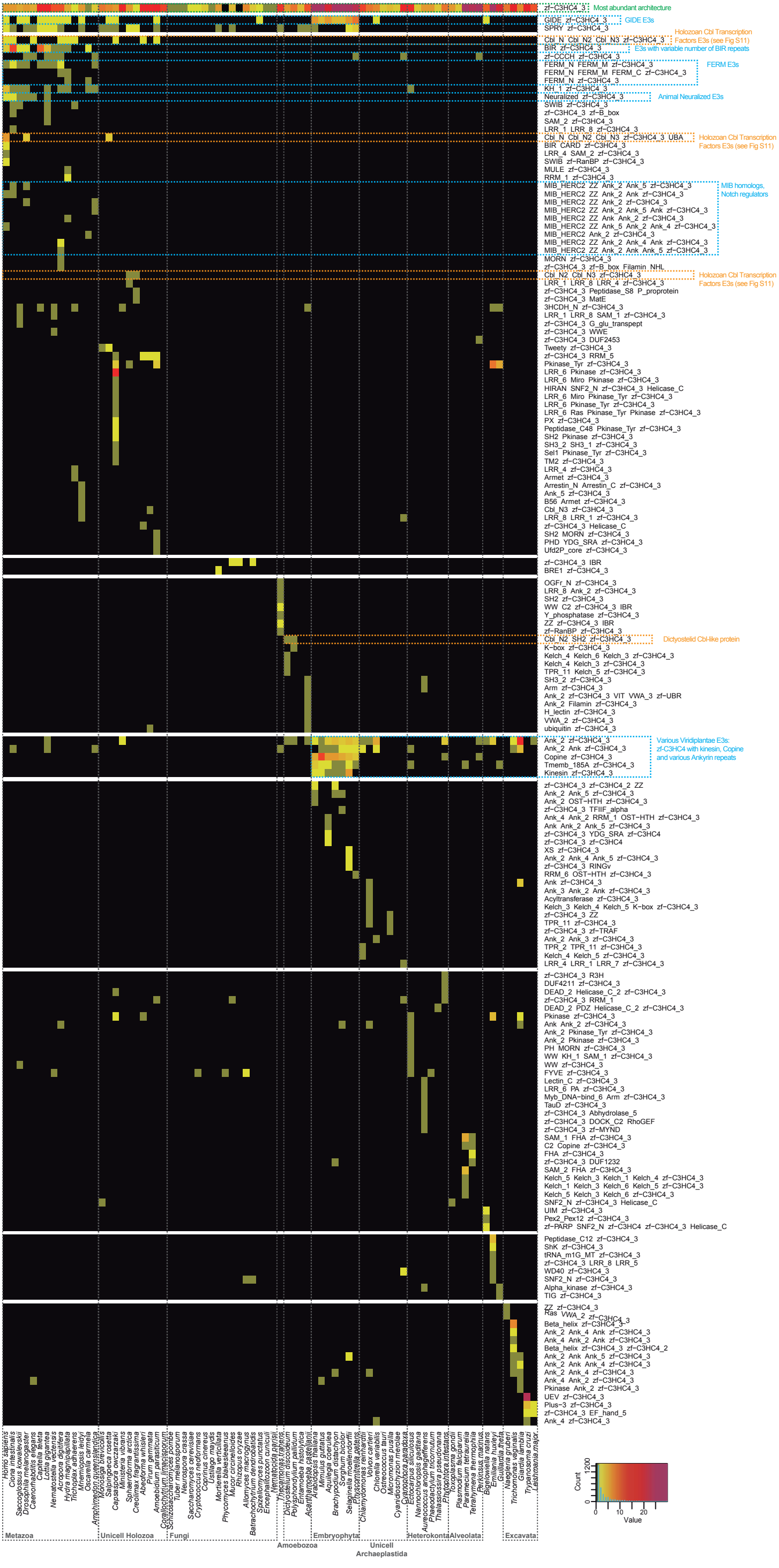


Figure S5H – Cbl_N

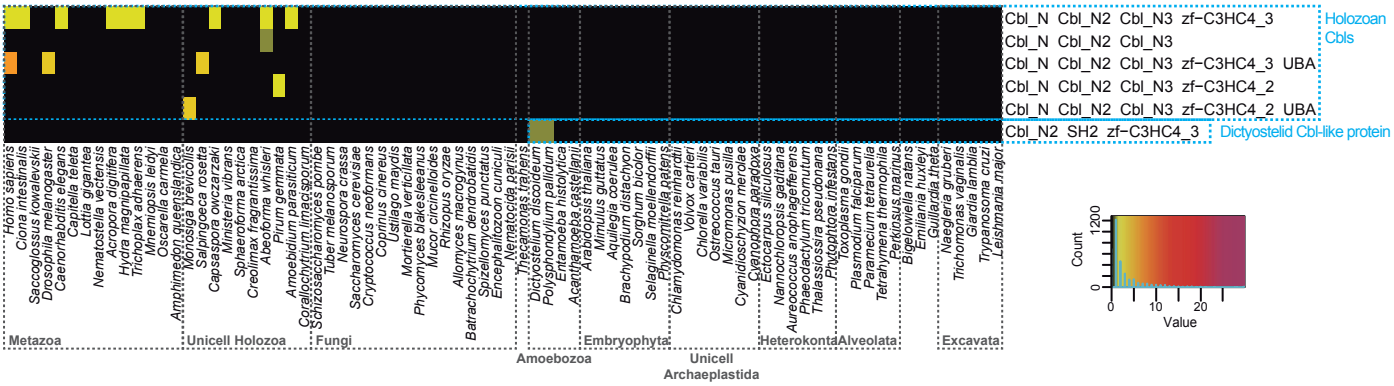


Figure S5l – U-box

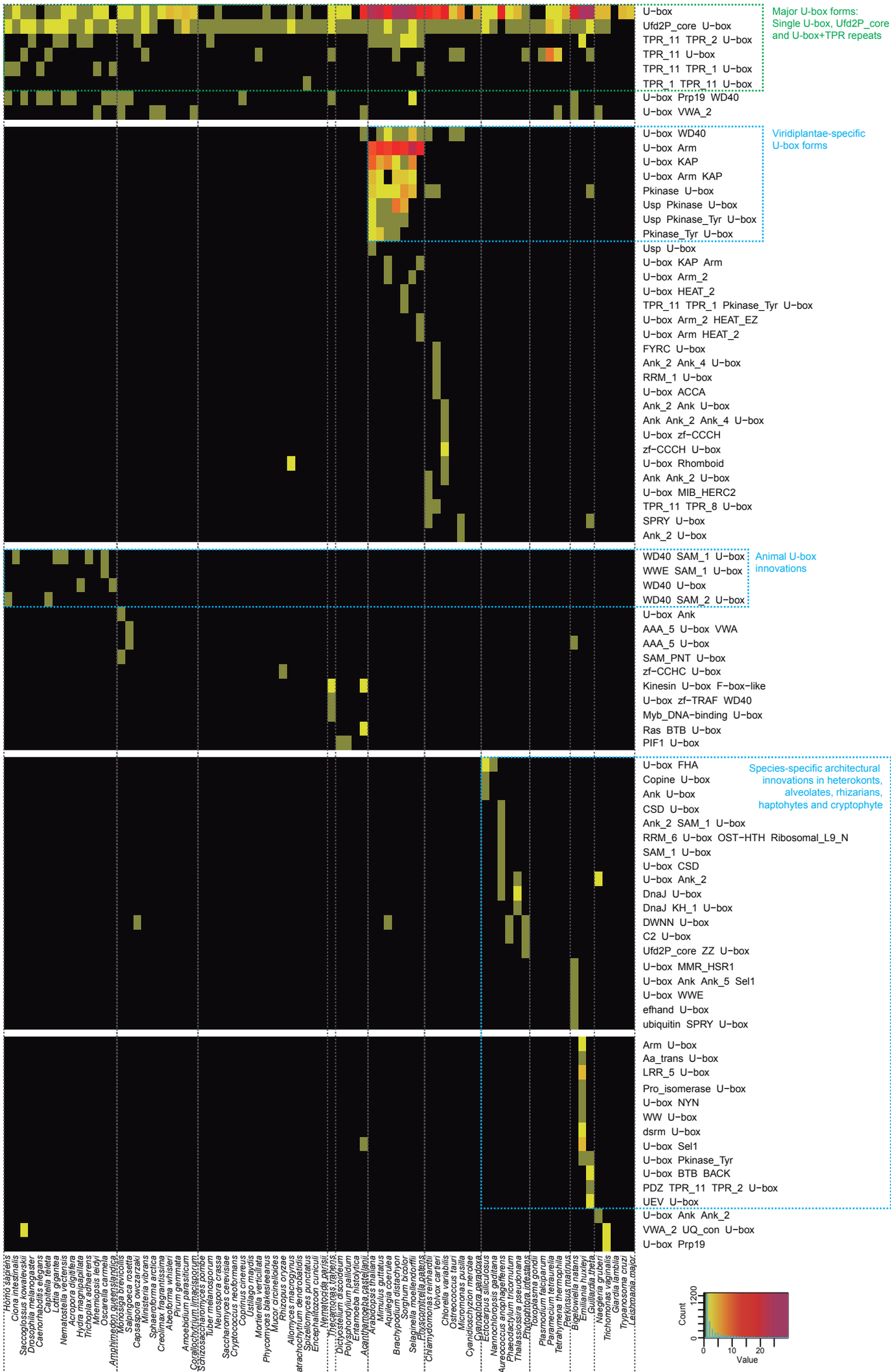


Figure S5J – zf-RING_LisH

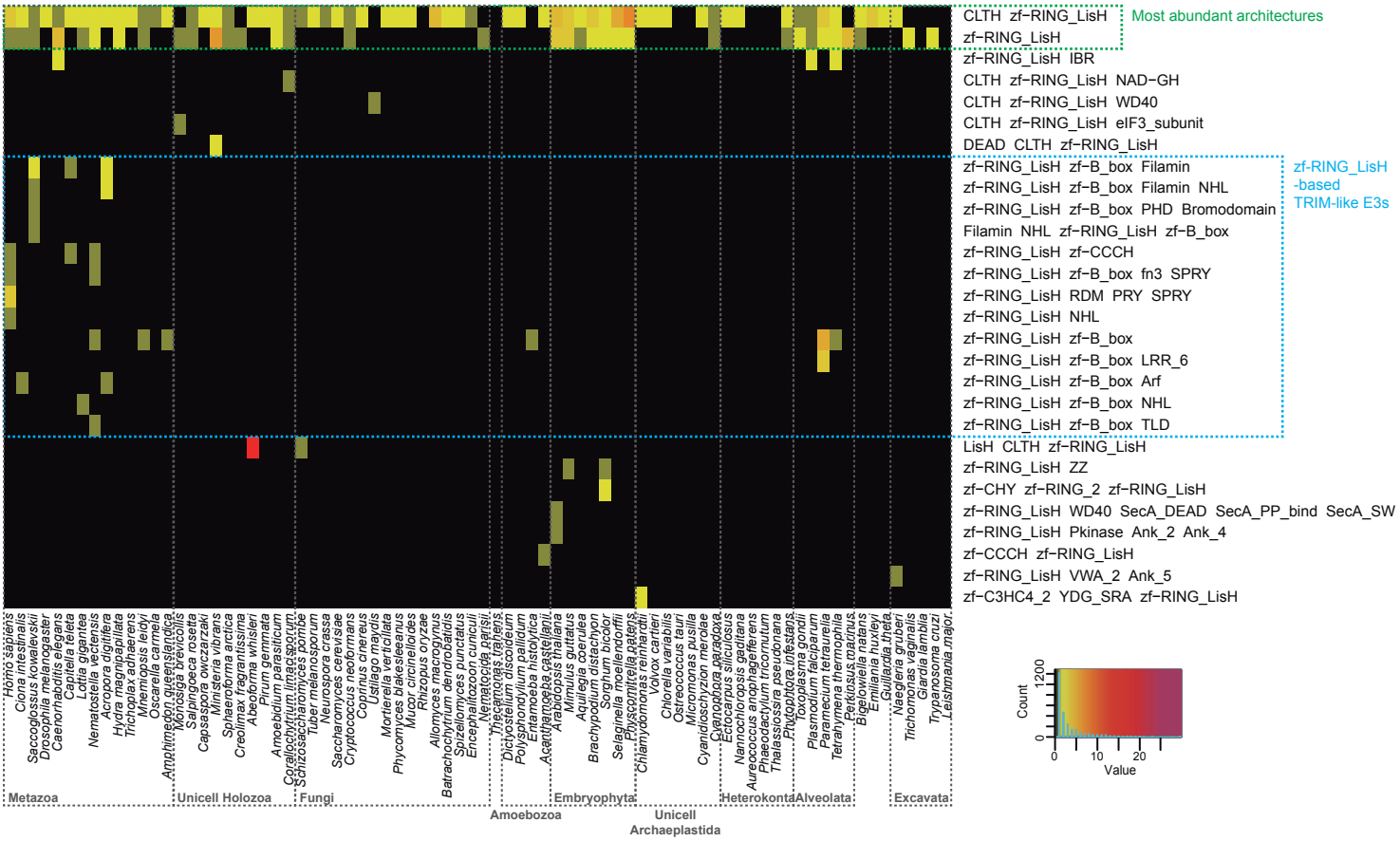


Figure S5K – RINGv

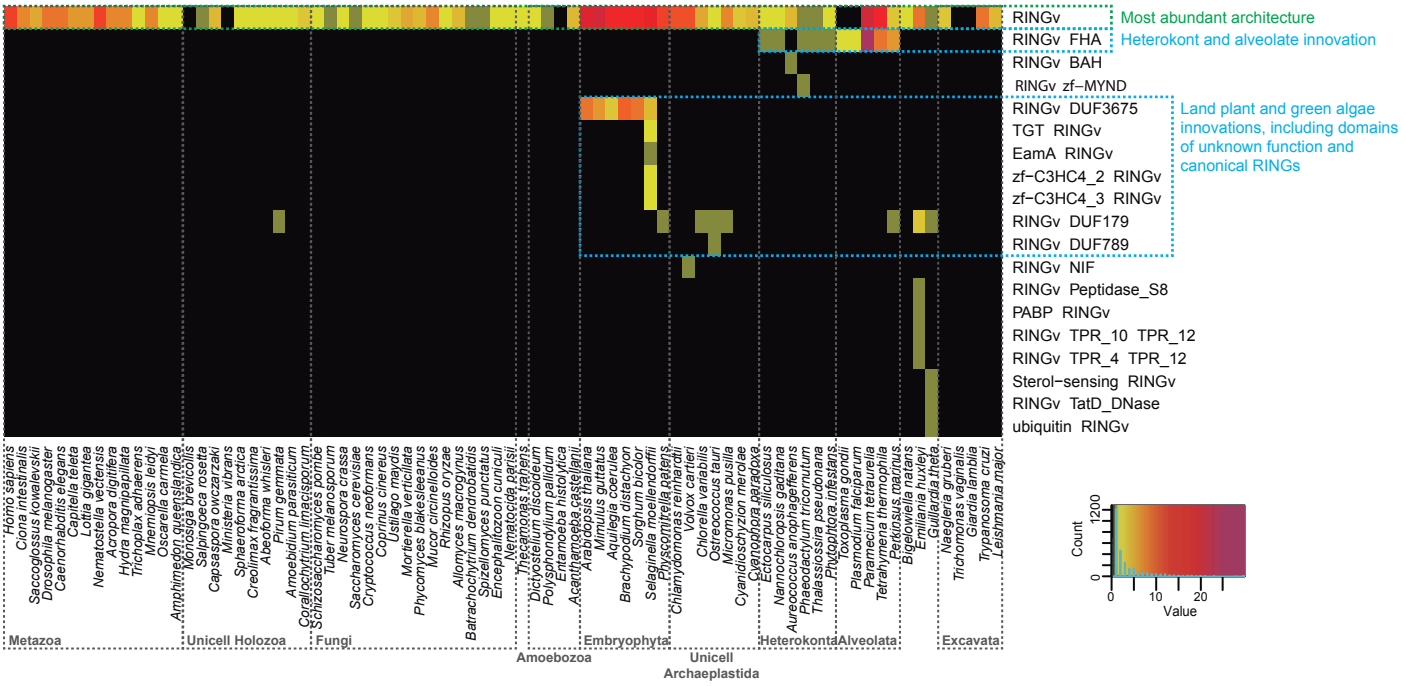


Figure S5L – FANCL_C

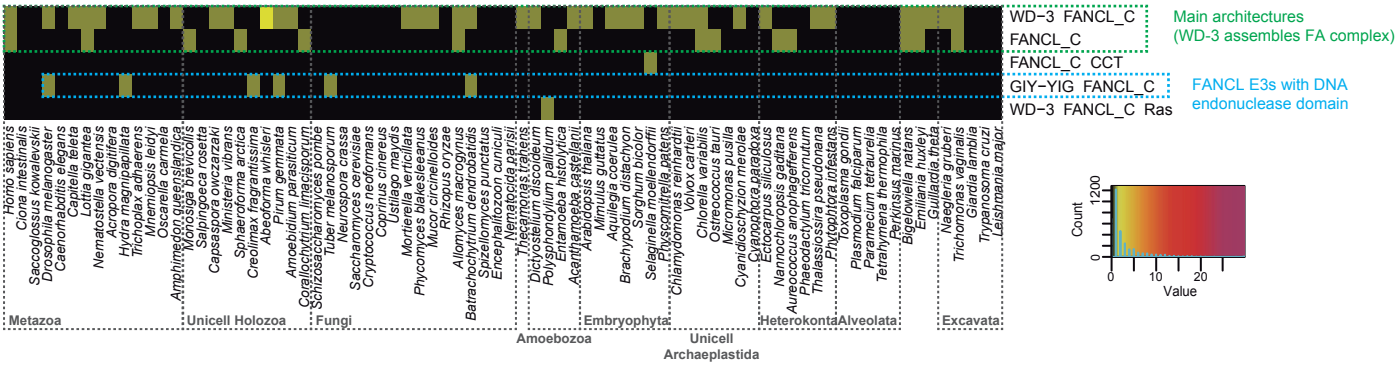


Figure S5M – IBR

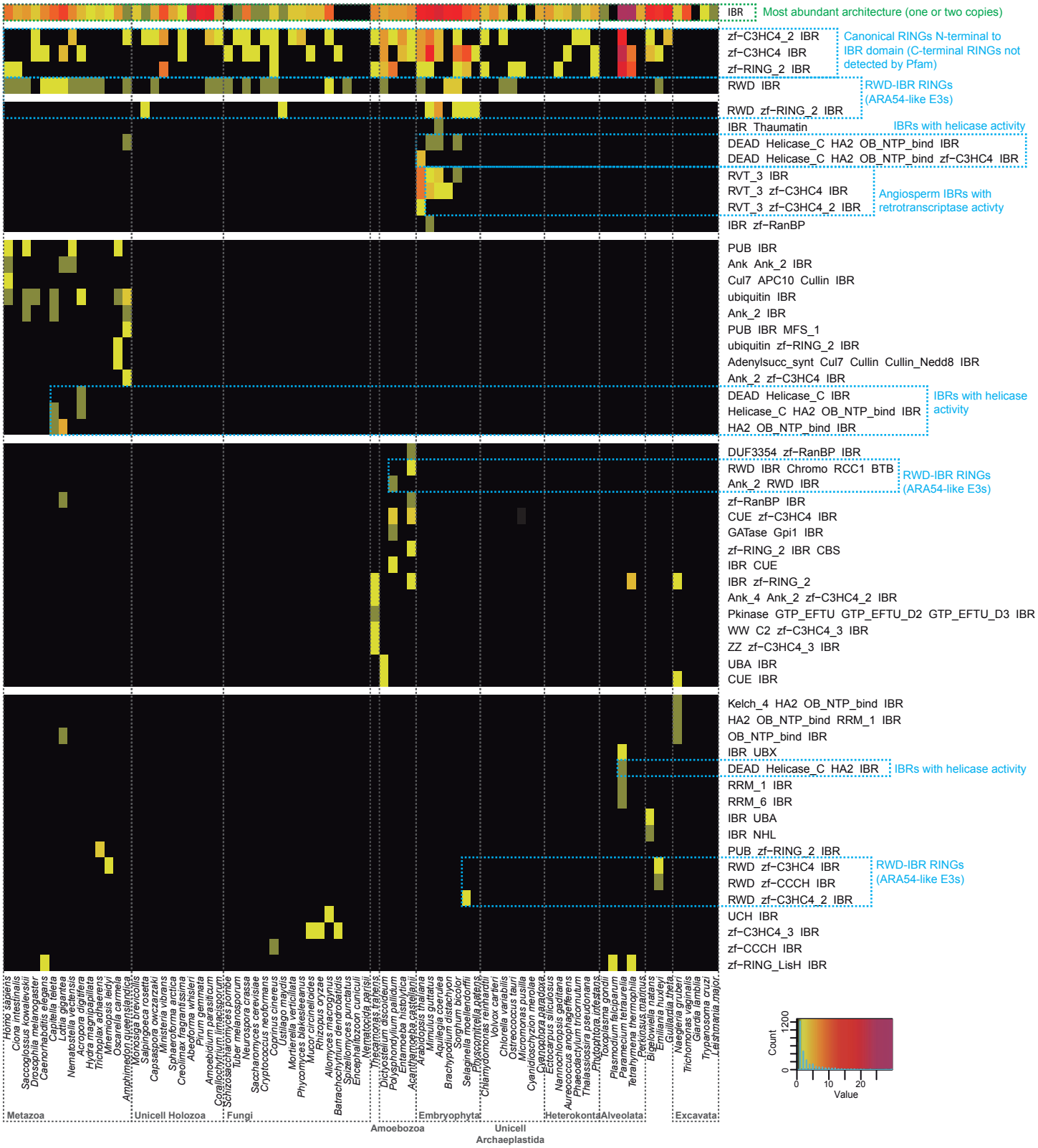


Figure S5N – Cullin

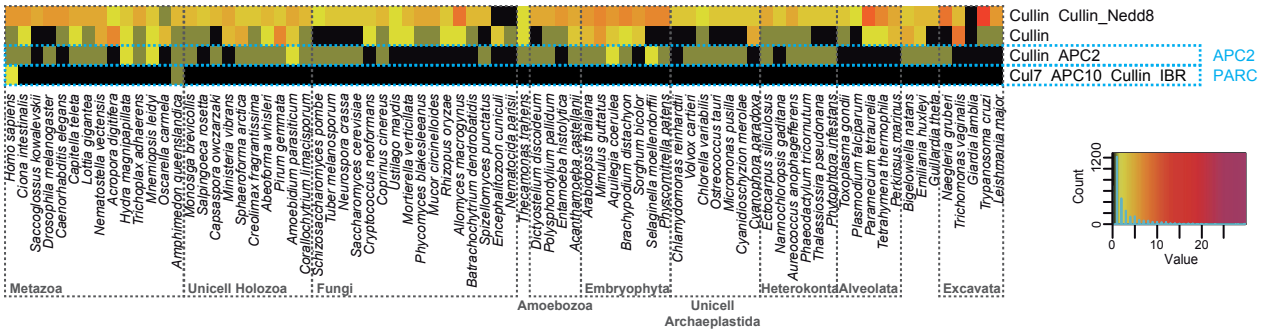


Figure S5O – F-box/F-box-like

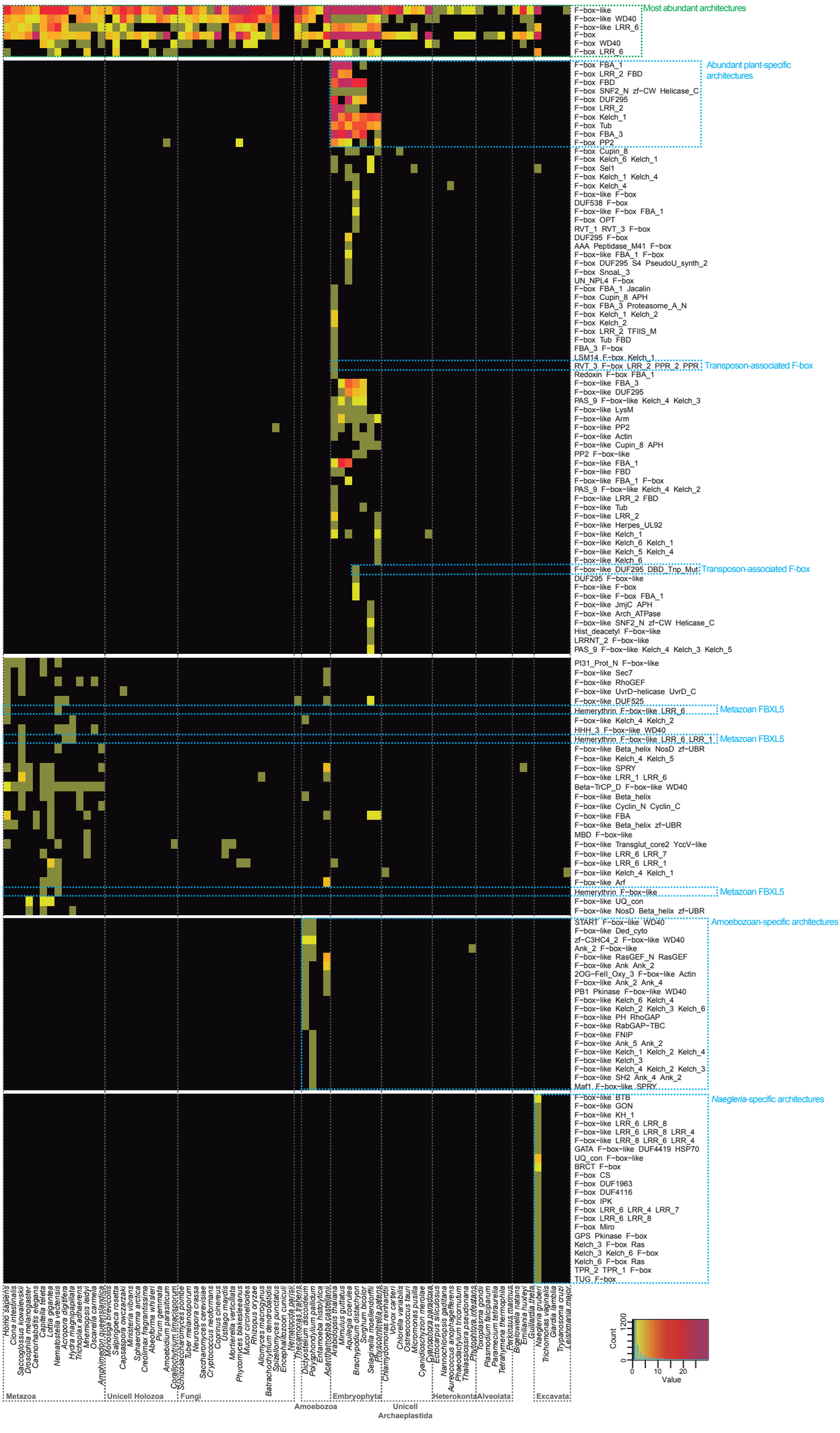


Figure S5P – SOCS_box

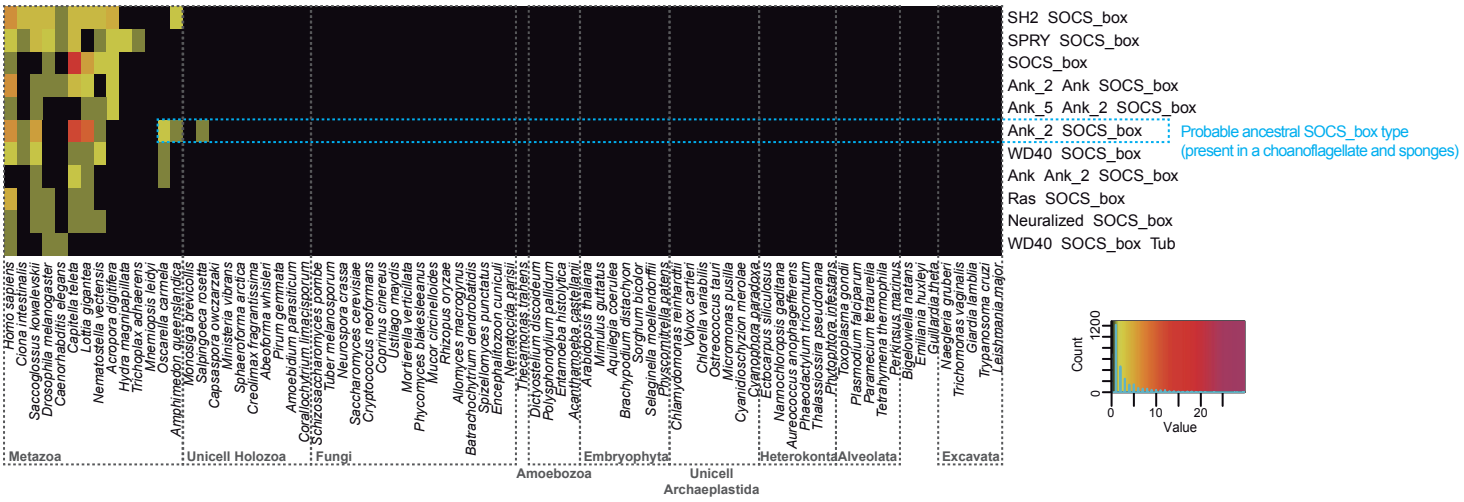


Figure S5Q – BTB

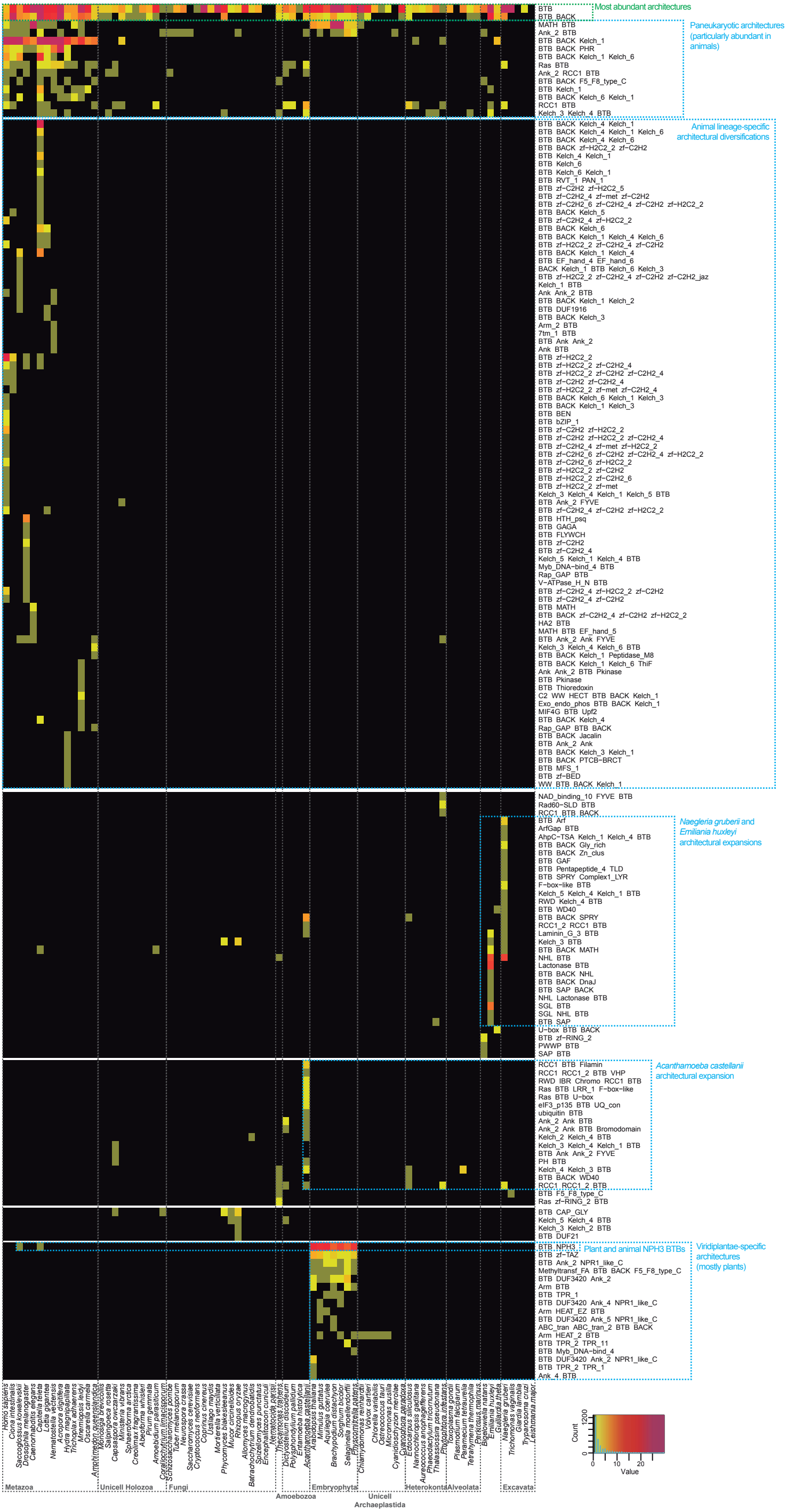


Figure S5R – UCH/UCH_1

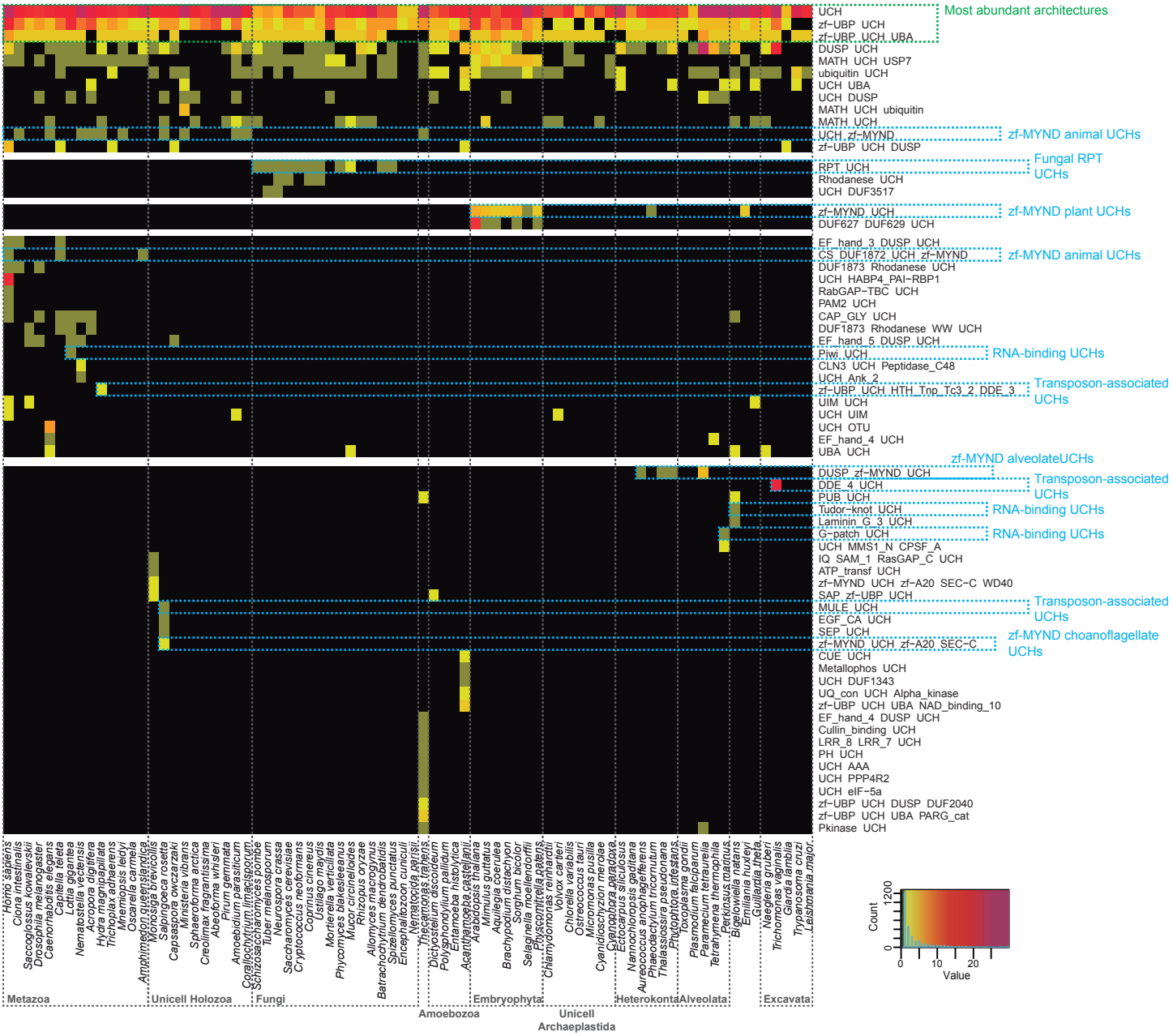


Figure S5S – Josephin

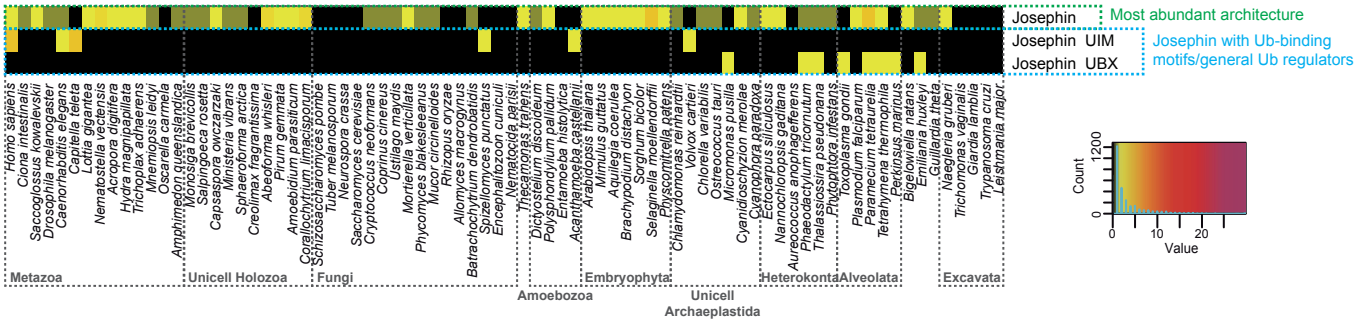


Figure S5T – OTU

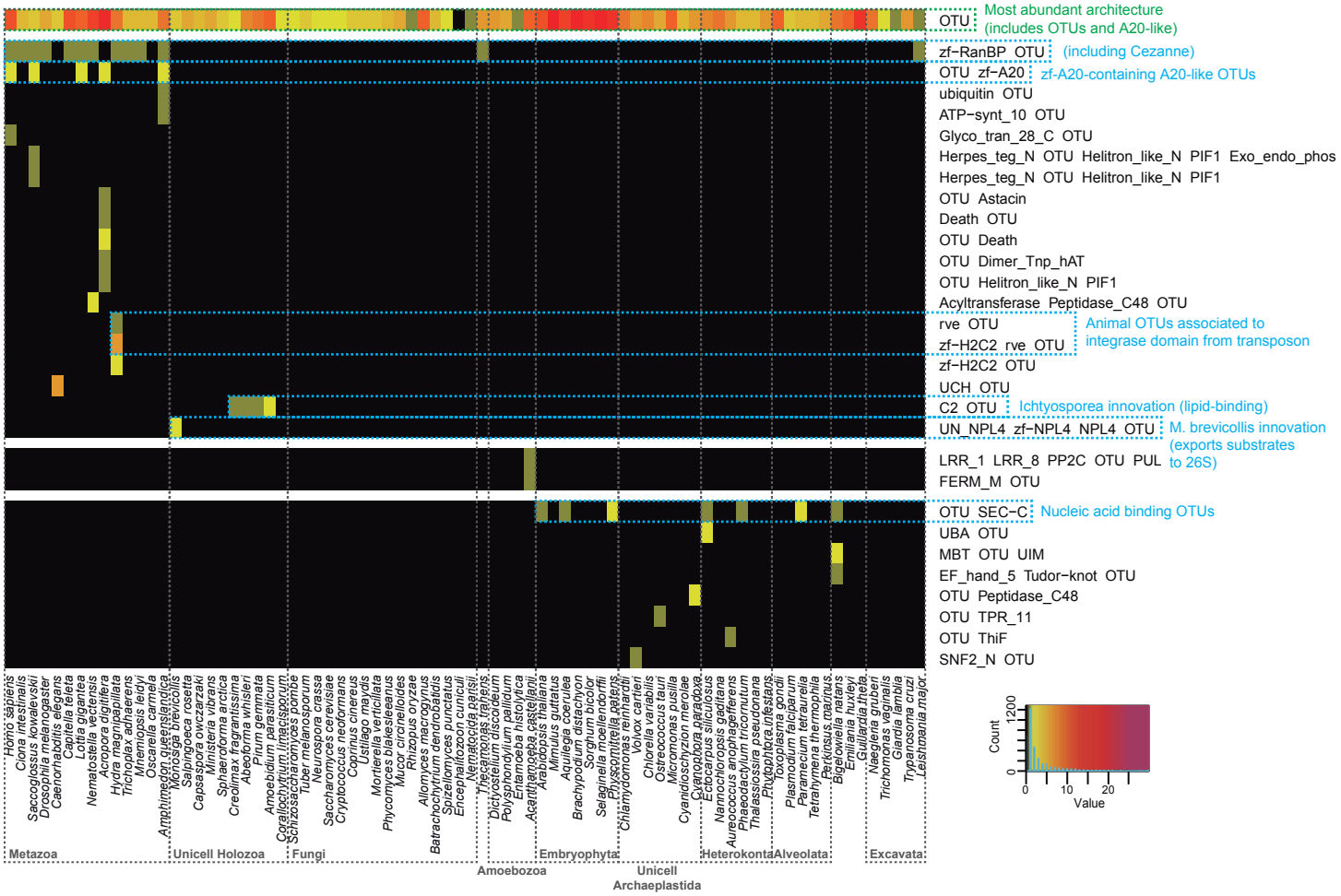


Figure S5U – Peptidase_C65

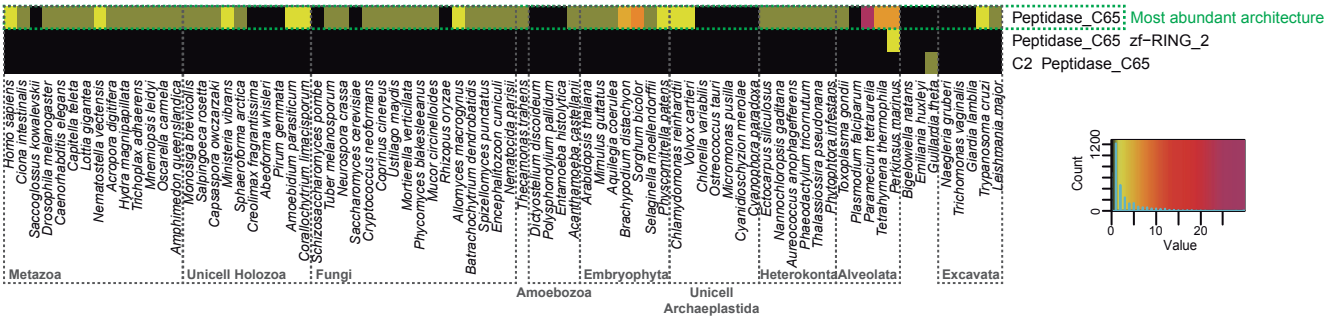


Figure S5V – JAB

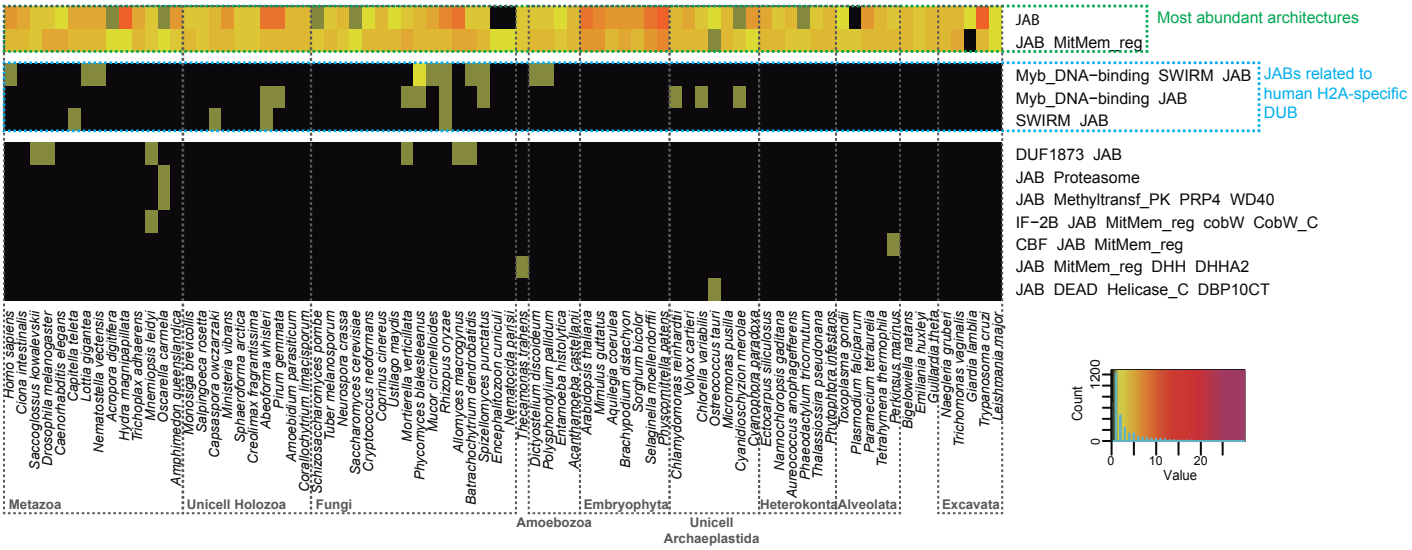


Figure S5W – zf-MIZ

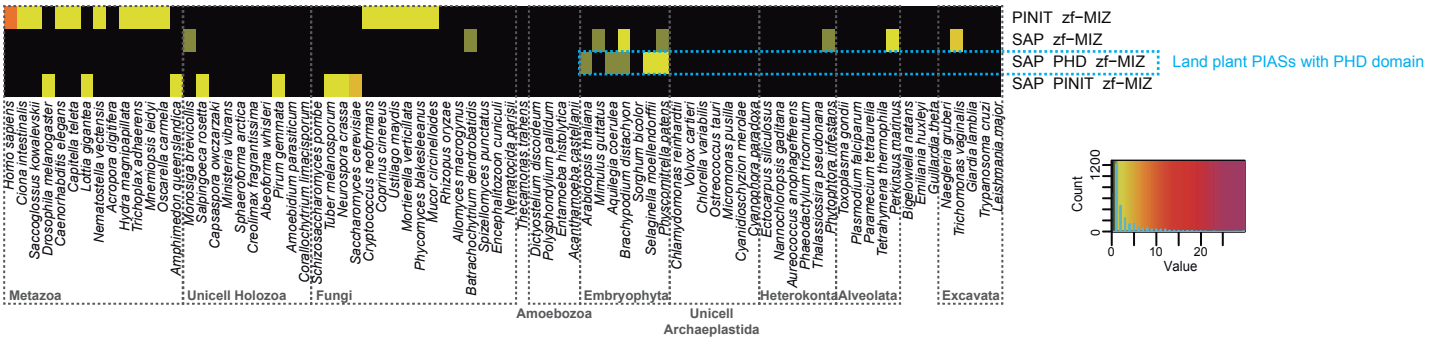


Figure S5X – zf-Nse

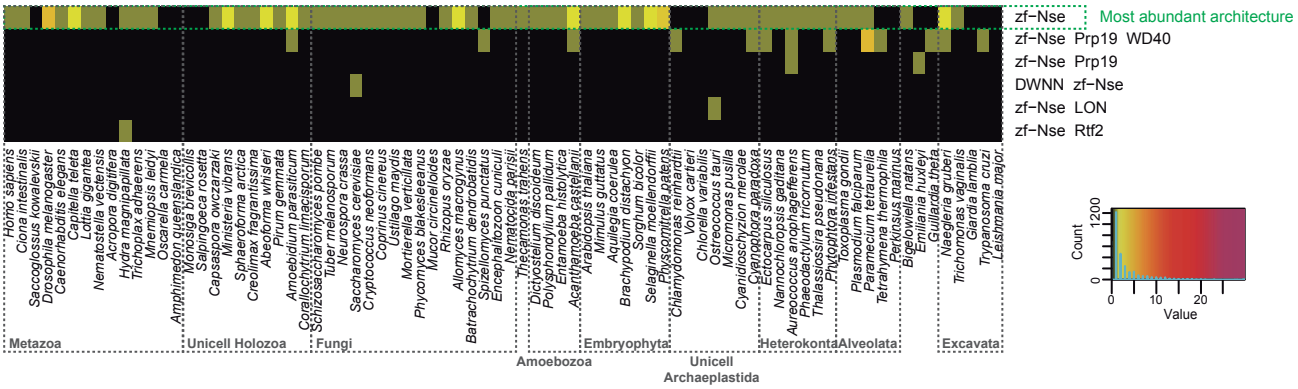


Figure S5Y – Peptidase_C48

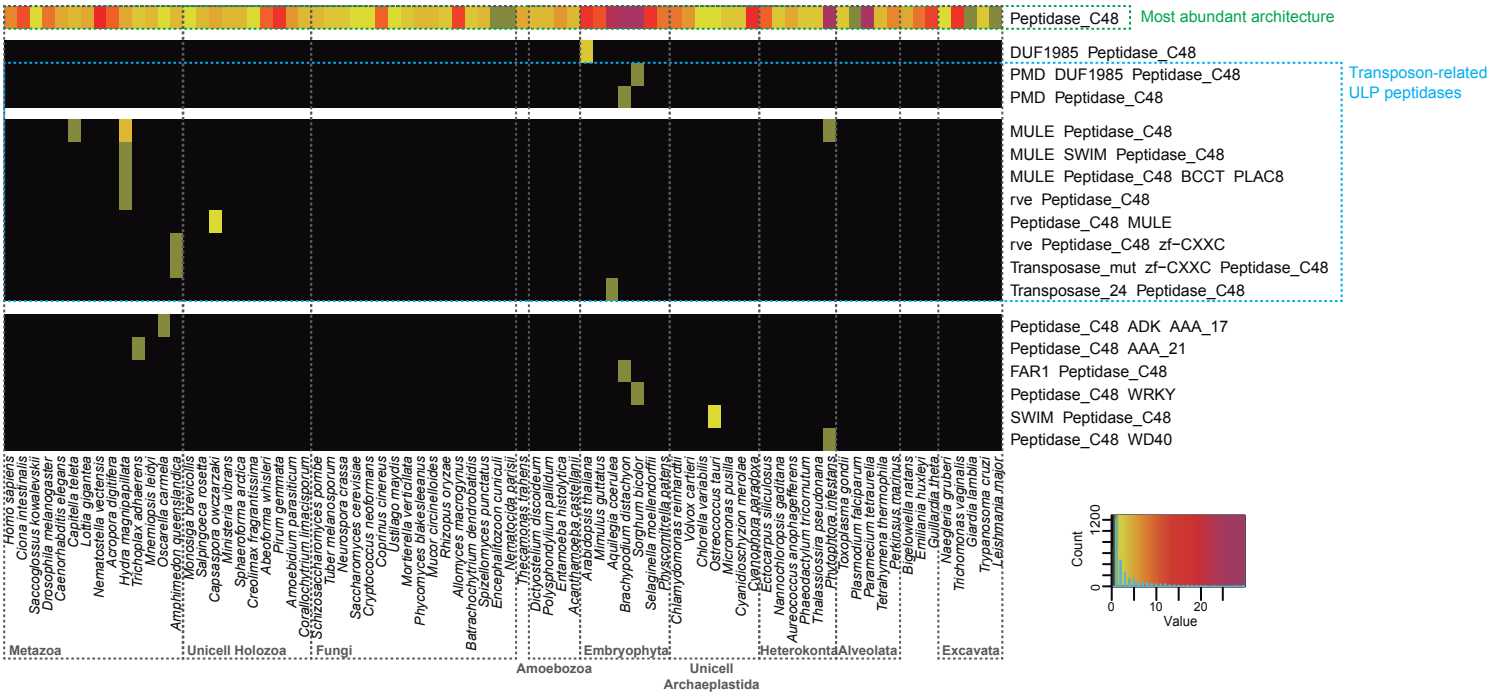


Figure S5Z – WLM

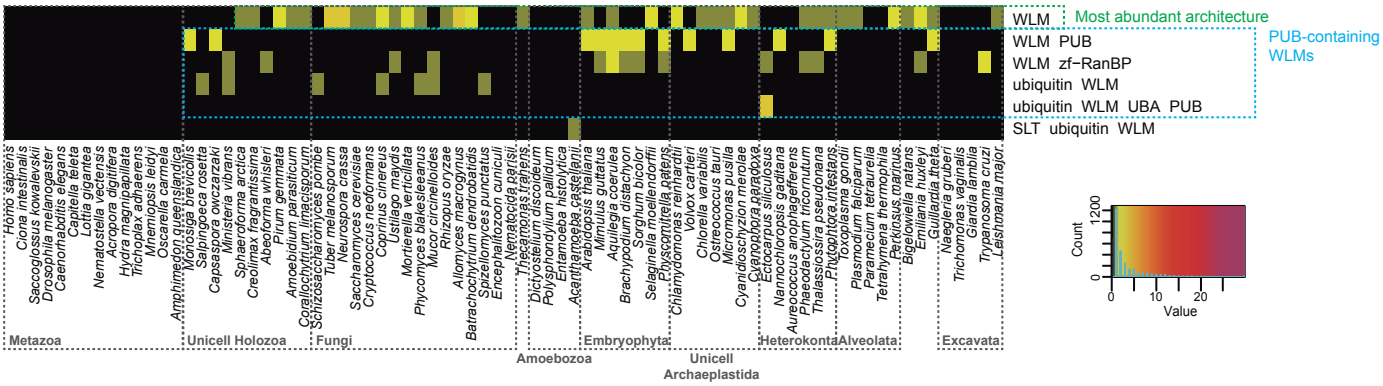


Figure S5AA – DUF862

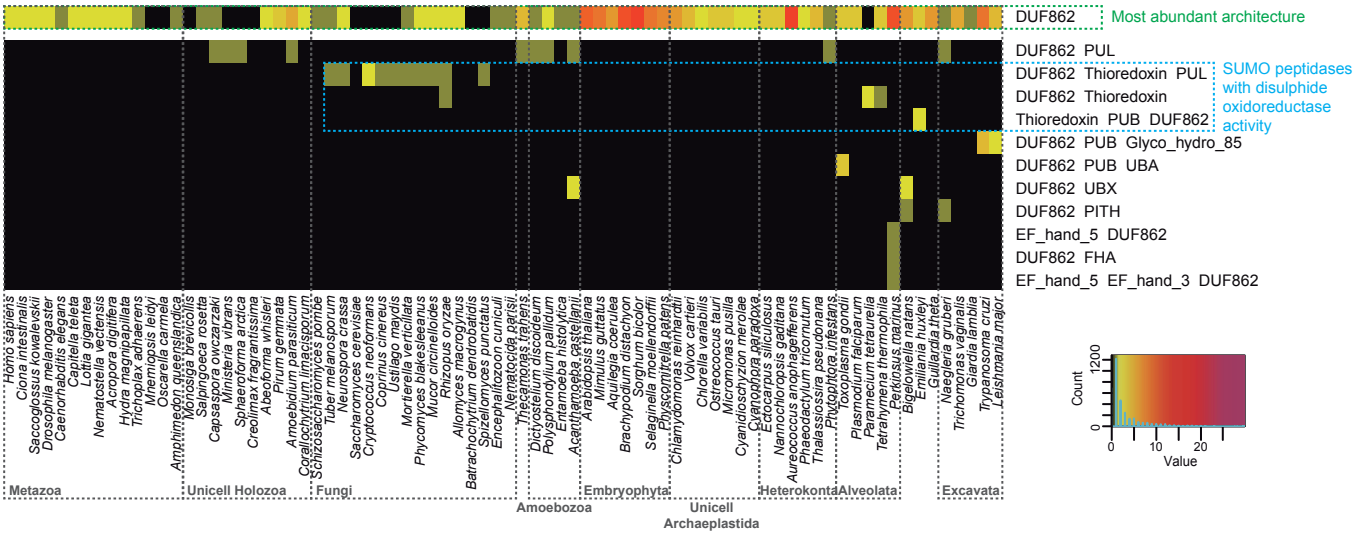


Figure S5AB – Peptidase_C78

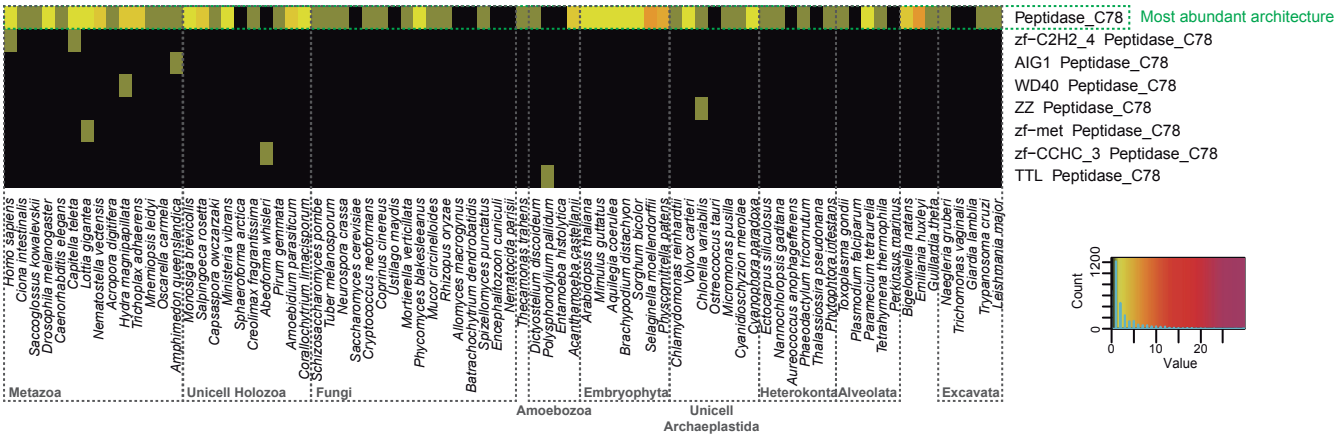
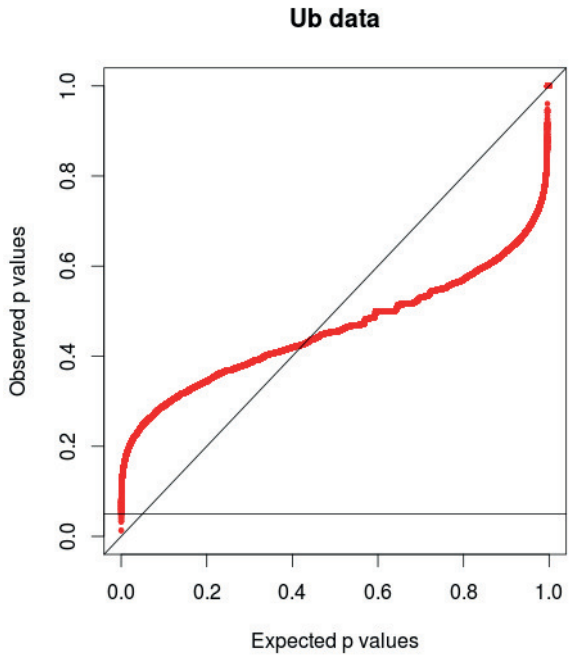
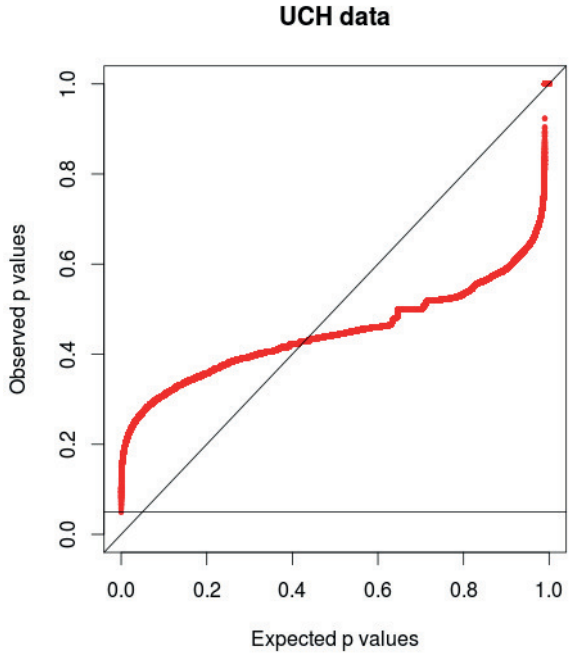


Fig. S6A
P-P plots of
matched-pairs symmetry tests





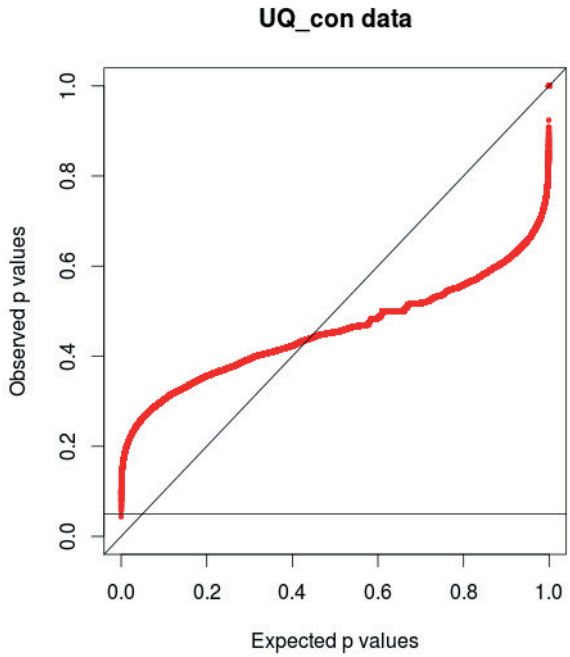


Fig. S6B Ubiquitin ML

Fig. S4C Ubiquitin P6

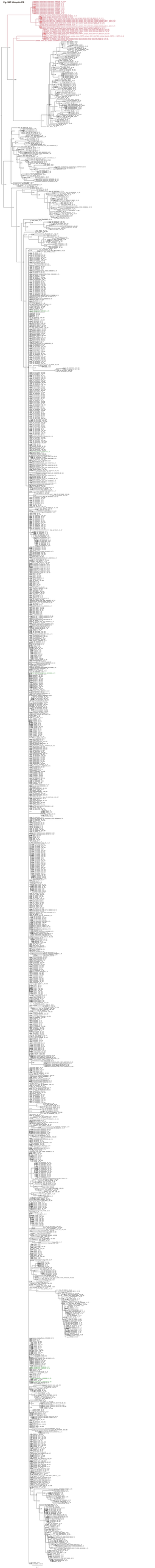


Fig. S10 UCA ML

Out_CALOSOMA_
Out_CARABUS_
Out_CYCHRUS_
Out_DAMAGER_
Out_DAMAGER_
Out_DAMAGER

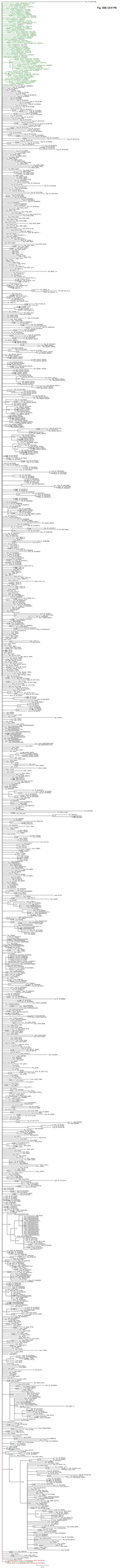


Fig. S6E UCH PB

Fig. S6F UQ_con ML

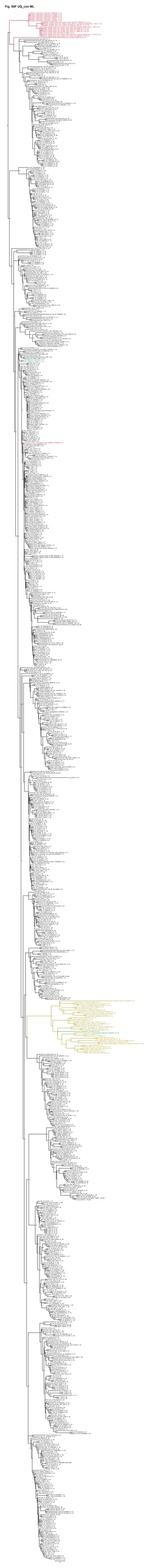


Fig. SIG UQ_con PB

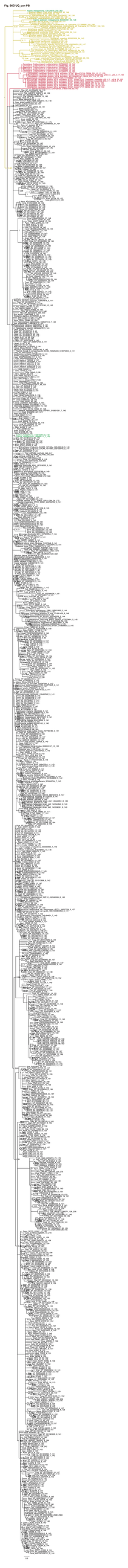
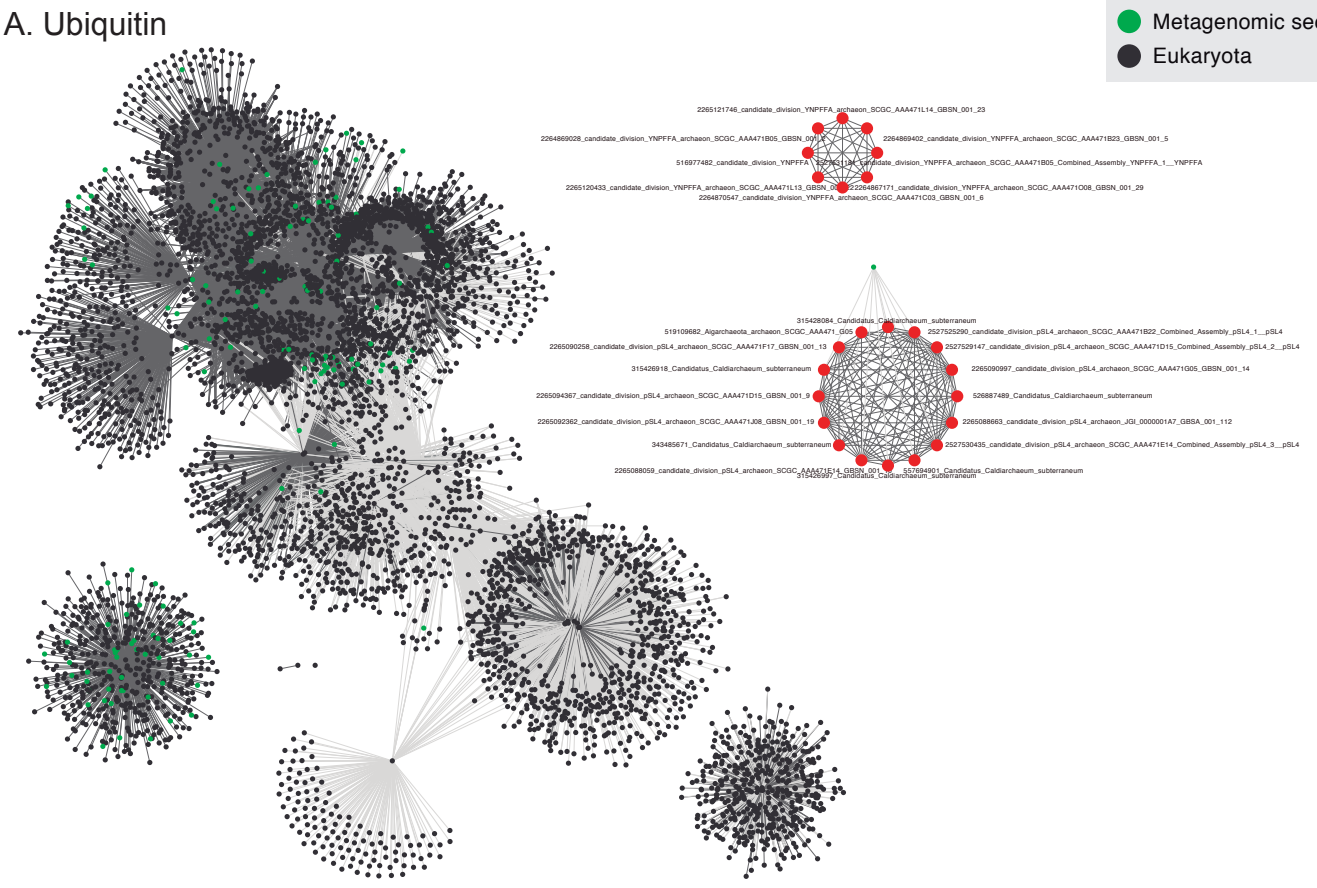


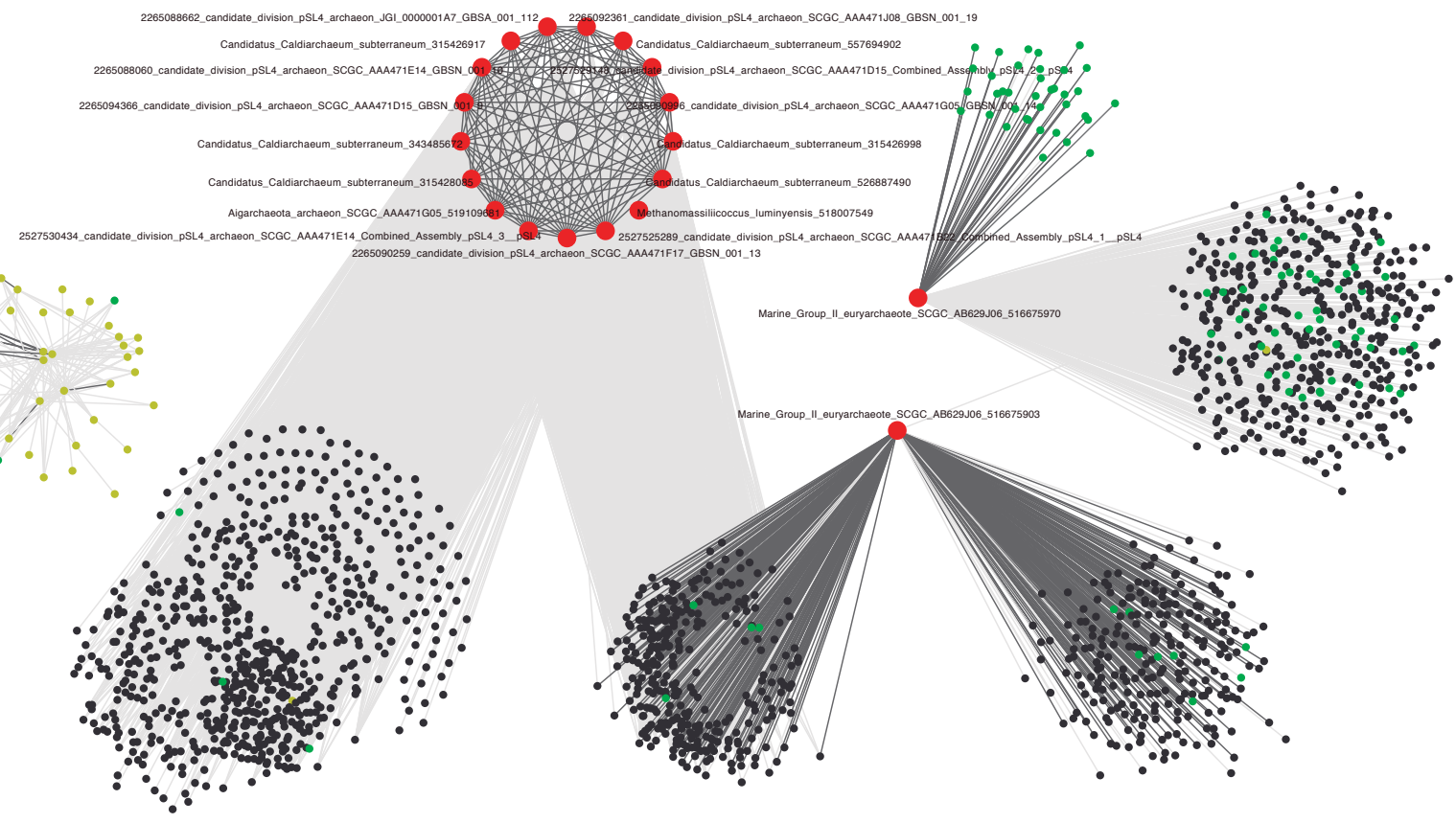
Figure S7

Archaea
Bacteria
Metagenomic sequence
Eukaryota

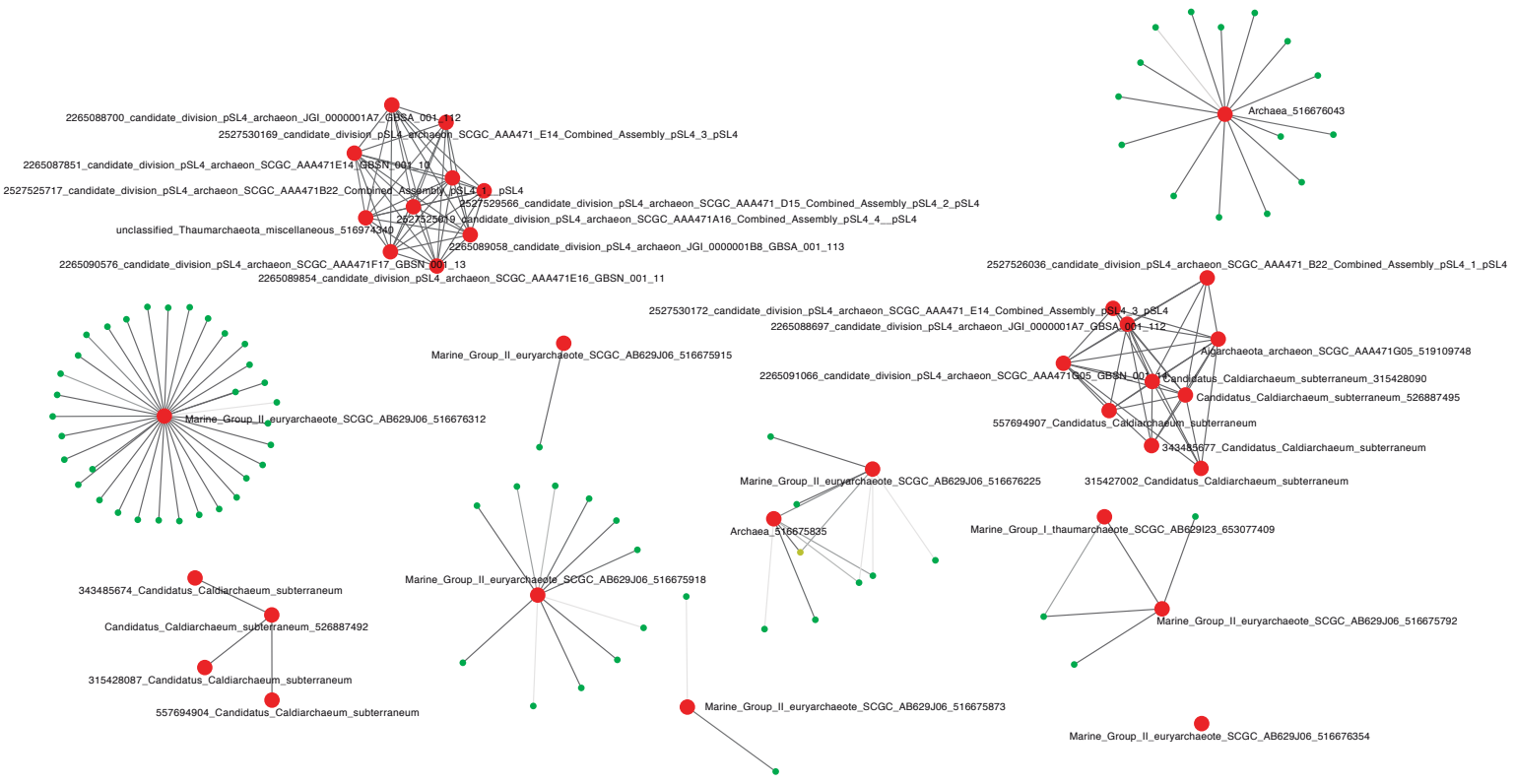
A. Ubiquitin



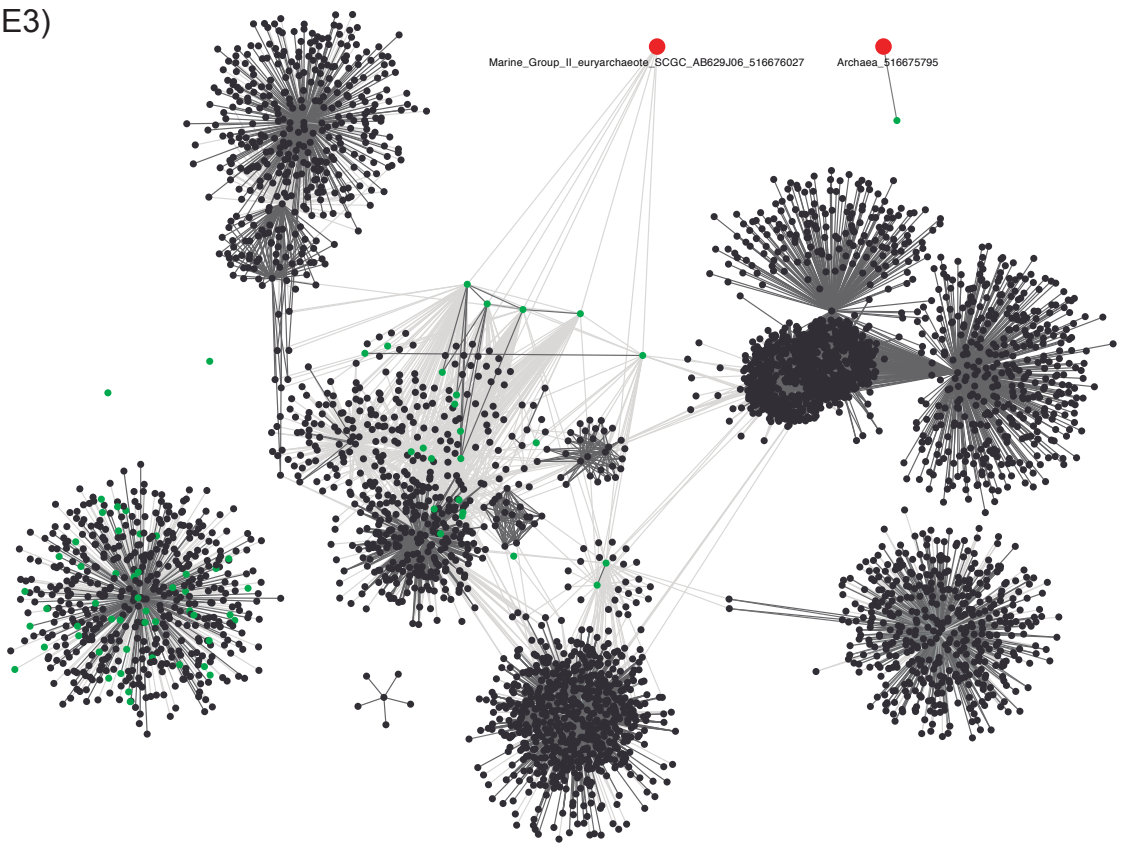
B. UQ_con (E2)



C. zf-RING_2 (E3)



D. RINGv (E3)



E. UCH (DUB)

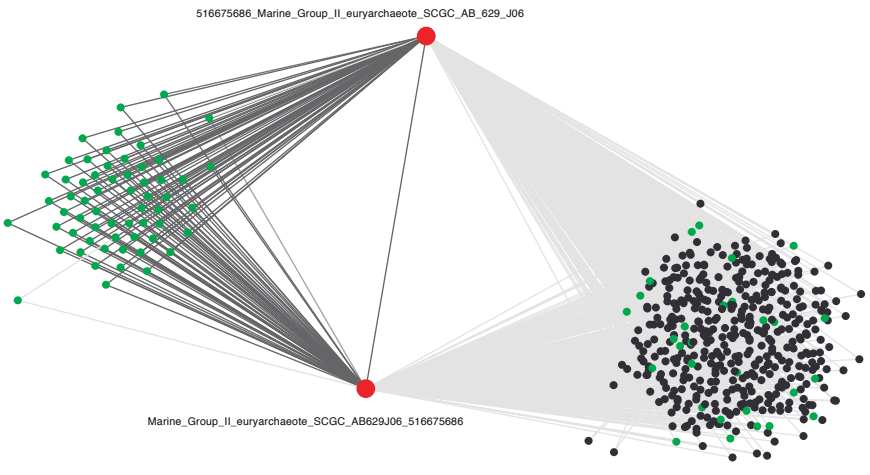


Table S1. Taxon sampling used in this study, including the taxonomic classification, the acronym used in the present study (between brackets) and the source of the proteome data.

Taxonomic classification		Species	Source
METAZOA		*Homo sapiens (Hsap)*	Ensembl
		Ciona intestinalis (Cint)	Ensembl
		Saccoglossus kowalevskii (Skow)	NCBI
		Drosophila melanogaster (Dmel)	Flybase *http://flybase.org/*
		Caenorhabditis elegans (Cele)	Ensembl
		Lottia gigantea (Lgig)	JGI *http://genome.jgi.doe.gov/*
		Capitella teleta (Ctel)	JGI
		Nematostella vectensis (Nvec)	NCBI
		Acropora digitifera (Adig)	*Acropora digitifera* Genome Project webpage *http://marinegenomics.oist.jp/*
		Hydra magnipapillata (Hmag)	NCBI
		Trichoplax adhaerens (Tadh)	NCBI
		Mnemiopsis leidyi (Mlei)	*M. leidyi* Genome Project webpage *http://research.nhgri.nih.gov/mnemiopsis/*
		Oscarella carmela (Ocar)	Courtesy of Scott Nichols
		Amphimedon queenslandica (Aque)	NCBI
CHOANOFLAGELLATA		*Monosiga brevicollis (Mbre)*	NCBI
		Salpingoeca rosetta (Sros)	Broad Institute *http://www.broadinstitute.org/annotation/genome/multicellularity_project/MultiHome.html*
FILASTEREA		*Capsaspora owczarzaki (Cowc)*	Broad Institute
		Ministeria vibrans (Mvib)	RNASeq data
ICHTHYOSPOREA		*Sphaeroforma arctica (Sarc)*	Broad Institute
		Creolimax fragrantissima (Cfra)	*Ab initio protein prediction*
		Abeoforma whisleri (Awhi)	RNASeq data
		Pirum gemmata (Pgem)	RNASeq data
		Amoebidium parasiticum (Apar)	RNASeq data
	Incertae sedis	*Corallochytrium limacisporum (Clim)*	RNASeq data
FUNGI	Ascomycota	*Aspergillus oryzae (Aory)*	NCBI
		Schizosaccharomyces pombe (Spom)	NCBI
		Tuber melanosporum (Tmel)	NCBI
		Neurospora crassa (Ncra)	Broad Institute *http://www.broadinstitute.org/scientific-community/science/projects/fungal-genome-initiative*
		Saccharomyces cerevisiae (Scer)	Broad Institute
	Basidiomycota	*Cryptococcus neoformans (Cneo)*	NCBI
		Coprinopsis cinerea (Ccin)	Broad Institute
		Ustilago maydis (Umay)	NCBI
	Incertae sedis	*Mortierella verticillata (Mver)*	Broad Institute
	Mucoromycotina	*Phyomyces blakesleeanus (Pbla)*	JGI
		Mucor circinelloides (Mcir)	JGI
		Rhizopus oryzae (Rory)	Broad Institute
	Blastocladio-mycota	*Allomyces macrogynus (Amac)*	Broad Institute
	Chytridiomycota	*Batrachochytrium dendrobatidis (Bden)*	JGI
		Spizellomyces punctatus (Spun)	Broad Institute
	Microsporidia	*Encephalitozoon cuniculi (Ecun)*	NCBI
		Nematocida parisii (Npar)	NCBI
APUSOZOA		*Thecamonas trahens (Ttra)*	Broad Institute

AMOEBOZOA	Mycetozoa	*Dictyostelium discoideum (Ddis)*	NCBI
		Polysphondylium pallidum (Ppal)	NCBI
	Archamoeba	*Entamoeba histolytica (Ehis)*	Wellcome Trust Sanger Institute *http://www.sanger.ac.uk/resources/downloads/protozoa/entamoeba.html*
	Centramoebida	*Acanthamoeba castellanii (Acas)*	*Ab initio protein prediction*
VIRIDIPLANTAE	Embryophyta	*Arabidopsis thaliana (Atha)*	NCBI
		Mimulus guttatus (Mgut)	Phytozome (JGI) *http://www.phytozome.net/*
		Aquilegia coerulea (Acoe)	Phytozome (JGI)
		Brachypodium distachyon (Bdis)	Phytozome (JGI)
		Sorghum bicolor (Sbic)	Phytozome (JGI)
		Selaginella moellendorffii (Smoe)	NCBI
		Physcomitrella patens (Ppat)	NCBI
	Chlorophyta	*Chlamydomonas reinhardtii (Crei)*	NCBI
		Volvox cartieri (Vcar)	NCBI
		Chlorella variabilis (Cvar)	NCBI
		Ostreococcus tauri (Otau)	NCBI
		Micromonas pusilla (Mpus)	JGI
	Rhodophyta	*Cyanidioschyzon merolae (Cmer)*	*C. merolae* Genome Project webpage *http://merolae.biol.s.u-tokyo.ac.jp/*
	Glaucophyta	*Cyanophora paradoxa (Cpar)*	*C. paradoxa* Genome Project webpage *http://cyanophora.rutgers.edu/cyanophora/*
HETERO-KONTA	Brown algae/ Phaeophyceae	*Ectocarpus siliculosus (Esil)*	EMBL
		Nannochloropsis gaditana (Ngad)	*N. gaditana* Genome Project webpage *http://nannochloropsis.genomeprojectsolutions-databases.com/*
		Aureococcus anophagefferens (Aano)	Uniprot
		Phaeodactylum tricornutum (Ptri)	NCBI
		Thalassiossira pseudonana (Tpse)	NCBI
	Oomycota	*Phytophthora infestans (Pinf)*	NCBI
ALVEOLATA	Apicomplexa	*Toxoplasma gondii (Tgon)*	NCBI
		Plasmodium falciparum (Pfal)	Uniprot
	Ciliophora	*Paramecium tetraurelia (Ptet)*	Uniprot
		Tetrahymena thermophila (Tthe)	NCBI
	Perkinsidae	*Perkinsus marinus (Pmar)*	NCBI
RHIZARIA		*Bigelowiella natans (Bnat)*	JGI
HAPTOPHYTA		*Emiliania huxleyi (Ehux)*	JGI
CRYPTOPHYTA		*Guillardia theta (Gthe)*	JGI
EXCAVATA	Heterolobosea	*Naegleria gruberi (Ngru)*	NCBI
	Kinetoplastida	*Trypanosoma cruzi (Tcru)*	NCBI
		Leishmania major (Lmaj)	NCBI
	Metamonada	*Trichomonas vaginalis (Tvag)*	NCBI
		Giardia lamblia (Glam)	NCBI
ARCHAEA & BACTERIA		-	Non-redundant database NCBI

Table S2. List of elements of the ubiquitin, SUMO and Ufm1 pathways sampled in our study, including their defining Pfam domain IDs. Examples of each element in the model systems *Homo sapiens, Saccharomyces cerevisiae* and *Arabidopsis thaliana* are also included.

	Type	Domain	Pfam ID	Human	Yeast	Arabidopsis
General	**E1**	ThiF	PF10585 *(See Material and Methods)*	UBA1 (Ub)… UBA2 (SUMO)… UBA5 (Ufm1)	UBA1 (Ub) UBA2 (SUMO/SMT3) - (Ufm1)	UBA1,2 (Ub)… SAE1/SAE2 (SUMO)… UBA5 (Ufm1)
	E2	UQ_con	PF00179	UBE2E1, UBE2E2, UBE2D1, UBE2D2, UBE2D3 (Ub)… UBE2I/UBC9 (SUMO) - (Ufm1)	UBC1-8 (Ub) UBC9 (SUMO) - (Ufm1)	UBC1-8, UBC10-37 (Ub)… UBC9, SCE1 (SUMO) - (Ufm1)
Ubiquitin	**Label**	ubiquitin	PF00240	Various	Various	Various
	E3s	HECT	PF00632	Trip12, Tom1, E6-AP, Nedd4...	Ufd4, Tom1...	UPL1-7
		U-box	PF04564	Prp19, CHIP...	Prp19, Ufd2P...	Prp19, CHIP...
		zf-C3HC4	PF00097	Various; see Deshaies and Joazeiro 2009	Various; see Deshaies and Joazeiro 2009	See Stone et al. 2005; Deshaies and Joazeiro 2009
		zf-C3HC4_2	PF13923			
		zf-C3HC4_3	PF13920			
		Sina	PF03145	Siah1 (Seven in absentia homolog 1)	-	SINAT5 (root development), SINAT1...
		zf-RING_2	PF13639	Various; see Deshaies and Joazeiro 2009	Various; see Deshaies and Joazeiro 2009	See Stone et al. 2005
		zf-RING_LisH	PF13445	Rmd5, Trim32	Rmd5/Gid2, -	LisH/CRA/RING-U-box domain-containing protein (not to be confused with Gid2/SLEEPY1, a F-box protein from the SCF complex), -
		RINGv	PF12906	MARCH1-9	Doa10/SSM4	MARCH6, Pitchoun 1/PIT1
		FANCL_C	PF11793	FANCL	-	unnamed NP_001032152
		IBR	PF01485	Park2, Ariadne/PARC, RNFs…	YKR017C, ITT1…	RING/U-box protein with C6HC-type zinc finger…
		zf-rbx1	PF12678	RBX1	Hrt1p	RING-box protein 1
		Cullin	PF00888	Cul1-7	Cullin	Cullin
		Skp1_POZ	PF03931	Skp1	Skp1p	Skp1-like protein
		MMS1_N	PF10433	DDB1	MSS1	DDB1
		F-box, F-box-like	PF00646, PF12937	F-box only protein X (Fbw1, Fbl1, Fbx1) See more examples in Cardozo et al. 2004	Mfb1p	F-box protein X (See more examples in Gagne et al. 2002)
		VHL	PF01847	Von Hippel-Lindau disease tumor suppressor	-	-
		SOCS_box	PF07525	Suppressor of cytokine signaling	-	-
		BTB	PF00651	Bcl6, ZBTB48…	YIL001Wp-like protein	NPR3…
		DCAF	PF00400 *(WD40; see Material and Methods)*	DCAF, RFWD2, COP1	DCAF	COP1, RFWD2, SPA1
	DUBs	Peptidase_C12	PF01088	UCHL1, BAP1	Yuh1p	Ubiquitin carboxyl-terminal hydrolase L5
		UCH, UCH_1	PF00443, PF13423	USP1	Ubp1p	Ubiquitin carboxyl-terminal hydrolase 1
		Josephin	PF02099	ATXN3, JOSD1	-	Ataxin-3
		JAB	PF01398	COP9 signalosome complex subunit 5; Histone H2A deubiquitinase MYSM1	Rpn11p, Rri1p	26S proteasome, non-ATPase regulatory subunit

		Peptidase_C65	PF10275	Otubains: OTUB1,2	-	Ubiquitin thioesterase otubain-like
		OTU	PF02338	OTUs: OTUD1; A20-like; A20, Cezanne, TRABID	Otu1p	OTU-like cysteine type protease
SUMO	**Label**	Rad60-SLD	PF11976	SUMO-1, SUMO-2, SUMO-3, SUMO-4	Smt3p	SUMO-1
	E3	zf-MIZ	PF02891 *(See Material and Methods)*	PIAS1, PIASxα, PIASxβ, PIASγ, and PIAS3	Siz1p, Nfi1p	SIZ1
		zf-Nse	PF11789	Nse1, Nse2	MMS21	MMS21
		IR1-M	PF12185	RanBP2	-	-
	Pepti-dase	Peptidase_C48	PF02902	SENP1, SENP2, SENP3,...,SENP7	Ulp1p, Ulp2p	Ubiquitin-like-specific protease 1,Ubiquitin-like-specific protease 2
		WLM	PF08325	-	Wss1p	no name (ex: NP_564704)
		DUF862	PF05903	DeSI-1 or PPPDE peptidase domain-containing protein	- (*S.pombe* has UPF0326 protein hag1)	PPPDE putative thiol peptidase family protein
Ufm1	**Label**	Ufm1	PF03671	Ufm1	-	Ufm1
	E2	UFC1	PF08694	UFC1	-	ubiquitin-fold modifier-conjugating enzyme 1
	E3	DUF2042	PF09743	E3 UFM1-protein ligase 1	-	E3 UFM1-protein ligase 1-like
	Pepti-dase	Peptidase_C78	PF07910	UfSP2	?	Probable Ufm1-specific protease