

# Output results of CLIME (CLustering by Inferred Models of Evolution)

## Dataset:

Num of genes in input gene set: 8

Total number of genes: 20834

Prediction LLR threshold: 0

The CLIME PDF output two sections:

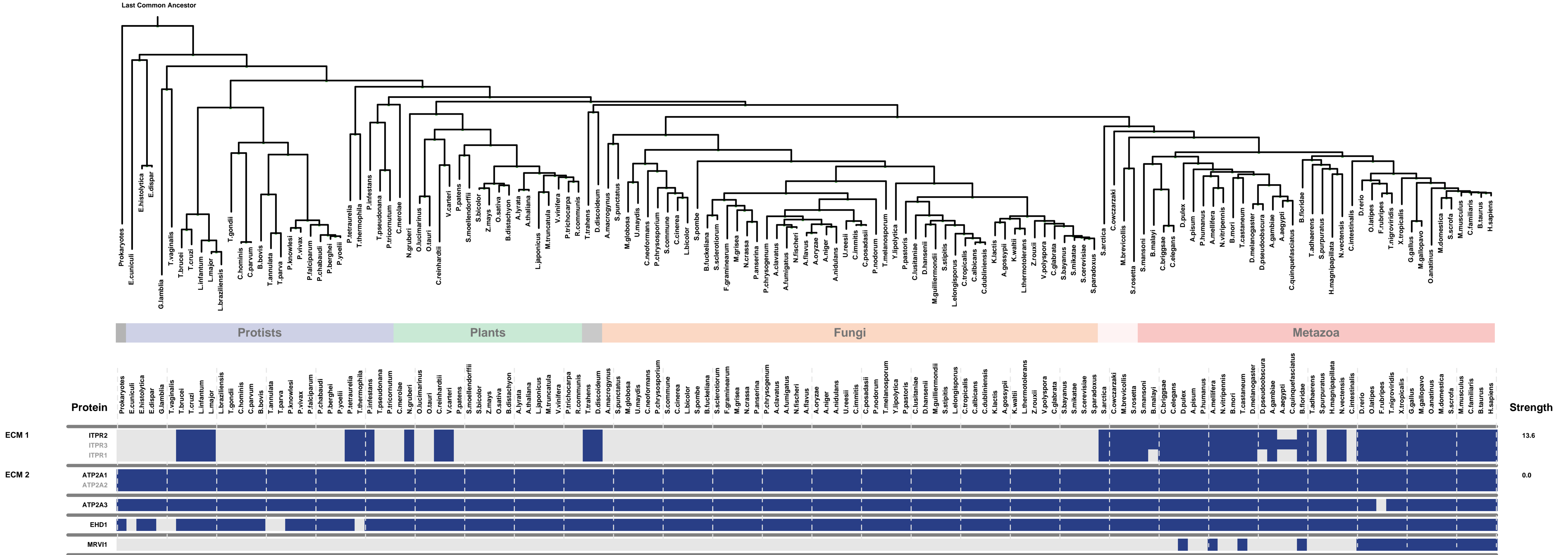
### 1) Overview of Evolutionarily Conserved Modules (ECMs)

- Top panel shows the predefined species tree.
- Bottom panel shows the partition of input genes into Evolutionary Conserved Modules (ECMs), ordered by ECM strength (shown at right), and separated by horizontal lines.
- Each row show one gene, where the phylogenetic profile indicates presence (blue) or absence (gray) of homologs in each species (column).
- Gene symbols are shown at left. Gray color indicates that the gene is a paralog to a higher scoring gene within the same ECM (based on BLASTP  $E < 1e-3$ ).

### 2) Details of each ECM and its expansion ECM+

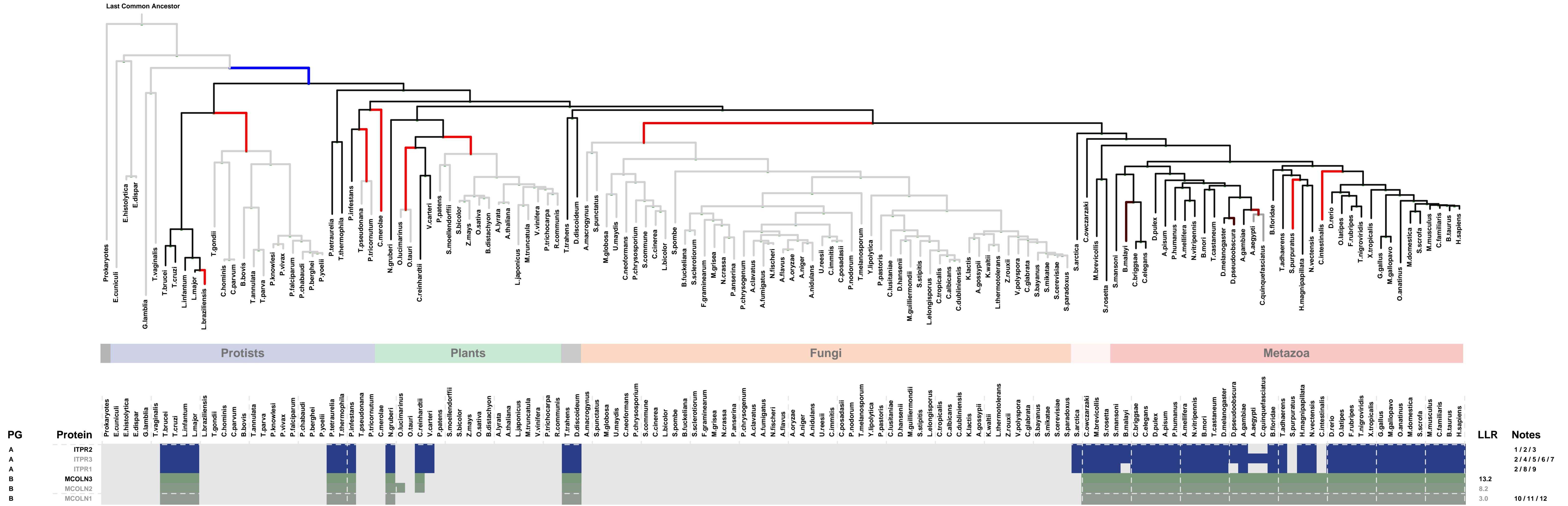
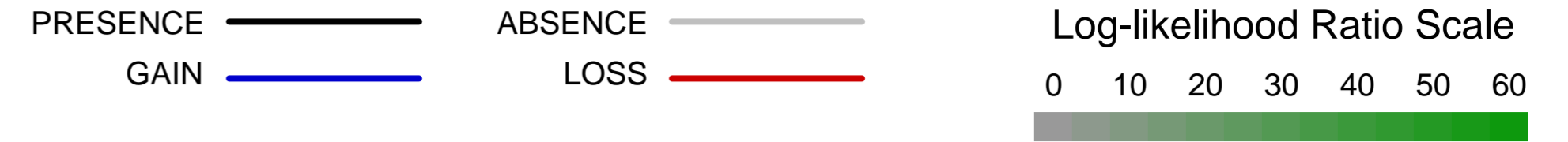
- Top panel shows the inferred evolutionary history on the predefined species tree. Branch color shows the gain event (blue) and loss events (red color, with brighter color indicating higher confidence in loss). Branches before the gain or after a loss are shown in gray.
- Bottom panel shows the input genes that are within the ECM (blue/white rows) as well as all genes in the expanded ECM+ (green/gray rows). The ECM+ includes genes likely to have arisen under the inferred model of evolution relative to a background model, and scored using a log likelihood ratio (LLR).
- PG indicates "paralog group" and are labeled alphabetically (i.e., A, B). The first gene within each paralog group is shown in black color. All other genes sharing sequence similarity (BLAST  $E < 1e-3$ ) are assigned to the same PG label and displayed in gray.

# Overview of Evolutionarily Conserved Modules (ECMs)



**ECM 1, Gene set "platelet dense tubular network membrane", Page 1**

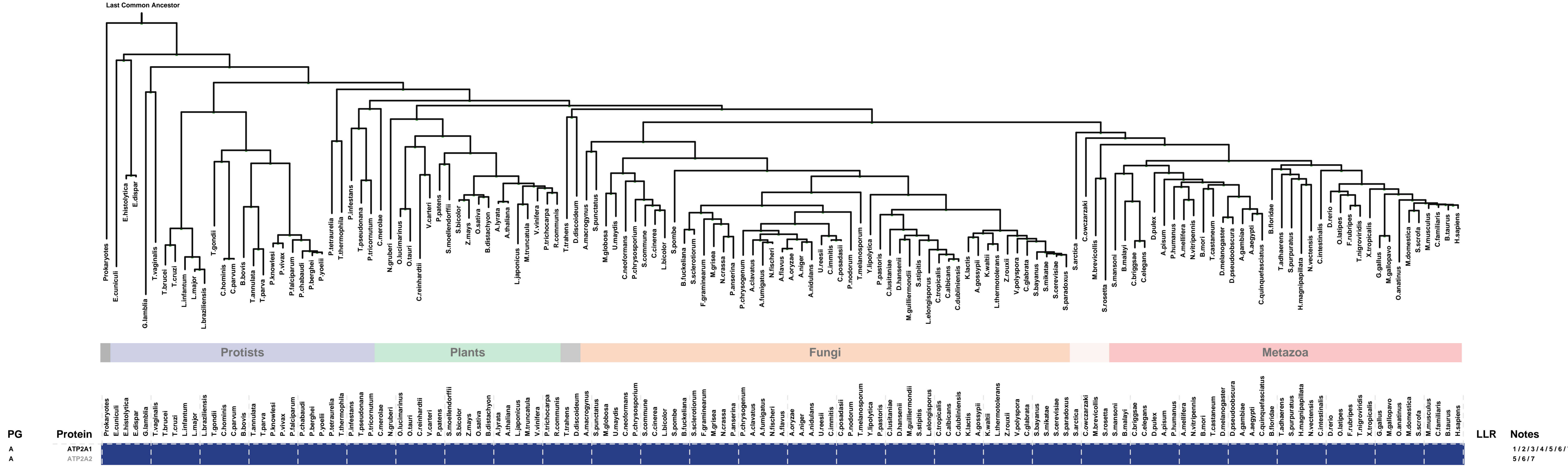
Num of ECM Genes: 3. Num of Predicted Genes: 3. ECM Strength: 13.6



1: cell cortex || 2: platelet dense tubular network membrane || 3: sarcoplasmic reticulum membrane || 4: apical part of cell || 5: brush border || 6: myelin sheath || 7: nuclear outer membrane || 8: platelet dense granule membrane || 9: platelet dense tubular network || 10: endosome membrane || 11: late endosome membrane || 12: lysosomal membrane

ECM 2, Gene set "platelet dense tubular network membrane", Page 1

Num of ECM Genes: 2. Num of Predicted Genes: 0. ECM Strength: 0.0

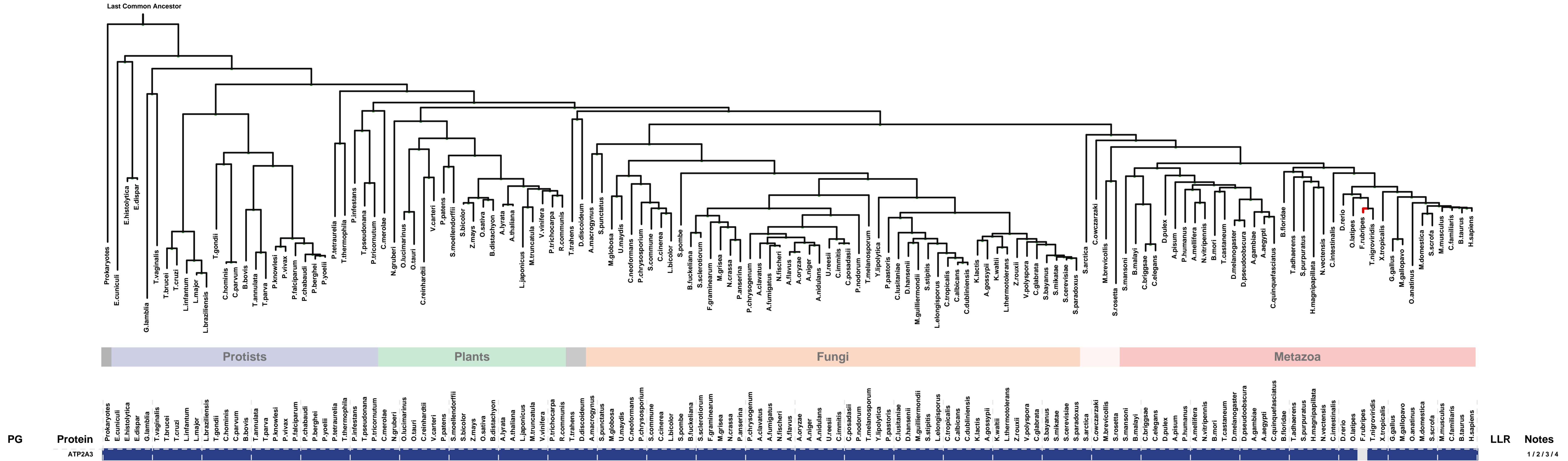


1: calcium channel complex || 2: endoplasmic reticulum-Golgi intermediate compartment || 3: H zone || 4: I band || 5: platelet dense tubular network membrane || 6: sarcoplasmic reticulum || 7: sarcoplasmic reticulum membrane

LLR Notes  
1/2/3/4/5/6/7  
5/6/7

ECM 3, Gene set "platelet dense tubular network membrane", Page 1

Num of ECM Genes: 1. Num of Predicted Genes: 0



1: nuclear membrane || 2: platelet dense tubular network membrane || 3: sarcoplasmic reticulum || 4: sarcoplasmic reticulum membrane



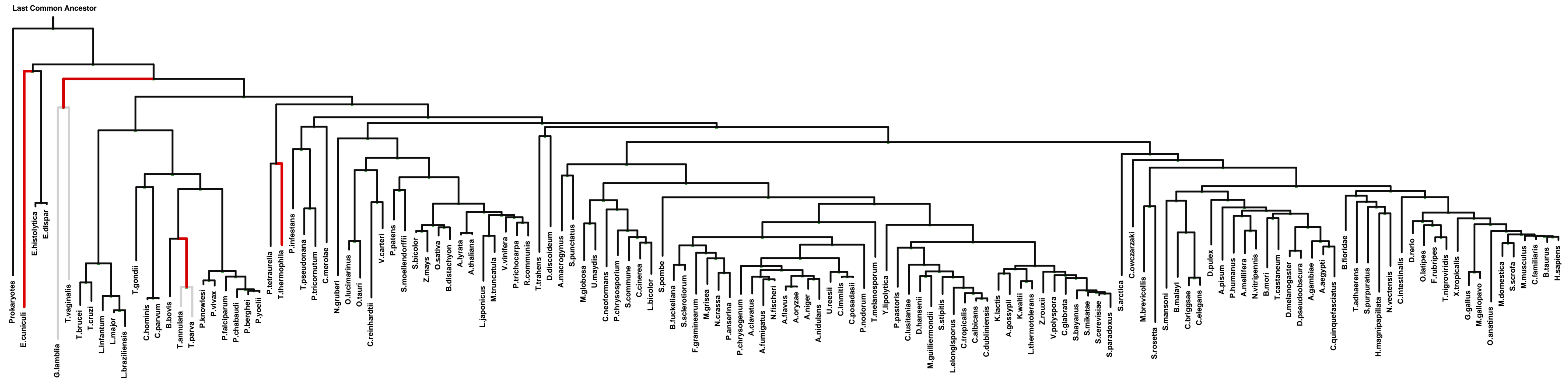
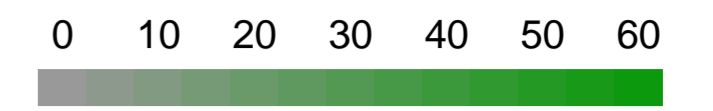
ECM 4, Gene set "platelet dense tubular network membrane", Page 2

Num of ECM Genes: 1. Num of Predicted Genes: 500

PRESENCE ———  
GAIN ———

ABSENCE ———  
LOSS ———

Log-likelihood Ratio Scale

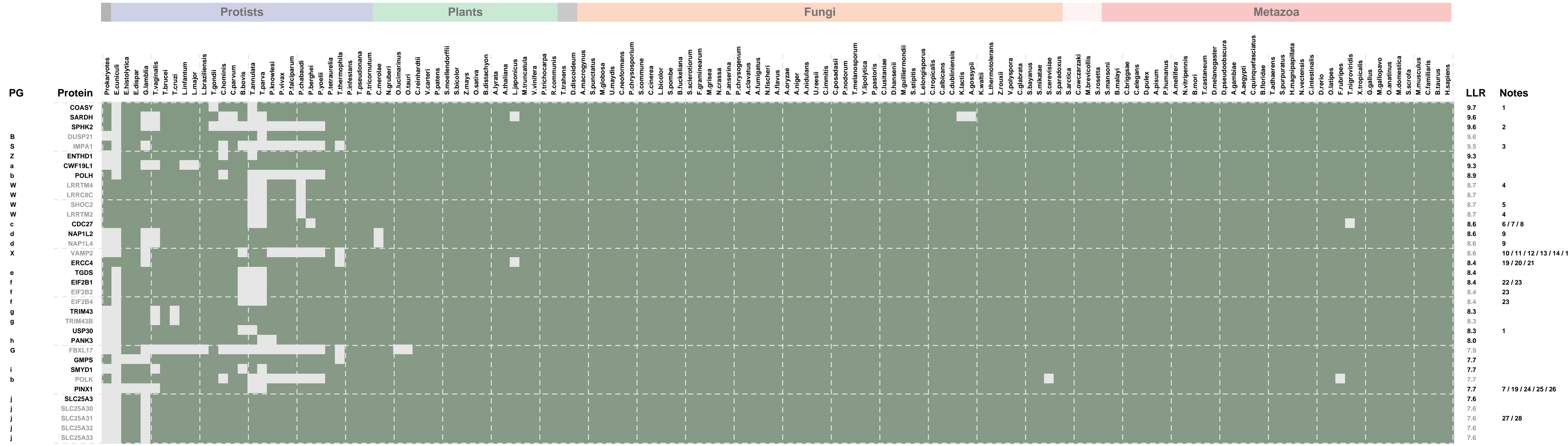
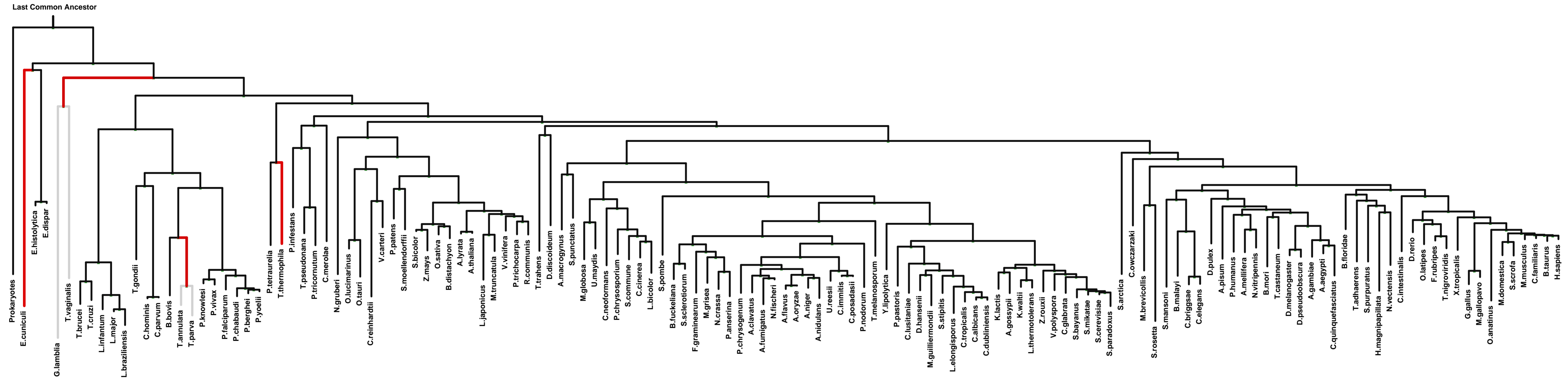


PG	Protein	Prokaryotes	Eukaryotes	Metazoa	LLR	Notes
H	UCHL3				16.3	
I	PFKFB2				16.0	
J	DNAJC6				15.7	
K	MCCC1				14.8	
L	SEC14L5				14.8	
M	IPO4				14.8	1
L	SEC14L1				14.8	
N	STX5				14.4	2 / 3
N	100510546				14.4	
O	EBNA1BP2				14.3	
O	CUL5				13.6	4
H	ABCC3				13.3	
H	UCHL5				13.2	5 / 6
P	PTPLAD1				12.9	
P	LDHB				12.8	
F	LOC128322				12.1	
Q	SV2C				11.8	7
C	HSD17B4				11.6	8 / 9 / 10
R	AMPD3				11.5	
R	AMPD1				11.5	
R	AMPD2				11.5	
S	IMPA2				11.3	
T	TMED4				10.8	
T	TMED9				10.8	2 / 11 / 12
T	TMED2				10.8	2 / 11 / 13 / 14 / 15 / 16
E	GNA11				10.8	17 / 18
B	DUSP27				10.5	
U	ZADH2				10.3	10
V	SNX7				10.3	19
V	SNX30				10.2	
H	UCHL1				10.1	
W	PHLPP2				10.0	
X	VAMP3				9.7	
Y	COX18				9.7	3 / 20 / 21 / 22 / 23 / 24
Y	MOCOS				9.7	25

1: nuclear pore || 2: endoplasmic reticulum-Golgi intermediate compartment membrane || 3: SNARE complex || 4: Cul5-RING ubiquitin ligase complex || 5: Ino80 complex || 6: proteasome complex || 7: synaptic vesicle membrane || 8: peroxisomal matrix || 9: peroxisomal membrane || 10: peroxisome || 11: endoplasmic reticulum-Golgi intermediate compartment || 12: trans-Golgi network transport vesicle || 13: COPI-coated vesicle || 14: COPI-coated vesicle membrane || 15: Golgi cisterna membrane || 16: zymogen granule membrane || 17: extrinsic to internal side of plasma membrane || 18: heterotrimeric G-protein complex || 19: cytoplasmic vesicle membrane || 20: clathrin-coated vesicle || 21: clathrin-coated vesicle membrane ||

ECM 4, Gene set "platelet dense tubular network membrane", Page 3

Num of ECM Genes: 1. Num of Predicted Genes: 500

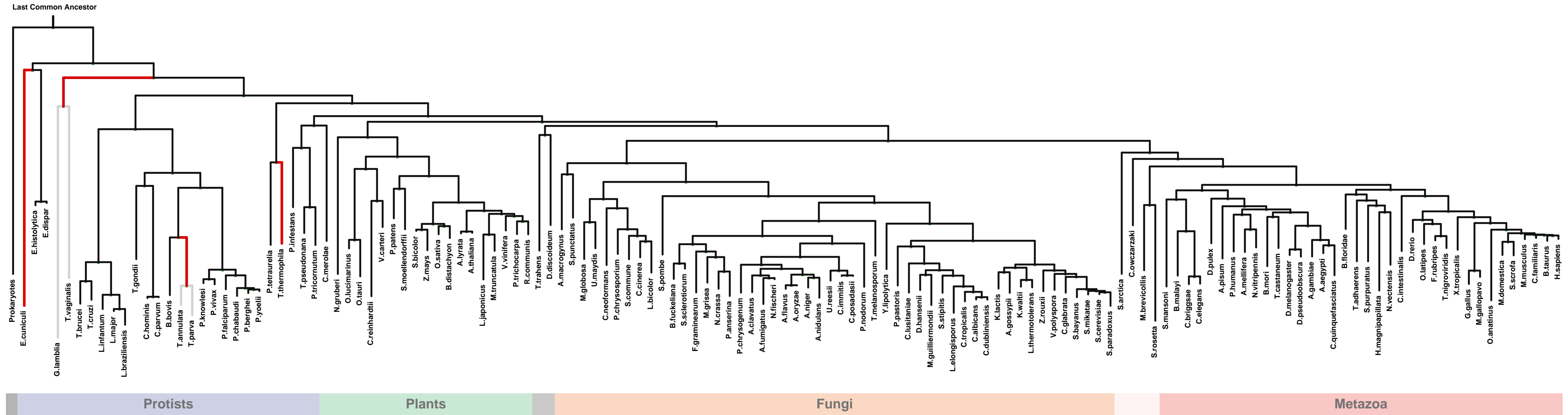


1: mitochondrial outer membrane || 2: lysosomal membrane || 3: axon || 4: postsynaptic membrane || 5: protein phosphatase type 1 complex || 6: anaphase-promoting complex || 7: spindle || 8: spindle microtubule || 9: chromatin assembly complex || 10: clathrin-coated vesicle || 11: clathrin-sculpted gamma-aminobutyric acid transport vesicle membrane || 12: clathrin-sculpted glutamate transport vesicle membrane || 13: clathrin-sculpted monoamine transport vesicle membrane || 14: endocytic vesicle membrane || 15: neuron projection || 16: secretory granule membrane || 17: SNARE complex || 18: synaptic vesicle membrane || 19: chromosome, telomeric region || 20: nuclear chromosome, telomeric region || 21: nucleotide-excision repair complex ||



ECM 4, Gene set "platelet dense tubular network membrane", Page 4

Num of ECM Genes: 1. Num of Predicted Genes: 500



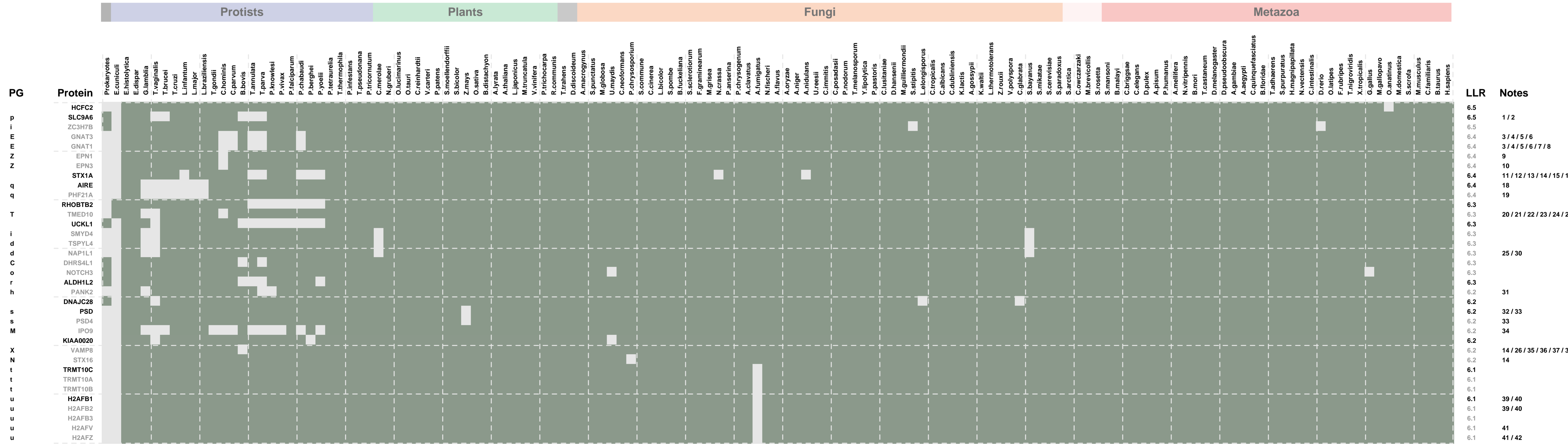
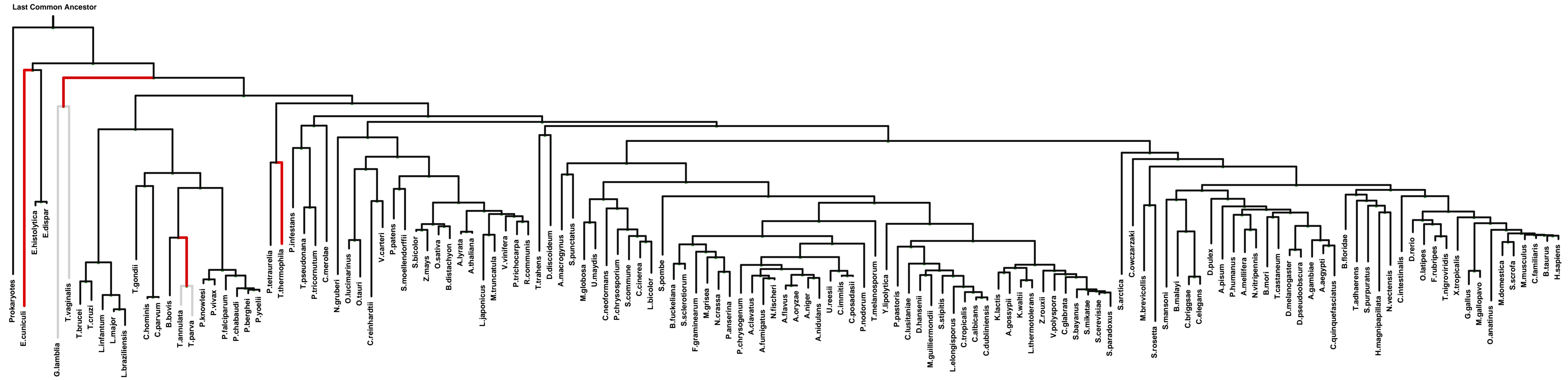
PG	Protein	LLR	Notes
j	SLC25A34	7.6	
j	SLC25A36	7.6	
j	SLC25A37	7.6	
j	SLC25A38	7.6	
j	SLC25A39	7.6	
j	SLC25A4	7.6	1
j	SLC25A40	7.6	
j	SLC25A41	7.6	
j	SLC25A42	7.6	
j	SLC25A43	7.6	
j	SLC25A44	7.6	
j	SLC25A45	7.6	
j	SLC25A48	7.6	
j	SLC25A5	7.6	2/3
j	SLC25A6	7.6	4
k	EIF2A	7.6	5
i	PRMT8	7.6	
i	CHMP2A	7.6	6
i	RBM15B	7.6	
A	ITSN2	7.6	
C	DECR2	7.6	7
	CHKA	7.6	
m	SF3B3	7.6	8/9/10/11
k	EIF3B	7.6	12
j	SLC25A1	7.6	
j	SLC25A10	7.6	
j	SLC25A11	7.6	
j	SLC25A12	7.6	
j	SLC25A13	7.6	
j	SLC25A14	7.6	
j	SLC25A15	7.6	
M	TNPO1	7.6	13
M	TNPO2	7.6	13
j	SLC25A16	7.6	
j	SLC25A17	7.6	7/14/15

1: mitochondrial outer membrane || 2: mitochondrial nucleoid || 3: MMXD complex || 4: mitochondrial inner membrane presequence translocase complex || 5: eukaryotic translation initiation factor 2 complex || 6: late endosome membrane || 7: peroxisome || 8: catalytic step 2 spliceosome || 9: small nuclear ribonucleoprotein complex || 10: spliceosomal complex || 11: U12-type spliceosomal complex || 12: eukaryotic translation initiation factor 3 complex || 13: nuclear pore || 14: integral to peroxisomal membrane || 15: peroxisomal membrane



ECM 4, Gene set "platelet dense tubular network membrane", Page 6

Num of ECM Genes: 1. Num of Predicted Genes: 500



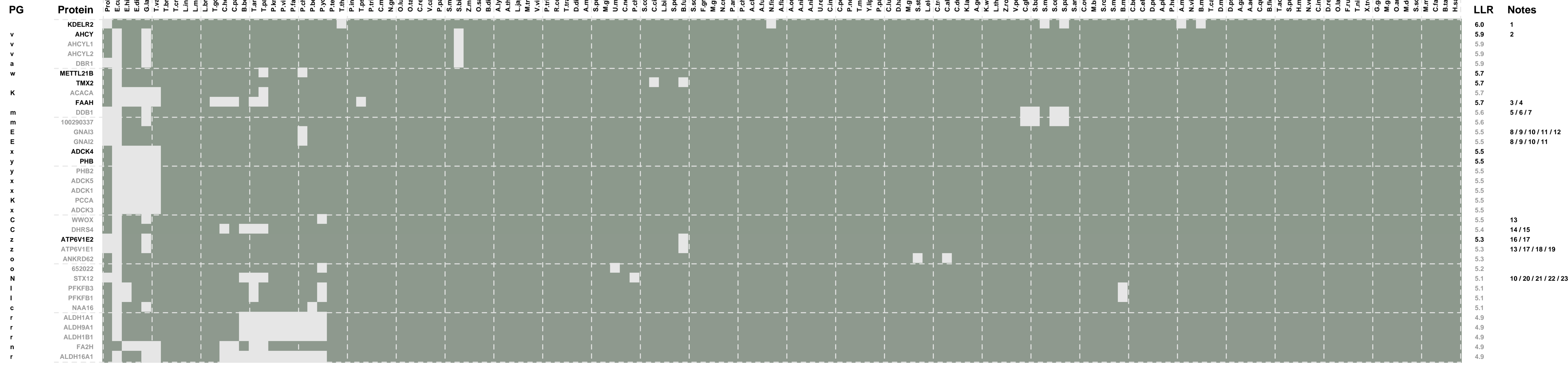
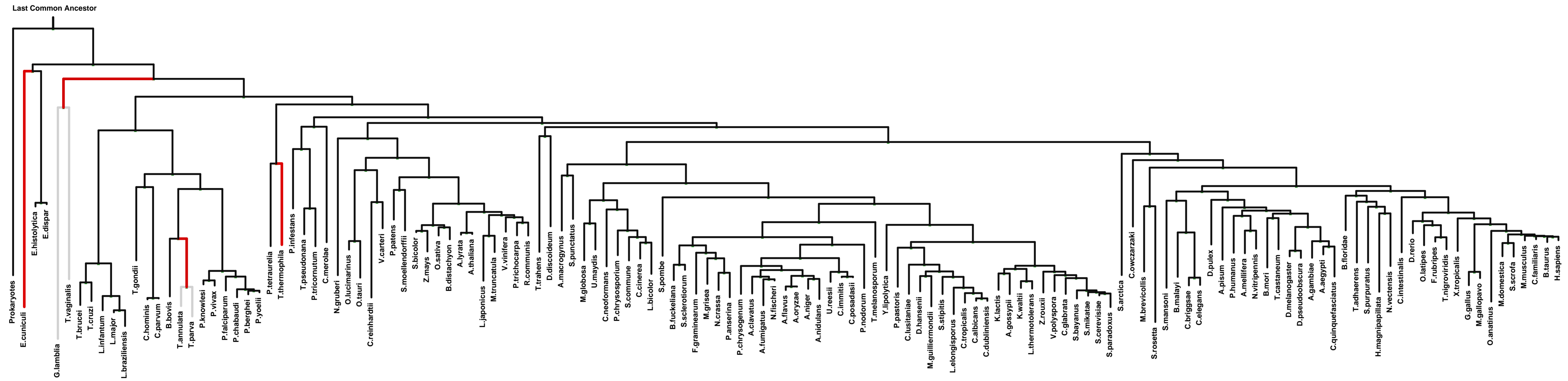
PG  
p  
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E  
Z  
Z  
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X  
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u

Protein	Prokaryotes	Protists	Plants	Fungi	Metazoa	LLR	Notes
HCF2						6.5	
SLC9A6						6.5	1 / 2
ZC3H7B						6.5	
GNAT3						6.4	3 / 4 / 5 / 6
GNAT1						6.4	3 / 4 / 5 / 6 / 7 / 8
EPN1						6.4	9
EPN3						6.4	10
STX1A						6.4	11 / 12 / 13 / 14 / 15 / 16
AIRE						6.4	18
PHF21A						6.4	19
RHOB2						6.3	
TMED10						6.3	20 / 21 / 22 / 23 / 24 / 25
UCKL1						6.3	
SMYD4						6.3	
TSPYL4						6.3	
NAP1L1						6.3	25 / 30
DHRS4L1						6.3	
NOTCH3						6.3	
ALDH1L2						6.3	
PANK2						6.2	31
DNAJC28						6.2	
PSD						6.2	
PSD4						6.2	32 / 33
IPO9						6.2	33
KIAA0020						6.2	34
VAMP8						6.2	
STX16						6.2	14 / 26 / 35 / 36 / 37 / 38
TRMT10C						6.2	14
TRMT10A						6.1	
TRMT10B						6.1	
H2AFB1						6.1	39 / 40
H2AFB2						6.1	39 / 40
H2AFB3						6.1	
H2AFV						6.1	41
H2AFZ						6.1	41 / 42

1: early endosome membrane || 2: recycling endosome membrane || 3: extrinsic to internal side of plasma membrane || 4: heterotrimeric G-protein complex || 5: photoreceptor inner segment || 6: photoreceptor outer segment || 7: photoreceptor connecting cilium || 8: photoreceptor outer segment membrane || 9: coated pit || 10: clathrin-coated vesicle || 11: actomyosin || 12: neuron projection || 13: secretory granule || 14: SNARE complex || 15: synaptic vesicle membrane || 16: synaptobrevin 2-SNAP-25-syntaxin-1a complex || 17: synaptobrevin 2-SNAP-25-syntaxin-1a-complexin I complex || 18: actin cytoskeleton || 19: histone deacetylase complex || 20: cis-Golgi network || 21: COPI-coated vesicle || 22: endoplasmic reticulum-Golgi intermediate compartment ||

ECM 4, Gene set "platelet dense tubular network membrane", Page 7

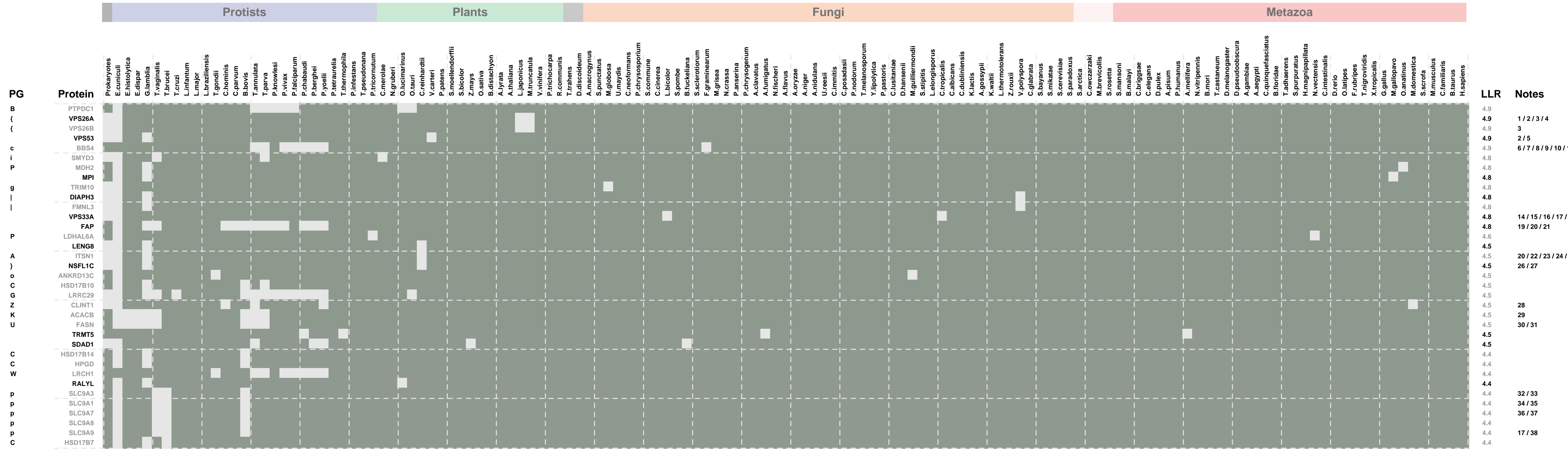
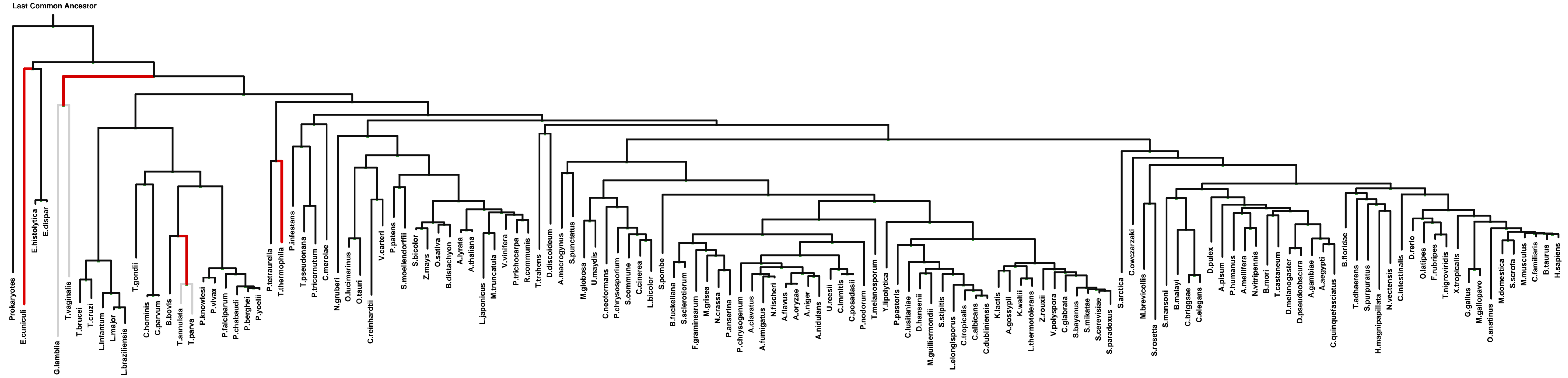
Num of ECM Genes: 1. Num of Predicted Genes: 500



1: cis-Golgi network || 2: melanosome || 3: endomembrane system || 4: organelle membrane || 5: Cul4A-RING ubiquitin ligase complex || 6: Cul4B-RING ubiquitin ligase complex || 7: Cul4-RING ubiquitin ligase complex || 8: extrinsic to internal side of plasma membrane || 9: heterotrimeric G-protein complex || 10: membrane raft || 11: midbody || 12: zymogen granule || 13: microvillus || 14: peroxisomal membrane || 15: peroxisome || 16: acrosomal vesicle || 17: proton-transporting two-sector ATPase complex, catalytic domain || 18: endosome || 19: proton-transporting two-sector ATPase complex || 20: BLOC-1 complex || 21: endosome membrane || 22: phagocytic vesicle || 23: SNARE complex

ECM 4, Gene set "platelet dense tubular network membrane", Page 8

Num of ECM Genes: 1. Num of Predicted Genes: 500



1: endosome || 2: endosome membrane || 3: retromer complex || 4: vesicle || 5: GARP complex || 6: BBSome || 7: centriolar satellite || 8: centriole || 9: cilium membrane || 10: microtubule basal body || 11: motile cilium || 12: nonmotile primary cilium || 13: pericentriolar material || 14: early endosome || 15: HOPS complex || 16: late endosome || 17: late endosome membrane || 18: lysosomal membrane || 19: invadopodium membrane || 20: lamellipodium || 21: lamellipodium membrane || 22: coated pit || 23: endocytic vesicle || 24: neuron projection || 25: synapse || 26: chromosome || 27: Golgi stack || 28: clathrin-coated vesicle || 29: endomembrane system || 30: glycogen granule ||



**ECM 4, Gene set "platelet dense tubular network membrane", Page 10**

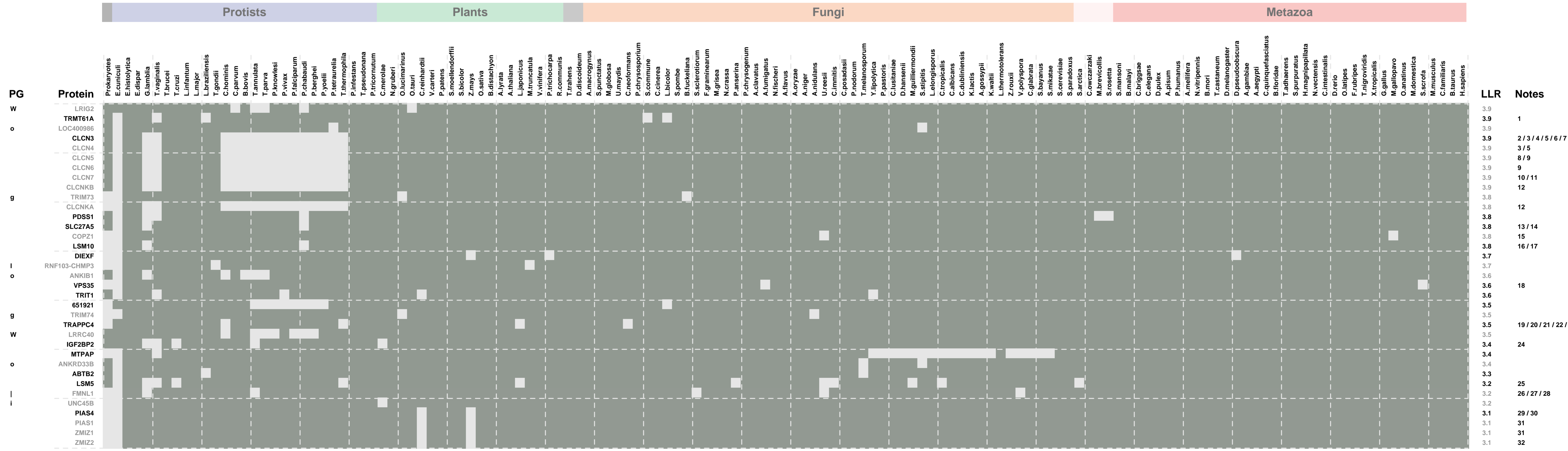
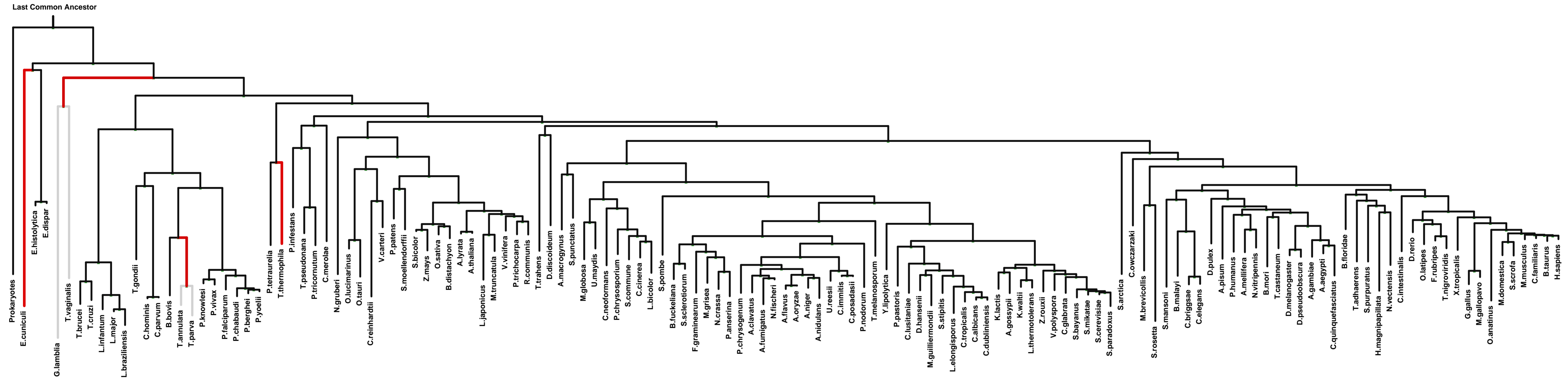
Num of ECM Genes: 1. Num of Predicted Genes: 500

PRESENCE ————  
GAIN ————

ABSENCE ————  
LOSS ————

Log-likelihood Ratio Scale

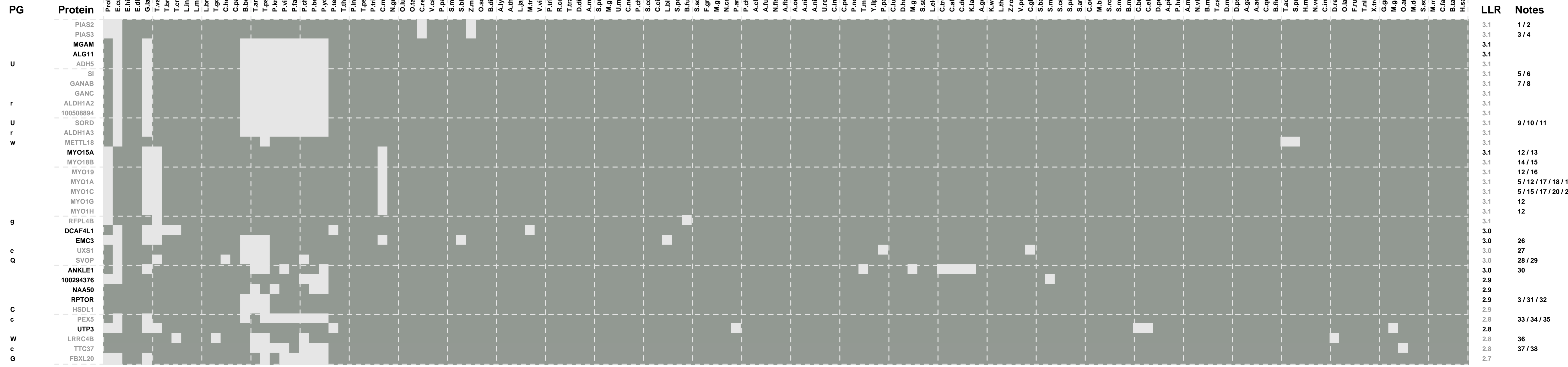
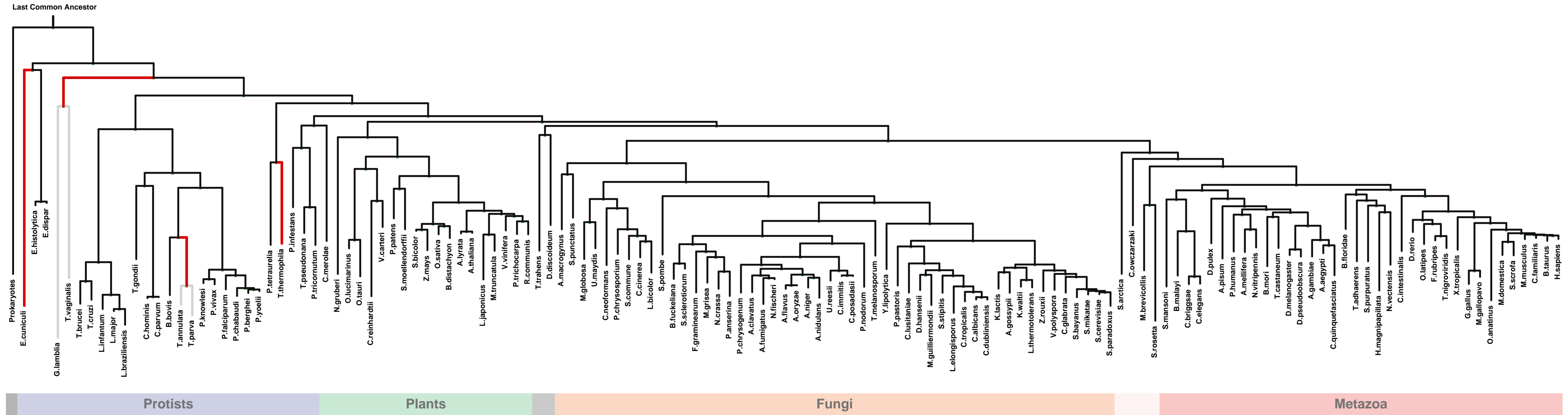
0 10 20 30 40 50 60



1: tRNA (m1A) methyltransferase complex || 2: early endosome || 3: early endosome membrane || 4: late endosome || 5: late endosome membrane || 6: transport vesicle membrane || 7: vesicle membrane || 8: apical part of cell ||  
 9: endosome membrane || 10: cytoplasmic vesicle || 11: lysosomal membrane || 12: chloride channel complex || 13: basal plasma membrane || 14: integral to endoplasmic reticulum membrane || 15: COPI vesicle coat || 16: Cajal body ||  
 17: U7 snRNP || 18: endosome || 19: dendrite || 20: Golgi stack || 21: synapse || 22: synaptic vesicle || 23: TRAPP complex || 24: cytoskeletal part || 25: ribonucleoprotein complex || 26: bleb || 27: cell cortex ||

ECM 4, Gene set "platelet dense tubular network membrane", Page 11

Num of ECM Genes: 1. Num of Predicted Genes: 500

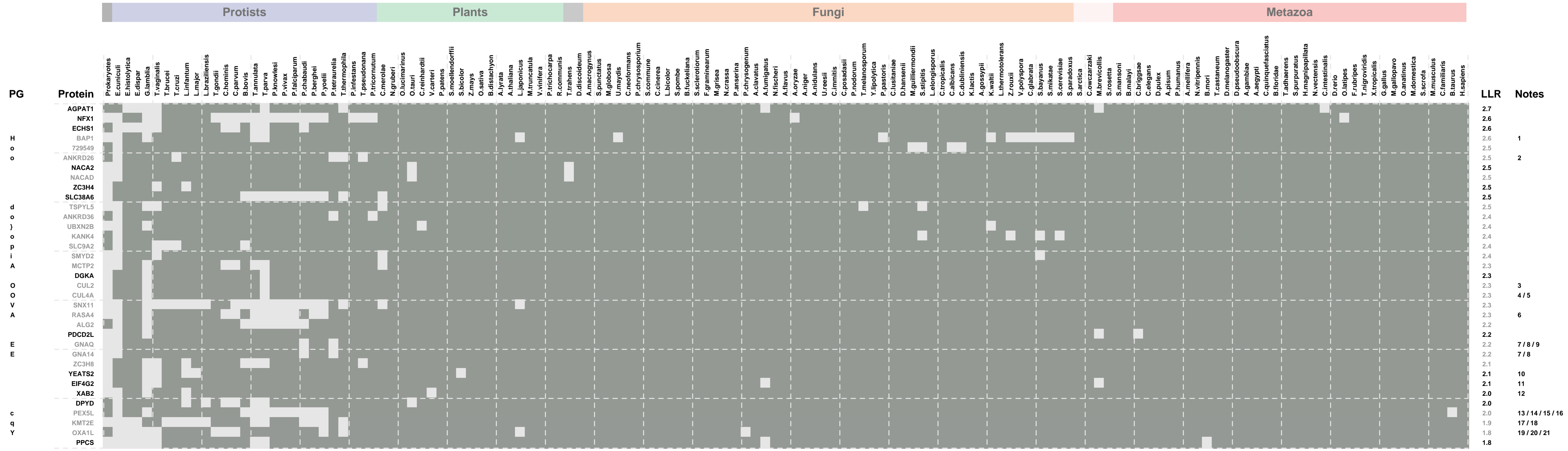
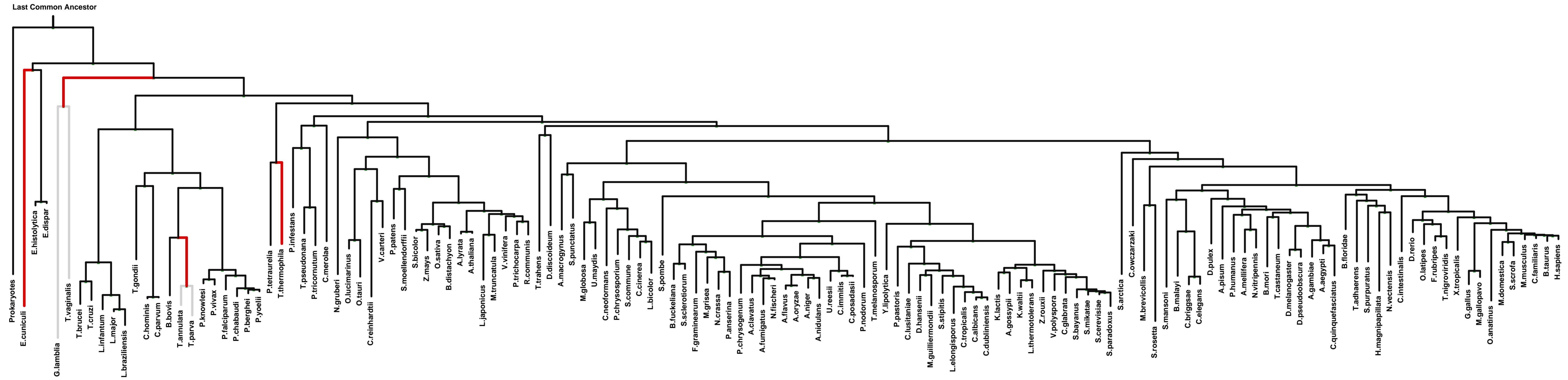


1: nuclear speck || 2: PML body || 3: dendrite || 4: synapse || 5: brush border || 6: membrane raft || 7: endoplasmic reticulum lumen || 8: melanosome || 9: cilium || 10: flagellum || 11: mitochondrial membrane || 12: myosin complex || 13: stereocilium || 14: sarcomere || 15: unconventional myosin complex || 16: mitochondrial outer membrane || 17: basal plasma membrane || 18: basolateral plasma membrane || 19: cortical actin cytoskeleton || 20: filamentous actin || 21: lateral plasma membrane || 22: microvillus || 23: nuclear pore || 24: stereocilium membrane || 25: stress fiber || 26: ER membrane protein complex || 27: Golgi cisterna membrane || 28: synaptic vesicle ||



ECM 4, Gene set "platelet dense tubular network membrane", Page 12

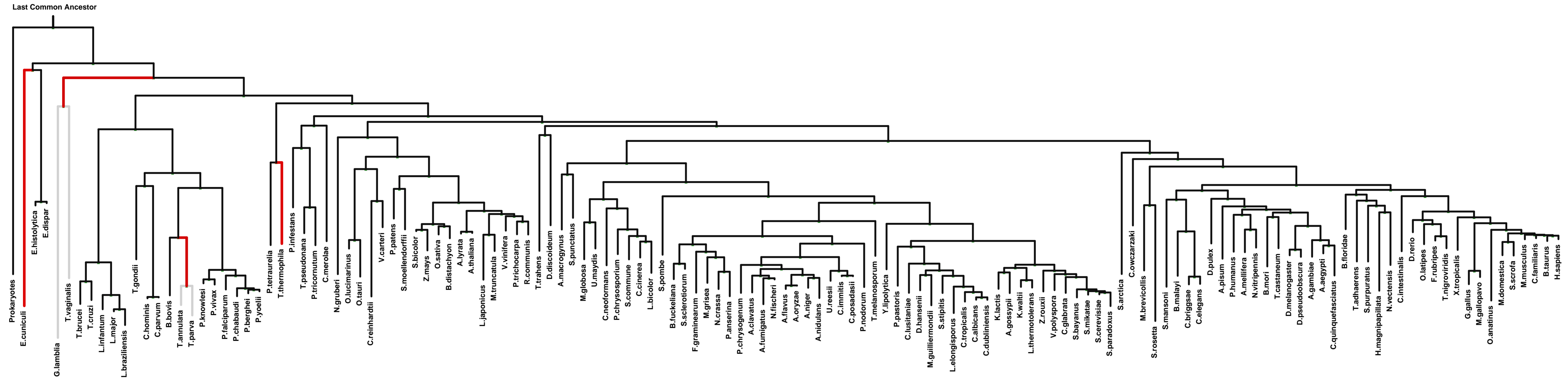
Num of ECM Genes: 1. Num of Predicted Genes: 500



1: PR-DUB complex || 2: actin filament || 3: Cul2-RING ubiquitin ligase complex || 4: Cul4A-RING ubiquitin ligase complex || 5: Cul4-RING ubiquitin ligase complex || 6: intrinsic to internal side of plasma membrane || 7: extrinsic to internal side of plasma membrane || 8: heterotrimeric G-protein complex || 9: nuclear membrane || 10: Ada2/Gcn5/Ada3 transcription activator complex || 11: eukaryotic translation initiation factor 4F complex || 12: catalytic step 2 spliceosome || 13: cell tip || 14: dendrite || 15: intracellular cyclic nucleotide activated cation channel complex || 16: peroxisomal membrane || 17: MLL5-L complex || 18: nuclear speck || 19: integral to mitochondrial membrane || 20: mitochondrial membrane || 21: mitochondrial respiratory chain

ECM 4, Gene set "platelet dense tubular network membrane", Page 13

Num of ECM Genes: 1. Num of Predicted Genes: 500



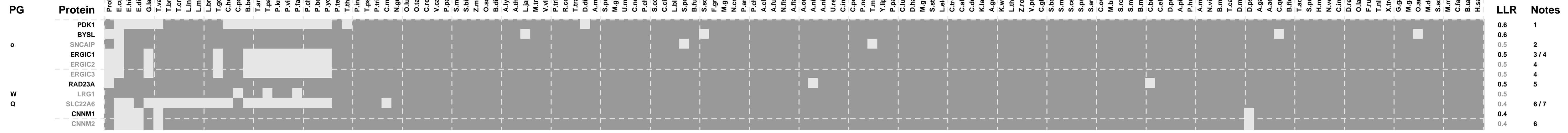
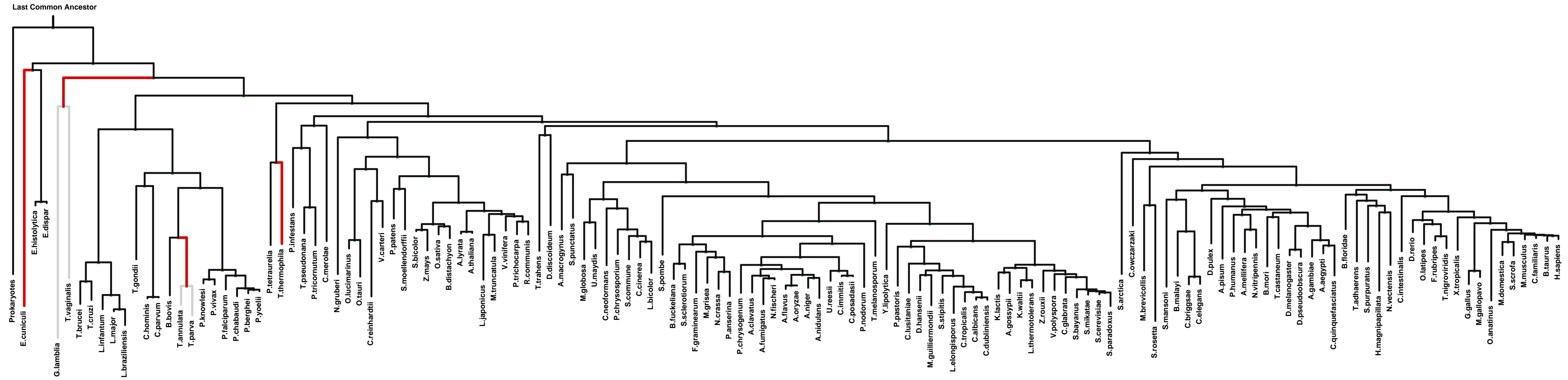
PG	Protein	Prokaryotes	Protists	Plants	Fungi	Metazoa	LLR	Notes
	RBBP6						1.8	1 / 2
	MYO18A						1.8	3 / 4 / 5
	CCNC						1.7	6 / 7
	LOC729468						1.7	
w	100287382						1.7	
	METTL21C						1.7	
	RABL6						1.7	
	PRPS2						1.7	
	PRPS1						1.7	
	PRPS1L1						1.7	
	TRMT2A						1.7	
K	PCCB						1.6	
w	METTL21A						1.6	
	ARHGAP22						1.6	
	SRI						1.5	8 / 9 / 10
e	NSDHL						1.5	11
o	ANKRD33						1.5	
	ZBTB17						1.5	
	BTF3						1.5	
	NOS3						1.5	12 / 13 / 14
	NAPB						1.5	15
	NAPA						1.5	15
	NOL6						1.5	16
	MYO6						1.4	6 / 12 / 17 / 18 / 19 / 20 / 21
	CAPN3						1.4	10 / 30 / 31
	GAPVD1						1.4	32
	TRAPPC3						1.4	33
	DBI						1.4	
	PRPSAP2						1.3	
	PRPSAP1						1.3	
E	TAF1L						1.3	34
	GNAZ						1.3	35 / 36 / 37
W	LRCH4						1.2	38
	MYO1D						1.2	5 / 39 / 40
	PPCDC						1.2	

1: chromosome || 2: microtubule organizing center || 3: actomyosin || 4: endoplasmic reticulum-Golgi intermediate compartment || 5: myosin complex || 6: DNA-directed RNA polymerase II, holoenzyme || 7: mediator complex || 8: sarcoplasmic reticulum membrane || 9: vesicle || 10: Z disc || 11: lipid particle || 12: apical part of cell || 13: caveola || 14: endocytic vesicle membrane || 15: synaptobrevin 2-SNAP-25-syntaxin-1a complex || 16: condensed nuclear chromosome || 17: axon || 18: cell cortex || 19: clathrin-coated endocytic vesicle || 20: clathrin-coated vesicle membrane || 21: coated pit || 22: cytoplasmic membrane-bounded vesicle || 23: endocytic vesicle || 24: filamentous actin || 25: microvillus ||



ECM 4, Gene set "platelet dense tubular network membrane", Page 15

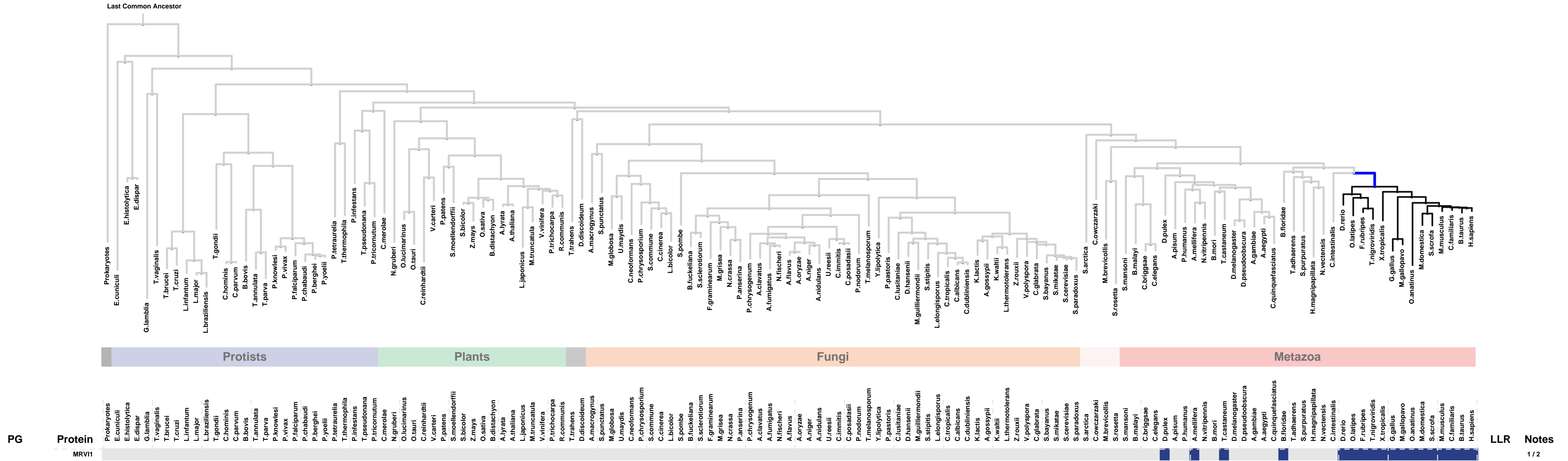
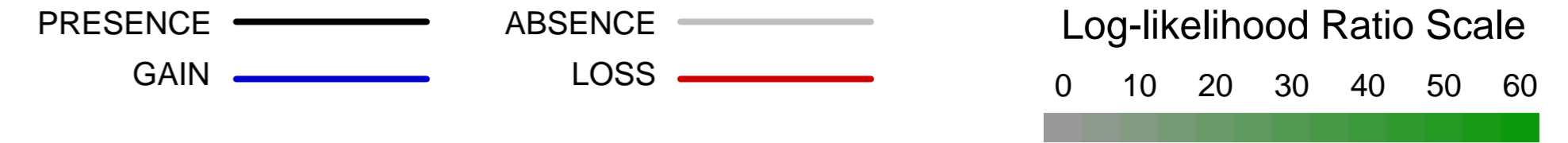
Num of ECM Genes: 1. Num of Predicted Genes: 500



1: pyruvate dehydrogenase complex || 2: presynaptic membrane || 3: endoplasmic reticulum-Golgi intermediate compartment || 4: endoplasmic reticulum-Golgi intermediate compartment membrane || 5: proteasome complex || 6: basolateral plasma membrane || 7: caveola

ECM 5, Gene set "platelet dense tubular network membrane", Page 1

Num of ECM Genes: 1. Num of Predicted Genes: 0



1: platelet dense tubular network membrane || 2: sarcoplasmic reticulum