

Supplemental Data

A single ancient origin for prototypical SR splicing factors

Sophie Califice, Denis Baurain[¶], Marc Hanikenne and Patrick Motte[¶]

[¶]To whom correspondence should be addressed.

E-mail: denis.baurain@ulg.ac.be, patrick.motte@ulg.ac.be

Table of contents

Supplemental Texts

Text S1. Detailed description of computational procedures.	4
---	---

Supplemental Table Legends.	17
------------------------------------	----

Supplemental Figure Legends.	19
-------------------------------------	----

Supplemental References.	28
---------------------------------	----

Supplemental Tables

Table S1. Taxonomic distribution of RRM-containing proteins.	Table S1 File
Table S2. Hand-curated corpus of RRM-containing proteins collected in the primary literature.	30
Table S3. Qualitative comparison of the five large RRM domain trees.	56
Table S4. Summary of the groupings observed for SR protein RRM1 domains.	58
Table S5. Compositional features specific of one or more SR subfamilies.	59
Table S6. Determination key for SR families and subfamilies.	60
Table S7. Statistics for the curated inventory of SR proteins in 20 selected proteomes.	61

Supplemental Figures

Figure S1. Scheme of the analysis pipeline.	62
Figure S2. Optimization of clustering parameters for RRM domains.	63
Figure S3. Evaluation of the selection algorithm for cluster representatives.	68
Figure S4. Color key for KOG annotation.	69
Figure S5. Maximum Parsimony tree of representative RRM domains.	70
Figure S6. RAXML tree of representative RRM domains obtained under the WAG+ Γ_4 model.	81
Figure S7. TREEFINDER tree of representative RRM domains obtained under the WAG+ Γ_4 model.	92
Figure S8. RAXML tree of representative RRM domains obtained under the LG+F+ Γ_4 model.	103
Figure S9. RAXML tree of the enlarged RRM dataset obtained under the WAG+ Γ_4 model.	114
Figure S10. Qualitative consensus of phylogenetic analyses of representative RRM domains.	130
Figure S11. Mutual affinities of SR protein RRM domains in the five large trees.	131
Figure S12. RAXML tree of the largest RRM clusters obtained under the LG+F+ Γ_4 model.	132
Figure S13. Exhaustive RAXML tree of SR-associated RRM1 domains (WAG+ Γ_4 model).	133
Figure S14. Exhaustive TREEFINDER tree of SR-associated RRM1 domains (WAG+ Γ_4 model).	137

Figure S15. RAXML tree of RRM1 domains from RNPS1-like proteins (WAG+ Γ_4 model).	141
Figure S16. TREEFINDER tree of RRM1 domains from RNPS1-like proteins (WAG+ Γ_4 model).	142
Figure S17. RAXML tree of RRM2 domains from dual RRM SR proteins (WAG+ Γ_4 model).	143
Figure S18. TREEFINDER tree of RRM2 domains from dual RRM SR proteins (WAG+ Γ_4 model).	147
Figure S19. RAXML tree of slowly evolving SR-associated RRM1 domains (WAG+ Γ_4 model).	151
Figure S20. TREEFINDER tree of slowly evolving SR-associated RRM1 domains (WAG+ Γ_4 model).	154
Figure S21. Sequence conservation in the first RRM domain of SR proteins.	157
Figure S22. Sequence conservation across prokaryotic RRM domains.	161
Figure S23. Sequence conservation across ZnK domains of SR proteins.	162
Figure S24. Distributions of relevant compositional features within SR subfamilies.	163
Figure S25. Architecture, conservation and compositional profile of SR subfamilies.	173
Figure S26. RAXML RRM tree of candidate SR proteins from selected proteomes (WAG+ Γ_4 model).	175
Figure S27. TREEFINDER RRM tree of candidate SR proteins from selected proteomes (WAG+ Γ_4 model).	178
Figure S28. RAXML tree of candidate SR proteins from selected proteomes (LG+F+ Γ_4 model).	181
Figure S29. PHYLOBAYES tree of candidate SR proteins from selected proteomes (CAT+ Γ_4 model).	184

Datasets

Dataset S1. HMM profiles for SR-associated RRM domains.	Dataset S1 File
Dataset S2. Accessions and sequences of SR proteins identified in the inventory.	Dataset S2 File
Dataset S3a. Architectures of candidate SR proteins from selected proteomes.	Dataset S3 File
Dataset S3b. 1-AA word densities in candidate SR proteins from selected proteomes.	Dataset S3 File
Dataset S3c. 2-AA word densities in candidate SR proteins from selected proteomes.	Dataset S3 File
Dataset S3d. 3-AA word densities in candidate SR proteins from selected proteomes.	Dataset S3 File
Dataset S4. Alignments in FASTA format.	Dataset S4 File

Text S1. Detailed description of computational procedures

1. RRM distribution across the Tree of Life

1.1. Data downloads

All complete prokaryotic and eukaryotic proteomes available on Ensembl and NCBI FTP servers were downloaded in November 2007 (<http://www.ncbi.nlm.nih.gov/sites/genome/>). Additional complete proteomes from photosynthetic eukaryotes were downloaded from JGI (*Aureococcus anophagefferens*, *Chlamydomonas reinhardtii*, *Ostreococcus lucimarinus*, *Ostreococcus tauri*, *Phaeodactylum tricornutum*, *Physcomitrella patens*, *Phytophthora ramorum*, *Phytophthora sojae*, *Thalassiosira pseudonana*, and *Volvox carteri*; <http://genome.jgi-psf.org/>) and TIGR (*Ricinus communis* and *Zea mays*; now located at <http://cmr.jcvi.org/>) servers. *Cyanidioschyzon merolae* and *Medicago truncatula* complete proteomes were downloaded from their respective project websites (<http://merolae.biol.s.u-tokyo.ac.jp/> and <http://medicago.org/>).

1.2. Prediction of RRM domains

The PFAM (Finn et al., 2010) alignment for the RRM domain (pfam00076; 79 domain sequences from 57 proteins) was downloaded from the NCBI Conserved Domain Database (CDD) (Marchler-Bauer et al., 2009) and used to build a HMM profile with the HMMBUILD component of the HMMER software package (<http://hmmer.org/>, see also Durbin et al., 1998). As mentioned on the PFAM website (<http://pfam.sanger.ac.uk/family?acc=PF00076>), the C-terminal β -strand and final helix are hard to align and have been omitted in the seed alignment, thus yielding a 72-amino-acid (AA) profile slightly truncated relative to the complete RRM structure. RRM domains were predicted in each complete proteome with the program HMMSEARCH (HMMER) using the HMM profile and a loose domain E-value threshold of 1e-5.

1.3. Extraction of RRM domains and RRM-containing proteins

HMMER reports were parsed to extract both the predicted RRM domains and the corresponding full-length proteins in FASTA format. To determine the best domain E-value threshold, sequences were repeatedly extracted using five increasingly stringent thresholds (1e-5, 1e-10, 1e-15, 1e-20, and 1e-25). Eventually, the threshold was set to 1e-10 as this value appeared to give the best compromise between sensitivity and specificity. RRM domains were numbered according to their N-term relative position within each protein (e.g., the second RRM domain of any given protein is numbered RRM2). Consequently, RRM domains located downstream of at least one unpredicted RRM domain (owing to an evolutionarily divergent sequence) were

assigned an incorrect number. This shortcoming was taken into account during annotation and manual analyses of RRM trees (see Sections 2.4-2.5). Finally, proteins containing more than one predicted RRM were extracted only once to ensure accurate statistics.

1.4. Prediction of putative SR proteins

Extracted RRM-containing proteins were tagged as 'putative SR' when they met the rather crude criterion proposed in reference (Boucher et al., 2001), i.e., having at least one occurrence of either quadripeptide 'RSRS' or 'SRSR'. Tagging was carried out for annotation purposes only; thus the absence of the 'SR' tag was never used to exclude a protein from subsequent analyses. For Figure 1C, RS/SR dipeptides were counted either in the complete dataset of non-redundant 8,042 RRM-containing proteins or in a subset of 197 proteins displaying at least 95% identity to reference sequences confirmed as SR or SRrp proteins (see Table S2 below for details).

1.5. Taxonomic distribution of RRM-containing proteins

For each domain E-value threshold, the numbers of RRM domains, RRM-containing proteins and putative SR proteins predicted in each complete proteome were compiled, along with proteome size and lineage, as fetched from the NCBI Taxonomy server (Benson et al., 2009; Sayers et al., 2009). Proteomes were further categorized according to domain (Archaea, Bacteria, or Eukaryota), complexity (unicellular vs. multicellular) and metabolism (standard vs. capable of oxygenic photosynthesis) and the influence of these factors was assessed using F-tests performed with the R statistical software (R Development Core Team, 2010). Though all eukaryotic and 126 prokaryotic proteomes yielded at least a few RRM-containing proteins, most prokaryotic and viral proteomes appeared devoid of RRM domains (Figure 1A-B and Table S1). These were nevertheless included for completeness.

2. Origin and evolution of SR proteins

2.1. Clustering of RRM domains

To allow phylogenetic analyses, the large number of RRM domains extracted in Section 1.3 (12,023 at the 1e-10 threshold) was reduced to a more tractable dataset through a two-step clustering based on sequence similarity.

First, exactly identical domains were consolidated and renamed after the most inclusive taxonomic group of each cluster members (e.g., a RRM domain found in both *Mus musculus* and *Rattus norvegicus* proteomes would be renamed 'Murinae'). Most of the time, merged domains corresponded to orthologues of closely related organisms or to in-paralogues (i.e.,

terminal gene duplications specific to an organism or to a small clade) or to protein isoforms. This step roughly reduced the number of RRM domains by 50% (6,633 at the 1e-10 threshold). Second, these unique RRM domains were more aggressively clustered by single-linkage using the (now deprecated) BLASTCLUST component of the NCBI C toolkit (Altschul et al., 1997). Two main parameters control the granularity of the clustering: these are the similarity threshold (fraction of identical residues in the local pairwise alignment) and the coverage threshold (fraction of the longest sequence covered by the alignment) that are to be reached to consider two domains as neighbors. To ensure the best clustering (C_k), we explored the parameter space for both thresholds (by steps of 0.05) and chose the combination of values that maximized a composite score rewarding normalized entropy (Cover and Thomas, 2006) but penalizing the number of singleton clusters (i.e., having only one domain) :

$$Sc = \frac{H(C_k)}{\log K} - 0.8 \frac{N_1}{N}$$

where

$$H(C_k) = - \sum_{k=1}^K \frac{N_k}{N} \log \frac{N_k}{N}$$

with N = total number of domains

K = number of clusters

N_k = number of domains in cluster k

N_1 = number of singleton clusters

As shown in Figure S2, optimal parameters were as follow: similarity threshold = 0.60 and coverage threshold = 0.85. These values held for domain E-value thresholds ranging from 1e-5 to 1e-20 and this step further reduced the cluster number by 80% (down to 1266 at the 1e-10 threshold). In the clustered datasets, each cluster was represented by the sequence of one of its domains and names were attributed as in the first step, albeit often resulting into much higher level taxa (e.g., Viridiplantae, Eukaryota, cellular organisms).

By default, BLASTCLUST selects the longest sequence as the cluster representative. Since longer sequences are also more prone to be evolutionarily divergent (due to the accumulation of non-conserved insertions), we modified BLASTCLUST to instead allow the selection of the most slowly evolving cluster sequence. In practice, for each cluster, the domain showing the highest average similarity with non-cluster domains was selected as the cluster representative. Our algorithm is an independent re-implementation of the approach used in the SCAFOS software package (Roure et al., 2007). The usefulness of this modification was evaluated by comparing

the length of the phylogenetic trees inferred by parsimony (see Section 2.3 for details) from three alternative datasets based on the selection strategy applied: (i) longest sequence; (ii) most slowly evolving sequence; (iii) fastest-evolving sequence (control experiment). Out of 1266 clusters, there were 352 differences when comparing cluster representatives between strategy (i) and (ii); 299 between (i) and (iii); and 479 between (ii) and (iii). In terms of performance, Figure S3 shows that strategy (ii) generally yielded the shortest trees, followed by strategies (i) and (iii). These results indicate that our algorithmic modification to BLASTCLUST should help to reduce the occurrence of phylogenetic artifacts by actively avoiding the selection of evolutionarily divergent sequences.

In the following, the 1266-cluster dataset built by selection of the most slowly evolving RRM domains was used as the basis of all analyses.

2.2. Alignment of RRM domains

Due to weak conservation combined to a large number of RRM domains to consider, standard alignment methods (e.g., CLUSTALW) led to overly wide alignments with so many gaps that they were practically unusable (data not shown). Alternatively, RRM domains were aligned with HMMALIGN (HMMER) against the HMM profile already used for their prediction (see Section 1.2). To control alignment width, amino acids that did not align to match states of the profile were discarded (option -m), thus literally 'splicing' autapomorphic (and unalignable) insertions out of longer domain sequences. Consequently, the resulting alignment had only 72 AA positions, as many as the HMM profile. Visual inspection of the 1266 domain sequences indicated that this alignment was suitable for large-scale analyses.

2.3. Phylogenetic analyses of RRM domains

The large alignment of RRM domains was analysed by Maximum Parsimony (MP) using PAUP* (Swofford, 2002) (Figure S5) and by Maximum Likelihood (ML) using either TREEFINDER (Jobb et al., 2004) with a WAG+ Γ_4 model (Yang, 1993; Whelan and Goldman, 2001) (Figure S7) or RAXML with the very similar PROTMIXWAG model (Stamatakis et al., 2005) (Figure S6) or with the LG+F+ Γ_4 model (Le and Gascuel, 2008) (Figure S8). SEQBOOT and CONSENSE from the PHYLIP software package (Felsenstein, 2005) were used respectively to generate 100 bootstrap replicates (Felsenstein, 1985) for each analysis and to compute support values. Bayesian inference with the CAT model known to reduce phylogenetic artifacts (Lartillot and Philippe, 2004; Lartillot et al., 2009; Philippe et al., 2011) was also investigated. However, this sophisticated model designed for phylogenomics did not yield useful results on our sequence-

rich but position-poor dataset, even after having run two independent PHYLOBAYES chains for more than 85,000 cycles (data not shown).

To evaluate our selection algorithm for representative cluster sequences (see Section 2.1) in a reasonable time, PAUP* was invoked with the following options: NREPS=1; ADDSEQ=RANDOM; SWAP=TBR; MAXTREE=10. In contrast, the tree built for phylogenetic purposes was inferred using more time-consuming options: NREPS=10; ADDSEQ=RANDOM; SWAP=TBR; MAXTREE=1000. As a consequence, the latter MP tree (Figure S5; 36,439 parsimony steps) was slightly shorter than the former (Figure S3; 36,617 parsimony steps).

Trees were rooted and left-ladderized using the TREEPLOT component of the MUST software package (Philippe, 1993). Since prokaryotic (and prokaryotic-containing) clusters were mostly concentrated in a small region of the tree, the root was set on the branch separating the bulk of these predominantly prokaryotic clusters from eukaryote-specific clusters. Automatic ladderization based on subtree content helped to order branches so that similarly composed subtrees were easily recognizable by eye across analyses.

2.4. Annotation of RRM trees

Prior to manual examination, RRM trees were automatically annotated using several data sources. To maximize the sensitivity, annotation was actually performed on the individual proteins corresponding to the RRM domains clustered in the trees. Thus, the main challenge was to keep track of the relationships between individual RRM domains (12,023) and RRM-containing proteins (8,042) on one side and cluster representative RRM domains (1266) on the other side, especially considering the two-step clustering and the taxonomic renaming of cluster representatives (see Section 2.1). Another challenge was to efficiently summarize the annotation of potentially numerous domains on the single tree leaf corresponding to each cluster representative. This was addressed by adding to leaf labels all annotation pieces that qualified at least 5% of cluster members, ordered by relevance within each data source. In addition to this relative measurement, stretches of stars (*) growing with the natural logarithm of the absolute number of domains qualified by each annotation piece were included. Finally, the color code of the most relevant (i.e., with the highest percentage) KOG annotation (see next paragraph and Figure S4) was applied to all labels for which the information was available. Altogether, this considerably facilitated visual comparison of the trees.

Two main data sources were used for annotation: (i) the KOG (Tatusov et al., 2003) component of NCBI CDD and (ii) a hand-curated corpus of about 500 RRM-containing proteins collected in the primary literature (Table S2). In preliminary experiments, other components (SMART, PFAM, COG, and PRK) of NCBI CDD were evaluated, but KOG was ultimately selected as the

most complete source. KOG was mined using RPS-BLAST (a variant of PSI-BLAST) (Altschul et al., 1997) with an E-value threshold of $1e-10$, whereas reference proteins were searched using BLASTP (or TBLASTN for reference mRNAs) with an identity threshold of 75%. More stringent thresholds (respectively $1e-25$ and 95%) were also considered but eventually abandoned due to a general lack of sensitivity that left most leafs without annotation. The flip side of adopting such a sensitive approach was a potential lack of specificity. That is why we took the resulting annotation with a grain of salt when analyzing the trees.

Other annotation bits added to leaf labels included: (iii) the number of domains in the cluster; (iv) the distribution of RRM numbers in the cluster (see Section 1.3 for the caveat about unpredicted RRM domains); (v) the amount of prokaryotic proteins; and (vi) the amount of 'putative SR' proteins. Notably, all annotation also applied to singleton clusters, except that numbers were dropped for simplicity. Furthermore, the following typographical conventions were enforced: (vii) prokaryotic-containing clusters in italic and (viii) clusters with domains from more than one species in boldface.

2.5. Analyses of an enlarged RRM dataset

Phylogenetic accuracy is known to be difficult to achieve. Consequently, robustness of phylogenetic inference is often assessed by analyzing the same alignment with multiple reconstruction methods and/or evolutionary models. Orthogonal to this approach, it is possible to enlarge or reduce the set of sequences included in the alignment. Experience has indeed shown that varying 'taxon sampling' is very efficient at uncovering phylogenetic artifacts (for reviews, see Delsuc et al., 2005; Philippe et al., 2005; Philippe et al., 2011). Here, both strategies were used to generate five different large RRM trees that were carefully compared to test the hypothesis of a single origin for SR splicing factors (see Section 2.6). As stated in Section 2.3, the first four trees (Figures S5-8) were inferred from the same 1266-cluster alignment. The purpose of this section is to explain how we assembled the huge alignment used for the fifth (even larger) tree (Figure S9).

As an alternative to complete proteomes used throughout this study, two other protein databases were mined for RRM domains: (i) NCBI RefSeq release 26 (Pruitt et al., 2007) and (ii) SMART 6 (Letunic et al., 2009). While RefSeq proteins were processed exactly as in Sections 1.2-1.3 (using the HMM profile for prediction), RRM domains and RRM-containing proteins were directly downloaded through the batch interface of the SMART website (<http://smart.embl-heidelberg.de/>). In both cases, the usual $1e-10$ domain E-value threshold was used for extraction, which respectively yielded 10,739 and 9,978 RRM domains (see Table S1 for taxonomic distributions).

RRM domains from all three sources (including complete proteomes) were then merged into one huge (yet overlapping) dataset and clustered using the same parameter values as in Section 2.1 to give a non-redundant dataset of 1831 clusters (to be compared to the 1266 clusters of complete proteomes alone). Automated alignment with HMMALIGN resulted in an alignment that had again 72 AA positions and that was analyzed using RAXML with the WAG+ Γ_4 model. Finally, the tree was rooted on most prokaryotic domains, left-ladderized and annotated, even if its assembly from multiple sources made the process more difficult.

2.6. Comparison of large RRM trees and phylogenetic analysis of the largest RRM clusters

The overall congruence of the large RRM trees was manually assessed by taking advantage of the multiple annotation pieces described in Section 2.4. The primary criterion was the KOG color coding, along with matches to RRM-containing reference proteins. The RRM number was also heavily used for proteins with multiple (up to six) RRM domains. For practical reasons, we mainly focused on leafs (clusters) representing a large number of RRM domains and/or including matches to reference RRM-containing proteins. When comparing the five different trees, two types of issues pertaining to RRM associations were examined: (i) *do proteins from a given KOG consistently group together?* and (ii) *do different KOG consistently group together?* These analyses allowed us to identify 88 groupings that were generally stable across the trees (Table S3). Associations between these groupings are summarized in a qualitative consensus tree (Figure S10). Altogether, mutual affinities among groups of SR-associated RRM domains suggested that most SR proteins share a single origin (Figure S11 and Table S4).

To check that SR proteins indeed derive from a common ancestor, an additional ML tree focusing on the 152 largest multi-species RRM clusters was computed using RAXML with the LG+F+ Γ_4 model (Figures 2 and S12). Briefly, the 1266-cluster RRM alignment was filtered to discard sequences that did not represent at least 8 RRM domains. We also removed 5 more sequences that represented larger RRM clusters, of which sequences all came from a single species, as these corresponded to multiple in-paralogues and/or mis-predicted proteins: *Caenorhabditis*@F42A6_7a_1_RRM_2, (8 domains), *Caenorhabditis*@Y46G5A_13_RRM_3 (10), *Caenorhabditis*@Y73B6BL_6a_3_RRM_2 (10), *Caenorhabditis*@Y73B6BL_6b_3_RRM_1 (10), and *Danio* @ENSDARP00000091192_RRM_1 (14). Therefore, the 152 retained sequences represented 10,101 of the 12,023 originally retrieved RRM domains (84%). Strikingly, in this sparser yet still unbiased tree, the RRM1 domains of most SR proteins were resolved as a single clade, while the global phylogenetic resolution was much improved (Figures 2 and S12). This result greatly strengthened our confidence in a single origin of main SR protein architectures.

2.7. Phylogenetic analyses of SR-associated RRM domains

To analyze the subsequent evolution of SR proteins, we decided to focus on three subtrees (shown in pink in Figure S6). For each subtree, RRM domains hidden behind each leaf were extracted from the 6,633-cluster dataset obtained after the first clustering step (see Section 2.1). Starting from this non-redundant dataset allowed us to greatly refine our sampling and to discard any potential mis-clustering caused by the greedy single linkage algorithm of BLASTCLUST, while ensuring that no duplicate domains were included. RRM domains were anew aligned using the HMM profile but this time without discarding insertions to preserve as much phylogenetic information as possible. The resulting alignments were cursorily optimized by hand using the interactive editor ED (MUST) then analyzed by ML using both TREEFINDER and RAXML with the WAG+ Γ_4 model, yielding six small RRM trees (Figures S13-18) out of three datasets. After automatic annotation as already described, the trees computed from the RRM1 of SR45/RNPS1 proteins (42 domains x 73 AA; Figures S15-16) and from the RRM2 of dual RRM SR proteins (349 domains x 97 AA; Figures S17-18) were directly interpretable, whereas the poor phylogenetic resolution of those inferred from the RRM1 of SR proteins (434 domains x 93 AA; Figures S13-14) prompted us to experiment with variations in taxon sampling.

In a first variant, we removed 130 fast-evolving domains (i.e., having long branches in the trees) to reduce the occurrence of phylogenetic artifacts, which helps to improve resolution. The two trees inferred from this curated dataset (304 domains x 87 AA) are shown in Figures S19-20. Then, we produced three more variants of this curated dataset by removing domains either from RS proteins (292 domains x 85 AA) or from dual ZnK SR proteins (297 domains x 87 AA) or from both subfamilies at the same time (285 domains x 85 AA). The trees obtained from these additional datasets are not shown but were used to monitor the effect of alternative samplings on the phylogenetic resolution of the relationships among the remaining SR-protein families and subfamilies (Table 1).

Along with RRM1/RRM2 and ZnK sequence logos (see Section 3.2), thorough comparison and integration of 5 (+1) large and 14 small RRM trees (see Section 4.2 for 4 more small trees) together laid the basis of our scenario for the single origin and subsequent diversification of SR proteins into 4 natural families (Figures 2-3 and S10-11 and Tables 1 and S3-4).

3. Profiling of sequence features in SR families

3.1. Extraction of RRM domains of SR-protein subfamilies

Based on the curated RAXML tree of SR-associated RRM domains (Figure S19), RRM1 domain sequences corresponding to each SR-protein subfamily were extracted from the initial 12,023-domain dataset (see Figure 3 for an up-to-date nomenclature). Subfamilies defined in this tree were (i) SC35; (ii) SCL; (iii) SRp; (iv) 9G8; (v) SRp20; (vi) RSZ; (vii) RS2Z; (viii) animal ASF-like; (ix) plant ASF-like; (x) SRp40-55-75; and (xi) RS. Similarly, the two remaining small RAXML trees were used to extract the RRM1 of (xii) SR45 and of (xiii) RNPS1 (Figure S15), as well as the RRM2 of animal ASF-like and of SRp40-55-75 (Figure S17). Owing to its evolutionary divergence, the RRM2 of the RS family had to be extracted from the large RAXML/WAG tree inferred from complete proteomes (Figure S6). Furthermore, to complete our subfamily-specific RRM domain datasets, the missed RRM2 of the plant ASF-like subfamily was predicted anew using a very loose domain E-value threshold (0.1) directly on the corresponding proteins.

As explained in the main text, the RRM of human SRp54 was also too divergent to be detected by the universal HMM profile. This SR protein was thus not investigated in our study as it would have featured a very long branch prone to phylogenetic artifacts. To complicate matters, the official SRP54 symbol actually corresponds to another protein, the signal recognition particle 54 kDa (ENSG00000100883), which is a ribonucleoprotein belonging to the GTP-binding SRP family and devoid of RRM domain... yet interacting with RNPS1! See <http://www.uniprot.org/uniprot/P61011> for details.

3.2. Sequence logos of aligned RRM and ZnK domains of SR-protein subfamilies

Within each subfamily, RRM1 domains were carefully aligned with ED (MUST) using the secondary structure as a guide. To improve alignments, minor domain-specific insertions (1-2 AA) were occasionally spliced out, while a handful of divergent domains were excluded. Then, RRM2 domains from dual RRM SR subfamilies were separately aligned. Finally, subfamilies were aligned with each other based on their consensus sequences to yield a high-quality structural alignment including RRM1 and RRM2 domains from all SR-protein subfamilies. Using different excerpts of this alignment, sequence logos (Schneider and Stephens, 1990) for each subfamily (Figure 4; see also Figure S21) were computed with WEBLOGO (Crooks et al., 2004) after enabling the correction for small samples.

Two overlapping strategies were used to sample prokaryotic RRM domains: (i) either all prokaryotic domains found in the initial dataset or (ii) only those located in the mainly prokaryotic subtrees used to root the large RAXML/WAG tree (Figure S6). The resulting

prokaryotic RRM datasets (cleared of potential eukaryotic contaminants) were processed as SR-protein subfamilies to generate the corresponding sequence logos (Figure S22).

To predict ZnK domains, a HMM profile was built from the PFAM alignment for the zf-CCHC domain (pfam00098; 182 domain sequences from 109 proteins). As for RRM domains before, ZnK domains were predicted in all complete proteomes. However, only those corresponding to single RRM ZnK-like SR subfamilies were actually extracted, thus resulting in four small datasets: 9G8, RSZ, RS2Z (left) and RS2Z (right). To increase the sampling for RSZ and RS2Z, ZnK domains from SR proteins identified in the inventory of additional proteomes (see Sections 4.1-4.4) were also included. Alignments and logos were easy to obtain due to the apparent constraint on size characterizing these domains (Figure S23).

3.3. Profiling of compositional features in SR-protein subfamilies

Full-length proteins corresponding to subfamily datasets used for RRM logos were collected and submitted to blind compositional analyses. First, a 24-AA sliding window was moved (1 AA at a time) along every individual protein. At each step, the numbers of occurrences for all possible overlapping unordered words of size 1 to 3 AA were recorded. Unordered means that occurrences of, e.g., SR and RS dipeptides were consolidated, while overlapping means that, e.g., the SRR tripeptide was counted as either (i) 1xS and 2xR or (ii) 1xRS/SR and 1xRR or (iii) 1xRRS/RSR/SRR, depending on word size. These word densities were then plotted for all proteins of each subfamily (data not shown, but see Dataset S3b-d for an illustration of a similar procedure). To avoid unnecessary clutter, density curves that did not reach a predefined threshold (1 AA: 8; 2-3 AA: 6) for any protein within a subfamily were discarded. After visual inspection of the resulting graphs, a series of words were identified as potentially useful for discriminating the different SR subfamilies (Table S5). Second, this preselection was refined by comparing the distribution (across all proteins of a given subfamily) of each word between subfamilies. Since we were mostly interested in inter-domain compositional features, promising words were tracked in particular protein regions: (i) before the first domain; (ii) between the first and the second domain; and (iii) after the last domain. This process led to one graph per word/region combination, each displaying the distribution of the compositional feature in every SR subfamily (Figure S24). Third, one representative protein was selected out of each subfamily, except for SRp40-55-75 and animal ASF-like, from which were selected three (SRp40, SRp55, SRp75) and two (ASF/SF2 and SRp30c) representatives, respectively. These proteins were used to graphically summarize the results of the compositional profiling (Figures 5 and S25).

3.4. Profiling of conservation in SR-protein subfamilies

The same full-length protein datasets were automatically aligned with CLUSTALW (Thompson et al., 1994). Alignments were then analyzed with the program PLOTCON (EMBOSS software package, Rice et al., 2000) to profile sequence conservation in every subfamily. Briefly, conservation along aligned proteins was computed by averaging all possible pairwise scores (using the EBLOSUM62 similarity matrix) at each position within a 24-AA sliding window. To allow a perfect juxtaposition with composition profiles, subfamily alignments were first cleared of sequence insertions relative to the representative proteins selected in Section 3.3. In practice, columns corresponding to positions missing in these proteins were removed from the alignments using the program NET (MUST), which implies that, for each subfamily, PLOTCON actually analyzed an alignment of exactly the same length as the protein representing the subfamily (Figures 5 and S25).

3.5. Development of a determination key for classifying SR proteins

To help classifying uncharacterized SR proteins, a determination key was developed by integrating most of our analyses: (i) protein architecture; (ii) conserved motifs in RRM domains; and (iii) compositional features (Table S6). This key was validated on candidate SR proteins identified in Sections 4.1-4.4.

4. Inventory of SR proteins in selected organisms

4.1. Optimized prediction of SR-associated RRM1 domains

Our original HMM profile for the RRM domain was deliberately universal in order to sample as much functional diversity as possible. This allowed us to investigate the origin and evolution of SR proteins using the ubiquitous RRM domain as a proxy for whole proteins. However, for uncharacterized proteomes, directly predicting domains that belong to SR proteins is more advantageous. To this end, six new HMM profiles optimized for the prediction of SR-associated RRM1 domains were computed from our alignments. The first three profiles were built from two sequence-rich but automatically HMM-aligned RRM1 subtrees (Figures S12,14; outgroups excluded), whereas the three remaining profiles were derived from RRM1 sequence logos (Figure S21), which had been structurally aligned by hand but lacked fast-evolving sequences.

These six new profiles were then tested on 20 selected proteomes: 13 model organisms already used in the previous analyses and 7 recently sequenced photosynthetic species (downloaded in June 2009; see Tables 2 and S7 for species list). HMMSEARCH was run with the same loose domain E-value threshold as in Section 1.2 ($1e^{-5}$) but each HMMER report ($6 \times 20 = 120$) was

individually examined to determine the optimal threshold. In practice, we set the threshold in the valley between the best hits (normally derived from SR proteins) and the remaining (non-SR) hits. For most reports, this task was rather easy to perform as the valley was unambiguous (except for *Aspergillus fumigatus* that did not yield any obvious SR-associated RRM1 domain). After consolidation of duplicates (i.e., predicted by more than one profile), a total of 247 candidate SR proteins were retained out of 19 proteomes.

4.2. Phylogenetic analyses of candidate SR protein RRM domains

RRM1 (and RRM2) domains from candidate SR proteins were extracted and automatically aligned on our structural alignment of SR-protein subfamily consensus sequences (see Section 3.2). This was carried out with the BABA component of the MUST software package, which also affiliated each candidate RRM domain to the most appropriate SR-protein subfamily.

The resulting high-quality alignment was then analyzed as in Section 2.3 (with both TREEFINDER and RAXML heuristics, as well as with PHYLOBAYES). Again, different variants of the dataset were considered: (i) with or without RRM2 domains; (ii) including or excluding positions corresponding to subfamily-specific insertions. Finally, we settled on a dataset containing all SR-associated RRM1 domains, along with RRM2 domains from plant RS proteins to test the duplication hypothesis (see main text), but no outgroup domains to minimize phylogenetic artifacts (Philippe et al., 2011). The trees, which eventually excluded subfamily-specific insertions, were rooted on the SR45/RNPS1 RRM domains (for convenience) and automatically annotated (Figures S26-29; see also Table 1 for the phylogenetic resolution of relationships among SR-protein families and subfamilies).

4.3. Architectural and compositional analyses of candidate SR proteins

The architecture of every candidate SR protein was elucidated by scripting the NCBI Conserved Domain Database web server (<http://www.ncbi.nlm.nih.gov/cdd/>). Consequently, domain identification was not restricted to RRM and ZnK domains but took advantage of the full breadth of domains available in CDD (Dataset S3a).

In parallel, candidate SR proteins were submitted to the blind compositional analyses already described, except that all candidate SR proteins were processed at the same time, rather than subfamily by subfamily as when selecting discriminating features (Dataset S3b-d).

4.4. Curation of candidate SR proteins

To assemble our curated inventory of SR proteins, candidates were validated by integrating the results of all aforementioned analyses. At the domain level, we considered the subfamily attributed by the alignment procedure as well as the phylogenetic position of the RRM1 domain in the last trees (Figures S26-29). At the protein level, we applied our determination key (Table S6) based on the architectural and compositional profiling of candidates (Dataset S3a-d). For dubious cases, confirmatory searches were conducted on the NCBI BLAST website (<http://blast.ncbi.nlm.nih.gov/>). This stepwise validation led to the confirmation of 192 proteins as genuine SR proteins along with 52 isoforms, of which the overwhelming majority could be classified into one of the previously identified subfamilies (Table 2; see also Table S7).

Table S1. Taxonomic distribution of RRM-containing proteins. The three Excel sheets summarize the statistics for RRM domain, RRM-containing and putative SR protein content per proteome for each data source: (i) complete proteomes; (ii) NCBI RefSeq; and (iii) SMART database. Statistics are given for the five domain E-value thresholds (1e-5, 1e-10, 1e-15, 1e-20 and 1e-25) used in the prediction of RRM domains. Proteomes are sorted by taxonomic lineage, except that proteomes devoid of RRM domains are listed at the bottom.

Table S2. Hand-curated corpus of RRM-containing proteins collected in the primary literature. Reference proteins are organized by family. For convenience, an independent bibliography is provided at the end of the corresponding file.

Table S3. Qualitative comparison of the five large RRM domain trees. The Table is a companion to Figure S10. Node numbers match those given in tree annotations (Figures S5-9) and in other comparative display elements (Figures S10-11 and Table S4). Unstable subgroups are enclosed in brackets. RRM#: RRM number; KOG#: abridged KOG number and name; MP: 1266-cluster parsimony tree; RW: 1266-cluster RAXML (WAG+ Γ_4) tree; TW: 1266-cluster TREEFINDER (WAG+ Γ_4) tree; RL: 1266-cluster RAXML (LG+F+ Γ_4) tree; mRX: 1831-cluster RAXML tree; y/n: does/does not exist in the corresponding tree.

Table S4. Summary of the groupings observed for SR protein RRM1 domains. The Table is a companion to Figure S11. Datasets are described in the text. Node numbers are as in Figure S10 and Table S3: (16) RRM1 domains of dual RRM SR proteins; (17) RRM1 domains of single RRM ZnK-like SR proteins; (22-23) RRM1 domains of single RRM SR proteins; (26-27) RRM1 domains of the atypical RNPS1/SR45 proteins.

Table S5. Compositional features specific of one or more SR subfamilies. For each subfamily, discriminating features used in the SR determination key and secondary features are listed. Features correspond to single, unordered 2-AA or 3-AA words, respectively. The SRp40-55-75 (SRSF5-6-4) and animal ASF-like (SRSF1-ASF/SF2 and SRSF9/SRp30c) subfamilies were split in their individual component proteins thus resulting in 16 rows in the Table.

Table S6. Determination key for SR families and subfamilies. The key was constructed by integrating architectural and compositional features that are specific either of SR natural families or subfamilies.

Table S7. Statistics for the curated inventory of SR proteins in 20 selected proteomes. The Table is a companion to Table 2 found in the main text. It provides detailed numbers for the stepwise validation of candidate SR proteins from RRM prediction to phylogenetic analysis and determination key classification. cand: candidate SR proteins; rej: candidates rejected as non-SR proteins; iso: isoforms of confirmed SR proteins (mis-modeling or alternative splicing); conf: candidates confirmed as SR proteins; key: confirmed candidates correctly classified by the determination key; trunc: truncated candidates (mis-modeling or alternative splicing) that were incorrectly classified by the determination key. The 7 recently sequenced photosynthetic added for the inventory are shown in boldface.

Figure S1. Scheme of the analysis pipeline. The four sections of the main text results are shown by discontinuous shaded areas (labeled 1 to 4). Within an area, each colored box corresponds to a logical analysis step (e.g., program execution followed by processing of its output). For simplicity, data and execution flows are confounded in the same arrows. Input data sources and pipeline outputs are symbolized by distinct icons. Both main and Supplemental Figure and Table numbers are indicated on the corresponding icons. See Text S1 for detailed methods and technical results.

Figure S2. Optimization of clustering parameters for RRM domains. Non-redundant RRM domains were clustered by single-linkage based on sequence similarity (fraction of identical residues). The parameter space for both similarity and coverage thresholds was explored to determine the combination that maximized a composite score rewarding normalized entropy but penalizing the number of singleton clusters. The analysis was conducted for each of the five non-redundant RRM datasets that were obtained at the following domain E-value thresholds: (A) 1e-5, (B) 1e-10, (C) 1e-15, (D) 1e-20 and (E) 1e-25.

Figure S3. Evaluation of the selection algorithm for cluster representatives. Three clustered datasets were assembled using either of the following selection criteria for cluster representatives: (i) longest sequence (orange); (ii) most slowly evolving sequence (green); (iii) fastest-evolving sequence (red). For each dataset, the corresponding tree was inferred by Maximum Parsimony along with 100 bootstrap replicates. The resulting tree lengths (in parsimony steps) are plotted either as a vertical line for the original tree or as a cumulative distribution for bootstrap replicates.

Figure S4. Color key for KOG annotation. A unique combination of background and text color has been attributed to each KOG, which are listed by descending occurrence count in the RRM-containing protein dataset.

Figure S5. Maximum Parsimony tree of representative RRM domains. The tree was obtained using PAUP* from the analysis of 72 aligned amino acid positions across 1266 sequences and rooted using prokaryotic RRM domains as outgroups. The length of the tree is 36,439 parsimony steps. Leaves were automatically annotated and colored based on cluster content using (i) KOG annotation and (ii) reference RRM-containing proteins (Figure S4 and Table S2). Furthermore, the following information is provided: (iii) the number of domains in the cluster; (iv) the distribution of RRM numbers in the clusters; (v) the amount of prokaryotic proteins; and

(vi) the amount of putative SR proteins. All numbers are given as percentages as well as logarithmic estimates represented as stretches of stars (*). Clusters that contain domains from more than one species or at least one prokaryotic RRM are shown in bold and italic, respectively. Stable groupings are indicated and follow the numbering of Figure S10 and Table S3. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S6. RAXML tree of representative RRM domains obtained under the WAG+ Γ_4 model.

The tree was actually obtained under the very similar PROTMIXWAG model from the analysis of 72 aligned amino acid positions across 1266 sequences and rooted using prokaryotic RRM domains as outgroups. Leaves were automatically annotated and colored based on cluster content using (i) KOG annotation and (ii) reference RRM-containing proteins (Figure S4 and Table S2). Furthermore, the following information is provided: (iii) the number of domains in the cluster; (iv) the distribution of RRM numbers in the clusters; (v) the amount of prokaryotic proteins; and (vi) the amount of putative SR proteins. All numbers are given as percentages as well as logarithmic estimates represented as stretches of stars (*). Clusters that contain domains from more than one species or at least one prokaryotic RRM are shown in bold and italic, respectively. Stable groupings are indicated and follow the numbering of Figure S10 and Table S3. SR-associated subtrees that were further analyzed are shown in pink. Subtrees prok-1 to prok-3 used to compute prokaryotic RRM logos are also indicated. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S7. TREEFINDER tree of representative RRM domains obtained under the WAG+ Γ_4 model.

The tree was obtained from the analysis of 72 aligned amino acid positions across 1266 sequences and rooted using prokaryotic RRM domains as outgroups. Leaves were automatically annotated and colored based on cluster content using (i) KOG annotation and (ii) reference RRM-containing proteins (Figure S4 and Table S2). Furthermore, the following information is provided: (iii) the number of domains in the cluster; (iv) the distribution of RRM numbers in the clusters; (v) the amount of prokaryotic proteins; and (vi) the amount of putative SR proteins. All numbers are given as percentages as well as logarithmic estimates represented as stretches of stars (*). Clusters that contain domains from more than one species or at least one prokaryotic RRM are shown in bold and italic, respectively. Stable groupings are indicated and follow the numbering of Figure S10 and Table S3. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S8. RAxML tree of representative RRM domains obtained under the LG+F+ Γ_4 model.

The tree was obtained from the analysis of 72 aligned amino acid positions across 1266 sequences and rooted using prokaryotic RRM domains as outgroups. Leaves were automatically annotated and colored based on cluster content using (i) KOG annotation and (ii) reference RRM-containing proteins (Figure S4 and Table S2). Furthermore, the following information is provided: (iii) the number of domains in the cluster; (iv) the distribution of RRM numbers in the clusters; (v) the amount of prokaryotic proteins; and (vi) the amount of putative SR proteins. All numbers are given as percentages as well as logarithmic estimates represented as stretches of stars (*). Clusters that contain domains from more than one species or at least one prokaryotic RRM are shown in bold and italic, respectively. Stable groupings are indicated and follow the numbering of Figure S10 and Table S3. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S9. RAxML tree of the enlarged RRM dataset obtained under the WAG+ Γ_4 model.

The tree was actually obtained under the very similar PROTMIXWAG model from the analysis of 72 aligned amino acid positions across 1831 sequences and rooted using prokaryotic RRM domains as outgroups. Leaves were automatically annotated and colored based on cluster content using (i) KOG annotation and (ii) reference RRM-containing proteins (Figure S4 and Table S2). Furthermore, the following information is provided: (iii) the number of domains in the cluster; (iv) the distribution of RRM numbers in the clusters; (v) the amount of prokaryotic proteins; and (vi) the amount of putative SR proteins. All numbers are given as percentages as well as logarithmic estimates represented as stretches of stars (*). Clusters that contain domains from more than one species or at least one prokaryotic RRM are shown in bold and italic, respectively. Stable groupings are indicated and follow the numbering of Figure S10 and Table S3. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S10. Qualitative consensus of phylogenetic analyses of representative RRM domains.

The consensus is based on a manual comparison of the 5 large trees (Figures S5-9). Recurrent nodes across analyses were uniquely numbered by descending grouping level. Unstable subgroups are enclosed in brackets. Notes about individual nodes and trees can be found in companion Table S3. Simple terminal branches correspond to functionally homogenous groupings, whereas open triangles represent mixed functionality. SR-associated subtrees are indicated by shaded boxes and the corresponding branches are color-coded to match Figures 2, 3 and S11: RRM1 of single RRM SR proteins (green); RRM1 of single RRM ZnK-like SR proteins

(blue); RRM1 of dual RRM SR proteins (red); RRM1 of RNPS1/SR45 proteins (orange); RRM2 of non-plant dual RRM SR proteins (violet); RRM2 of the plant-specific 'RS' group of SR proteins (brown). Note that node names are based on automated KOG annotation without manual curation, hence the presence of occasional inaccuracies (e.g., node 83 labelled as 'splicing factor RNPS1' while it actually includes PABP proteins; see Table S3).

Figure S11. Mutual affinities of SR protein RRM domains in the five large trees. Cartoons (A) to (E) summarize the trees given in Figures S5 to S9, respectively, and leaf node numbers are described in Figure S10 and Table S3. Simple terminal branches correspond to functionally homogenous groupings, whereas open triangles represent mixed functionality. SR-associated RRM domains are color-coded as in Figures 2, 3 and S10, while outgroup RRM domains are shown in black. Companion Table S4 summarizes the groupings observed in each tree for the RRM1 domains of SR splicing factors.

Figure S12. RAXML tree of the largest RRM clusters obtained under the LG+F+ Γ_4 model. The tree was obtained from the analysis of 72 aligned amino acid positions across 152 slowly evolving RRM sequences representative of all multi-species RRM clusters with ≥ 8 member domains (i.e., 10,101 out of 12,023 retrieved domains), and rooted using prokaryotic RRM clusters as outgroups (in italic). Leaves were automatically annotated and colored based on cluster content using (i) KOG annotation and (ii) reference RRM-containing proteins (Figure S4 and Table S2). Furthermore, the following information is provided: (iii) the number of domains in the cluster; (iv) the distribution of RRM numbers in the clusters; (v) the amount of prokaryotic proteins; and (vi) the amount of putative SR proteins. All numbers are given as percentages as well as logarithmic estimates represented as stretches of stars (*). Stable groupings are indicated and follow the numbering of Figure S10 and Table S3. All non-zero bootstrap proportions are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S13. Exhaustive RAXML tree of SR-associated RRM1 domains (WAG+ Γ_4 model). The tree was actually obtained under the very similar PROTMIXWAG model from the analysis of 93 aligned amino acid positions across 434 sequences and was left unrooted as 'outgroups' are not monophyletic. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM1 of SR proteins' subtree (in pink in Figure S6). Annotation is as described for Figures S5-9. Bootstrap proportions $>50\%$ are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S14. Exhaustive TREEFINDER tree of SR-associated RRM1 domains (WAG+ Γ_4 model).

The unrooted tree was obtained from the analysis of 93 aligned amino acid positions across 434 sequences and was left unrooted as 'outgroups' are not monophyletic. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM1 of SR proteins' subtree (in pink in Figure S6). Annotation is as described for Figures S5-9. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S15. RAXML tree of RRM1 domains from RNPS1-like proteins (WAG+ Γ_4 model).

The tree was actually obtained under the very similar PROTMIXWAG model from the analysis of 73 aligned amino acid positions across 42 sequences and rooted between RNPS1 and SR45 domains. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM1 of SR45/RNPS1' subtree (in pink in Figure S6). Annotation is as described for Figures S5-9. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S16. TREEFINDER tree of RRM1 domains from RNPS1-like proteins (WAG+ Γ_4 model).

The unrooted tree was obtained from the analysis of 73 aligned amino acid positions across 42 sequences and rooted between RNPS1 and SR45 domains. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM1 of SR45/RNPS1' subtree (in pink in Figure S6). Annotation is as described for Figures S5-9. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S17. RAXML tree of RRM2 domains from dual RRM SR proteins (WAG+ Γ_4 model).

The tree was actually obtained under the very similar PROTMIXWAG model from the analysis of 97 aligned amino acid positions across 349 sequences and rooted between SR-associated and outgroup domains. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM2 of dual RRM SR proteins' subtree (in pink in Figure S6). Annotation is as described for Figures S5-9. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S18. TREEFINDER tree of RRM2 domains from dual RRM SR proteins (WAG+ Γ_4 model).

The unrooted tree was obtained from the analysis of 97 aligned amino acid positions across 349 sequences and rooted between SR-associated and outgroup domains. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM2 of dual RRM SR proteins'

subtree (in pink in Figure S6). Annotation is as described for Figures S5-9. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S19. RAXML tree of slowly evolving SR-associated RRM1 domains (WAG+ Γ_4 model).

The tree was actually obtained under the very similar PROTMIXWAG model from the analysis of 87 aligned amino acid positions across 304 sequences and was left unrooted as 'outgroups' are not monophyletic. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM1 of SR proteins' subtree (in pink in Figure S6), of which 130 fast-evolving (i.e., long-branched) sequences have been removed. Annotation is as described for Figures S5-9. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S20. TREEFINDER tree of slowly evolving SR-associated RRM1 domains (WAG+ Γ_4 model).

The tree was obtained from the analysis of 87 aligned amino acid positions across 304 sequences and was left unrooted as 'outgroups' are not monophyletic. Leaves correspond to unique domain sequences belonging to clusters present in the 'RRM1 of SR proteins' subtree (in pink in Figure S6), of which 130 fast-evolving (i.e., long-branched) sequences have been removed. Annotation is as described for Figures S5-9. Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S21. Sequence conservation in the first RRM domain of SR proteins.

RRM sequence logos are aligned based on secondary structure (bottom). At a given position, the height of any residue is proportional to its frequency while overall stack height corresponds to sequence conservation. Error bars reflect the uncertainty of conservation estimates. Small sample sizes lead to conservatively downscaled letters (e.g., RS2Z subfamily and SR45). RNP1 and RNP2 motifs are shaded, as are conserved aromatic residues in these motifs. β 1-4, α 1-2 and L1-5 respectively stand for β -sheets, α -helices and linkers of the RRM secondary structure. The Figure contains four panels, one for each natural family of SR proteins: (A) single RRM; (B) single RRM ZnK-like; (C) dual RRM; and (D) RNPS1-like. In (C), RS2Z proteins were grouped with other ZnK-containing proteins even if their RRM is quite different, including RNP motifs.

Figure S22. Sequence conservation across prokaryotic RRM domains.

RRM sequence logos are aligned based on secondary structure (bottom). At a given position, the height of any residue is proportional to its frequency while overall stack height corresponds to sequence conservation. Error bars reflect the uncertainty of conservation estimates. RNP1 and RNP2 motifs are shaded,

as are conserved aromatic residues in these motifs. β 1-4, α 1-2 and L1-5 respectively stand for β -sheets, α -helices and linkers of the RRM secondary structure. The 2 upper logos respectively include all prokaryotic or cyanobacterial RRM domains independently of their actual position in the phylogenetic tree (Figure S6). The 3 lower logos each correspond to one of the mainly prokaryotic subtrees used as outgroups, of which non-prokaryotic domains were excluded. Grey boxes highlight motifs specific of the discrete cyanobacterial subtree (middle).

Figure S23. Sequence conservation across ZnK domains of SR proteins. Thanks to their very constraint size, ZnK sequence logos were easily aligned by hand. At a given position, the height of any residue is proportional to its frequency while overall stack height corresponds to sequence conservation. Error bars reflect the uncertainty of conservation estimates. To increase sampling for RSZ and RS2Z logos, ZnK domains from SR proteins identified in the inventory of the seven additional photosynthetic proteomes were also included. Left and right ZnK domains from RS2Z proteins were considered separately in an attempt to determine their respective ancestry by comparison with SRSF7/9G8 and RSZ homologues (grey boxes). However, this analysis proved inconclusive due to the short size of ZnKs. Universally conserved CCHC motifs (yellow) and glycine residues (orange) are also shaded. ZnKs of the CCHC family have amino acid arrangements with the consensus sequence 'C- Φ -X-C-G- $\pm$ -X-G-H-X3- δ -C,' where X is a variable amino acid, Φ is an aromatic amino acid, ($\pm$) is a charged amino acid, and δ is a carbonyl-containing residue (Green and Berg, 1989; Cavaloc et al., 1994; Cavaloc et al., 1999; Armas et al., 2008).

Figure S24. Distributions of relevant compositional features within SR subfamilies. Each panel corresponds to the distributions of the density of a particular word (1, 2 or 3 unordered residues) in a specific region across all subfamilies. Regions are bounded by RRM and ZnK domains and defined as follows: (i) before the first domain; (ii) between the first and the second domain; and (iii) after the last domain (e.g., RS/SR before RRM1 or GG between RRM1 and ZnK1). For a given word/region combination, density is computed as the number of overlapping word occurrences in a sliding-window of 24 amino acid residues scanning the region in each protein. Maximal word densities (i.e., highest peaks) are then pooled by subfamily to allow joint plotting of resulting distributions on a single graph. Numbers in panel legends indicate the number of analyzed proteins in each subfamily. This number can vary between word/region combinations because of (i) mis-modeled proteins lacking one or more canonical domains of the family and (ii) non-prediction of divergent domains. Similarly, not all

combinations can be analyzed for every subfamily, e.g., single RRM SR proteins do not possess an interdomain region.

Figure S25. Architecture, conservation and compositional profile of SR subfamilies. Within each panel, an individual protein was selected as representative for compositional profiling while conservation was computed on the alignment of all subfamily sequences. The SRp40-55-75 (SRSF5-6-4) and animal ASF-like (SRSF1-ASF/SF2 and SRSF9/SRp30c) subfamilies were split in their individual component proteins thus resulting in 16 panels. In these cases, a single subfamily alignment was used for conservation profiling in respectively three (K, L, M) and two (H, I) panels. Only informative features (Table S5) are shown, with discriminating features used in the key (Table S6) in plain style and secondary features in dashed style. (A) SC35: human SRSF2/SC35 (ENSP00000293233); (B) SCL: Arabidopsis At-SCL33 (NP_001031195); (C) SRp: mouse SRSF10/SRp40 (ENSMUSP00000030437); (D) 9G8: human SRSF7/9G8 (ENSP00000325905); (E) SRp20: human SRSF3/SRp20 (ENSP00000362820); (F) RSZ: Arabidopsis At-RSZ21 (NP_564208); (G) RS2Z: rice Os-RS2Z36 (NP_001054489); (H) ASF/SF2: human SRSF1-ASF/SF2 (ENSP00000258962); (I) SRp30c: human SRSF9/SRp30c (ENSP00000229390); (J) ASF-like: rice Os-SR32 (NP_001050082); (K) SRp40: human SRSF5/SRp40 (ENSP00000342294); (L) SRp55: human SRSF6/SRp55 (ENSP00000244020); (M) SRp75: human SRSF4/SRp75 (ENSP00000362900); (N) RS: Arabidopsis At-RS41 (NP_200017); (O) SR45: Arabidopsis SR45 (NP_173107); (P) RNPS1: human RNPS1 (ENSP00000380275).

Figure S26. RAXML RRM tree of candidate SR proteins from selected proteomes (WAG+Γ4 model). The tree was actually obtained under the very similar PROTMIXWAG model from the analysis of 64 unambiguously aligned amino acid positions across 270 sequences and arbitrarily rooted using RNPS1-like proteins. Positions corresponding to subfamily-specific insertions were discarded from the full alignment (82 amino acid positions) prior to analysis. RRM2 domains from RS proteins were also included to test the duplication hypothesis (see main text). Annotation was limited to KOG identifiers and reference RRM-containing proteins, supplemented with a subfamily code added during automatic alignment on subfamily consensus (e.g., asflkpl stands for plant ASF-like). Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S27. TREEFINDER RRM tree of candidate SR proteins from selected proteomes (WAG+Γ4 model). The tree was obtained from the analysis of 64 unambiguously aligned amino acid positions across 270 sequences and arbitrarily rooted using RNPS1-like proteins. Positions

corresponding to subfamily-specific insertions were discarded from the full alignment (82 amino acid positions) prior to analysis. RRM2 domains from RS proteins were also included to test the duplication hypothesis. Annotation was limited to KOG identifiers and reference RRM-containing proteins, supplemented with a subfamily code added during automatic alignment on subfamily consensus (e.g., asflkpl stands for plant ASF-like). Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S28. RAXML tree of candidate SR proteins from selected proteomes (LG+F+ Γ 4 model).

The tree was obtained from the analysis of 64 unambiguously aligned amino acid positions across 270 sequences and arbitrarily rooted using RNPS1-like proteins. Positions corresponding to subfamily-specific insertions were discarded from the full alignment (82 amino acid positions) prior to analysis. RRM2 domains from RS proteins were also included to test the duplication hypothesis. Annotation was limited to KOG identifiers and reference RRM-containing proteins, supplemented with a subfamily code added during automatic alignment on subfamily consensus (e.g., asflkpl stands for plant ASF-like). Bootstrap proportions >50% are shown. The scale bar at the bottom gives the number of substitutions per site.

Figure S29. PHYLOBAYES tree of candidate SR proteins from selected proteomes (CAT+ Γ 4 model).

The tree was obtained from the analysis of 64 unambiguously aligned amino acid positions across 270 sequences. It is the consensus of two independent chains ran for 55,000 cycles (burn-in = 5000 cycles; one tree sampled every 100 cycles) and is arbitrarily rooted using RNPS1-like proteins. Positions corresponding to subfamily-specific insertions were discarded from the full alignment (82 amino acid positions) prior to analysis. RRM2 domains from RS proteins were also included to test the duplication hypothesis. Annotation was limited to KOG identifiers and reference RRM-containing proteins, supplemented with a subfamily code added during automatic alignment on subfamily consensus (e.g., asflkpl stands for plant ASF-like). Posterior probabilities (PP) >50% are shown (whereas nodes with PP <5% are collapsed). The scale bar at the bottom gives the number of substitutions per site.

Supplemental References

- Altschul SF, Madden TL, Schaffer AA, Zhang J, Zhang Z, Miller W, Lipman DJ** (1997) Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. *Nucleic Acids Res* **25**: 3389-3402
- Armas P, Nasif S, Calcaterra NB** (2008) Cellular nucleic acid binding protein binds G-rich single-stranded nucleic acids and may function as a nucleic acid chaperone. *J Cell Biochem* **103**: 1013-1036
- Benson DA, Karsch-Mizrachi I, Lipman DJ, Ostell J, Sayers EW** (2009) GenBank. *Nucleic Acids Res* **37**: D26-31
- Boucher L, Ouzounis CA, Enright AJ, Blencowe BJ** (2001) A genome-wide survey of RS domain proteins. *RNA* **7**: 1693-1701
- Cavaloc Y, Bourgeois CF, Kister L, Stevenin J** (1999) The splicing factors 9G8 and SRp20 transactivate splicing through different and specific enhancers. *RNA* **5**: 468-483
- Cavaloc Y, Popielarz M, Fuchs JP, Gattoni R, Stevenin J** (1994) Characterization and cloning of the human splicing factor 9G8: a novel 35 kDa factor of the serine/arginine protein family. *EMBO J* **13**: 2639-2649
- Cover TM, Thomas JA** (2006) *Elements of Information Theory*. Wiley-Interscience, New York, Ed Second Edition
- Crooks GE, Hon G, Chandonia JM, Brenner SE** (2004) WebLogo: a sequence logo generator. *Genome Res* **14**: 1188-1190
- Delsuc F, Brinkmann H, Philippe H** (2005) Phylogenomics and the reconstruction of the tree of life. *Nat Rev Genet* **6**: 361-375
- Durbin R, Eddy S, Krogh A, Mitchinson G** (1998) *Biological sequence analysis: probabilistic models of proteins and nucleic acids*. Cambridge University Press, Cambridge
- Felsenstein J** (1985) Confidence Limits on Phylogenies: An Approach Using the Bootstrap. *Evolution* **39**: 783-791
- Felsenstein J** (2005) PHYLIP (Phylogeny Inference Package) version 3.6. Distributed by the author, Seattle, Department of Genome Sciences, University of Washington
- Finn RD, Mistry J, Tate J, Coghill P, Heger A, Pollington JE, Gavin OL, Gunasekaran P, Ceric G, Forslund K, Holm L, Sonnhammer EL, Eddy SR, Bateman A** (2010) The Pfam protein families database. *Nucleic Acids Res* **38**: D211-222
- Green LM, Berg JM** (1989) A retroviral Cys-Xaa2-Cys-Xaa4-His-Xaa4-Cys peptide binds metal ions: spectroscopic studies and a proposed three-dimensional structure. *Proc Natl Acad Sci U S A* **86**: 4047-4051
- Jobb G, von Haeseler A, Strimmer K** (2004) TREEFINDER: a powerful graphical analysis environment for molecular phylogenetics. *BMC Evol Biol* **4**: 18
- Lartillot N, Lepage T, Blanquart S** (2009) PhyloBayes 3: a Bayesian software package for phylogenetic reconstruction and molecular dating. *Bioinformatics* **25**: 2286-2288
- Lartillot N, Philippe H** (2004) A Bayesian mixture model for across-site heterogeneities in the amino-acid replacement process. *Molecular biology and evolution* **21**: 1095-1109
- Le SQ, Gascuel O** (2008) An improved general amino acid replacement matrix. *Molecular biology and evolution* **25**: 1307-1320
- Letunic I, Doerks T, Bork P** (2009) SMART 6: recent updates and new developments. *Nucleic Acids Res* **37**: D229-232
- Marchler-Bauer A, Anderson JB, Chitsaz F, Derbyshire MK, DeWeese-Scott C, Fong JH, Geer LY, Geer RC, Gonzales NR, Gwadz M, He S, Hurwitz DI, Jackson JD, Ke Z, Lanczycki CJ, Liebert CA, Liu C, Lu F, Lu S, Marchler GH, Mullokandov M, Song JS, Tasneem A, Thanki N, Yamashita RA, Zhang D, Zhang N, Bryant SH** (2009) CDD: specific functional annotation with the Conserved Domain Database. *Nucleic Acids Res* **37**: D205-210

- Philippe H** (1993) MUST, a computer package of Management Utilities for Sequences and Trees. *Nucleic Acids Res* **21**: 5264-5272
- Philippe H, Brinkmann H, Lavrov DV, Littlewood DT, Manuel M, Worheide G, Baurain D** (2011) Resolving difficult phylogenetic questions: why more sequences are not enough. *PLoS biology* **9**: e1000602
- Philippe H, Delsuc F, Brinkmann H, Lartillot N** (2005) Phylogenomics. *Annu Rev Ecol Evol Syst* **36**: 541-562
- Pruitt KD, Tatusova T, Maglott DR** (2007) NCBI reference sequences (RefSeq): a curated non-redundant sequence database of genomes, transcripts and proteins. *Nucleic Acids Res* **35**: D61-65
- R Development Core Team** (2010) A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria
- Rice P, Longden I, Bleasby A** (2000) EMBOSS: the European Molecular Biology Open Software Suite. *Trends Genet* **16**: 276-277
- Roure B, Rodriguez-Ezpeleta N, Philippe H** (2007) SCAFoS: a tool for selection, concatenation and fusion of sequences for phylogenomics. *BMC Evol Biol* **7 Suppl 1**: S2
- Sayers EW, Barrett T, Benson DA, Bryant SH, Canese K, Chetvernin V, Church DM, DiCuccio M, Edgar R, Federhen S, Feolo M, Geer LY, Helmberg W, Kapustin Y, Landsman D, Lipman DJ, Madden TL, Maglott DR, Miller V, Mizrahi I, Ostell J, Pruitt KD, Schuler GD, Sequeira E, Sherry ST, Shumway M, Sirotkin K, Souvorov A, Starchenko G, Tatusova TA, Wagner L, Yaschenko E, Ye J** (2009) Database resources of the National Center for Biotechnology Information. *Nucleic Acids Res* **37**: D5-15
- Schneider TD, Stephens RM** (1990) Sequence logos: a new way to display consensus sequences. *Nucleic Acids Res* **18**: 6097-6100
- Stamatakis A, Ludwig T, Meier H** (2005) RAXML-III: a fast program for maximum likelihood-based inference of large phylogenetic trees. *Bioinformatics* **21**: 456-463
- Swofford DL** (2002) PAUP*. Phylogenetic Analysis Using Parsimony (*and Other Methods). Version 4. Sinauer Associates, Inc., Sunderland, MA.
- Tatusov RL, Fedorova ND, Jackson JD, Jacobs AR, Kiryutin B, Koonin EV, Krylov DM, Mazumder R, Mekhedov SL, Nikolskaya AN, Rao BS, Smirnov S, Sverdlov AV, Vasudevan S, Wolf YI, Yin JJ, Natale DA** (2003) The COG database: an updated version includes eukaryotes. *BMC Bioinformatics* **4**: 41
- Thompson JD, Higgins DG, Gibson TJ** (1994) CLUSTAL W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice. *Nucleic Acids Res* **22**: 4673-4680
- Whelan S, Goldman N** (2001) A general empirical model of protein evolution derived from multiple protein families using a maximum-likelihood approach. *Mol Biol Evol* **18**: 691-699
- Yang Z** (1993) Maximum-likelihood estimation of phylogeny from DNA sequences when substitution rates differ over sites. *Mol Biol Evol* **10**: 1396-1401

organism	name	description	accession	#RRM	references
▷ ARRS — acidic rich RS protein (RRM and RS domains)					
<i>Mus musculus</i>	Psc1	–	AAS19274	1	Kavanagh et al. (2005)
<i>Mus musculus</i>	ARRS	–	BAC34721	1	Kavanagh et al. (2005)
<i>Homo sapiens</i>	KIAA1311	–	BAA92549	1	Kavanagh et al. (2005)
<i>Homo sapiens</i>	Se70-2	–	AAH41655	1	Kavanagh et al. (2005)
<i>Xenopus laevis</i>	RBM26	–	AAH43744	1	Kavanagh et al. (2005)
<i>Drosophila melanogaster</i>	ARRS	–	NP_609976	1	Kavanagh et al. (2005)
<i>Anopheles gambiae</i>	ARRS	–	XP_318628	1	Kavanagh et al. (2005)
<i>Caenorhabditis elegans</i>	ARRS	–	NP_498234	1	Kavanagh et al. (2005)
<i>Dictyostelium discoideum</i>	ARRS	–	AA051188	1	Kavanagh et al. (2005)
<i>Homo sapiens</i>	RBM 26	–	NP_071401	2	Kavanagh et al. (2005)
<i>Homo sapiens</i>	RBM 27	–	NP_061862	1	Kavanagh et al. (2005)
▷ Bruno — CUG-BP1 and ETR-3 like factors (CELF)/BRUNO-like proteins					
<i>Homo sapiens</i>	CUGBP 1	CUG triplet repeat, RNA-binding protein 1	NP_006551	3	Timchenko et al. (1996)
<i>Homo sapiens</i>	CUGBP 2	ETR-3	NP_001020247	3	Lu et al. (1999)
<i>Homo sapiens</i>	CELF 3	Bruno-like 3	NP_064565	3	Ladd et al. (2001)
<i>Homo sapiens</i>	CELF 4	Bruno-like 4	Q9BZC1	3	Ladd et al. (2001)
<i>Homo sapiens</i>	CELF 5	Bruno-like 5	NP_068757	3	Ladd et al. (2001)
<i>Homo sapiens</i>	CELF 6	Bruno-like 6	NP_443072	3	Ladd et al. (2004)
<i>Mus musculus</i>	CUGBP 1	–	NP_059064	3	Timchenko et al. (2006)
<i>Mus musculus</i>	BRUNOL-4	–	NP_573458	3	Meins et al. (2002)
<i>Mus musculus</i>	BRUNOL-6	–	NP_780444	3	McKee et al. (2005)
<i>Gallus gallus</i>	CUGBP 1	–	NP_001012539	3	Brimacombe and Ladd (2007)
<i>Rattus norvegicus</i>	CUGBP 1	–	NP_001020592	3	Karagiannides et al. (2006)
<i>Danio rerio</i>	CUGBP 1	–	NP_571688	3	Hashimoto et al. (2006)
<i>Xenopus laevis</i>	EDEN-BP	embryo deadenylation element binding protein	NP_001084196	3	Paillard et al. (1998)
▷ CAPER — coactivator of activating protein-1 (AP-1) and estrogen receptors (Ers)					
<i>Homo sapiens</i>	CAPER	–	NP_909122	3	Jung et al. (2002)
<i>Mus musculus</i>	CAPER	–	NP_573505	3	Jung et al. (2002)
▷ CPEB — cytoplasmic polyadenylation element binding protein					
<i>Homo sapiens</i>	CPEB 1	–	NP_085097	2	Welk et al. (2001)
<i>Homo sapiens</i>	CPEB 2	–	NP_872587	2	Hagele et al. (2008)
<i>Homo sapiens</i>	CPEB 3	–	NP_055727	2	Salehi-Ashtiani et al. (2006)
<i>Homo sapiens</i>	CPEB 4	–	NP_085130	2	Kurihara et al. (2003)

organism	name	description	accession	#RRM	references
<i>Xenopus laevis</i>	CPEB	–	NP_001084072	2	Paris et al. (1991)
<i>Mus musculus</i>	CPEB 1	–	NP_031781	2	Gebauer and Richter (1996)
<i>Mus musculus</i>	CPEB 2	–	NP_787951	2	Kurihara et al. (2003)
<i>Mus musculus</i>	CPEB 3	–	NP_938042	2	Theis et al. (2003)
<i>Mus musculus</i>	CPEB 4	–	NP_080528	2	Theis et al. (2003)
<i>Rattus norvegicus</i>	CPEB 1	–	NP_001099746	2	Wu et al. (1998)
▷ Dazap — Deleted in azoospermia-associated protein					
<i>Homo sapiens</i>	Dazap1	DAZ associated protein 1	NP_061832	2	Tsui et al. (2000)
<i>Mus musculus</i>	Dazap1	DAZ associated protein 1	NP_573451	2	Dai et al. (2001)
<i>Mus musculus</i>	Dazap1	DAZ associated protein 1	NP_001116077	2	Dai et al. (2001)
<i>Rattus norvegicus</i>	Dazap1	DAZ associated protein 1	NP_001020913	2	Pan et al. (2005)
<i>Xenopus laevis</i>	Dazap1	DAZ associated protein 1 and Prpp (proline-rich RNA binding protein)	Q98SJ2	2	Zhao et al. (2001)
▷ ELAV — embryonic lethal, abnormal vision, Drosophila-like 1/Hu					
<i>Mus musculus</i>	ELAVL 1/HuR	Hu antigen R	NP_034615	3	Atasoy et al. (1998)
<i>Mus musculus</i>	ELAVL 2	Hu antigen B	NP_034616	3	Abe et al. (1996b)
<i>Mus musculus</i>	ELAVL 3	Hu antigen C	NP_034617	3	Okano and Darnell (1997)
<i>Mus musculus</i>	ELAVL 4	Hu antigen D	NP_034618	3	Abe et al. (1994)
<i>Homo sapiens</i>	ELAVL 1/HuR	Hu antigen R	NP_001410	3	Ma et al. (1996)
<i>Homo sapiens</i>	ELAVL 2/HuB	Hu antigen B	NP_004423	3	Levine et al. (1993)
<i>Homo sapiens</i>	ELAVL 3	Hu antigen C	NP_001411	3	Van Tine et al. (1998)
<i>Homo sapiens</i>	ELAVL 4	Hu antigen D	NP_068771	3	Szabo et al. (1991)
<i>Gallus gallus</i>	ELAVL 4	Hu antigen D	NP_990161	3	Wakamatsu and Weston (1997)
<i>Gallus gallus</i>	ELAVL 1/HuR	Hu antigen R	NP_990164	3	Wakamatsu and Weston (1997)
<i>Rattus norvegicus</i>	ELAVL 1/HuR	Hu antigen R	NP_001102318	3	Tang et al. (2002)
<i>Rattus norvegicus</i>	ELAVL 2/HuB	Hu antigen B	NP_775431	3	Fornaro et al. (2007)
<i>Rattus norvegicus</i>	ELAVL 3	Hu antigen C	NP_758827	3	Abe et al. (1996a)
<i>Rattus norvegicus</i>	ELAVL 4	Hu antigen D	NP_001071119	3	Steller et al. (1996)
▷ FCAFP — other Arabidopsis RRM proteins FCA and FPA					
<i>Arabidopsis thaliana</i>	FCA	–	CAB10407	2	Macknight et al. (1997)
<i>Arabidopsis thaliana</i>	FCA-like	–	AAB63831	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	FPA	–	AAB64314	3	Schomburg et al. (2001)
<i>Arabidopsis thaliana</i>	AtY14	–	AAG52616	1	Park and Muench (2007)
<i>Arabidopsis thaliana</i>	AtREF	–	NP_200803	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	AtREF	–	AAG51767	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	AtREF	–	CAB85990	1	Lorkovic and Barta (2002)

organism	name	description	accession	#RRM	references
<i>Arabidopsis thaliana</i>	AtREF	–	NP_198588	1	Lorkovic and Barta (2002)
▷ FOX — Feminizing locus on X					
<i>Caenorhabditis elegans</i>	Fox-1	–	NP_508446	1	Hodgkin et al. (1994)
<i>Homo sapiens</i>	Fox-1	ataxin 2-binding protein 1	NP_665898	1	Shibata et al. (2000)
<i>Homo sapiens</i>	Fox-2	RBM 9	NP_001076045	1	Lieberman et al. (2001)
<i>Homo sapiens</i>	Fox-3	hexaribonucleotide binding protein	NP_001076044	1	Underwood et al. (2005)
<i>Mus musculus</i>	Fox-1	ataxin 2-binding protein	NP_067452	1	Kiehl et al. (2001)
<i>Mus musculus</i>	Fox-2	RBM 9	NP_444334	1	Lieberman et al. (2001)
<i>Danio rerio</i>	Fox-1	ataxin 2-binding protein-like	NP_999940	1	Jin et al. (2003)
▷ G3BP — Ras-GTPase-activating protein SH3-domain-binding protein					
<i>Homo sapiens</i>	G3BP 1	–	NP_938405	1	Parker et al. (1996)
<i>Homo sapiens</i>	G3BP 2	–	NP_987100	1	Prigent et al. (2000)
<i>Mus musculus</i>	G3BP 1	–	NP_038744	1	Kennedy et al. (1996)
▷ GRSRBP — Glycine-Rich-RNA Binding (GR-RBP) and small RNA-binding protein (S-RBP)					
<i>Arabidopsis thaliana</i>	GR-RBP1	–	AAD22311	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	GR-RBP2	–	CAB36849	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	GR-RBP3	–	BAB10366	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	GR-RBP4	–	BAB03001	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	GR-RBP5	–	AAG52402	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	GR-RBP6	–	AAF98412	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	GR-RBP7	–	AAD23639	1	Heintzen et al. (1997)
<i>Arabidopsis thaliana</i>	GR-RBP8	–	CAB43641	1	Carpenter et al. (1994)
<i>Arabidopsis thaliana</i>	AtRZ-1a	–	BAB02203	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	AtRZ-1b	–	AAB71977	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	AtRZ-1c	–	NP_196048	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	AtRZ-1-like	–	AAG51392	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP1	–	CAB78428	1	Lorkovic and Barta (2002)
<i>Zea mays</i>	GRP	–	NP_001105707	1	Didierjean et al. (1992)
<i>Nicotiana sylvestris</i>	RZ-1	–	BAA06012	1	Hanano et al. (1996)
<i>Homo sapiens</i>	GRSF 1	G-rich RNA sequence binding factor 1	NP_002083	3	Qian and Wilusz (1994)
<i>Homo sapiens</i>	RBM3	–	NP_006734	1	Danno et al. (1997)
<i>Homo sapiens</i>	CIRP	–	NP_001271	1	Nishiyama et al. (1997)
<i>Mus musculus</i>	CIRP	–	NP_031731	1	Nishiyama et al. (1997)

organism	name	description	accession	#RRM	references
▷ IGF2BP — insulin-like growth factor 2 RNA binding protein					
<i>Homo sapiens</i>	IGF2BP 1	–	NP_006537	2	Nielsen et al. (1999)
<i>Homo sapiens</i>	IGF2BP 2	–	NP_006539	2	Nielsen et al. (1999)
<i>Homo sapiens</i>	IGF2BP 3	–	NP_006538	2	Nielsen et al. (1999)
▷ LA — LA					
<i>Homo sapiens</i>	La	–	NP_003133	1	Maraia and Intine (2001)
<i>Homo sapiens</i>	Larp 7	–	NP_056269	1	Krueger et al. (2008)
<i>Mus musculus</i>	Ssb	Sjogren syndrome antigen B	NP_001103615	1	Maraia and Intine (2001)
<i>Mus musculus</i>	Larp7	–	NP_613059	1	Krueger et al. (2008)
<i>Arabidopsis thaliana</i>	La1	–	NP_001031777	1	Fleurdepine et al. (2007)
<i>Arabidopsis thaliana</i>	La	–	NP_178106	2	Fleurdepine et al. (2007)
<i>Arabidopsis thaliana</i>	La	–	NP_974184	2	Fleurdepine et al. (2007)
<i>Arabidopsis thaliana</i>	La	–	NP_974185	2	Fleurdepine et al. (2007)
<i>Arabidopsis thaliana</i>	La	–	NP_188540	1	Fleurdepine et al. (2007)
<i>Arabidopsis thaliana</i>	La	–	NP_851141	1	Fleurdepine et al. (2007)
<i>Oryza sativa</i>	La	–	BAD19607	2	Fleurdepine et al. (2007)
<i>Oryza sativa</i>	La	–	CAE03115	2	Fleurdepine et al. (2007)
<i>Schizosaccharomyces pombe</i>	la1	–	NP_593315	1	Van Horn et al. (1997)
<i>Saccharomyces cerevisiae</i>	Lhp1	–	NP_010232	1	Yoo and Wolin (1994)
<i>Drosophila melanogaster</i>	La	–	NP_724257	1	Yoo and Wolin (1994)
▷ LARK — LARK					
<i>Homo sapiens</i>	RBM4	LARK	NP_002887	2	Markus and Morris (2006)
<i>Mus musculus</i>	RBM4	LARK	NP_033058	2	Kojima et al. (2007)
<i>Drosophila melanogaster</i>	LARK	–	NP_523957	2	McNeil et al. (2001)
<i>Bombyx mori</i>	LARK	–	NP_001037293	2	Wang et al. (2005)
▷ Musashi — Musashi					
<i>Homo sapiens</i>	musashi 1	neural-specific RNA binding protein	NP_002433	2	Good et al. (1998)
<i>Homo sapiens</i>	musashi 2	neural-specific RNA binding protein	NP_620412	2	Barbouti et al. (2003)
<i>Mus musculus</i>	Musashi 1	neural-specific RNA binding protein homolog 1	NP_032655	2	Sakakibara et al. (1996)
<i>Mus musculus</i>	Musashi 2	neural-specific RNA binding protein homolog 2	NP_473384	2	Sakakibara et al. (2001)
<i>Xenopus laevis</i>	nrp-1B	neural-specific RNA binding protein	NP_001084040	2	Richter et al. (1990)
<i>Caenorhabditis elegans</i>	Musashi-1	neural-specific RNA binding protein	NP_497799	2	Yoda et al. (2000)
<i>Ciona intestinalis</i>	Musashi	neural-specific RNA binding protein	NP_001027721	2	Kawashima et al. (2000)
<i>Halocynthia roretzi</i>	Musashi	neural-specific RNA binding protein	BAA82622	2	Kawashima et al. (2000)

organism	name	description	accession	#RRM	references
▷ NTF — RRM proteins containing the NTF domain					
<i>Arabidopsis thaliana</i>	NTF-RRM1	–	AAF20222	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM2	–	AAD20086	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM3	–	AAF27060	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM4	–	AAF81299	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM5	–	BAB09056	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM6	–	BAB10647	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM7	–	BAB10698	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM8	–	BAB02073	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	NTF-RRM9	–	AAF20221	2	Lorkovic and Barta (2002)
▷ P54nrb — 54 kD nuclear RNA-binding protein/ non-POU domain containing, octamer-binding					
<i>Homo sapiens</i>	p54nrb	–	NP_031389	2	Dong et al. (1993)
<i>Mus musculus</i>	NonO	–	NP_075633	2	Yang et al. (1993)
<i>Rattus norvegicus</i>	NonO/p54nrb	–	NP_001020442	2	Too et al. (1998)
<i>Rattus norvegicus</i>	NonO	–	NP_001012356	2	Brown et al. (2005)
<i>Xenopus laevis</i>	P54nrb	–	NP_001080735	2	Takahashi et al. (2005)
<i>Drosophila melanogaster</i>	NonA	no on or off transient A	NP_523367	2	Jones and Rubin (1990)
▷ PABP — poly(A)-binding proteins					
<i>Homo sapiens</i>	PABPC1	–	NP_002559	4	Hosoda et al. (2006)
<i>Homo sapiens</i>	PABP2	–	NP_004634	1	Wahle (1991)
<i>Homo sapiens</i>	PABPC3	–	NP_112241	3	Feral et al. (2001)
<i>Homo sapiens</i>	PABPC4	–	NP_003810	4	Yang et al. (1995)
<i>Homo sapiens</i>	PABPC5	–	NP_543022	4	Blanco et al. (2001)
<i>Mus musculus</i>	PAPB2	–	NP_001007463	1	Cosson et al. (2004)
<i>Mus musculus</i>	PABP1	–	NP_032800	4	Wang et al. (1992)
<i>Mus musculus</i>	PABP2	–	NP_035163	4	Kleene et al. (1998)
<i>Mus musculus</i>	PABPC5	–	NP_444344	4	Blanco et al. (2001)
<i>Rattus norvegicus</i>	PABP1	–	NP_599180	4	Lim et al. (2006)
<i>Drosophila melanogaster</i>	PABPC1	–	NP_725750	4	Behm-Ansmant et al. (2007)
<i>Drosophila melanogaster</i>	PABPN1	–	NP_476902	1	Behm-Ansmant et al. (2007)
<i>Xenopus laevis</i>	PABPC1	–	NP_001080204	4	Voeltz et al. (2001)
<i>Xenopus laevis</i>	ePAB	–	NP_001082094	4	Voeltz et al. (2001)
<i>Bos taurus</i>	PABPN1	–	NP_776994	1	Kuhn et al. (2003)
<i>Arabidopsis thaliana</i>	PABP1	–	NP_174676	3	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABP2	–	NP_195137	2	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABP3	–	NP_173690	4	Belostotsky (2003)

organism	name	description	accession	#RRM	references
<i>Arabidopsis thaliana</i>	PABP4	–	NP_179916	4	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABP5	–	NP_177322	4	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABP6	–	NP_188259	4	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABP7	–	NP_181204	4	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABP8	–	NP_564554	4	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABP9	–	NP_175125	4	Belostotsky (2003)
<i>Arabidopsis thaliana</i>	PABN1	–	NP_568751	1	Forbes et al. (2006)
<i>Chlamydomonas reinhardtii</i>	RB57	–	XP_001689671	4	Yohn et al. (1998)
<i>Saccharomyces cerevisiae</i>	Pab1p	–	NP_011092	4	Otero et al. (1999)
<i>Saccharomyces cerevisiae</i>	Rbp29	–	NP_012266	1	Winstall et al. (2000)
<i>Schizosaccharomyces pombe</i>	Pab2	–	CAB16904	1	Perreault et al. (2007)
▷ PDIP — DNA polymerase delta interacting protein 3					
<i>Homo sapiens</i>	PDIP3	PDIP46	NP_115687	1	Smyk et al. (2006)
<i>Mus musculus</i>	PDIP3	–	NP_848742	1	Liu et al. (2003)
▷ PSF — polypyrimidine tract binding protein associated, splicing factor proline/glutamine rich					
<i>Homo sapiens</i>	PSF	sfpq	NP_005057	2	Gozani et al. (1994)
<i>Mus musculus</i>	PSF	sfpq	NP_076092	2	Shav-Tal et al. (2001)
<i>Danio rerio</i>	PSF	sfpq	NP_998443	2	Lowery et al. (2007)
▷ PSP1 — paraspeckle protein					
<i>Homo sapiens</i>	PSP1	paraspeckle protein 1	NP_001035879	2	Fox et al. (2002)
<i>Mus musculus</i>	PSP1	paraspeckle protein 1	NP_079958	2	Myojin et al. (2004)
▷ PTBP — polypyrimidine tract-binding protein					
<i>Homo sapiens</i>	PTBP1	–	NP_114368	4	Gil et al. (1991)
<i>Homo sapiens</i>	PTBP2	–	NP_067013	4	Markovtsov et al. (2000)
<i>Mus musculus</i>	PTBP1	–	NP_032982	4	Bothwell et al. (1991)
<i>Mus musculus</i>	PTBP2	brPTB	NP_062423	4	Polydorides et al. (2000)
<i>Rattus norvegicus</i>	PTBP1	PTB4	NP_071961	4	Gooding et al. (2003)
<i>Rattus norvegicus</i>	PTBP	smPTB	NP_877970	4	Gooding et al. (2003)
<i>Rattus norvegicus</i>	PTBP2	nPTB	NP_001005555	4	Gooding et al. (2003)
▷ RALYL — RALY RNA binding protein and RALY-like					
<i>Homo sapiens</i>	RALYL	–	NP_776247	1	Ji et al. (2003)
<i>Homo sapiens</i>	RALY	hnRNP-associated with lethal yellow	NP_031393	1	Khrebtukova et al. (1999)

organism	name	description	accession	#RRM	references
<i>Mus musculus</i>	RALY	hnRNP-associated with lethal yellow	NP_075619	1	Khrebtukova et al. (1999)
▷ RBM — RNA Binding Motif proteins					
<i>Homo sapiens</i>	RBM1	RNPC1	NP_906270	1	Shu et al. (2006)
<i>Homo sapiens</i>	RBM5	–	NP_005769	2	Shu et al. (2007)
<i>Homo sapiens</i>	RBM6	–	NP_005768	2	Wang et al. (2007b)
<i>Homo sapiens</i>	RBM8A	–	NP_005096	1	Salicioni et al. (2000)
<i>Homo sapiens</i>	RBM8B	–	AAG16782	1	Salicioni et al. (2000)
<i>Homo sapiens</i>	RBM10	–	NP_690595	2	Inoue et al. (1996)
<i>Rattus norvegicus</i>	RBM10	–	NP_690600	2	Inoue et al. (1996)
<i>Homo sapiens</i>	RBM12	–	NP_690051	4	Stover et al. (2001)
<i>Pongo pygmaeus</i>	RBM12	–	Q5RBM8	4	GenBank
<i>Macaca mulatta</i>	RBM12	–	Q8SQ27	4	GenBank
<i>Mus musculus</i>	RBM12	–	Q8R4X3	4	GenBank
<i>Homo sapiens</i>	RBM14	–	NP_006319	2	Iwasaki et al. (2001)
<i>Homo sapiens</i>	RBM15	–	NP_073605	3	Ma et al. (2001)
<i>Mus musculus</i>	RBM15	–	NP_001039272	3	Ma et al. (2007)
<i>Homo sapiens</i>	RBM22	–	NP_060517	1	Montaville et al. (2006)
<i>Homo sapiens</i>	RBM25	–	NP_067062	1	Fortes et al. (2007)
<i>Homo sapiens</i>	RBM28	–	NP_060547	4	Damianov et al. (2006)
<i>Homo sapiens</i>	RBM40	–	Q96LT9	2	Zhao et al. (2003)
<i>Mus musculus</i>	RBM40	–	Q3UZ01	2	Zhao et al. (2003)
<i>Rattus norvegicus</i>	RBM40	–	Q4G055	2	GenBank
<i>Homo sapiens</i>	RBM45	–	NP_694453	4	Tamada et al. (2002)
<i>Mus musculus</i>	RBM45	–	NP_700454	4	Tamada et al. (2002)
▷ RBMS — RNA binding motif, single stranded interacting protein					
<i>Homo sapiens</i>	RBMS1	scr2/MSSP1	NP_002888	2	Kanaoka and Nojima (1994); Negishi et al. (1994)
<i>Homo sapiens</i>	RBMS2	scr3	NP_002889	2	Kanaoka and Nojima (1994)
<i>Homo sapiens</i>	RBMS3	–	NP_001003792	2	Penkov et al. (2000); Fritz and Stefanovic (2007)
<i>Mus musculus</i>	RBMS1	–	NP_064692	2	Fujimoto et al. (2000)
<i>Mus musculus</i>	RBMS2	–	NP_062685	2	Fujimoto et al. (2000)
<i>Gallus gallus</i>	RBMS1	–	NP_990355	2	Kimura et al. (1998)
▷ RBM Y — RNA binding motif protein, Y-linked, family 1					
<i>Homo sapiens</i>	RBM Y A1	–	NP_005049	1	Chai et al. (1998)
<i>Homo sapiens</i>	RBM Y B	–	NP_001006121	1	Chai et al. (1998)
<i>Homo sapiens</i>	RBM Y D	–	NP_001006120	1	Chai et al. (1998)

organism	name	description	accession	#RRM	references
<i>Homo sapiens</i>	RBM Y E	–	NP_001006118	1	Chai et al. (1998)
<i>Homo sapiens</i>	RBM Y F	–	NP_689798	1	Chai et al. (1998)
<i>Homo sapiens</i>	RBM Y J	–	NP_001006117	1	Chai et al. (1998)
▷ RDM1 — RAD52 motif 1					
<i>Homo sapiens</i>	RDM1	–	NP_663629	1	Hamimes et al. (2005)
<i>Gallus gallus</i>	RDM1	–	NP_989877	1	Hamimes et al. (2005)
<i>Mus musculus</i>	RDM1	–	NP_079930	1	Hamimes et al. (2005)
▷ RNPS1 — RNA-binding protein S1					
<i>Homo sapiens</i>	RNPS1	–	NP_006702	1	Badolato et al. (1995)
<i>Mus musculus</i>	RNPS1	–	NP_033096	1	Schmidt and Werner (1993)
▷ SART3 — squamous cell carcinoma antigen recognized by T cells 3					
<i>Homo sapiens</i>	SART 3	–	NP_055521	2	Harada et al. (2001)
<i>Mus musculus</i>	SART 3	–	NP_058622	2	Harada et al. (2000)
<i>Danio rerio</i>	SART 3	–	NP_001025289	2	Trede et al. (2007)
<i>Rattus norvegicus</i>	SART 3	–	NP_001100626	2	GenBank
▷ SR — SR proteins					
<i>Homo sapiens</i>	SRp20	–	P84103	1	Zahler et al. (1992)
<i>Homo sapiens</i>	SC35	–	NP_003007	1	Fu and Maniatis (1992)
<i>Homo sapiens</i>	SRp30c	–	AAA93069	2	Screaton et al. (1995)
<i>Homo sapiens</i>	9G8	–	NP_001026854	1	Cavaloc et al. (1994)
<i>Homo sapiens</i>	ASF/SF2	–	NP_008855	2	Krainer et al. (1990); Ge and Manley (1990)
<i>Homo sapiens</i>	SRp40	–	NP_008856	2	Screaton et al. (1995)
<i>Homo sapiens</i>	SRp46	–	NP_115285	1	Soret et al. (1998)
<i>Homo sapiens</i>	SRp55	–	Q13247	2	Screaton et al. (1995)
<i>Homo sapiens</i>	SRp54	–	NP_004759	1	Zhang and Wu (1996)
<i>Homo sapiens</i>	SRp75	–	Q08170	2	Zahler et al. (1993)
<i>Arabidopsis thaliana</i>	SRp30	–	NP_172386	2	Lopato et al. (1999b)
<i>Arabidopsis thaliana</i>	SR1/SRp34	–	O22315	2	Lazar et al. (1995)
<i>Arabidopsis thaliana</i>	SRp34a	–	NP_190512	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	SRp34b	–	NP_567235	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	RSp31	–	P92964	2	Lopato et al. (1996)
<i>Arabidopsis thaliana</i>	RSp31a	–	NP_182184	2	Kalya and Barta (2004)
<i>Arabidopsis thaliana</i>	RSp40/SRp35	–	P92965	2	Lopato et al. (1996)

organism	name	description	accession	#RRM	references
<i>Arabidopsis thaliana</i>	RSp41	–	P92966	2	Lopato et al. (1996)
<i>Arabidopsis thaliana</i>	SRZ21/RSZ21	–	AAD12770	1	Golovkin and Reddy (1998)
<i>Arabidopsis thaliana</i>	SRZ22/RSZ22	–	NP_194886	1	Golovkin and Reddy (1998)
<i>Arabidopsis thaliana</i>	RSZ22a	–	NP_180035	1	Lopato et al. (1999a)
<i>Arabidopsis thaliana</i>	RSZ32	–	NP_190918	1	Lopato et al. (2002)
<i>Arabidopsis thaliana</i>	RSZ33	–	CAC03605	1	Lopato et al. (2002)
<i>Arabidopsis thaliana</i>	SC35	–	NP_201225	1	Lopato et al. (2002)
<i>Arabidopsis thaliana</i>	SR33/SCL33	–	NP_564685	1	Golovkin and Reddy (1999)
<i>Arabidopsis thaliana</i>	SCL30	–	NP_567021	1	Lopato et al. (2002)
<i>Arabidopsis thaliana</i>	SCL30a	–	NP_187966	1	Lopato et al. (2002)
<i>Arabidopsis thaliana</i>	SCL28	–	NP_197382	1	Lopato et al. (2002)
<i>Arabidopsis thaliana</i>	SR45	–	Q9SEE9	1	Golovkin and Reddy (1999)
<i>Oryza sativa</i>	SRp32	–	AK061903	2	Isshiki et al. (2006)
<i>Oryza sativa</i>	SRp33a	–	AK106176	2	Isshiki et al. (2006)
<i>Oryza sativa</i>	SRp33b	–	AK071503	2	Isshiki et al. (2006)
<i>Oryza sativa</i>	SR20	–	AK103534	2	Isshiki et al. (2006)
<i>Oryza sativa</i>	SC35a	–	AK103676	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	SC35b	–	AK070292	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	SC35c	–	AK073057	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	SCL25	–	AK073451	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	SCL30a	–	AK062577	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	SCL30b	–	AK065531	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSZp21a	–	AK063879	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSZp21b	–	AK073210	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSZp23	–	AK060088	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSp29	–	AK102071	2	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSp33	–	AK121372	2	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSZ36	–	AK103897	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSZ37a	–	AK060171	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSZ37b	–	AK073348	1	Isshiki et al. (2006)
<i>Oryza sativa</i>	RSZ39	–	AK063518	1	Isshiki et al. (2006)
<i>Zea mays</i>	SRp30	–	AAU29331	2	Gao et al. (2004)
<i>Zea mays</i>	SRp30'	–	Q64HB9	2	Gao et al. (2004)
<i>Zea mays</i>	SRp31	–	Q64HB5	2	Gao et al. (2004)
<i>Zea mays</i>	SRp31"	–	Q64HB8	2	Gao et al. (2004)
<i>Zea mays</i>	SRp32	–	AAU29328	2	Gao et al. (2004)
<i>Zea mays</i>	SRp32'	–	Q64HC2	2	Gao et al. (2004)
<i>Caenorhabditis elegans</i>	CeSRp75/rsp-1	–	Q23121	2	Longman et al. (2000)

organism	name	description	accession	#RRM	references
<i>Caenorhabditis elegans</i>	CeSRp40/rsp-2	–	Q23120	2	Longman et al. (2000)
<i>Caenorhabditis elegans</i>	CeSF2/ASF/rsp-3	–	Q9NEW6	2	Longman et al. (2000)
<i>Caenorhabditis elegans</i>	CeSC35/rsp-4	–	Q09511	1	Longman et al. (2000)
<i>Caenorhabditis elegans</i>	CeSC35-2/rsp-5	–	Q10021	1	Longman et al. (2000)
<i>Caenorhabditis elegans</i>	CeSRp20/rsp-6	–	Q18409	1	Longman et al. (2000)
<i>Caenorhabditis elegans</i>	Cep54/rsp-7	–	O01159	2	Longman et al. (2000)
<i>Drosophila melanogaster</i>	SC35	–	NP_652612	1	Allemand et al. (2001)
<i>Drosophila melanogaster</i>	9G8	–	AAF43414	1	Allemand et al. (2001)
<i>Drosophila melanogaster</i>	SRp55	–	CAA41556	2	Roth et al. (1991)
<i>Schizosaccharomyces pombe</i>	Srp1	–	AAC49909	1	Gross et al. (1998)
<i>Chironomus tentans</i>	Hrp45	–	Z54163	2	Alzhanova-Ericsson et al. (1996)
▷ SRrp — SR related protein					
<i>Homo sapiens</i>	SRp40	–	AAL57514	1	Cowper et al. (2001)
<i>Homo sapiens</i>	SRp35	–	Q8WXF0	1	Cowper et al. (2001)
<i>Homo sapiens</i>	SRp86	–	NP_001070667	2	Barnard and Patton (2000)
<i>Homo sapiens</i>	SRp38	–	NP_473357	1	Shin et al. (2004)
▷ TARDBP — TAR DNA binding protein					
<i>Homo sapiens</i>	TARDBP	–	NP_031401	2	Ou et al. (1995)
<i>Mus musculus</i>	TARDBP	–	NP_663531	2	Buratti and Baralle (2008)
▷ TIAT1AR — T-cell internal antigen-1 (TIA-1) and TIA-1-related protein (TIAR)					
<i>Homo sapiens</i>	TIAR	–	NP_003243	3	Kawakami et al. (1992)
<i>Homo sapiens</i>	TIA-1	–	NP_071320	3	Tian et al. (1991)
<i>Mus musculus</i>	TIA-1	–	NP_035715	3	Lowin et al. (1996)
<i>Gallus gallus</i>	TIA-1	–	NP_989687	3	Le Guiner et al. (2003)
<i>Bombyx mori</i>	TIA-1	–	NP_001036895	3	Kotani et al. (2003)
<i>Rattus norvegicus</i>	TIA-1	–	NP_001012096	3	GenBank
<i>Mus musculus</i>	TiaL1	–	NP_033409	3	Beck et al. (1996)
<i>Rattus norvegicus</i>	TiaL1	–	NP_001013211	3	GenBank
▷ TIF3 — Translation initiation factor 3					
<i>Arabidopsis thaliana</i>	TIF3	–	AAG51445	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	TIF3	–	BAB10805	1	Lorkovic and Barta (2002)

organism	name	description	accession	#RRM	references
▷ UMH — Proteins with the UHM domain (RRM variant)					
<i>Homo sapiens</i>	KIS	kinase interacting stathmin	NP_787062	1	Bieche et al. (2003)
<i>Mus musculus</i>	KIS	kinase interacting stathmin	NP_034763	1	Maucuer et al. (1995)
<i>Rattus norvegicus</i>	KIS	kinase interacting stathmin	NP_058989	1	Maucuer et al. (1997)
<i>Homo sapiens</i>	PUF60	poly-U binding splicing factor 60KDa	NP_510965	3	Page-McCaw et al. (1999)
<i>Drosophila melanogaster</i>	PUF60	poly-U binding splicing factor 60KDa	NP_525123	2	Van Buskirk and Schupbach (2002)
<i>Mus musculus</i>	PUF60	poly-U binding splicing factor 60KDa	AAH10601	2	Kielkopf et al. (2004)
<i>Danio rerio</i>	PUF60	poly-U binding splicing factor 60KDa	CAD61099	2	Kielkopf et al. (2004)
<i>Anopheles gambiae</i>	PUF60	poly-U binding splicing factor 60KDa	EAA09944	2	Kielkopf et al. (2004)
<i>Caenorhabditis elegans</i>	PUF60	poly-U binding splicing factor 60KDa	AAF60676	2	Kielkopf et al. (2004)
<i>Homo sapiens</i>	SPF45	RBM17	NP_116294	1	Sampath et al. (2003)
<i>Mus musculus</i>	SPF45	RBM17	NP_690037	1	Kielkopf et al. (2004)
<i>Danio rerio</i>	SPF45	–	AAH45473	1	Kielkopf et al. (2004)
<i>Anopheles gambiae</i>	SPF45	–	EAA15153	1	Kielkopf et al. (2004)
<i>Drosophila melanogaster</i>	SPF45	–	EAA46008	1	Chaouki and Salz (2006)
<i>Caenorhabditis elegans</i>	SPF45	–	CAA97799	1	Kielkopf et al. (2004)
<i>Homo sapiens</i>	Tat-SF1	–	AAB18823	1	Zhou and Sharp (1996)
<i>Mus musculus</i>	Tat-SF1	–	AAH37711	1	Kielkopf et al. (2004)
<i>Danio rerio</i>	Tat-SF1	–	AAH55565	1	Kielkopf et al. (2004)
<i>Drosophila melanogaster</i>	Tat-SF1	–	AAF51719	1	Kielkopf et al. (2004)
<i>Anopheles gambiae</i>	Tat-SF1	–	EAA10753	1	Kielkopf et al. (2004)
<i>Caenorhabditis elegans</i>	Tat-SF1	–	AAK29956	1	Kielkopf et al. (2004)
<i>Homo sapiens</i>	HCC1	Hepatocellular carcinoma protein 1	Q14498	2	Imai et al. (1993)
<i>Mus musculus</i>	HCC1	–	Q8VH51	2	Kielkopf et al. (2004)
<i>Danio rerio</i>	HCC1	–	AAH44487	2	Kielkopf et al. (2004)
<i>Drosophila melanogaster</i>	HCC1	–	AAF52478	2	Kielkopf et al. (2004)
<i>Anopheles gambiae</i>	HCC1	–	EAA12873	2	Kielkopf et al. (2004)
<i>Caenorhabditis elegans</i>	HCC1	–	AAM97977	2	Kielkopf et al. (2004)
<i>Arabidopsis thaliana</i>	HCC1	–	AAM20703	2	Kielkopf et al. (2004)
▷ ZCRB1 — zinc finger CCHC-type and RNA binding motif					
<i>Homo sapiens</i>	ZCRB1	–	NP_149105	1	Wang et al. (2007a)
<i>Mus musculus</i>	ZCRB1	–	NP_080301	1	Wang et al. (2007a)
▷ cpRNP — chloroplast RRM containing proteins					
<i>Arabidopsis thaliana</i>	cpRNP28	–	AAD14476	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	cpRNP28b	–	AAF26472	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	cpRNP29	–	CAB67653	2	Ohta et al. (1995)

organism	name	description	accession	#RRM	references
<i>Arabidopsis thaliana</i>	cpRNP29b	–	AAC98043	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	cpRNP31	–	CAA22986	2	Ohta et al. (1995)
<i>Arabidopsis thaliana</i>	cpRNP31b	–	BAB09396	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	cpRNP33	–	CAB43448	2	Ohta et al. (1995)
<i>Arabidopsis thaliana</i>	cpRNP33b	–	AAC36180	2	Lorkovic and Barta (2002)
▷ cyclophilin — cyclophilins					
<i>Arabidopsis thaliana</i>	AtCyp59	–	NP_175776	1	Gullerova et al. (2006)
<i>Rattus norvegicus</i>	CypE	–	NP_001041333	1	GenBank
<i>Caenorhabditis elegans</i>	cyp-13	–	NP_503034	1	Zorio and Blumenthal (1999)
<i>Mus musculus</i>	Cyp-33	–	Q9QZH3	1	Anderson et al. (2002)
<i>Drosophila melanogaster</i>	Cyp-33	–	Q9V3G3	1	Anderson et al. (2002)
<i>Homo sapiens</i>	Cyp-33	–	Q9UNP9	1	Mi et al. (1996)
<i>Homo sapiens</i>	PPIL4	–	Q8WUA2	1	Zeng et al. (2001)
<i>Mus musculus</i>	PPIL4	–	Q9CXG3	1	Zeng et al. (2001)
<i>Schizosaccharomyces pombe</i>	PPIL4	–	Q9UUE4	1	Pemberton and Kay (2005)
<i>Haemonchus contortus</i>	CYP	–	AAW82658	1	Valle et al. (2005)
▷ eIF4B — eukaryotic translation initiation factor 4B					
<i>Homo sapiens</i>	eIF-4B	–	NP_001408	1	Milburn et al. (1990)
<i>Mus musculus</i>	eIF-4B	–	NP_663600	1	Shahbazian et al. (2006)
▷ hnRNP — Heterogeneous nuclear ribonucleoprotein					
<i>Arabidopsis thaliana</i>	AtRNP A/B1	–	CAB10209	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP A/B2	–	AAB80680	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP A/B3	–	BAB08572	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP A/B4	–	CAB43861	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP A/B5	–	BAB09088	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP A/B6	–	AAF21191	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP H/F1	–	BAB10406	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP H/F2	–	BAB02497	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP I/PTB	–	BAB08421	2	Lorkovic et al. (2000b)
<i>Arabidopsis thaliana</i>	AtRNP I/PTB	–	AAF26159	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	AtRNP I/PTB	–	NP_175010	4	Lorkovic and Barta (2002)
<i>Homo sapiens</i>	hnRNP A2/B1	–	NP_112533	2	Burd et al. (1989)
<i>Homo sapiens</i>	hnRNP A1/A1	–	NP_002127	2	Buvoli et al. (1988)
<i>Homo sapiens</i>	hnRNP A/B	–	NP_112556	2	Khan et al. (1991)
<i>Homo sapiens</i>	hnRNP A0	–	NP_006796	2	Myer and Steitz (1995)

organism	name	description	accession	#RRM	references
<i>Homo sapiens</i>	hnRNP C1/C2	–	AAH07052	1	Swanson et al. (1987)
<i>Homo sapiens</i>	hnRNP C	–	NP_001070910	1	Swanson et al. (1987)
<i>Homo sapiens</i>	hnRNP D	–	NP_112737	2	Park et al. (2007)
<i>Homo sapiens</i>	hnRNP F	–	NP_001091676	3	Matunis et al. (1994)
<i>Homo sapiens</i>	hnRNP G	–	P38159	1	Soulard et al. (1993)
<i>Homo sapiens</i>	hnRNP H3	–	NP_036339	2	Mahe et al. (1997)
<i>Homo sapiens</i>	hnRNP L	–	NP_001524	4	Pinol-Roma et al. (1989)
<i>Homo sapiens</i>	hnRNP L-like	–	NP_612403	3	Shur et al. (2004)
<i>Homo sapiens</i>	hnRNP R	–	NP_005817	3	Hassfeld et al. (1998)
<i>Rattus norvegicus</i>	hnRNP A2/B1	–	NP_001098083	2	Kamma et al. (1999)
<i>Rattus norvegicus</i>	hnRNP M	–	NP_001103381	3	Kafasla et al. (2000)
<i>Chironomus tentans</i>	Hrp59 protein	–	CAH05070	3	Kiesler et al. (2005)
<i>Mus musculus</i>	HNRP A/B	–	NP_034578	2	Inoue et al. (2001)
<i>Mus musculus</i>	HNRP L	–	NP_796275	3	Costain and Mishra (2003)
<i>Mus musculus</i>	HNRP M	–	NP_084080	3	Mahe et al. (2000)
<i>Drosophila melanogaster</i>	Hrp36	–	CAA44502	2	Matunis et al. (1992)
▷ nucleolin — nucleolins					
<i>Arabidopsis thaliana</i>	nucleolin	AtNUC-L1	NP_175322	2	Pontvianne et al. (2007)
<i>Arabidopsis thaliana</i>	nucleolin	AtNUC-L2	NP_188491	2	Pontvianne et al. (2007)
<i>Homo sapiens</i>	nucleolin/C23	–	NP_005372	4	Srivastava et al. (1989)
<i>Rattus norvegicus</i>	nucleolin/C23	–	NP_036881	4	Bourbon et al. (1988b)
<i>Schizosaccharomyces pombe</i>	GAR2	–	NP_593531	2	Gulli et al. (1995)
<i>Saccharomyces cerevisiae</i>	NSR1	–	NP_011675	2	Edwards et al. (2000)
<i>Xenopus laevis</i>	NCL	–	P20397	4	Heine et al. (1993)
<i>Mus musculus</i>	NCL	–	NP_035010	4	Bourbon et al. (1988a)
▷ oligoU — oligouridylated-specific RRM proteins (UBP1, RBP45, RBP47, UBA1 et UBA2)					
<i>Arabidopsis thaliana</i>	RBP45b	–	NP_172630	3	Lorkovic et al. (2000a)
<i>Arabidopsis thaliana</i>	RBP47a	–	AAG13046	3	Lorkovic et al. (2000a)
<i>Arabidopsis thaliana</i>	RBP47b	–	BAB02953	3	Lorkovic et al. (2000a)
<i>Arabidopsis thaliana</i>	RBP47c	–	AAD46038	3	Lorkovic et al. (2000a)
<i>Arabidopsis thaliana</i>	RBP47c'	–	AAD46037	3	Lorkovic et al. (2000a)
<i>Nicotiana glauca</i>	RBP45	–	CAC01237	3	Lorkovic et al. (2000a)
<i>Arabidopsis thaliana</i>	UBP1a	–	AAD25780	3	Lambermon et al. (2000)
<i>Arabidopsis thaliana</i>	UBP1b	–	AAF79492	3	Lambermon et al. (2000)
<i>Arabidopsis thaliana</i>	UBP1c	–	BAB02974	3	Lambermon et al. (2000)
<i>Nicotiana glauca</i>	UBP1	–	CAB75429	3	Lambermon et al. (2000)

organism	name	description	accession	#RRM	references
<i>Arabidopsis thaliana</i>	UBA2a	–	NP_850711	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	UBA2b	–	NP_001078035	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	UBA2c	–	BAA97064	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	UBA1a	–	AAD25815	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	UBA1b	–	AAD25814	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	UBA1c	–	AAC16468	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP2	–	BAB09544	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP3	–	AAC61284	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP4	–	CAB88326	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP5	–	CAB78306	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP7	–	AAG51218	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP8	–	AAD20390	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP9	–	AAC23648	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP10	–	AAF21210	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP11	–	BAB09686	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP12	–	BAB09337	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP13	–	BAB08354	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP14	–	AAB88654	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	S-RBP15	–	BAB09540	1	Lorkovic and Barta (2002)
▷ snRNP — small nuclear ribonucleoprotein (snRNP)					
<i>Solanum tuberosum</i>	U1A	–	CAA90282	2	Simpson et al. (1995)
<i>Homo sapiens</i>	U1A	–	NP_004587	2	Sillekens et al. (1987)
<i>Mus musculus</i>	U1A	–	NP_056597	2	Bennett et al. (1993)
<i>Xenopus laevis</i>	U1A	–	CAA41021	2	Scherly et al. (1991)
<i>Solanum tuberosum</i>	U2B ^{''}	–	AAA33847	2	Simpson et al. (1991)
<i>Arabidopsis thaliana</i>	U1A	–	NP_182280	2	Simpson et al. (1995)
<i>Arabidopsis thaliana</i>	U170K	–	CAB62436	1	Golovkin and Reddy (1996)
<i>Arabidopsis thaliana</i>	U2B	–	NP_180585	2	Simpson et al. (1995)
<i>Arabidopsis thaliana</i>	U2B	–	AAF82223	2	Simpson et al. (1991)
<i>Arabidopsis thaliana</i>	U2AF65a	–	CAB80335	2	Domon et al. (1998)
<i>Arabidopsis thaliana</i>	U2AF65b	–	AAG51641	3	Domon et al. (1998)
<i>Arabidopsis thaliana</i>	U2SF3b53a	–	AAD12222	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	U2SF3b53b	–	AAD15475	2	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	U11-35kD	–	AAB64330	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	U2AF35	–	BAB10638	1	Domon et al. (1998)
<i>Nicotiana glauca</i>	U2AF65	–	CAA77136	3	Domon et al. (1998)
<i>Zea mays</i>	U170K	–	AAT64945	1	Gupta et al. (2006)

organism	name	description	accession	#RRM	references
<i>Danio rerio</i>	U170K	–	Q6DRE8	1	Amsterdam et al. (2004)
<i>Mus musculus</i>	U11/U1235K	–	Q9D384	1	GenBank
<i>Homo sapiens</i>	U2AF35	–	NP_006749	1	Zhang et al. (1992)
<i>Mus musculus</i>	U2AF35	–	Q9D883	1	Pacheco et al. (2004)
<i>Danio rerio</i>	U2AF35	–	AAM34646	1	Pacheco et al. (2004)
<i>Drosophila melanogaster</i>	U2AF35	–	AAB17271	1	Rudner et al. (1996)
<i>Caenorhabditis elegans</i>	U2AF35	–	CAB55137	1	Zorio and Blumenthal (1999)
<i>Gallus gallus</i>	U2AF35	–	NP_989986	1	Pacheco et al. (2004)
<i>Schizosaccharomyces pombe</i>	U2AF23	–	AAC49805	1	Wentz-Hunter and Potashkin (1996)
<i>Homo sapiens</i>	U2AF65	–	NP_009210	3	Zamore et al. (1992)
<i>Mus musculus</i>	U2AF65	–	NP_598432	3	Sailer et al. (1992)
<i>Danio rerio</i>	U2AF65	–	AAH65869	3	Kielkopf et al. (2004)
<i>Caenorhabditis elegans</i>	U2AF65	–	AAC26982	3	Zorio et al. (1997)
<i>Homo sapiens</i>	U11/U12 35K	–	NP_073208	1	Will et al. (2004)
<i>Mus musculus</i>	U2AF1-rs 1	–	NP_035793	1	Kitagawa et al. (1995)
<i>Homo sapiens</i>	U2A1L3	–	Q8WU68	1	Shepard et al. (2002)
<i>Homo sapiens</i>	U2AF1L4	–	NP_001035515	1	Shepard et al. (2002)
▷ 30kRRM — 30K-RRM proteins					
<i>Arabidopsis thaliana</i>	30K-RRM1	–	CAB77597	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	30K-RRM2	–	AAF27001	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	30K-RRM3	–	AAD30604	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	30K-RRM4	–	AAG51948	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	30K-RRM5	–	AAF87259	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	30K-RRM6	–	AAF71806	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	30K-RRM7	–	AAC33496	1	Lorkovic and Barta (2002)
<i>Arabidopsis thaliana</i>	30K-RRM8	–	AAK32921	1	Lorkovic and Barta (2002)

References

- R. Abe, Y. Uyeno, K. Yamamoto, and H. Sakamoto. Tissue-specific expression of the gene encoding a mouse RNA binding protein homologous to human HuD antigen. *DNA Res*, 1:175–80, 1994.
- R. Abe, E. Sakashita, K. Yamamoto, and H. Sakamoto. Two different RNA binding activities for the AU-rich element and the poly(A) sequence of the mouse neuronal protein mHuC. *Nucleic Acids Res*, 24:4895–901, 1996a.
- R. Abe, K. Yamamoto, and H. Sakamoto. Target specificity of neuronal RNA-binding protein, Mel-N1: direct binding to the 3' untranslated region of its own mRNA. *Nucleic Acids Res*, 24:2011–6, 1996b.
- E. Allemand, R. Gattoni, H. M. Bourbon, J. Stevenin, J. F. Caceres, J. Soret, and J. Tazi. Distinctive features of Drosophila alternative splicing factor RS domain: implication for specific phosphorylation, shuttling, and splicing activation. *Mol Cell Biol*, 21:1345–59, 2001.
- A. T. Alzhanova-Ericsson, X. Sun, N. Visa, E. Kiseleva, T. Wurtz, and B. Daneholt. A protein of the SR family of splicing factors binds extensively to exonic Balbiani ring pre-mRNA and accompanies the RNA from the gene to the nuclear pore. *Genes Dev*, 10:2881–93, 1996.
- A. Amsterdam, R. M. Nissen, Z. Sun, E. C. Swindell, S. Farrington, and N. Hopkins. Identification of 315 genes essential for early zebrafish development. *Proc Natl Acad Sci U S A*, 101:12792–7, 2004.
- M. Anderson, K. Fair, S. Amero, S. Nelson, P. J. Harte, and M. O. Diaz. A new family of cyclophilins with an RNA recognition motif that interact with members of the trx/MLL protein family in Drosophila and human cells. *Dev Genes Evol*, 212:107–13, 2002.
- U. Atasoy, J. Watson, D. Patel, and J. D. Keene. ELAV protein HuA (HuR) can redistribute between nucleus and cytoplasm and is upregulated during serum stimulation and T cell activation. *J Cell Sci*, 111 (Pt 21): 3145–56, 1998.
- J. Badolato, E. Gardiner, N. Morrison, and J. Eisman. Identification and characterisation of a novel human RNA-binding protein. *Gene*, 166:323–7, 1995.
- A. Barbouti, M. Hoglund, B. Johansson, C. Lassen, P. G. Nilsson, A. Hagemeijer, F. Mitelman, and T. Fioretos. A novel gene, MS12, encoding a putative RNA-binding protein is recurrently rearranged at disease progression of chronic myeloid leukemia and forms a fusion gene with HOXA9 as a result of the cryptic t(7;17)(p15;q23). *Cancer Res*, 63:1202–6, 2003.
- D. C. Barnard and J. G. Patton. Identification and characterization of a novel serine-arginine-rich splicing regulatory protein. *Mol Cell Biol*, 20:3049–57, 2000.
- A. R. Beck, Q. G. Medley, S. O'Brien, P. Anderson, and M. Streuli. Structure, tissue distribution and genomic organization of the murine RRM-type RNA binding proteins TIA-1 and TIAR. *Nucleic Acids Res*, 24:3829–35, 1996.
- I. Behm-Ansmant, D. Gatfield, J. Rehwinkel, V. Hilgers, and E. Izauralde. A conserved role for cytoplasmic poly(A)-binding protein 1 (PABPC1) in nonsense-mediated mRNA decay. *Embo J*, 26:1591–601, 2007.
- D. A. Belostotsky. Unexpected complexity of poly(A)-binding protein gene families in flowering plants: three conserved lineages that are at least 200 million years old and possible auto- and cross-regulation. *Genetics*, 163: 311–9, 2003.
- M. M. Bennett, M. A. Baron, and J. Craft. Nucleotide sequence analysis of the A protein of the U1 small nuclear ribonucleoprotein particle: the murine protein contains a 5' amino-terminal tag. *Nucleic Acids Res*, 21:4404, 1993.
- I. Bieche, V. Manceau, P. A. Curmi, I. Laurendeau, S. Lachkar, K. Leroy, D. Vidaud, A. Sobel, and A. Maucuer. Quantitative RT-PCR reveals a ubiquitous but preferentially neural expression of the KIS gene in rat and human. *Brain Res Mol Brain Res*, 114:55–64, 2003.
- P. Blanco, C. A. Sargent, C. A. Boucher, G. Howell, M. Ross, and N. A. Affara. A novel poly(A)-binding protein gene (PABPC5) maps to an X-specific subinterval in the Xq21.3/Yp11.2 homology block of the human sex chromosomes. *Genomics*, 74:1–11, 2001.
- A. L. Bothwell, D. W. Ballard, W. M. Philbrick, G. Lindwall, S. E. Maher, M. M. Bridgett, S. F. Jamison, and M. A. Garcia-Blanco. Murine polypyrimidine tract binding protein. Purification, cloning, and mapping of the RNA binding domain. *J Biol Chem*, 266:24657–63, 1991.
- H. M. Bourbon, B. Lapeyre, and F. Amalric. Structure of the mouse nucleolin gene. The complete sequence reveals that each RNA binding domain is encoded by two independent exons. *J Mol Biol*, 200:627–38, 1988a.
- H. M. Bourbon, M. Prudhomme, and F. Amalric. Sequence and structure of the nucleolin promoter in rodents: characterization of a strikingly conserved CpG island. *Gene*, 68:73–84, 1988b.

- K. R. Brimacombe and A. N. Ladd. Cloning and embryonic expression patterns of the chicken CELF family. *Dev Dyn*, 236:2216–24, 2007.
- S. A. Brown, J. Ripperger, S. Kadener, F. Fleury-Olela, F. Vilbois, M. Rosbash, and U. Schibler. PERIOD1-associated proteins modulate the negative limb of the mammalian circadian oscillator. *Science*, 308:693–6, 2005.
- E. Buratti and F. E. Baralle. Multiple roles of TDP-43 in gene expression, splicing regulation, and human disease. *Front Biosci*, 13:867–78, 2008.
- C. G. Burd, M. S. Swanson, M. Gorlach, and G. Dreyfuss. Primary structures of the heterogeneous nuclear ribonucleoprotein A2, B1, and C2 proteins: a diversity of RNA binding proteins is generated by small peptide inserts. *Proc Natl Acad Sci U S A*, 86:9788–92, 1989.
- M. Buvoli, G. Biamonti, P. Tsoulfas, M. T. Bassi, A. Ghetti, S. Riva, and C. Morandi. cDNA cloning of human hnRNP protein A1 reveals the existence of multiple mRNA isoforms. *Nucleic Acids Res*, 16:3751–70, 1988.
- C. D. Carpenter, J. A. Kreps, and A. E. Simon. Genes encoding glycine-rich Arabidopsis thaliana proteins with RNA-binding motifs are influenced by cold treatment and an endogenous circadian rhythm. *Plant Physiol*, 104:1015–25, 1994.
- Y. Cavaloc, M. Popielarz, J. P. Fuchs, R. Gattoni, and J. Stevenin. Characterization and cloning of the human splicing factor 9G8: a novel 35 kDa factor of the serine/arginine protein family. *Embo J*, 13:2639–49, 1994.
- N. N. Chai, H. Zhou, J. Hernandez, H. Najmabadi, S. Bhasin, and P. H. Yen. Structure and organization of the RBMY genes on the human Y chromosome: transposition and amplification of an ancestral autosomal hnRNP gene. *Genomics*, 49:283–9, 1998.
- A. S. Chaouki and H. K. Salz. Drosophila SPF45: a bi-functional protein with roles in both splicing and DNA repair. *PLoS Genet*, 2:e178, 2006.
- B. Cosson, F. Braun, L. Paillard, P. Blackshear, and H. Beverley Osborne. Identification of a novel Xenopus laevis poly (A) binding protein. *Biol Cell*, 96:519–27, 2004.
- W. J. Costain and R. K. Mishra. PLG regulates hnRNP-L expression in the rat striatum and pre-frontal cortex: identification by ddPCR. *Peptides*, 24:137–46, 2003.
- A. E. Cowper, J. F. Caceres, A. Mayeda, and G. R. Screaton. Serine-arginine (SR) protein-like factors that antagonize authentic SR proteins and regulate alternative splicing. *J Biol Chem*, 276:48908–14, 2001.
- T. Dai, Y. Vera, E. C. Salido, and P. H. Yen. Characterization of the mouse Dazap1 gene encoding an RNA-binding protein that interacts with infertility factors DAZ and DAZL. *BMC Genomics*, 2:6, 2001.
- A. Damianov, M. Kann, W. S. Lane, and A. Bindereif. Human RBM28 protein is a specific nucleolar component of the spliceosomal snRNPs. *Biol Chem*, 387:1455–60, 2006.
- S. Danno, H. Nishiyama, H. Higashitsuji, H. Yokoi, J. H. Xue, K. Itoh, T. Matsuda, and J. Fujita. Increased transcript level of RBM3, a member of the glycine-rich RNA-binding protein family, in human cells in response to cold stress. *Biochem Biophys Res Commun*, 236:804–7, 1997.
- L. Didierjean, P. Frendo, and G. Burkard. Stress responses in maize: sequence analysis of cDNAs encoding glycine-rich proteins. *Plant Mol Biol*, 18:847–9, 1992.
- C. Domon, Z. J. Lorkovic, J. Valcarcel, and W. Filipowicz. Multiple forms of the U2 small nuclear ribonucleoprotein auxiliary factor U2AF subunits expressed in higher plants. *J Biol Chem*, 273:34603–10, 1998.
- B. Dong, D. S. Horowitz, R. Kobayashi, and A. R. Krainer. Purification and cDNA cloning of HeLa cell p54nrb, a nuclear protein with two RNA recognition motifs and extensive homology to human splicing factor PSF and Drosophila NONA/BJ6. *Nucleic Acids Res*, 21:4085–92, 1993.
- T. K. Edwards, A. Saleem, J. A. Shaman, T. Dennis, C. Gerigk, E. Oliveros, M. R. Gartenberg, and E. H. Rubin. Role for nucleolin/Nsr1 in the cellular localization of topoisomerase I. *J Biol Chem*, 275:36181–8, 2000.
- C. Feral, G. Guellaen, and A. Pawlak. Human testis expresses a specific poly(A)-binding protein. *Nucleic Acids Res*, 29:1872–83, 2001.
- S. Fleurdepine, J. M. Deragon, M. Devic, J. Guillemot, and C. Bousquet-Antonelli. A bona fide La protein is required for embryogenesis in Arabidopsis thaliana. *Nucleic Acids Res*, 35:3306–21, 2007.
- K. P. Forbes, B. Addepalli, and A. G. Hunt. An Arabidopsis Fip1 homolog interacts with RNA and provides conceptual links with a number of other polyadenylation factor subunits. *J Biol Chem*, 281:176–86, 2006.
- M. Fornaro, S. Raimondo, J. M. Lee, and M. G. Giacobini-Robecchi. Neuron-specific Hu proteins subcellular localization in primary sensory neurons. *Ann Anat*, 189:223–8, 2007.
- P. Fortes, D. Longman, S. McCracken, J. Y. Ip, R. Poot, I. W. Mattaj, J. F. Caceres, and B. J. Blencowe. Identification and characterization of RED120: a conserved PWI domain protein with links to splicing and 3'-end formation. *FEBS Lett*, 581:3087–97, 2007.
- A. H. Fox, Y. W. Lam, A. K. Leung, C. E. Lyon, J. Andersen, M. Mann, and A. I. Lamond. Paraspeckles: a novel nuclear domain. *Curr Biol*, 12:13–25, 2002.
- D. Fritz and B. Stefanovic. RNA-binding protein RBMS3 is expressed in activated hepatic stellate cells and liver

REFERENCES

- fibrosis and increases expression of transcription factor Prx1. *J Mol Biol*, 371:585–95, 2007.
- X. D. Fu and T. Maniatis. Isolation of a complementary DNA that encodes the mammalian splicing factor SC35. *Science*, 256:535–8, 1992.
- M. Fujimoto, K. I. Matsumoto, S. M. Iguchi-Ariga, and H. Ariga. Structures and comparison of genomic and complementary DNAs of mouse MSSP, a c-Myc binding protein. *Int J Oncol*, 16:245–51, 2000.
- H. Gao, W. J. Gordon-Kamm, and L. A. Lyznik. ASF/SF2-like maize pre-mRNA splicing factors affect splice site utilization and their transcripts are alternatively spliced. *Gene*, 339:25–37, 2004.
- H. Ge and J. L. Manley. A protein factor, ASF, controls cell-specific alternative splicing of SV40 early pre-mRNA in vitro. *Cell*, 62:25–34, 1990.
- F. Gebauer and J. D. Richter. Mouse cytoplasmic polyadenylation element binding protein: an evolutionarily conserved protein that interacts with the cytoplasmic polyadenylation elements of c-mos mRNA. *Proc Natl Acad Sci U S A*, 93:14602–7, 1996.
- A. Gil, P. A. Sharp, S. F. Jamison, and M. A. Garcia-Blanco. Characterization of cDNAs encoding the polypyrimidine tract-binding protein. *Genes Dev*, 5:1224–36, 1991.
- M. Golovkin and A. S. Reddy. An SC35-like protein and a novel serine/arginine-rich protein interact with Arabidopsis U1-70K protein. *J Biol Chem*, 274:36428–38, 1999.
- M. Golovkin and A. S. Reddy. Structure and expression of a plant U1 snRNP 70K gene: alternative splicing of U1 snRNP 70K pre-mRNAs produces two different transcripts. *Plant Cell*, 8:1421–35, 1996.
- M. Golovkin and A. S. Reddy. The plant U1 small nuclear ribonucleoprotein particle 70K protein interacts with two novel serine/arginine-rich proteins. *Plant Cell*, 10:1637–48, 1998.
- P. Good, A. Yoda, S. Sakakibara, A. Yamamoto, T. Imai, H. Sawa, T. Ikeuchi, S. Tsuji, H. Satoh, and H. Okano. The human Musashi homolog 1 (MSI1) gene encoding the homologue of Musashi/Nrp-1, a neural RNA-binding protein putatively expressed in CNS stem cells and neural progenitor cells. *Genomics*, 52:382–4, 1998.
- C. Gooding, P. Kemp, and C. W. Smith. A novel polypyrimidine tract-binding protein paralog expressed in smooth muscle cells. *J Biol Chem*, 278:15201–7, 2003.
- O. Gozani, J. G. Patton, and R. Reed. A novel set of spliceosome-associated proteins and the essential splicing factor PSF bind stably to pre-mRNA prior to catalytic step II of the splicing reaction. *Embo J*, 13:3356–67, 1994.
- T. Gross, K. Richert, C. Mierke, M. Lutzelberger, and N. F. Kaufer. Identification and characterization of srp1, a gene of fission yeast encoding a RNA binding domain and a RS domain typical of SR splicing factors. *Nucleic Acids Res*, 26:505–11, 1998.
- M. Gullerova, A. Barta, and Z. J. Lorkovic. AtCyp59 is a multidomain cyclophilin from Arabidopsis thaliana that interacts with SR proteins and the C-terminal domain of the RNA polymerase II. *Rna*, 12:631–43, 2006.
- M. P. Gulli, J. P. Girard, D. Zabetakis, B. Lapeyre, T. Melese, and M. Caizergues-Ferrer. gar2 is a nuclear protein from Schizosaccharomyces pombe required for 18S rRNA and 40S ribosomal subunit accumulation. *Nucleic Acids Res*, 23:1912–8, 1995.
- S. Gupta, A. Ciungu, N. Jameson, and S. K. Lal. Alternative splicing expression of U1 snRNP 70K gene is evolutionary conserved between different plant species. *DNA Seq*, 17:254–61, 2006.
- S. Hagele, U. Kuhn, M. Boning, and D. M. Katschinski. Cytoplasmic polyadenylation element binding protein (CPEB)1 and 2 bind to the HIF-1alpha mRNA 3'UTR and modulate HIF-1 alpha protein expression. *Biochem J*, 2008.
- S. Hamimes, H. Arakawa, A. Z. Stasiak, A. M. Kierzek, S. Hirano, Y. G. Yang, M. Takata, A. Stasiak, J. M. Buerstedde, and E. Van Dyck. RDM1, a novel RNA recognition motif (RRM)-containing protein involved in the cell response to cisplatin in vertebrates. *J Biol Chem*, 280:9225–35, 2005.
- S. Hanano, M. Sugita, and M. Sugiura. Isolation of a novel RNA-binding protein and its association with a large ribonucleoprotein particle present in the nucleoplasm of tobacco cells. *Plant Mol Biol*, 31:57–68, 1996.
- K. Harada, A. Yamada, T. Mine, N. Kawagoe, H. Takasu, and K. Itoh. Mouse homologue of the human SART3 gene encoding tumor-rejection antigen. *Jpn J Cancer Res*, 91:239–47, 2000.
- K. Harada, A. Yamada, D. Yang, K. Itoh, and S. Shichijo. Binding of a SART3 tumor-rejection antigen to a pre-mRNA splicing factor RNPS1: a possible regulation of splicing by a complex formation. *Int J Cancer*, 93:623–8, 2001.
- Y. Hashimoto, H. Suzuki, Y. Kageyama, K. Yasuda, and K. Inoue. Bruno-like protein is localized to zebrafish germ plasm during the early cleavage stages. *Gene Expr Patterns*, 6:201–5, 2006.
- W. Hassfeld, E. K. Chan, D. A. Mathison, D. Portman, G. Dreyfuss, G. Steiner, and E. M. Tan. Molecular definition of heterogeneous nuclear ribonucleoprotein R (hnRNP R) using autoimmune antibody: immunological relationship with hnRNP P. *Nucleic Acids Res*, 26:439–45, 1998.

- M. A. Heine, M. L. Rankin, and P. J. DiMario. The Gly/Arg-rich (GAR) domain of *Xenopus* nucleolin facilitates in vitro nucleic acid binding and in vivo nucleolar localization. *Mol Biol Cell*, 4:1189–204, 1993.
- C. Heintzen, M. Nater, K. Apel, and D. Staiger. At-GRP7, a nuclear RNA-binding protein as a component of a circadian-regulated negative feedback loop in *Arabidopsis thaliana*. *Proc Natl Acad Sci U S A*, 94:8515–20, 1997.
- J. Hodgkin, J. D. Zellan, and D. G. Albertson. Identification of a candidate primary sex determination locus, *fox-1*, on the X chromosome of *Caenorhabditis elegans*. *Development*, 120:3681–9, 1994.
- N. Hosoda, F. Lejeune, and L. E. Maquat. Evidence that poly(A) binding protein C1 binds nuclear pre-mRNA poly(A) tails. *Mol Cell Biol*, 26:3085–97, 2006.
- H. Imai, E. K. Chan, K. Kiyosawa, X. D. Fu, and E. M. Tan. Novel nuclear autoantigen with splicing factor motifs identified with antibody from hepatocellular carcinoma. *J Clin Invest*, 92:2419–26, 1993.
- A. Inoue, K. P. Takahashi, M. Kimura, T. Watanabe, and S. Morisawa. Molecular cloning of a RNA binding protein, S1-1. *Nucleic Acids Res*, 24:2990–7, 1996.
- A. Inoue, A. Omori, S. Ichinose, K. P. Takahashi, Y. Kinoshita, and S. Mita. S1 proteins C2 and D2 are novel hnRNPs similar to the transcriptional repressor, CARG box motif-binding factor A. *Eur J Biochem*, 268:3654–63, 2001.
- M. Isshiki, A. Tsumoto, and K. Shimamoto. The serine/arginine-rich protein family in rice plays important roles in constitutive and alternative splicing of pre-mRNA. *Plant Cell*, 18:146–58, 2006.
- T. Iwasaki, W. W. Chin, and L. Ko. Identification and characterization of RRM-containing coactivator activator (CoAA) as TRBP-interacting protein, and its splice variant as a coactivator modulator (CoAM). *J Biol Chem*, 276:33375–83, 2001.
- C. N. Ji, J. Z. Chen, Y. Xie, S. Wang, J. Qian, E. Zhao, W. Jin, X. Z. Wu, W. X. Xu, K. Ying, and Y. M. Mao. A novel cDNA encodes a putative hRALY-like protein, hRALYL. *Mol Biol Rep*, 30:61–7, 2003.
- Y. Jin, H. Suzuki, S. Maegawa, H. Endo, S. Sugano, K. Hashimoto, K. Yasuda, and K. Inoue. A vertebrate RNA-binding protein Fox-1 regulates tissue-specific splicing via the pentanucleotide GCAUG. *Embo J*, 22:905–12, 2003.
- K. R. Jones and G. M. Rubin. Molecular analysis of no-on-transient A, a gene required for normal vision in *Drosophila*. *Neuron*, 4:711–23, 1990.
- D. J. Jung, S. Y. Na, D. S. Na, and J. W. Lee. Molecular cloning and characterization of CAPER, a novel coactivator of activating protein-1 and estrogen receptors. *J Biol Chem*, 277:1229–34, 2002.
- P. Kafasla, M. Patrino-Georgoula, and A. Guialis. The 72/74-kDa polypeptides of the 70-110 S large heterogeneous nuclear ribonucleoprotein complex (LH-nRNP) represent a discrete subset of the hnRNP M protein family. *Biochem J*, 350 Pt 2:495–503, 2000.
- M. Kalyna and A. Barta. A plethora of plant serine/arginine-rich proteins: redundancy or evolution of novel gene functions? *Biochem Soc Trans*, 32:561–4, 2004.
- H. Kamma, H. Horiguchi, L. Wan, M. Matsui, M. Fujiwara, M. Fujimoto, T. Yazawa, and G. Dreyfuss. Molecular characterization of the hnRNP A2/B1 proteins: tissue-specific expression and novel isoforms. *Exp Cell Res*, 246:399–411, 1999.
- Y. Kanaoka and H. Nojima. SCR: novel human suppressors of *cdc2/cdc13* mutants of *Schizosaccharomyces pombe* harbour motifs for RNA binding proteins. *Nucleic Acids Res*, 22:2687–93, 1994.
- I. Karagiannides, T. Thomou, T. Tchkonja, T. Pirtskhalava, K. E. Kypreos, A. Cartwright, G. Dalagiorgou, T. L. Lash, S. R. Farmer, N. A. Timchenko, and J. L. Kirkland. Increased CUG triplet repeat-binding protein-1 predisposes to impaired adipogenesis with aging. *J Biol Chem*, 281:23025–33, 2006.
- S. J. Kavanagh, T. C. Schulz, P. Davey, C. Claudianos, C. Russell, and P. D. Rathjen. A family of RS domain proteins with novel subcellular localization and trafficking. *Nucleic Acids Res*, 33:1309–22, 2005.
- A. Kawakami, Q. Tian, X. Duan, M. Streuli, S. F. Schlossman, and P. Anderson. Identification and functional characterization of a TIA-1-related nucleolysin. *Proc Natl Acad Sci U S A*, 89:8681–5, 1992.
- T. Kawashima, A. R. Murakami, M. Ogasawara, K. Tanaka, R. Isoda, Y. Sasakura, T. Nishikata, H. Okano, and K. W. Makabe. Expression patterns of musashi homologs of the ascidians, *Halocynthia roretzi* and *Ciona intestinalis*. *Dev Genes Evol*, 210:162–5, 2000.
- D. Kennedy, S. A. Wood, T. Ramsdale, P. P. Tam, K. A. Steiner, and J. S. Mattick. Identification of a mouse orthologue of the human ras-GAP-SH3-domain binding protein and structural confirmation that these proteins contain an RNA recognition motif. *Biomed Pept Proteins Nucleic Acids*, 2:93–9, 1996.
- F. A. Khan, A. K. Jaiswal, and W. Szer. Cloning and sequence analysis of a human type A/B hnRNP protein. *FEBS Lett*, 290:159–61, 1991.
- I. Khrebtkova, A. Kuklin, R. P. Woychik, and E. J. Michaud. Alternative processing of the human and mouse raly genes(1). *Biochim Biophys Acta*, 1447:107–12, 1999.
- T. R. Kiehl, H. Shibata, T. Vo, D. P. Huynh, and S. M. Pulst. Identification and expression of a mouse ortholog of A2BP1. *Mamm Genome*, 12:595–601, 2001.

- C. L. Kielkopf, S. Lucke, and M. R. Green. U2AF homology motifs: protein recognition in the RRM world. *Genes Dev*, 18:1513–26, 2004.
- E. Kiesler, M. E. Hase, D. Brodin, and N. Visa. Hrp59, an hnRNP M protein in *Chironomus* and *Drosophila*, binds to exonic splicing enhancers and is required for expression of a subset of mRNAs. *J Cell Biol*, 168:1013–25, 2005.
- K. Kimura, H. Saga, K. Hayashi, H. Obata, Y. Chimori, H. Ariga, and K. Sobue. c-Myc gene single-strand binding protein-1, MSSP-1, suppresses transcription of alpha-smooth muscle actin gene in chicken visceral smooth muscle cells. *Nucleic Acids Res*, 26:2420–5, 1998.
- K. Kitagawa, X. Wang, I. Hatada, T. Yamaoka, H. Nojima, J. Inazawa, T. Abe, K. Mitsuya, M. Oshimura, A. Murata, and et al. Isolation and mapping of human homologues of an imprinted mouse gene U2af1-rs1. *Genomics*, 30:257–63, 1995.
- K. C. Kleene, E. Mulligan, D. Steiger, K. Donohue, and M. A. Mastrangelo. The mouse gene encoding the testis-specific isoform of Poly(A) binding protein (Pabp2) is an expressed retroposon: intimations that gene expression in spermatogenic cells facilitates the creation of new genes. *J Mol Evol*, 47:275–81, 1998.
- S. Kojima, K. Matsumoto, M. Hirose, M. Shimada, M. Nagano, Y. Shigeyoshi, S. Hoshino, K. Ui-Tei, K. Saigo, C. B. Green, Y. Sakaki, and H. Tei. LARK activates posttranscriptional expression of an essential mammalian clock protein, PERIOD1. *Proc Natl Acad Sci U S A*, 104:1859–64, 2007.
- E. Kotani, T. Ohba, T. Niwa, K. B. Storey, J. S. Storey, S. Hara, H. Saito, Y. Sugimura, and T. Furusawa. De novo gene expression and antisense inhibition in cultured cells of BmTRN-1, cloned from the midgut of the silkworm, *Bombyx mori*, which is homologous with mammalian TIA-1/R. *Gene*, 320:67–79, 2003.
- A. R. Krainer, G. C. Conway, and D. Kozak. Purification and characterization of pre-mRNA splicing factor SF2 from HeLa cells. *Genes Dev*, 4:1158–71, 1990.
- B. J. Krueger, C. Jeronimo, B. B. Roy, A. Bouchard, C. Barrandon, S. A. Byers, C. E. Searcey, J. J. Cooper, O. Bensaude, E. A. Cohen, B. Coulombe, and D. H. Price. LARP7 is a stable component of the 7SK snRNP while P-TEFb, HEXIM1 and hnRNP A1 are reversibly associated. *Nucleic Acids Res*, 36:2219–29, 2008.
- U. Kuhn, A. Nemeth, S. Meyer, and E. Wahle. The RNA binding domains of the nuclear poly(A)-binding protein. *J Biol Chem*, 278:16916–25, 2003.
- Y. Kurihara, M. Tokuriki, R. Myojin, T. Hori, A. Kuroiwa, Y. Matsuda, T. Sakurai, M. Kimura, N. B. Hecht, and S. Uesugi. CPEB2, a novel putative translational regulator in mouse haploid germ cells. *Biol Reprod*, 69:261–8, 2003.
- A. N. Ladd, N. Charlet, and T. A. Cooper. The CELF family of RNA binding proteins is implicated in cell-specific and developmentally regulated alternative splicing. *Mol Cell Biol*, 21:1285–96, 2001.
- A. N. Ladd, N. H. Nguyen, K. Malhotra, and T. A. Cooper. CELF6, a member of the CELF family of RNA-binding proteins, regulates muscle-specific splicing enhancer-dependent alternative splicing. *J Biol Chem*, 279:17756–64, 2004.
- M. H. Lambermon, G. G. Simpson, D. A. Wiczorek Kirk, M. Hemmings-Mieszczak, U. Klahre, and W. Filipowicz. UBP1, a novel hnRNP-like protein that functions at multiple steps of higher plant nuclear pre-mRNA maturation. *Embo J*, 19:1638–49, 2000.
- G. Lazar, T. Schaal, T. Maniatis, and H. M. Goodman. Identification of a plant serine-arginine-rich protein similar to the mammalian splicing factor SF2/ASF. *Proc Natl Acad Sci U S A*, 92:7672–6, 1995.
- C. Le Guiner, M. C. Gesnel, and R. Breathnach. TIA-1 or TIAR is required for DT40 cell viability. *J Biol Chem*, 278:10465–76, 2003.
- T. D. Levine, F. Gao, P. H. King, L. G. Andrews, and J. D. Keene. Hel-N1: an autoimmune RNA-binding protein with specificity for 3' uridylate-rich untranslated regions of growth factor mRNAs. *Mol Cell Biol*, 13:3494–504, 1993.
- A. P. Lieberman, D. L. Friedlich, G. Harmison, B. W. Howell, C. L. Jordan, S. M. Breedlove, and K. H. Fischbeck. Androgens regulate the mammalian homologues of invertebrate sex determination genes tra-2 and fox-1. *Biochem Biophys Res Commun*, 282:499–506, 2001.
- N. S. Lim, G. Kozlov, T. C. Chang, O. Groover, N. Siddiqui, L. Volpon, G. De Crescenzo, A. B. Shyu, and K. Gehring. Comparative peptide binding studies of the PABC domains from the ubiquitin-protein isopeptide ligase HYD and poly(A)-binding protein. Implications for HYD function. *J Biol Chem*, 281:14376–82, 2006.
- L. Liu, E. M. Rodriguez-Belmonte, N. Mazloum, B. Xie, and M. Y. Lee. Identification of a novel protein, PDIP38, that interacts with the p50 subunit of DNA polymerase delta and proliferating cell nuclear antigen. *J Biol Chem*, 278:10041–7, 2003.
- D. Longman, I. L. Johnstone, and J. F. Caceres. Functional characterization of SR and SR-related genes in *Caenorhabditis elegans*. *Embo J*, 19:1625–37, 2000.
- S. Lopato, E. Waigmann, and A. Barta. Characterization of a novel arginine/serine-rich splicing factor in *Arabidopsis*. *Plant Cell*, 8:2255–64, 1996.
- S. Lopato, R. Gattoni, G. Fabini, J. Stevenin, and A. Barta. A novel family of plant splicing factors with a Zn knuckle motif: examination of RNA binding and splicing activities. *Plant Mol Biol*, 39:761–73, 1999a.

- S. Lopato, M. Kalyna, S. Dorner, R. Kobayashi, A. R. Krainer, and A. Barta. atSRp30, one of two SF2/ASF-like proteins from *Arabidopsis thaliana*, regulates splicing of specific plant genes. *Genes Dev*, 13:987–1001, 1999b.
- S. Lopato, C. Forstner, M. Kalyna, J. Hilscher, U. Langhammer, K. Indrapichate, Z. J. Lorkovic, and A. Barta. Network of interactions of a novel plant-specific Arg/Ser-rich protein, atRSZ33, with atSC35-like splicing factors. *J Biol Chem*, 277:39989–98, 2002.
- Z. J. Lorkovic and A. Barta. Genome analysis: RNA recognition motif (RRM) and K homology (KH) domain RNA-binding proteins from the flowering plant *Arabidopsis thaliana*. *Nucleic Acids Res*, 30:623–35, 2002.
- Z. J. Lorkovic, D. A. Wieczorek Kirk, U. Klahre, M. Hemmings-Mieszczak, and W. Filipowicz. RBP45 and RBP47, two oligouridylate-specific hnRNP-like proteins interacting with poly(A)⁺ RNA in nuclei of plant cells. *Rna*, 6:1610–24, 2000a.
- Z. J. Lorkovic, D. A. Wieczorek Kirk, M. H. Lambermon, and W. Filipowicz. Pre-mRNA splicing in higher plants. *Trends Plant Sci*, 5:160–7, 2000b.
- L. A. Lowery, J. Rubin, and H. Sive. Whitesnake/sfpq is required for cell survival and neuronal development in the zebrafish. *Dev Dyn*, 236:1347–57, 2007.
- B. Lowin, L. French, J. C. Martinou, and J. Tschopp. Expression of the CTL-associated protein TIA-1 during murine embryogenesis. *J Immunol*, 157:1448–54, 1996.
- X. Lu, N. A. Timchenko, and L. T. Timchenko. Cardiac elav-type RNA-binding protein (ETR-3) binds to RNA CUG repeats expanded in myotonic dystrophy. *Hum Mol Genet*, 8:53–60, 1999.
- W. J. Ma, S. Cheng, C. Campbell, A. Wright, and H. Furneaux. Cloning and characterization of HuR, a ubiquitously expressed Elav-like protein. *J Biol Chem*, 271:8144–51, 1996.
- X. Ma, M. J. Renda, L. Wang, E. C. Cheng, C. Niu, S. W. Morris, A. S. Chi, and D. S. Krause. Rbm15 modulates Notch-induced transcriptional activation and affects myeloid differentiation. *Mol Cell Biol*, 27:3056–64, 2007.
- Z. Ma, S. W. Morris, V. Valentine, M. Li, J. A. Herbrick, X. Cui, D. Bouman, Y. Li, P. K. Mehta, D. Nizetic, Y. Kaneko, G. C. Chan, L. C. Chan, J. Squire, S. W. Scherer, and J. K. Hitzler. Fusion of two novel genes, RBM15 and MKL1, in the t(1;22)(p13;q13) of acute megakaryoblastic leukemia. *Nat Genet*, 28:220–1, 2001.
- R. Macknight, I. Bancroft, T. Page, C. Lister, R. Schmidt, K. Love, L. Westphal, G. Murphy, S. Sherson, C. Cobbett, and C. Dean. FCA, a gene controlling flowering time in *Arabidopsis*, encodes a protein containing RNA-binding domains. *Cell*, 89:737–45, 1997.
- D. Mahe, P. Mahl, R. Gattoni, N. Fischer, M. G. Mattei, J. Stevenin, and J. P. Fuchs. Cloning of human 2H9 heterogeneous nuclear ribonucleoproteins. Relation with splicing and early heat shock-induced splicing arrest. *J Biol Chem*, 272:1827–36, 1997.
- D. Mahe, N. Fischer, D. Decimo, and J. P. Fuchs. Spatiotemporal regulation of hnRNP M and 2H9 gene expression during mouse embryonic development. *Biochim Biophys Acta*, 1492:414–24, 2000.
- R. J. Maraia and R. V. Intine. Recognition of nascent RNA by the human La antigen: conserved and divergent features of structure and function. *Mol Cell Biol*, 21:367–79, 2001.
- V. Markovtsov, J. M. Nikolic, J. A. Goldman, C. W. Turck, M. Y. Chou, and D. L. Black. Cooperative assembly of an hnRNP complex induced by a tissue-specific homolog of polypyrimidine tract binding protein. *Mol Cell Biol*, 20:7463–79, 2000.
- M. A. Markus and B. J. Morris. Lark is the splicing factor RBM4 and exhibits unique subnuclear localization properties. *DNA Cell Biol*, 25:457–64, 2006.
- E. L. Matunis, M. J. Matunis, and G. Dreyfuss. Characterization of the major hnRNP proteins from *Drosophila melanogaster*. *J Cell Biol*, 116:257–69, 1992.
- M. J. Matunis, J. Xing, and G. Dreyfuss. The hnRNP F protein: unique primary structure, nucleic acid-binding properties, and subcellular localization. *Nucleic Acids Res*, 22:1059–67, 1994.
- A. Maucuer, J. H. Camonis, and A. Sobel. Stathmin interaction with a putative kinase and coiled-coil-forming protein domains. *Proc Natl Acad Sci U S A*, 92:3100–4, 1995.
- A. Maucuer, S. Ozon, V. Manceau, O. Gavet, S. Lawler, P. Curmi, and A. Sobel. KIS is a protein kinase with an RNA recognition motif. *J Biol Chem*, 272:23151–6, 1997.
- A. E. McKee, E. Minet, C. Stern, S. Riahi, C. D. Stiles, and P. A. Silver. A genome-wide in situ hybridization map of RNA-binding proteins reveals anatomically restricted expression in the developing mouse brain. *BMC Dev Biol*, 5:14, 2005.
- G. P. McNeil, A. J. Schroeder, M. A. Roberts, and F. R. Jackson. Genetic analysis of functional domains within the *Drosophila* LARK RNA-binding protein. *Genetics*, 159:229–40, 2001.
- M. Meins, S. Schlickum, C. Wilhelm, J. Missbach, S. Yadav, B. Glaser, M. Grzmil, P. Burfeind, and F. Laccone. Identification and characterization of murine Brunol4, a new member of the elav/bruno family. *Cytogenet Genome Res*, 97:254–60, 2002.
- H. Mi, O. Kops, E. Zimmermann, A. Jaschke, and M. Tropschug. A nuclear RNA-binding cyclophilin in human T cells. *FEBS Lett*, 398:201–5, 1996.

- S. C. Milburn, J. W. Hershey, M. V. Davies, K. Kelleher, and R. J. Kaufman. Cloning and expression of eukaryotic initiation factor 4B cDNA: sequence determination identifies a common RNA recognition motif. *Embo J*, 9: 2783–90, 1990.
- P. Montaville, Y. Dai, C. Y. Cheung, K. Giller, S. Becker, M. Michalak, S. E. Webb, A. L. Miller, and J. Krebs. Nuclear translocation of the calcium-binding protein ALG-2 induced by the RNA-binding protein RBM22. *Biochim Biophys Acta*, 1763:1335–43, 2006.
- V. E. Myer and J. A. Steitz. Isolation and characterization of a novel, low abundance hnRNP protein: A0. *Rna*, 1: 171–82, 1995.
- R. Myojin, S. Kuwahara, T. Yasaki, T. Matsunaga, T. Sakurai, M. Kimura, S. Uesugi, and Y. Kurihara. Expression and functional significance of mouse paraspeckle protein 1 on spermatogenesis. *Biol Reprod*, 71:926–32, 2004.
- Y. Negishi, Y. Nishita, Y. Saegusa, I. Kakizaki, I. Galli, F. Kihara, K. Tamai, N. Miyajima, S. M. Iguchi-Ariga, and H. Ariga. Identification and cDNA cloning of single-stranded DNA binding proteins that interact with the region upstream of the human c-myc gene. *Oncogene*, 9: 1133–43, 1994.
- J. Nielsen, J. Christiansen, J. Lykke-Andersen, A. H. Johnsen, U. M. Wewer, and F. C. Nielsen. A family of insulin-like growth factor II mRNA-binding proteins represses translation in late development. *Mol Cell Biol*, 19:1262–70, 1999.
- H. Nishiyama, H. Higashitsuji, H. Yokoi, K. Itoh, S. Danno, T. Matsuda, and J. Fujita. Cloning and characterization of human CIRP (cold-inducible RNA-binding protein) cDNA and chromosomal assignment of the gene. *Gene*, 204:115–20, 1997.
- M. Ohta, M. Sugita, and M. Sugiura. Three types of nuclear genes encoding chloroplast RNA-binding proteins (cp29, cp31 and cp33) are present in *Arabidopsis thaliana*: presence of cp31 in chloroplasts and its homologue in nuclei/cytoplasm. *Plant Mol Biol*, 27:529–39, 1995.
- H. J. Okano and R. B. Darnell. A hierarchy of Hu RNA binding proteins in developing and adult neurons. *J Neurosci*, 17:3024–37, 1997.
- L. J. Otero, M. P. Ashe, and A. B. Sachs. The yeast poly(A)-binding protein Pab1p stimulates in vitro poly(A)-dependent and cap-dependent translation by distinct mechanisms. *Embo J*, 18:3153–63, 1999.
- S. H. Ou, F. Wu, D. Harrich, L. F. Garcia-Martinez, and R. B. Gaynor. Cloning and characterization of a novel cellular protein, TDP-43, that binds to human immunodeficiency virus type 1 TAR DNA sequence motifs. *J Virol*, 69:3584–96, 1995.
- T. R. Pacheco, A. Q. Gomes, N. L. Barbosa-Morais, V. Benes, W. Ansorge, M. Wollerton, C. W. Smith, J. Valcarcel, and M. Carmo-Fonseca. Diversity of vertebrate splicing factor U2AF35: identification of alternatively spliced U2AF1 mRNAs. *J Biol Chem*, 279:27039–49, 2004.
- P. S. Page-McCaw, K. Amonlirdviman, and P. A. Sharp. PUF60: a novel U2AF65-related splicing activity. *Rna*, 5:1548–60, 1999.
- L. Paillard, F. Omilli, V. Legagneux, T. Bassez, D. Maniey, and H. B. Osborne. EDEN and EDEN-BP, a cis element and an associated factor that mediate sequence-specific mRNA deadenylation in *Xenopus* embryos. *Embo J*, 17:278–87, 1998.
- H. A. Pan, Y. S. Lin, K. H. Lee, J. R. Huang, Y. H. Lin, and P. L. Kuo. Expression patterns of the DAZ-associated protein DAZAP1 in rat and human ovaries. *Fertil Steril*, 84 Suppl 2:1089–94, 2005.
- J. Paris, K. Swenson, H. Piwnicka-Worms, and J. D. Richter. Maturation-specific polyadenylation: in vitro activation by p34cdc2 and phosphorylation of a 58-kD CPE-binding protein. *Genes Dev*, 5:1697–708, 1991.
- H. G. Park, J. Y. Yoon, and M. Choi. Heterogeneous nuclear ribonucleoprotein D/AUF1 interacts with heterogeneous nuclear ribonucleoprotein L. *J Biosci*, 32:1263–72, 2007.
- N. I. Park and D. G. Muench. Biochemical and cellular characterization of the plant ortholog of PYM, a protein that interacts with the exon junction complex core proteins Mago and Y14. *Planta*, 225:625–39, 2007.
- F. Parker, F. Maurier, I. Delumeau, M. Duchesne, D. Faucher, L. Debussche, A. Dugue, F. Schweighofer, and B. Tocque. A Ras-GTPase-activating protein SH3-domain-binding protein. *Mol Cell Biol*, 16:2561–9, 1996.
- T. J. Pemberton and J. E. Kay. The cyclophilin repertoire of the fission yeast *Schizosaccharomyces pombe*. *Yeast*, 22:927–45, 2005.
- D. Penkov, R. Ni, C. Else, S. Pinol-Roma, F. Ramirez, and S. Tanaka. Cloning of a human gene closely related to the genes coding for the c-myc single-strand binding proteins. *Gene*, 243:27–36, 2000.
- A. Perreault, C. Lemieux, and F. Bachand. Regulation of the nuclear poly(A)-binding protein by arginine methylation in fission yeast. *J Biol Chem*, 282:7552–62, 2007.
- S. Pinol-Roma, M. S. Swanson, J. G. Gall, and G. Dreyfuss. A novel heterogeneous nuclear RNP protein with a unique distribution on nascent transcripts. *J Cell Biol*, 109:2575–87, 1989.
- A. D. Polydorides, H. J. Okano, Y. Y. Yang, G. Stefani, and R. B. Darnell. A brain-enriched polypyrimidine tract-binding protein antagonizes the ability of Nova to regulate neuron-specific alternative splicing. *Proc Natl Acad Sci U S A*, 97:6350–5, 2000.

- F. Pontvianne, I. Matia, J. Douet, S. Tourmente, F. J. Medina, M. Echeverria, and J. Saez-Vasquez. Characterization of AtNUC-L1 reveals a central role of nucleolin in nucleolus organization and silencing of AtNUC-L2 gene in Arabidopsis. *Mol Biol Cell*, 18:369–79, 2007.
- M. Prigent, I. Barlat, H. Langen, and C. Dargemont. IkappaBalpha and IkappaBalpha/NF-kappa B complexes are retained in the cytoplasm through interaction with a novel partner, RasGAP SH3-binding protein 2. *J Biol Chem*, 275:36441–9, 2000.
- Z. Qian and J. Wilusz. GRSF-1: a poly(A)+ mRNA binding protein which interacts with a conserved G-rich element. *Nucleic Acids Res*, 22:2334–43, 1994.
- K. Richter, P. J. Good, and I. B. Dawid. A developmentally regulated, nervous system-specific gene in *Xenopus* encodes a putative RNA-binding protein. *New Biol*, 2: 556–65, 1990.
- M. B. Roth, A. M. Zahler, and J. A. Stolk. A conserved family of nuclear phosphoproteins localized to sites of polymerase II transcription. *J Cell Biol*, 115:587–96, 1991.
- D. Z. Rudner, R. Kanaar, K. S. Breger, and D. C. Rio. Mutations in the small subunit of the *Drosophila* U2AF splicing factor cause lethality and developmental defects. *Proc Natl Acad Sci U S A*, 93:10333–7, 1996.
- A. Sailer, N. J. MacDonald, and C. Weissmann. Cloning and sequencing of the murine homologue of the human splicing factor U2AF65. *Nucleic Acids Res*, 20:2374, 1992.
- S. Sakakibara, T. Imai, K. Hamaguchi, M. Okabe, J. Aruga, K. Nakajima, D. Yasutomi, T. Nagata, Y. Kurihara, S. Uesugi, T. Miyata, M. Ogawa, K. Mikoshiba, and H. Okano. Mouse-Musashi-1, a neural RNA-binding protein highly enriched in the mammalian CNS stem cell. *Dev Biol*, 176:230–42, 1996.
- S. Sakakibara, Y. Nakamura, H. Satoh, and H. Okano. Rna-binding protein Musashi2: developmentally regulated expression in neural precursor cells and subpopulations of neurons in mammalian CNS. *J Neurosci*, 21: 8091–107, 2001.
- K. Salehi-Ashtiani, A. Luptak, A. Litovchick, and J. W. Szostak. A genomewide search for ribozymes reveals an HDV-like sequence in the human CPEB3 gene. *Science*, 313:1788–92, 2006.
- A. M. Salicioni, M. Xi, L. A. Vanderveer, B. Balsara, J. R. Testa, J. Dunbrack, R. L., and A. K. Godwin. Identification and structural analysis of human RBM8A and RBM8B: two highly conserved RNA-binding motif proteins that interact with OVCA1, a candidate tumor suppressor. *Genomics*, 69:54–62, 2000.
- J. Sampath, P. R. Long, R. L. Shepard, X. Xia, V. Devanarayan, G. E. Sandusky, r. Perry, W. L., A. H. Dantzig, M. Williamson, M. Rolfe, and R. E. Moore. Human SPF45, a splicing factor, has limited expression in normal tissues, is overexpressed in many tumors, and can confer a multidrug-resistant phenotype to cells. *Am J Pathol*, 163:1781–90, 2003.
- D. Scherly, C. Kambach, W. Boelens, W. J. van Venrooij, and I. W. Mattaj. Conserved amino acid residues within and outside of the N-terminal ribonucleoprotein motif of U1A small nuclear ribonucleoprotein involved in U1 RNA binding. *J Mol Biol*, 219:577–84, 1991.
- G. Schmidt and D. Werner. Sequence of a complete murine cDNA reflecting an S phase-prevalent transcript encoding a protein with two types of nucleic acid binding motifs. *Biochim Biophys Acta*, 1216:317–20, 1993.
- F. M. Schomburg, D. A. Patton, D. W. Meinke, and R. M. Amasino. FPA, a gene involved in floral induction in Arabidopsis, encodes a protein containing RNA-recognition motifs. *Plant Cell*, 13:1427–36, 2001.
- G. R. Screaton, J. F. Caceres, A. Mayeda, M. V. Bell, M. Plebanski, D. G. Jackson, J. I. Bell, and A. R. Krainer. Identification and characterization of three members of the human SR family of pre-mRNA splicing factors. *Embo J*, 14:4336–49, 1995.
- D. Shahbazian, P. P. Roux, V. Mieulet, M. S. Cohen, B. Raught, J. Taunton, J. W. Hershey, J. Blenis, M. Pende, and N. Sonenberg. The mTOR/PI3K and MAPK pathways converge on eIF4B to control its phosphorylation and activity. *Embo J*, 25:2781–91, 2006.
- Y. Shav-Tal, M. Cohen, S. Lapter, B. Dye, J. G. Patton, J. Vandekerckhove, and D. Zipori. Nuclear relocation of the pre-mRNA splicing factor PSF during apoptosis involves hyperphosphorylation, masking of antigenic epitopes, and changes in protein interactions. *Mol Biol Cell*, 12:2328–40, 2001.
- J. Shepard, M. Reick, S. Olson, and B. R. Graveley. Characterization of U2AF(6), a splicing factor related to U2AF(35). *Mol Cell Biol*, 22:221–30, 2002.
- H. Shibata, D. P. Huynh, and S. M. Pulst. A novel protein with RNA-binding motifs interacts with ataxin-2. *Hum Mol Genet*, 9:1303–13, 2000.
- C. Shin, Y. Feng, and J. L. Manley. Dephosphorylated SRp38 acts as a splicing repressor in response to heat shock. *Nature*, 427:553–8, 2004.
- L. Shu, W. Yan, and X. Chen. RNPC1, an RNA-binding protein and a target of the p53 family, is required for maintaining the stability of the basal and stress-induced p21 transcript. *Genes Dev*, 20:2961–72, 2006.
- Y. Shu, N. D. Rintala-Maki, V. E. Wall, K. Wang, C. A. Goard, C. E. Langdon, and L. C. Sutherland. The apoptosis modulator and tumour suppressor protein RBM5 is a phosphoprotein. *Cell Biochem Funct*, 25:643–53, 2007.

- I. Shur, D. Ben-Avraham, and D. Benayahu. Alternatively spliced isoforms of a novel stromal RNA regulating factor. *Gene*, 334:113–21, 2004.
- P. T. Sillekens, W. J. Habets, R. P. Beijer, and W. J. van Venrooij. cDNA cloning of the human U1 snRNA-associated A protein: extensive homology between U1 and U2 snRNP-specific proteins. *Embo J*, 6:3841–8, 1987.
- G. G. Simpson, P. Vaux, G. Clark, R. Waugh, J. D. Beggs, and J. W. Brown. Evolutionary conservation of the spliceosomal protein, U2B". *Nucleic Acids Res*, 19:5213–7, 1991.
- G. G. Simpson, G. P. Clark, H. M. Rothnie, W. Boelens, W. van Venrooij, and J. W. Brown. Molecular characterization of the spliceosomal proteins U1A and U2B" from higher plants. *Embo J*, 14:4540–50, 1995.
- A. Smyk, M. Szuminska, K. A. Uniewicz, L. M. Graves, and P. Kozlowski. Human enhancer of rudimentary is a molecular partner of PDIP46/SKAR, a protein interacting with DNA polymerase delta and S6K1 and regulating cell growth. *Febs J*, 273:4728–41, 2006.
- J. Soret, R. Gattoni, C. Guyon, A. Sureau, M. Popielarz, E. Le Rouzic, S. Dumon, F. Apiou, B. Dutrillaux, H. Voss, W. Ansorge, J. Stevenin, and B. Perbal. Characterization of SRp46, a novel human SR splicing factor encoded by a PR264/SC35 retropseudogene. *Mol Cell Biol*, 18:4924–34, 1998.
- M. Soulard, V. Della Valle, M. C. Siomi, S. Pinol-Roma, P. Codogno, C. Bauvy, M. Bellini, J. C. Lacroix, G. Monod, G. Dreyfuss, and et al. hnRNP G: sequence and characterization of a glycosylated RNA-binding protein. *Nucleic Acids Res*, 21:4210–7, 1993.
- M. Srivastava, P. J. Fleming, H. B. Pollard, and A. L. Burns. Cloning and sequencing of the human nucleolin cDNA. *FEBS Lett*, 250:99–105, 1989.
- U. Steller, S. Kohls, B. Muller, R. Soller, R. Muller, J. Schlender, and D. H. Blohm. The RNA binding protein HuD: rat cDNA and analysis of the alternative spliced mRNA in neuronal differentiating cell lines P19 and PC12. *Brain Res Mol Brain Res*, 35:285–96, 1996.
- C. Stover, G. Gradl, I. Jentsch, M. R. Speicher, R. Wieser, and W. Schwaeble. cDNA cloning, chromosome assignment, and genomic structure of a human gene encoding a novel member of the RBM family. *Cytogenet Cell Genet*, 92:225–30, 2001.
- M. S. Swanson, T. Y. Nakagawa, K. LeVan, and G. Dreyfuss. Primary structure of human nuclear ribonucleoprotein particle C proteins: conservation of sequence and domain structures in heterogeneous nuclear RNA, mRNA, and pre-rRNA-binding proteins. *Mol Cell Biol*, 7:1731–9, 1987.
- A. Szabo, J. Dalmau, G. Manley, M. Rosenfeld, E. Wong, J. Henson, J. B. Posner, and H. M. Furneaux. HuD, a paraneoplastic encephalomyelitis antigen, contains RNA-binding domains and is homologous to Elav and Sex-lethal. *Cell*, 67:325–33, 1991.
- N. Takahashi, N. Tochimoto, S. Y. Ohmori, H. Mamada, M. Itoh, M. Inamori, J. Shinga, S. Osada, and M. Taira. Systematic screening for genes specifically expressed in the anterior neuroectoderm during early Xenopus development. *Int J Dev Biol*, 49:939–51, 2005.
- H. Tamada, E. Sakashita, K. Shimazaki, E. Ueno, T. Hamamoto, Y. Kagawa, and H. Endo. cDNA cloning and characterization of Drb1, a new member of RRM-type neural RNA-binding protein. *Biochem Biophys Res Commun*, 297:96–104, 2002.
- K. Tang, E. C. Breen, and P. D. Wagner. Hu protein R-mediated posttranscriptional regulation of VEGF expression in rat gastrocnemius muscle. *Am J Physiol Heart Circ Physiol*, 283:H1497–504, 2002.
- M. Theis, K. Si, and E. R. Kandel. Two previously undescribed members of the mouse CPEB family of genes and their inducible expression in the principal cell layers of the hippocampus. *Proc Natl Acad Sci U S A*, 100:9602–7, 2003.
- Q. Tian, M. Streuli, H. Saito, S. F. Schlossman, and P. Anderson. A polyadenylate binding protein localized to the granules of cytolytic lymphocytes induces DNA fragmentation in target cells. *Cell*, 67:629–39, 1991.
- L. T. Timchenko, J. W. Miller, N. A. Timchenko, D. R. DeVore, K. V. Datar, L. Lin, R. Roberts, C. T. Caskey, and M. S. Swanson. Identification of a (CUG)_n triplet repeat RNA-binding protein and its expression in myotonic dystrophy. *Nucleic Acids Res*, 24:4407–14, 1996.
- L. T. Timchenko, E. Salisbury, G. L. Wang, H. Nguyen, J. H. Albrecht, J. W. Hershey, and N. A. Timchenko. Age-specific CUGBP1-eIF2 complex increases translation of CCAAT/enhancer-binding protein beta in old liver. *J Biol Chem*, 281:32806–19, 2006.
- C. K. Too, R. Knee, A. L. Pinette, A. W. Li, and P. R. Murphy. Prolactin induces expression of FGF-2 and a novel FGF-responsive NonO/p54nrb-related mRNA in rat lymphoma cells. *Mol Cell Endocrinol*, 137:187–95, 1998.
- N. S. Trede, J. Medenbach, A. Damianov, L. H. Hung, G. J. Weber, B. H. Paw, Y. Zhou, C. Hersey, A. Zapata, M. Keefe, B. A. Barut, A. B. Stuart, T. Katz, C. T. Amemiya, L. I. Zon, and A. Bindereif. Network of coregulated spliceosome components revealed by zebrafish mutant in recycling factor p110. *Proc Natl Acad Sci U S A*, 104:6608–13, 2007.
- S. Tsui, T. Dai, S. Roettger, W. Schempp, E. C. Salido, and P. H. Yen. Identification of two novel proteins that interact with germ-cell-specific RNA-binding proteins DAZ and DAZL1. *Genomics*, 65:266–73, 2000.
- J. G. Underwood, P. L. Boutz, J. D. Dougherty, P. Stoilov, and D. L. Black. Homologues of the *Caenorhabditis el-*

- egans Fox-1 protein are neuronal splicing regulators in mammals. *Mol Cell Biol*, 25:10005–16, 2005.
- C. Valle, A. R. Troiani, P. Lazzaretti, J. Bouvier, D. Cioli, and M. Q. Klinkert. Molecular and biochemical characterization of a protein cyclophilin from the nematode *Haemonchus contortus* (P). *Parasitol Res*, 96:199–205, 2005.
- C. Van Buskirk and T. Schupbach. Half pint regulates alternative splice site selection in *Drosophila*. *Dev Cell*, 2:343–53, 2002.
- D. J. Van Horn, C. J. Yoo, D. Xue, H. Shi, and S. L. Wolin. The La protein in *Schizosaccharomyces pombe*: a conserved yet dispensable phosphoprotein that functions in tRNA maturation. *Rna*, 3:1434–43, 1997.
- B. A. Van Tine, J. F. Knops, A. Butler, P. Deloukas, G. M. Shaw, and P. H. King. Localization of HuC (ELAVL3) to chromosome 19p13.2 by fluorescence in situ hybridization utilizing a novel tyramide labeling technique. *Genomics*, 53:296–9, 1998.
- G. K. Voeltz, J. Ongkasuwan, N. Standart, and J. A. Steitz. A novel embryonic poly(A) binding protein, ePAB, regulates mRNA deadenylation in *Xenopus* egg extracts. *Genes Dev*, 15:774–88, 2001.
- E. Wahle. A novel poly(A)-binding protein acts as a specificity factor in the second phase of messenger RNA polyadenylation. *Cell*, 66:759–68, 1991.
- Y. Wakamatsu and J. A. Weston. Sequential expression and role of Hu RNA-binding proteins during neurogenesis. *Development*, 124:3449–60, 1997.
- H. Wang, M. X. Gao, L. Li, B. Wang, N. Hori, and K. Sato. Isolation, expression, and characterization of the human ZCRB1 gene mapped to 12q12. *Genomics*, 89:59–69, 2007a.
- K. Wang, G. Ubriaco, and L. C. Sutherland. RBM6-RBM5 transcription-induced chimeras are differentially expressed in tumours. *BMC Genomics*, 8:348, 2007b.
- M. Y. Wang, M. Cutler, I. Karimpour, and K. C. Kleene. Nucleotide sequence of a mouse testis poly(A) binding protein cDNA. *Nucleic Acids Res*, 20:3519, 1992.
- Z. L. Wang, J. Li, Q. Y. Xia, P. Zhao, J. Duan, X. F. Zha, and Z. H. Xiang. Identification and expression pattern of Bmlark, a homolog of the *Drosophila* gene lark in *Bombyx mori*. *DNA Seq*, 16:224–9, 2005.
- J. F. Welk, A. Charlesworth, G. D. Smith, and A. M. MacNicol. Identification and characterization of the gene encoding human cytoplasmic polyadenylation element binding protein. *Gene*, 263:113–20, 2001.
- K. Wentz-Hunter and J. Potashkin. The small subunit of the splicing factor U2AF is conserved in fission yeast. *Nucleic Acids Res*, 24:1849–54, 1996.
- C. L. Will, C. Schneider, M. Hossbach, H. Urlaub, R. Rauhut, S. Elbashir, T. Tuschl, and R. Luhrmann. The human 18S U11/U12 snRNP contains a set of novel proteins not found in the U2-dependent spliceosome. *Rna*, 10:929–41, 2004.
- E. Winstall, M. Sadowski, U. Kuhn, E. Wahle, and A. B. Sachs. The *Saccharomyces cerevisiae* RNA-binding protein Rbp29 functions in cytoplasmic mRNA metabolism. *J Biol Chem*, 275:21817–26, 2000.
- L. Wu, D. Wells, J. Tay, D. Mendis, M. A. Abbott, A. Barnitt, E. Quinlan, A. Heynen, J. R. Fallon, and J. D. Richter. CPEB-mediated cytoplasmic polyadenylation and the regulation of experience-dependent translation of α -CaMKII mRNA at synapses. *Neuron*, 21:1129–39, 1998.
- H. Yang, C. S. Duckett, and T. Lindsten. iPABP, an inducible poly(A)-binding protein detected in activated human T cells. *Mol Cell Biol*, 15:6770–6, 1995.
- Y. S. Yang, J. H. Hanke, L. Carayannopoulos, C. M. Craft, J. D. Capra, and P. W. Tucker. NonO, a non-POU-domain-containing, octamer-binding protein, is the mammalian homolog of *Drosophila* nonAdiss. *Mol Cell Biol*, 13:5593–603, 1993.
- A. Yoda, H. Sawa, and H. Okano. MSI-1, a neural RNA-binding protein, is involved in male mating behaviour in *Caenorhabditis elegans*. *Genes Cells*, 5:885–895, 2000.
- C. B. Yohn, A. Cohen, C. Rosch, M. R. Kuchka, and S. P. Mayfield. Translation of the chloroplast psbA mRNA requires the nuclear-encoded poly(A)-binding protein, RB47. *J Cell Biol*, 142:435–42, 1998.
- C. J. Yoo and S. L. Wolin. La proteins from *Drosophila melanogaster* and *Saccharomyces cerevisiae*: a yeast homolog of the La autoantigen is dispensable for growth. *Mol Cell Biol*, 14:5412–24, 1994.
- A. M. Zahler, W. S. Lane, J. A. Stolk, and M. B. Roth. SR proteins: a conserved family of pre-mRNA splicing factors. *Genes Dev*, 6:837–47, 1992.
- A. M. Zahler, K. M. Neugebauer, J. A. Stolk, and M. B. Roth. Human SR proteins and isolation of a cDNA encoding SRp75. *Mol Cell Biol*, 13:4023–8, 1993.
- P. D. Zamore, J. G. Patton, and M. R. Green. Cloning and domain structure of the mammalian splicing factor U2AF. *Nature*, 355:609–14, 1992.
- L. Zeng, Z. Zhou, J. Xu, W. Zhao, W. Wang, Y. Huang, C. Cheng, M. Xu, Y. Xie, and Y. Mao. Molecular cloning, structure and expression of a novel nuclear RNA-binding cyclophilin-like gene (PPIL4) from human fetal brain. *Cytogenet Cell Genet*, 95:43–7, 2001.
- M. Zhang, P. D. Zamore, M. Carmo-Fonseca, A. I. Lamond, and M. R. Green. Cloning and intracellular localization of the U2 small nuclear ribonucleoprotein auxiliary factor small subunit. *Proc Natl Acad Sci U S A*, 89:8769–73, 1992.

REFERENCES

- W. J. Zhang and J. Y. Wu. Functional properties of p54, a novel SR protein active in constitutive and alternative splicing. *Mol Cell Biol*, 16:5400–8, 1996.
- E. Zhao, J. Li, Y. Xie, W. Jin, Z. Zhang, J. Chen, L. Zeng, G. Yin, J. Qian, H. Wu, K. Ying, R. C. Zhao, and Y. Mao. Cloning and identification of a novel human RNPC3 gene that encodes a protein with two RRM domains and is expressed in the cell nucleus. *Biochem Genet*, 41: 315–23, 2003.
- W. M. Zhao, C. Jiang, T. T. Kroll, and P. W. Huber. A proline-rich protein binds to the localization element of *Xenopus* Vg1 mRNA and to ligands involved in actin polymerization. *Embo J*, 20:2315–25, 2001.
- Q. Zhou and P. A. Sharp. Tat-SF1: cofactor for stimulation of transcriptional elongation by HIV-1 Tat. *Science*, 274:605–10, 1996.
- D. A. Zorio and T. Blumenthal. U2AF35 is encoded by an essential gene clustered in an operon with RRM/cyclophilin in *Caenorhabditis elegans*. *Rna*, 5: 487–94, 1999.
- D. A. Zorio, K. Lea, and T. Blumenthal. Cloning of *Caenorhabditis* U2AF65: an alternatively spliced RNA containing a novel exon. *Mol Cell Biol*, 17:946–53, 1997.

node	RRM# (KOG#) KOG name	reference sequences	MP	RW	TW	RL	mRW
1	RRM1 (0110) RBP	–	y	y	y	y ¹	y
2	RRM1 (0117) hnRNPr	hnRNP (excl. flowering plants)	y ²	y	y	y	y ¹
3	RRM1 (0123) PABP	PABP	y ³	y	y ¹	y	y
4	RRM2 (0123) PABP	PABP	y ⁴	y ⁵	y ⁴	y ⁴	y ⁵
5	RRM2 (0131) splicing factor 2b [RRM2 (0115) RBP p54 nrb]	– (fungi) p54 nrb/PSP1/PSF	y ³	y	y	y	y
6	RRM3 (0123) PABP	PABP (minor subgroup)	y ³	y	y	y	y
7	RRM4 (0123) PABP	PABP	y ³	y	y	y	y
8	RRM1 (0144) BRUNO	BRUNO FCAFP (land plants)	y ²	y	y	y	y
9	RRM2 (0144) BRUNO	BRUNO FCAFP (land plants)	y ²	y	y	y	y
10	RRM3 (0144) BRUNO	BRUNO	y ³	y	y	y	y
11	RRM1 (0145) ELAV/HU	ELAV	y ³	y	y	y	y
12	RRM2 (0145) ELAV/HU	ELAV/RBMS	y ³	y	y	y	y
13	RRM3 (0145) ELAV/HU	ELAV	y ³	y	y	y	y
14	[RRM1 (0151) predicted splicing regulator]	–	y ³	y	y ¹	y ¹	y ¹
15	[RRM1 (0153) RBP]	RBM	y ³	y	y ¹	y ¹	y ¹
16	–	–	n ⁶	y	y	n ⁶	y
17	RRM1 (0105) ASF/SF2 RRM1 (0106) SRp55/B52/SRp75	dual RRM SR proteins	y	y	y	y	y
18	[RRM1 (0107) SRp20/9G8]	single RRM Zn-K SR proteins	y	y	y	y	y
19	–	see footnote [7]	n	y	n	y	y
20	[RRM1 (0111) cyclophilin-type PPCTI ⁸]	cyclophilin	y ⁹	y	y ⁹	y ⁹	y
21	[RRM1 (0130) RBP RBM8 ¹⁰]	RBM	y ⁹	y	y ⁹	y	y
22	–	–	n	n	n	n	y
23	RRM1 (4207) predicted SR protein	single RRM SR proteins	y	y	y	y	y
24	RRM1 (0111) cyclophilin-type PPCTI ⁸	SRrp	y	y	y	y	y
25	[RRM1 (0121) CBP20]	–	y	y	y	y	y ⁹
26	–	–	y	y	y	y	n ¹¹
27	RRM1 (-)	SR45 (green plants)	y	y	y	y	y
28	RRM1 (4209) splicing factor RNPS1	RNPS1	y	y	y	y	y
29	–	–	y	y	y	y	y
30	RRM2 (0105) ASF/SF2 RRM2 (0106) SRp55/B52/SRp75	dual RRM SR proteins (excl. plants)	y	y	y	y	y
31	RRM1/2/3 (4212) hnRNPM	hnRNP	y ¹²	y ¹³	y ¹³	y ¹²	y ¹²
32	[RRM1 (0533) RRM-containing protein]	PDIP/FCAFP	y ¹²	y ¹³	y ¹³	y ¹²	y ¹²
33	RRM1 (0117) hnRNPr	– (flowering plants)	y	y	y	y	y
34	RRM3 (0110) RBP	–	y ¹⁴	y	y	y	y
35	[RRM1 (0115) RBP p54 nrb]	p54 nrb-PSP1-PSF	n	y	n	n	y
36	RRM1 (2277) CID1	–	y	y	y ¹⁵	y ¹⁵	y
37	RRM1 (0116) Rasputin	G3BP	y ¹⁶	y	n	y ¹⁶	y
38	RRM1 (0149) SEB4	RBM/30KRRM	y ¹⁶	y	n	y ¹⁶	y
39	RRM1/2 (4205) HRP1	hnRNP/Musashi/Dazap/TARDBP/OligoU	y ¹⁵	y	y	y	y
40	RRM1 (0113) U1 snRNP	snRNP	y ¹⁵	y	y	y	y
41	RRM2 (0128) SART3	SART3	y ¹⁵	y	y	y ¹⁷	y ¹⁷
42	[RRM1 (0415) PPCTI ⁸]	cyclophilin	y ¹⁵	y ¹⁵	y	y	y
43	–	–	n ⁶	n ¹⁸	y ¹⁹	y ²⁰	y ²⁰
44	RRM1 (4206) U1A/U2B snRNP	snRNP	y	y	y	y	y
45	RRM2 (4206) U1A/U2B snRNP	snRNP	y	y	y	y	y
46	RRM1 (4660) Mei2	–	y	y	y	y	y
47	RRM2 (4660) Mei2	–	y	y	y	y	y
48	[RRM1 (0114) RBP]	–	y	y	y	y	y
49	–	–	n ²¹	n ²²	n ²³	n ²⁴	n ²⁴
50	RRM1 (0131) splicing factor 2b	see footnote [25]	y	y	y	y	y
51	RRM1 (4454) RBP	–	y	y	y	y	y
52	[RRM1 (2193) IGF2BP]	IGF2BP	y	y	y	y	y

node	RRM# (KOG#) KOG name	reference sequences	MP	RW	TW	RL	mRW
49	–	–	y	y	n ²⁶	y	n ²⁶
50	RRM1 (0109) LARK	LARK	y	y	y	y	y
51	RRM2 (0109) LARK	LARK	y	y	y	y	y
52	–	–	n	y	y	n	y
53	RRM2 (0112) RBP	RBM	y	y	y	y	y ²⁷
54	RRM3 (0112) RBP	–	y	y	y	y	y ²⁷
55	–	–	n	y	y	y	y
56	RRM2 (0106) SRp55/B52/SRp75	plant-specific RS group of SR proteins	y	y	y	y	y
57	RRM1 (0108) RNA15	ZCRB1	y	y	y	y	y
58	RRM1 (0108) RNA15	GRSRBP/hnRNP/RBMY	y	y	y	y	y
59	RRM4/5 (0110) RBP	–	y	y	y	y	y
60	RRM4/5/6 (0110) RBP	–	y	y	y	y	y
61	RRM4 (0112) RBP	–	y	y	y	y	y
62	RRM1 (0117) hnRNPr	– (land plants)	y	y	y	y	y
63	RRM3 (0117) hnRNPr	hnRNP	n ²⁸	y	y	n ²⁸	n ²⁸
64	RRM2 (0120) U2AF	snRNP	y	y	y	y	y
65	RRM1 (0122) TIF3 (eIF3)	–	y	y	y	y	y
66	RRM3 (0123) PABP	PABP (major subgroup)	y ²⁹	y	y	y ²⁹³⁰	y ³⁰
	RRM2 (0124) PUF60	UMH					
67	RRM2 (0147) CAPER/UMH [RRM1 (0124) PUF60]	UMH UMH	y ³¹	y ³¹	y ³²	y ³²	y ³²
	RRM1 (0125) ataxin-2 binding protein	FOX					
68	RRM1 (0127) fibrillarin RRM1 (4661) SAF-B	– (land plants) –	n	y	y	y	y
69	RRM1 (0126) RBP	–	y	y	y	y	y
70	RRM1 (0127) fibrillarin	RBM	y	y	y	y	y
71	RRM2 (0127) fibrillarin	RBM	y	y	y	y	y
72	RRM3 (0127) fibrillarin	RBM	y	y	y	y	y
73	RRM1 (0128) SART3	SART3 (excl. green plants)	y	y	y	y	y
74	RRM1 (0128) SART3	– (green plants)	y	y	y	y	y
75	RRM1 (0147) CAPER/UMH	CAPER/UMH	y	y	y	y	y
76	RRM1 (0148) TIA1/TIAR	TIATIA/OligoU	y	n ⁶	y	y	y
77	RRM2 (0148) TIA1/TIAR RRM1 (0226) RBP	TIATIA/OligoU –	y	y	y	y	y
78	RRM3 (0148) TIA1/TIAR	OligoU	y	y	y	y	y
79	RRM3 (0148) TIA1/TIAR	TIATIA/OligoU	n ⁶	y	y	y	y
80	RRM? (1365) fusillin RRM2 (4211) hnRNPF	– hnRNP	y	y	y	y	y
81	RRM1 (1855) predicted RBP	La	y	y	y	y	y
82	RRM1 (4208) NIFK	–	y	y	y	y	y
83	RRM1 (4209) splicing factor RNPS1	PABP (26%)	y	y	y	y	y
84	RRM1 (4213) RBP La	La	y	y	y	y	y
85	RRM2 (4676) splicing factor SR rich	SRrp	y	y	y	y	y
86	RRM1 (–)	hnRNP/RALYL	y	y	y	y	y
87	RRM1 (–)	eIF4b	y	y	y	y	y
88	RRM1 (0108) ³³	prokaryotic RRM	n ⁶	y	y	y	y

¹not associated to node (15); ²also associated in MP tree but independently of node (15); ³forming a mini node in MP tree (15); ⁴RRM2 of p54 nrb not associated to the group; ⁵RRM2 of p54 nrb associated to the group; ⁶split; ⁷9G8 and SC35/SCL groups associated in TF and MP trees; ⁸PPCTI: peptidyl-propyl cis-trans isomerase; ⁹not associated to SR proteins; ¹⁰always associated to 9G8 SR proteins; ¹¹RRM1 of CBP20 not associated to the group; ¹²RRM1 of KOG0533 not associated to the group; ¹³RRM1 of KOG0533 associated to the group; ¹⁴fungal RBP missing from the group; ¹⁵not associated to the group; ¹⁶RRM1 of Rasputin not associated to the group; ¹⁷more distantly related to the group; ¹⁸nodes (36, 37) associated; ¹⁹nodes (36, 37, 38) associated; ²⁰nodes (36, 37) + (38) associated; ²¹4 groups: nodes (42, 44), node (40), node (41), and node (43); ²²2 groups: nodes (41, 42, 43, 44) and node (40); ²³2 groups: nodes (40, 41, 43, 44) and node (42); ²⁴4 groups: nodes (40, 43), node (41), node (42), and node (44); ²⁵snRNPs represent 8% of group proteins; ²⁶RRM1 of IGF2BP not associated to the group; ²⁷nodes (53) and (54) merged; ²⁸split into plant and animal groups; ²⁹associated to node (5); ³⁰associated to node (6); ³¹RRM1 of PUF60 not associated to the group; ³²RRM1 of PUF60 associated to the group; ³³mostly KOG0108, but also a lower % of KOG0116 and KOG0145

Table S4

dataset	seq#/AA#	meth.	heuristic	model	tree	node associations
original	1266x72	MP	PAUP*	–	Fig. S5	[16] vs. [17 + (22-23) + (26-27)]
original	1266x72	ML	RAxML	WAG + G4	Fig. S6	[16 + 17 + (22-23)] vs. [(26-27)]
original	1266x72	ML	TreeFinder	WAG + G4	Fig. S7	[16] vs. [17 + (22-23)] vs. [(26-27)]
original	1266x72	ML	RAxML	LG + F + G4	Fig. S8	[16 + 17 + (26-27)] vs. [(22-23)]
enlarged	1831x72	ML	RAxML	WAG + G4	Fig. S9	[16 + 17 + (26-27)] vs. [(22-23)]

Table S5

SR subfamily	key features	secondary features
SC35	K P S KS	R RS
SCL	P R GR RS	E G S
SRp	K P R S KS	RS
9G8	R RS	S
SRp20	G	P R S RS
RSZ	G GG GR	P R S RS
RS2Z		G P R S GR RS
ASF/SF2	G	P R S RS
SRp30c	G	P R S RS
ASF-like (plants)	G KS RS SS	R S
SRp40	G K S KS	R RS
SRp55	G K S KS	R RS
SRp75	G K S KS	R RS
RS		E P R S RS
SR45	K P R S PP RS SS SSS	
RNPS1	P R S PP RS SS ST SSS	

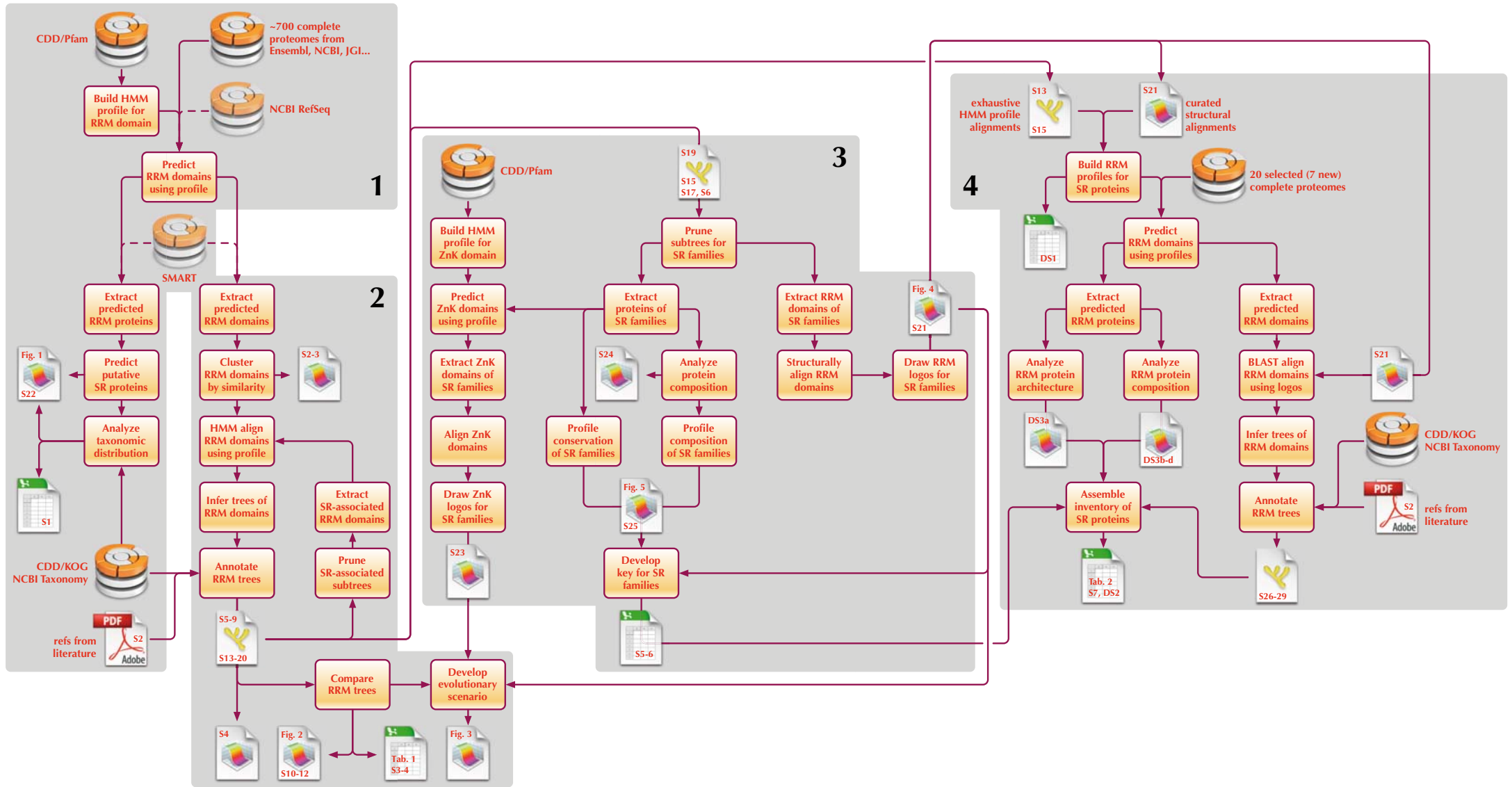
Table S6

step	criteria	result
1	one RRM domain	step 2
	two RRM domains	step 9
2	2 Zn knuckles	▷ RS2Z
	1 Zn knuckle	step 3
	no Zn knuckle	step 4
3	enriched in G, GG, GR, GGG between RRM and ZnK	▷ RSZ
	enriched in R, RS between RRM and ZnK	▷ 9G8
4	enriched in P, R, RS before RRM	step 5
	otherwise	step 7
5	enriched in GR before RRM	▷ SCL
	enriched in S, GS, SS before RRM and P, PP, PPP after RRM	step 6
6	enriched in R, ST, SSS before RRM	▷ RNPS1
	enriched in K, SSS after RRM	▷ SR45
7	enriched in K, KS after RRM and P, S before RRM	step 8
	enriched G before RRM	▷ SRp20
8	enriched in R before RRM	▷ SRrp
	otherwise	▷ SC35
9	second RRM lacks SWKDLKD motif	▷ RS
	enriched in G between RRMs	step 10
10	enriched in KS after second RRM	step 11
	enriched in G before first RRM	▷ ASF/SF2, SRp30c
11	enriched in RS, SS before RRM	▷ ASF-like (plant)
	enriched in S, K, KS after last domain	▷ SRp40-55-75

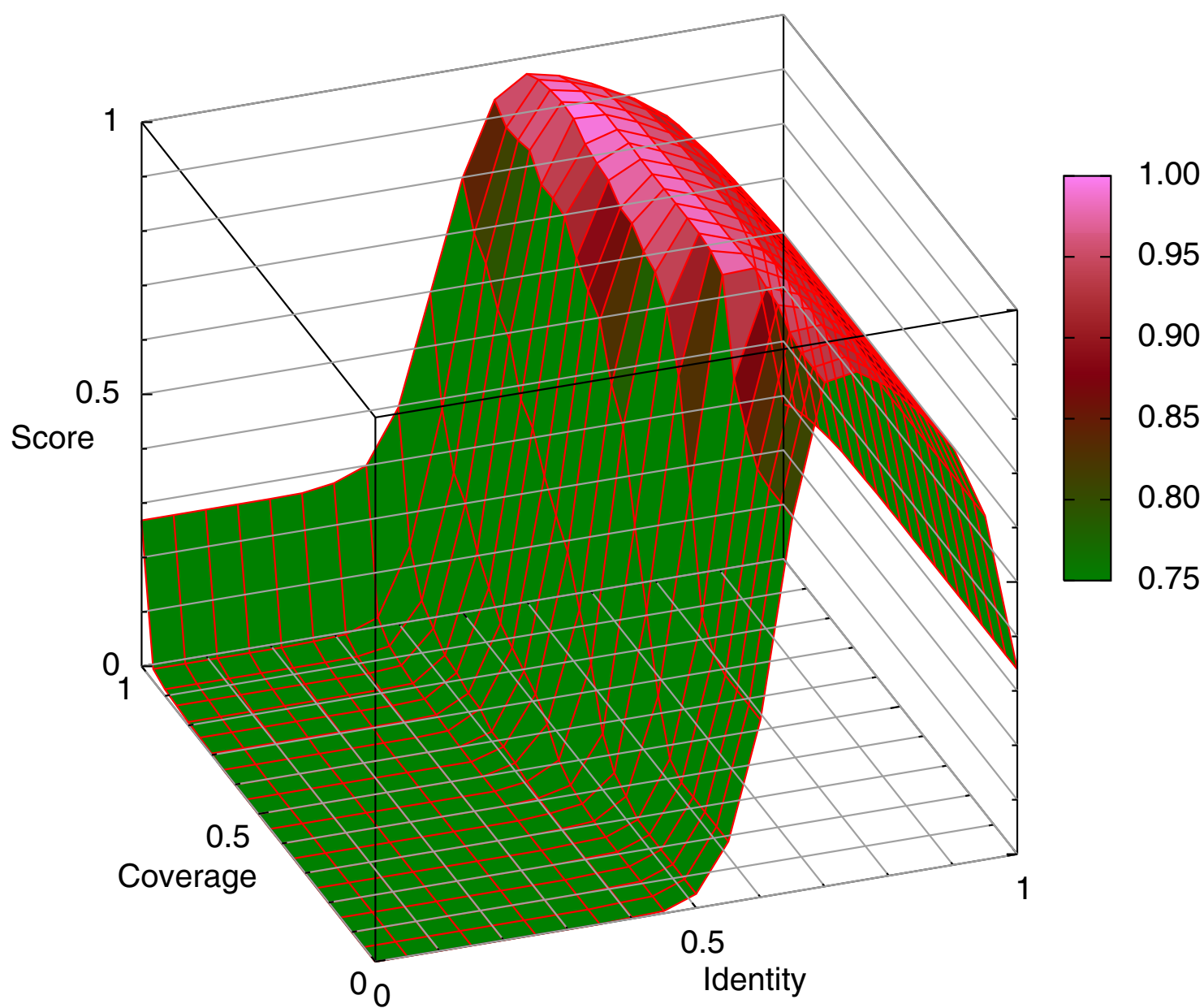
Table S7

organism	lineage	cand	rej	iso	conf	key	trunc
<i>Homo sapiens</i>	Eutheria	23	0	11	12	11	0
<i>Mus musculus</i>	Eutheria	26	1	13	12	12	0
<i>Drosophila melanogaster</i>	Insecta	15	0	6	9	5	0
<i>Caenorhabditis elegans</i>	Nematoda	14	0	7	7	4	0
<i>Aspergillus fumigatus</i>	Ascomycota	0	0	0	0	0	0
<i>Arabidopsis thaliana</i>	eudicotyledons	29	0	10	19	18	0
<i>Populus trichocarpa</i>	eudicotyledons	30	0	0	30	21	6
<i>Oryza sativa</i>	Liliopsida	23	1	0	22	17	0
<i>Sorghum bicolor</i>	Liliopsida	21	0	0	21	15	4
<i>Selaginella moellendorffii</i>	Lycopodiophyta	15	0	5	10	4	4
<i>Physcomitrella patens</i>	Bryophyta	12	0	0	12	11	0
<i>Chlamydomonas reinhardtii</i>	Chlorophyta	9	0	0	9	4	3
<i>Volvox carteri</i>	Chlorophyta	8	1	0	7	1	1
<i>Chlorella</i> sp. NC64A	Chlorophyta	7	0	0	7	3	1
<i>Micromonas pusilla</i> CCMP1545	Chlorophyta	3	0	0	3	0	3
<i>Micromonas pusilla</i> RCC299	Chlorophyta	3	0	0	3	1	1
<i>Ostreococcus</i> sp. RCC809	Chlorophyta	3	0	0	3	0	3
<i>Ostreococcus lucimarinus</i>	Chlorophyta	3	0	0	3	0	3
<i>Ostreococcus tauri</i>	Chlorophyta	1	0	0	1	0	1
<i>Cyanidioschyzon merolae</i>	Rhodophyta	2	0	0	2	1	0
Total		247	3	52	192	128	30

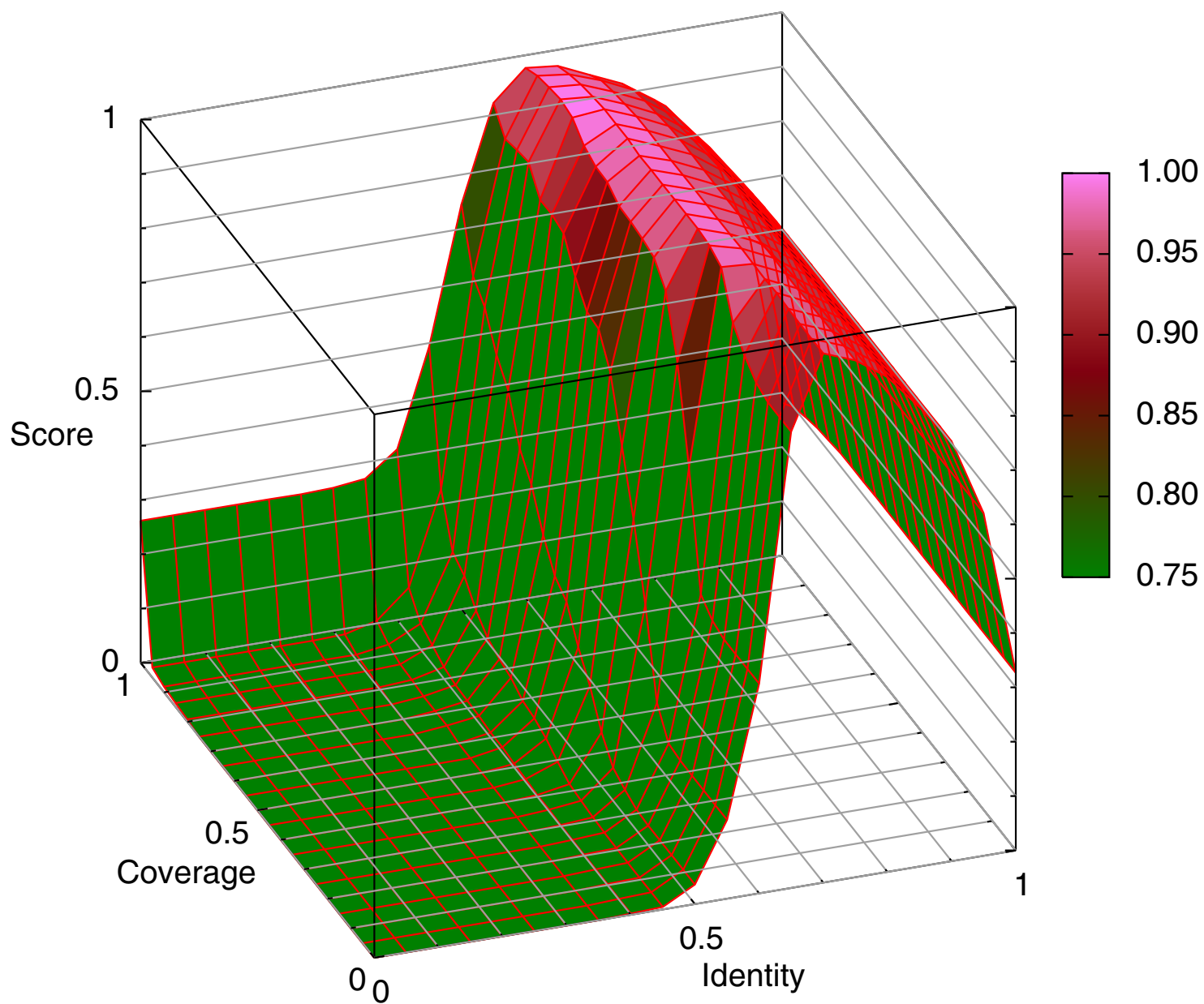
Fig. S1



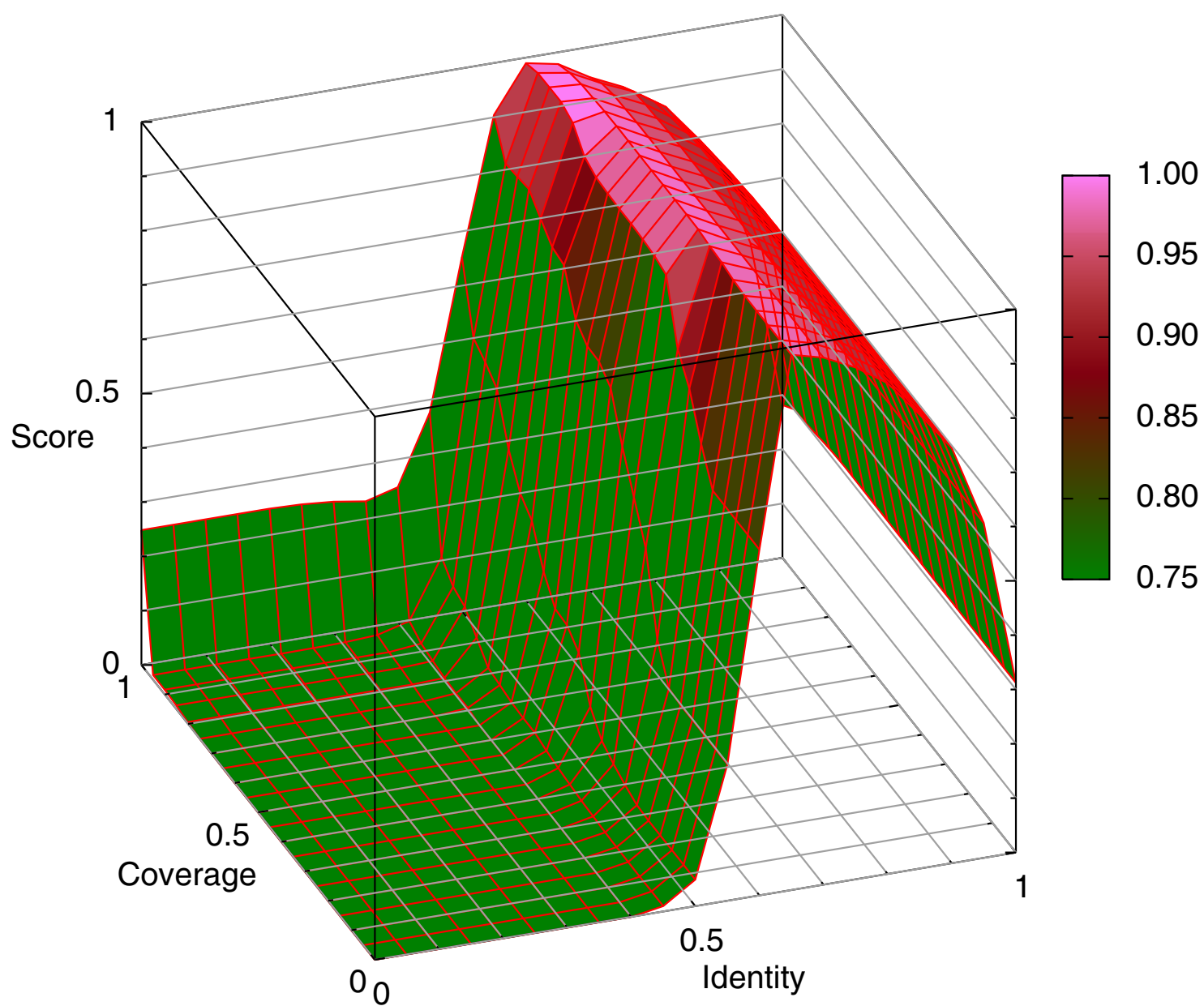
A. E-value threshold = $1\text{E-}05$ / # RRM domains = 8471



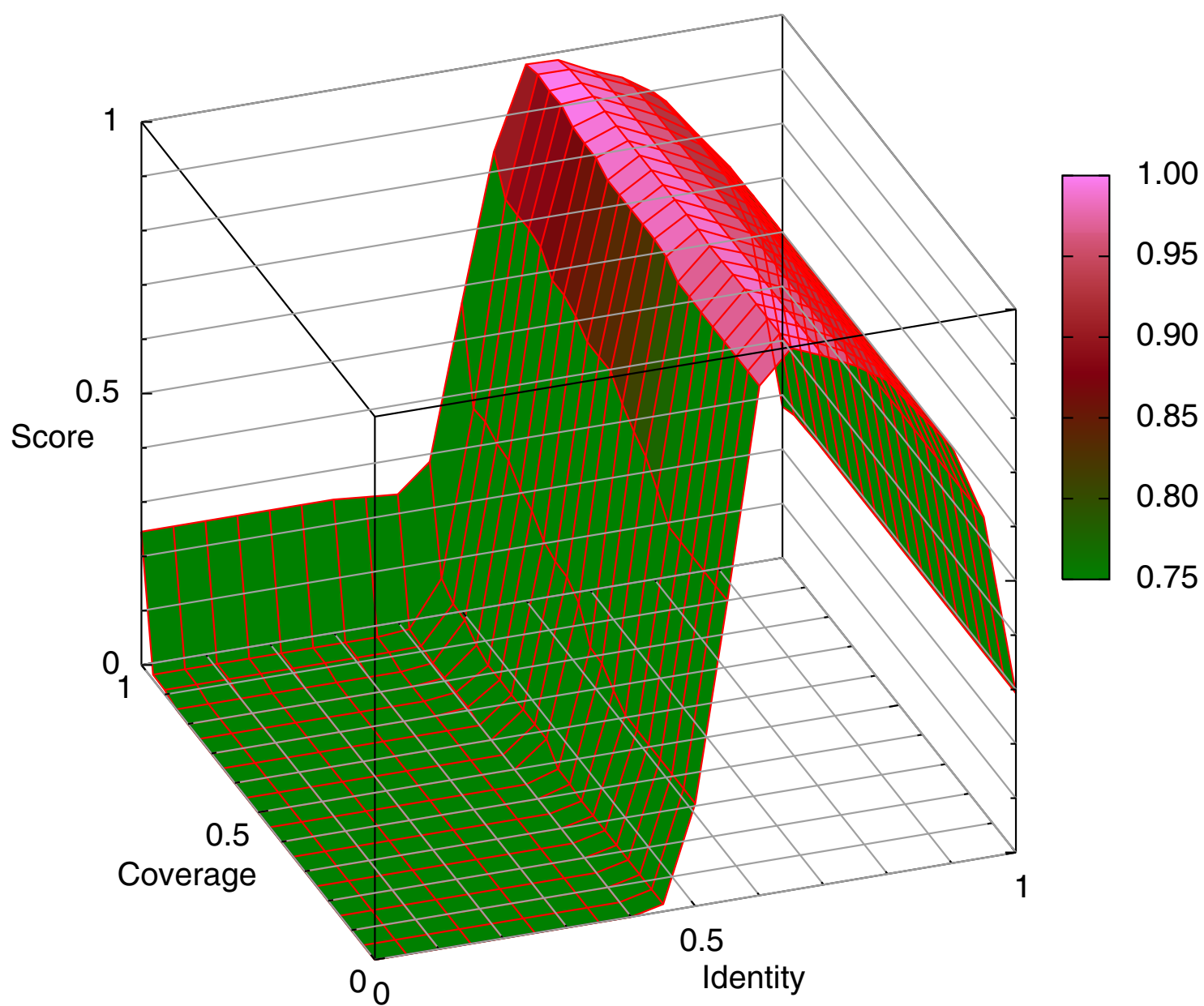
B. E-value threshold = $1\text{E-}10$ / # RRM domains = 6633



C. E-value threshold = $1\text{E-}15$ / # RRM domains = 4523



D. E-value threshold = $1\text{E-}20$ / # RRM domains = 2311



E. E-value threshold = $1\text{E-}25$ / # RRM domains = 597

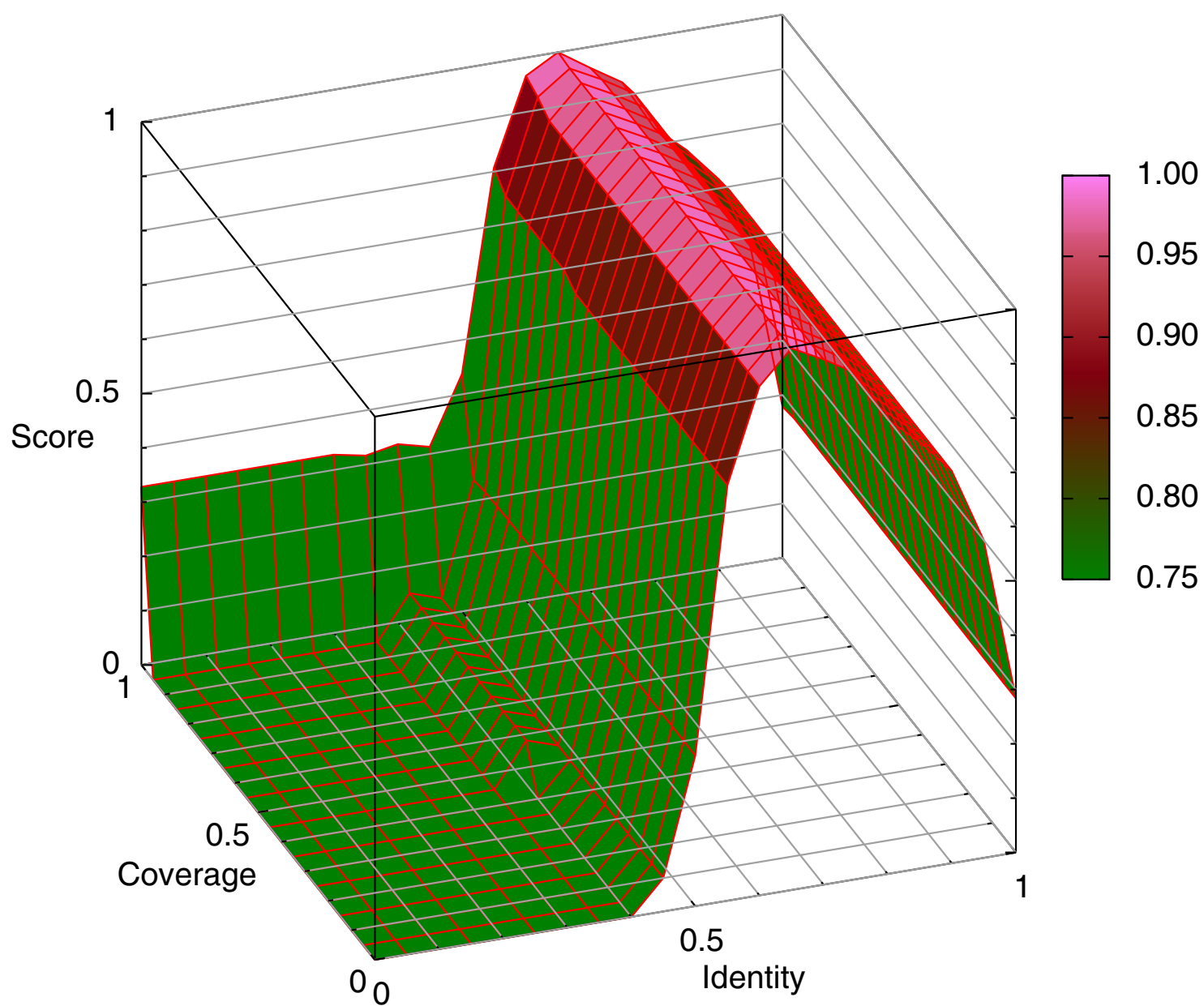


Fig. S3

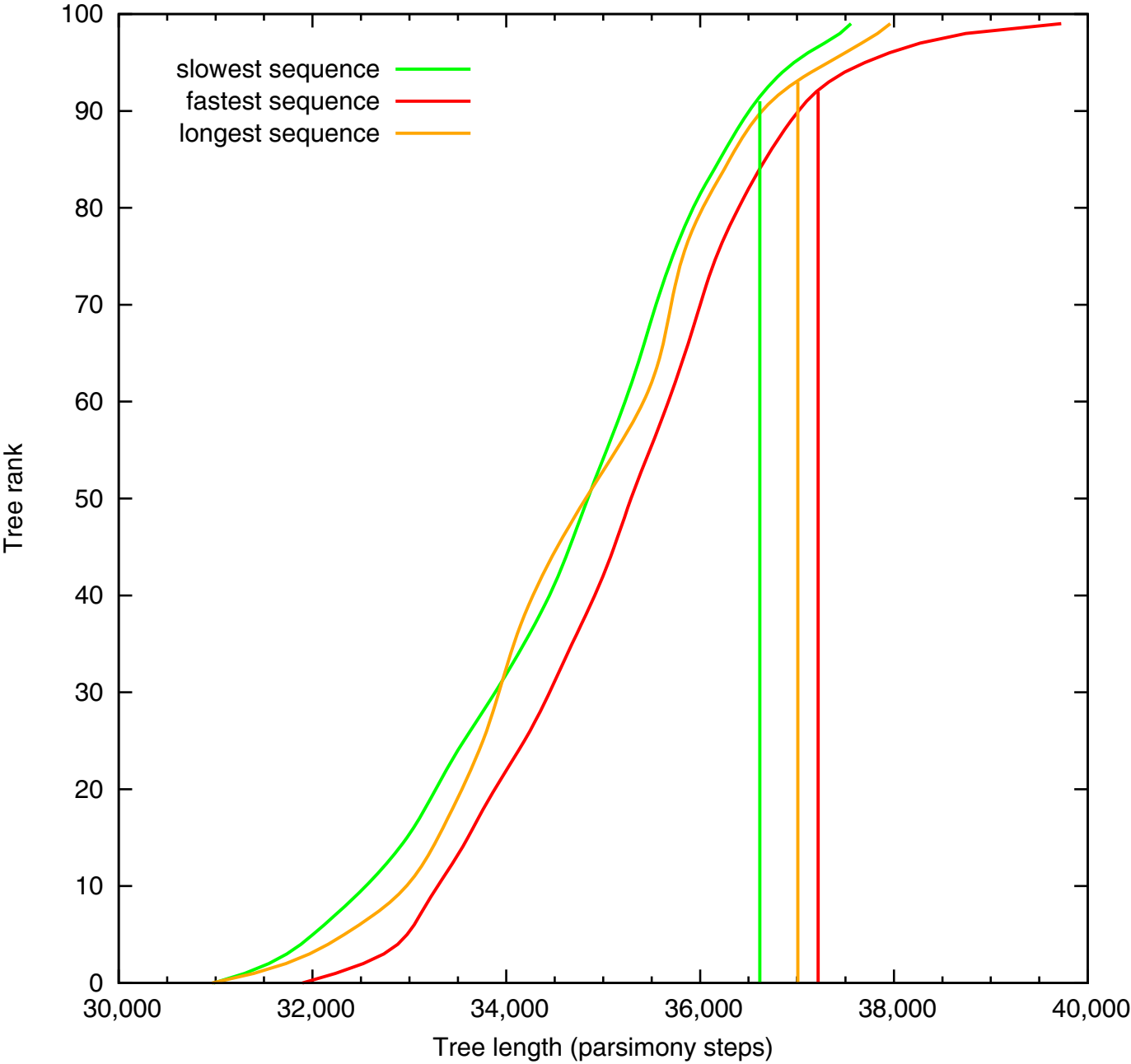


Fig. S5

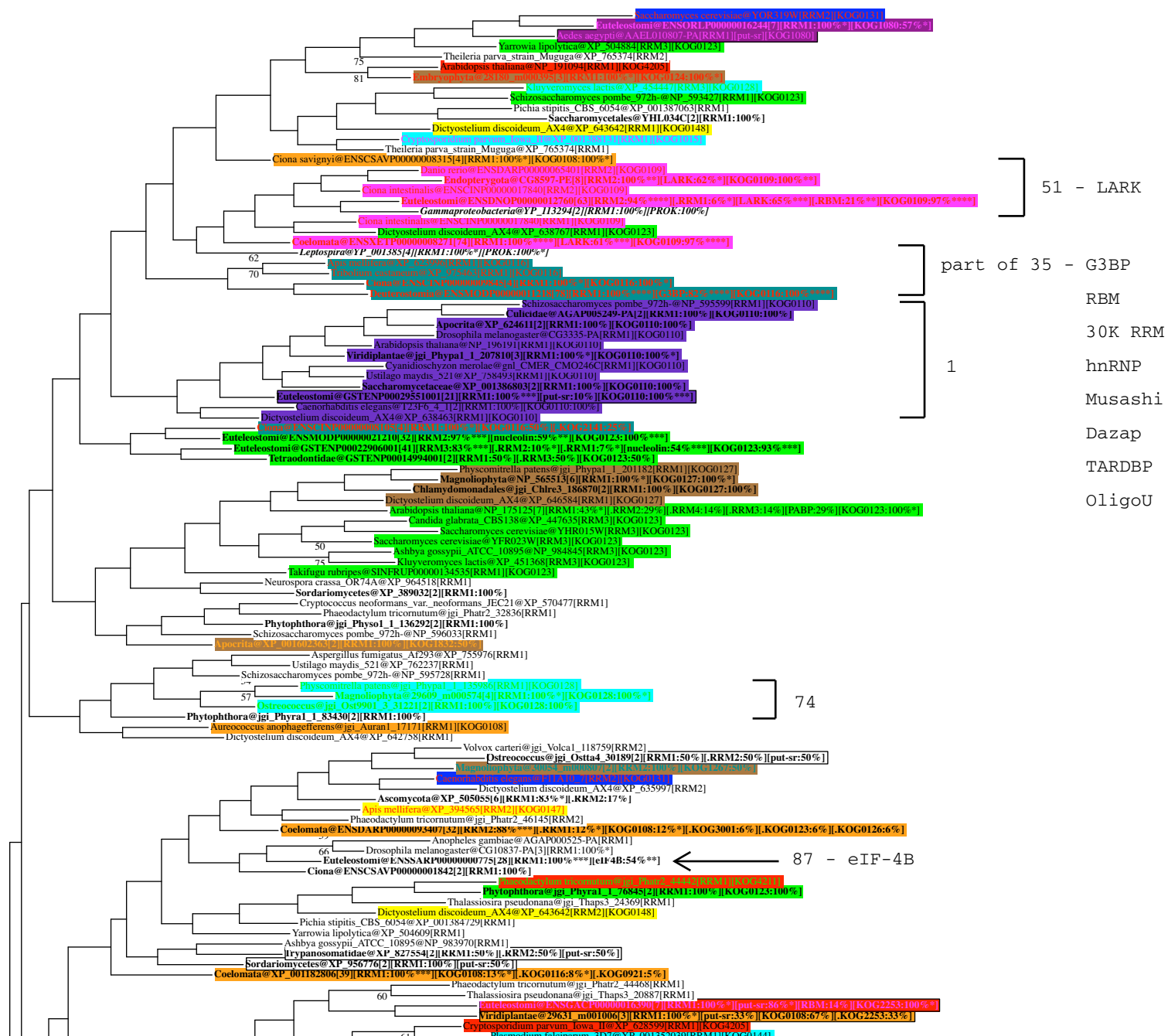


Fig. S5

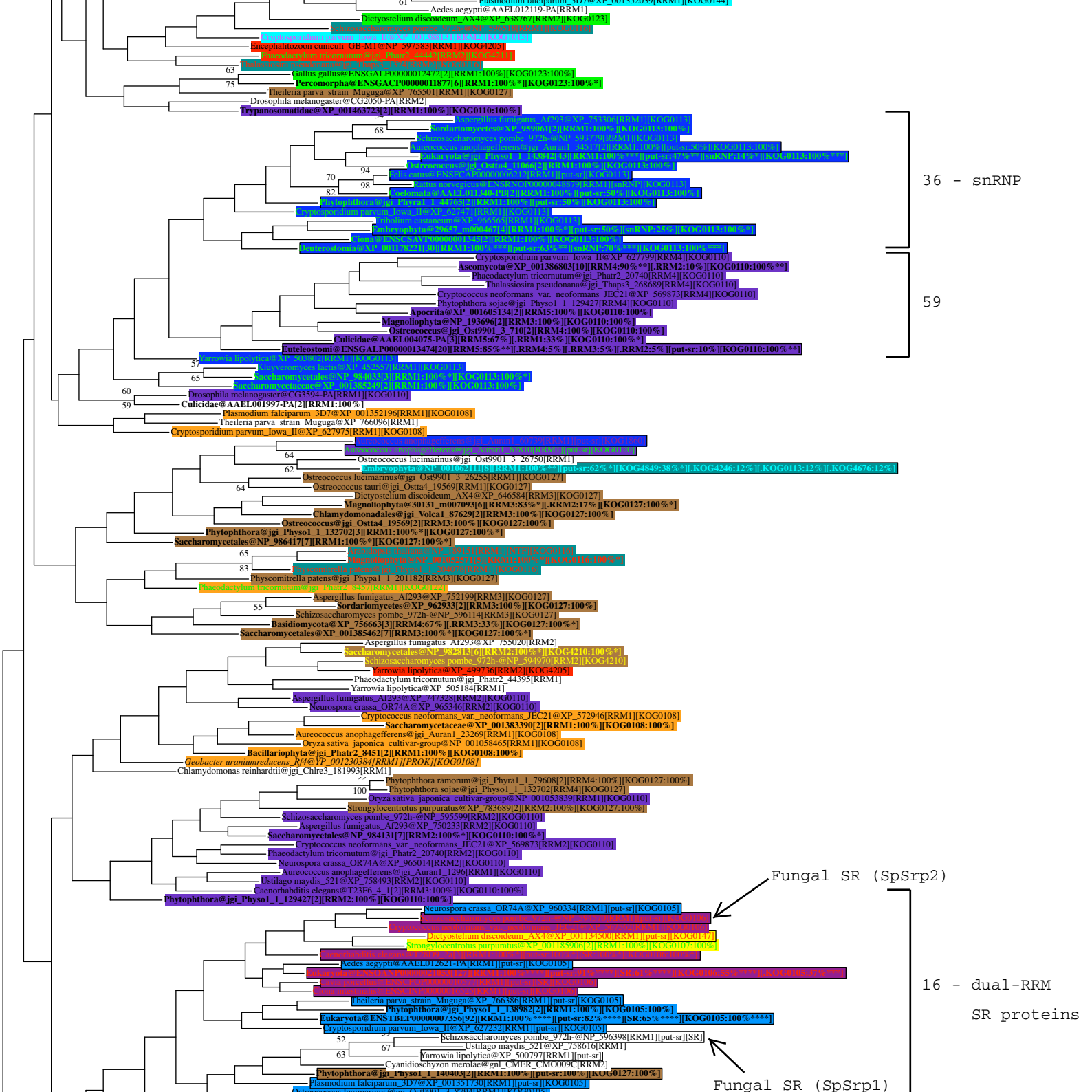


Fig. S5

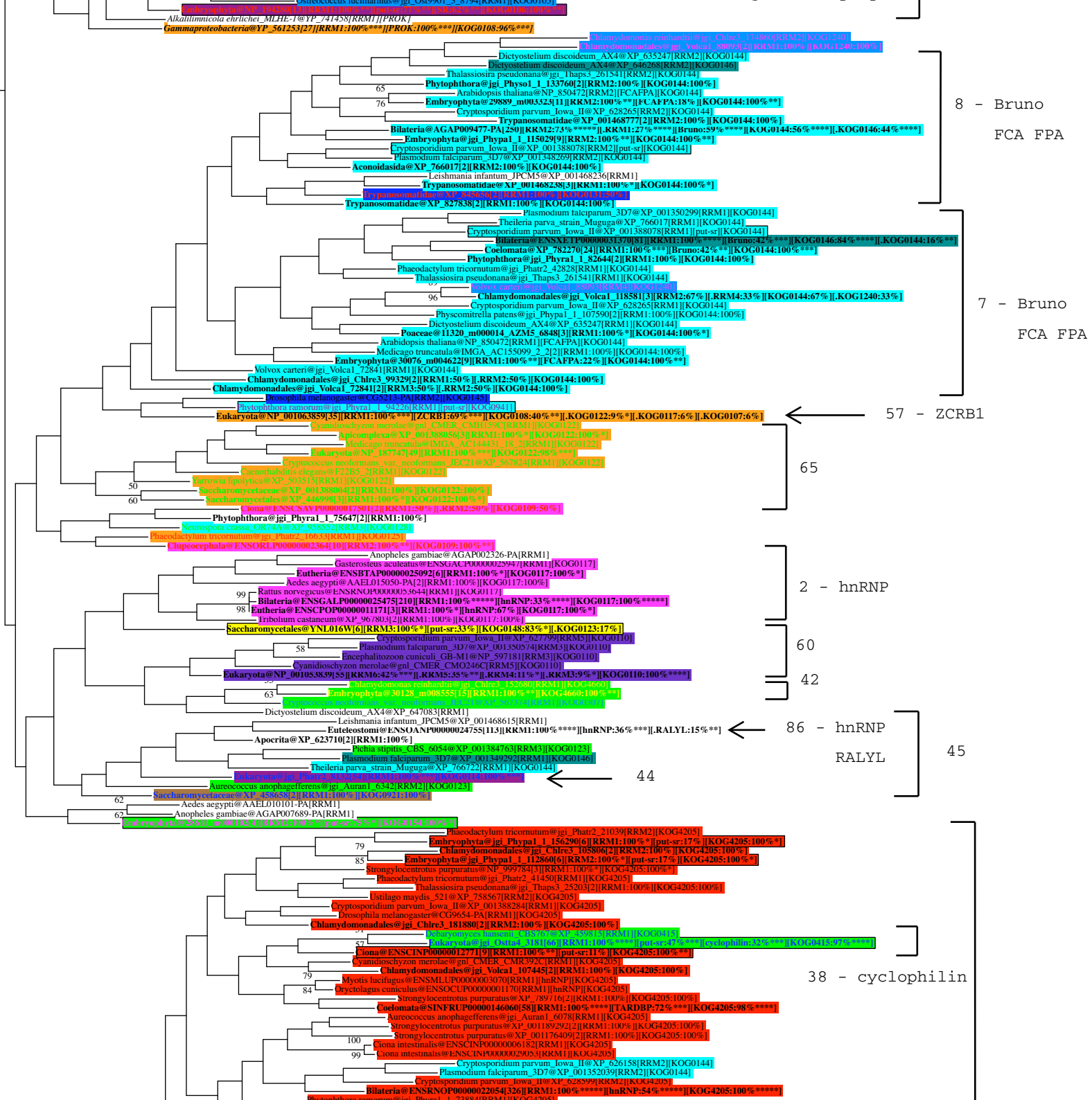


Fig. S5

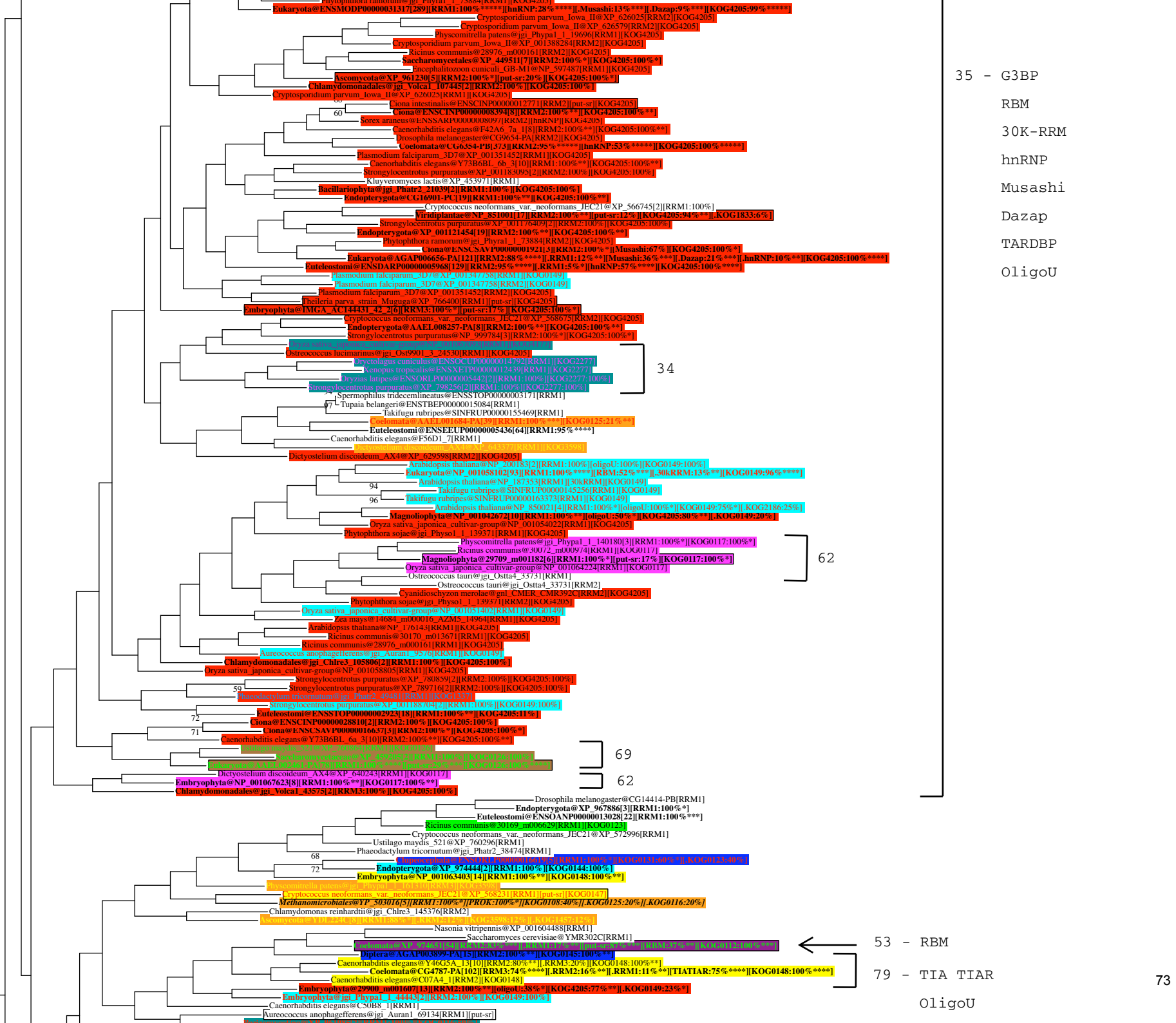


Fig. S5

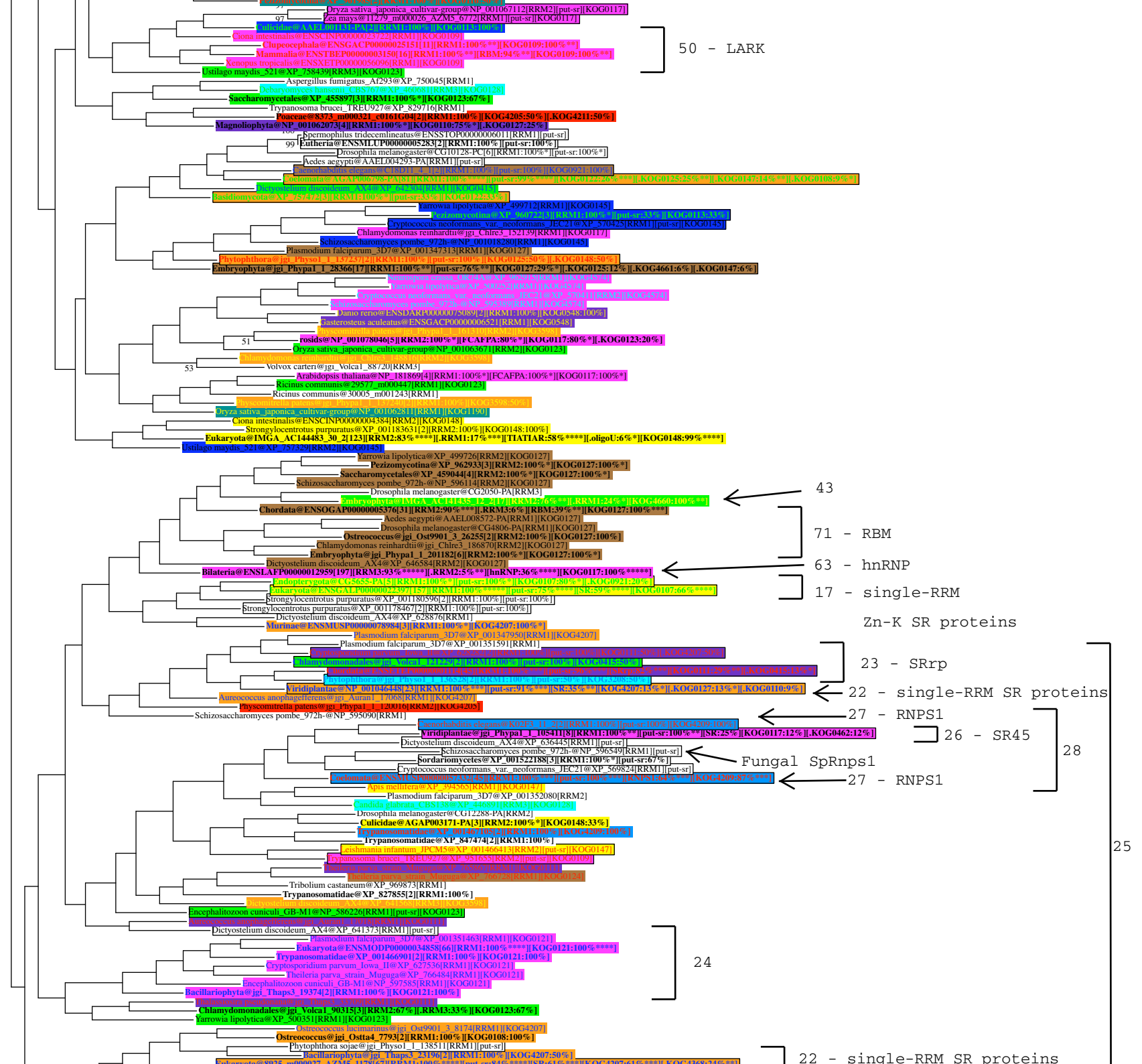


Fig. S5

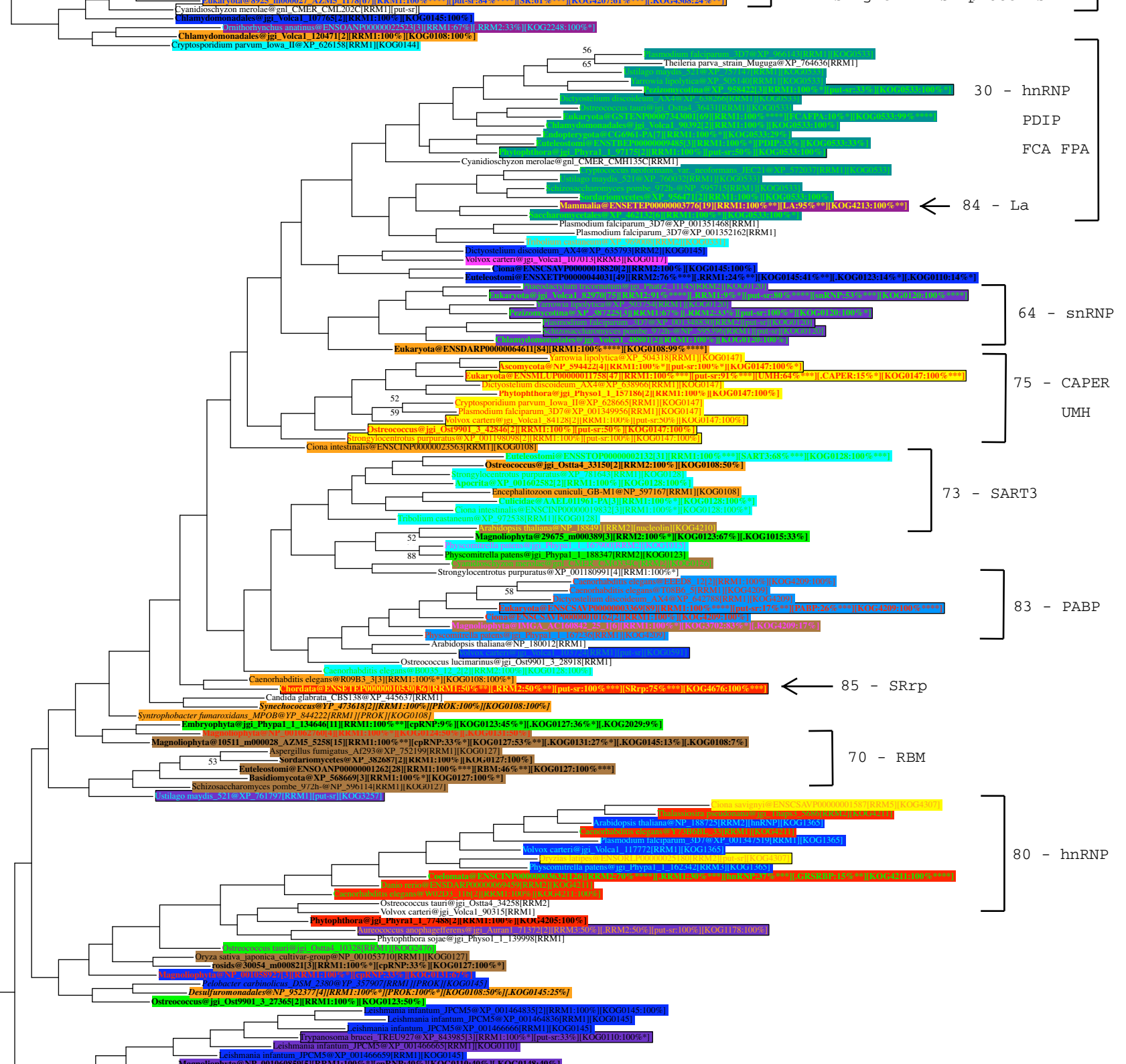


Fig. S5



Fig. S5

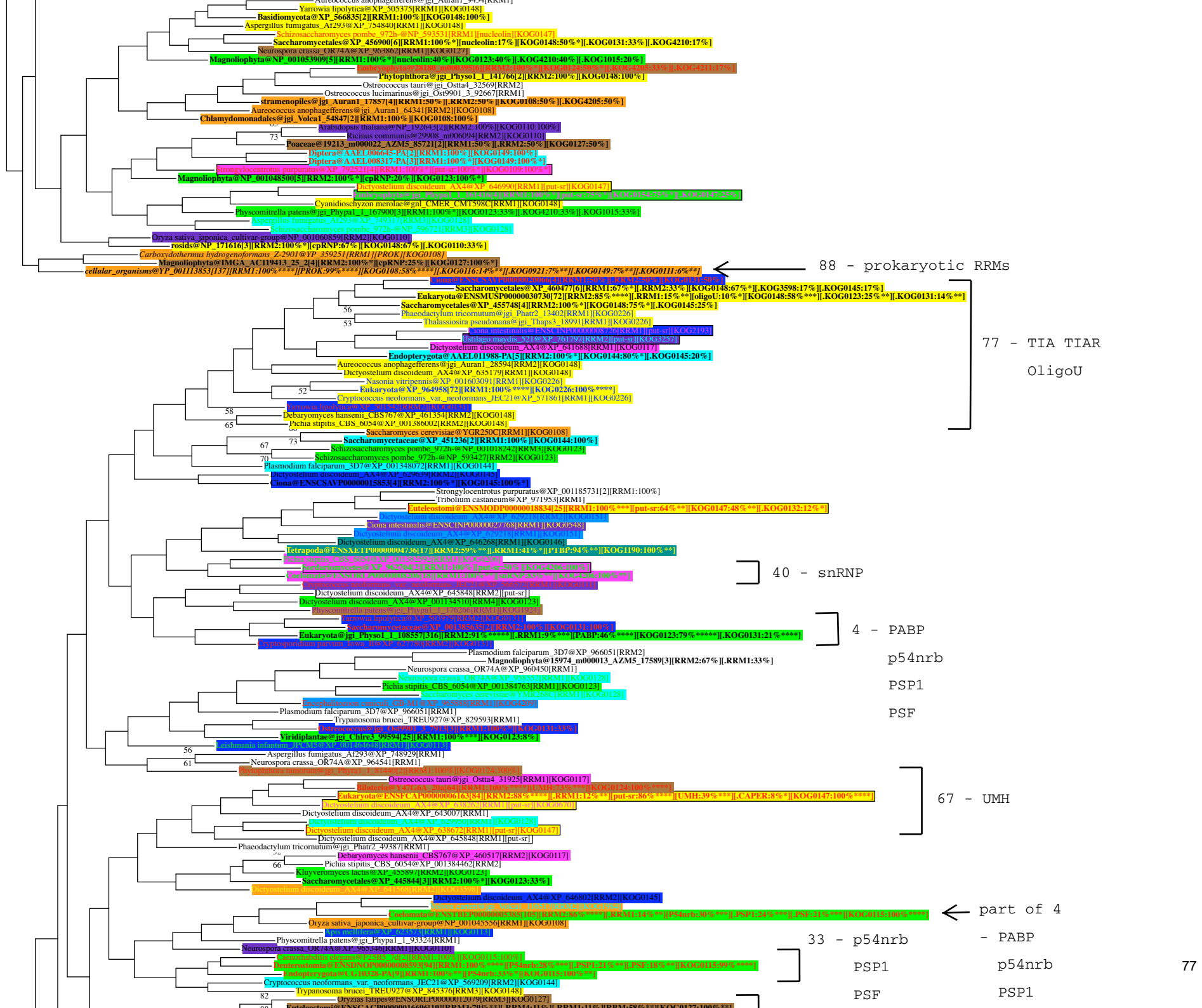


Fig. S5

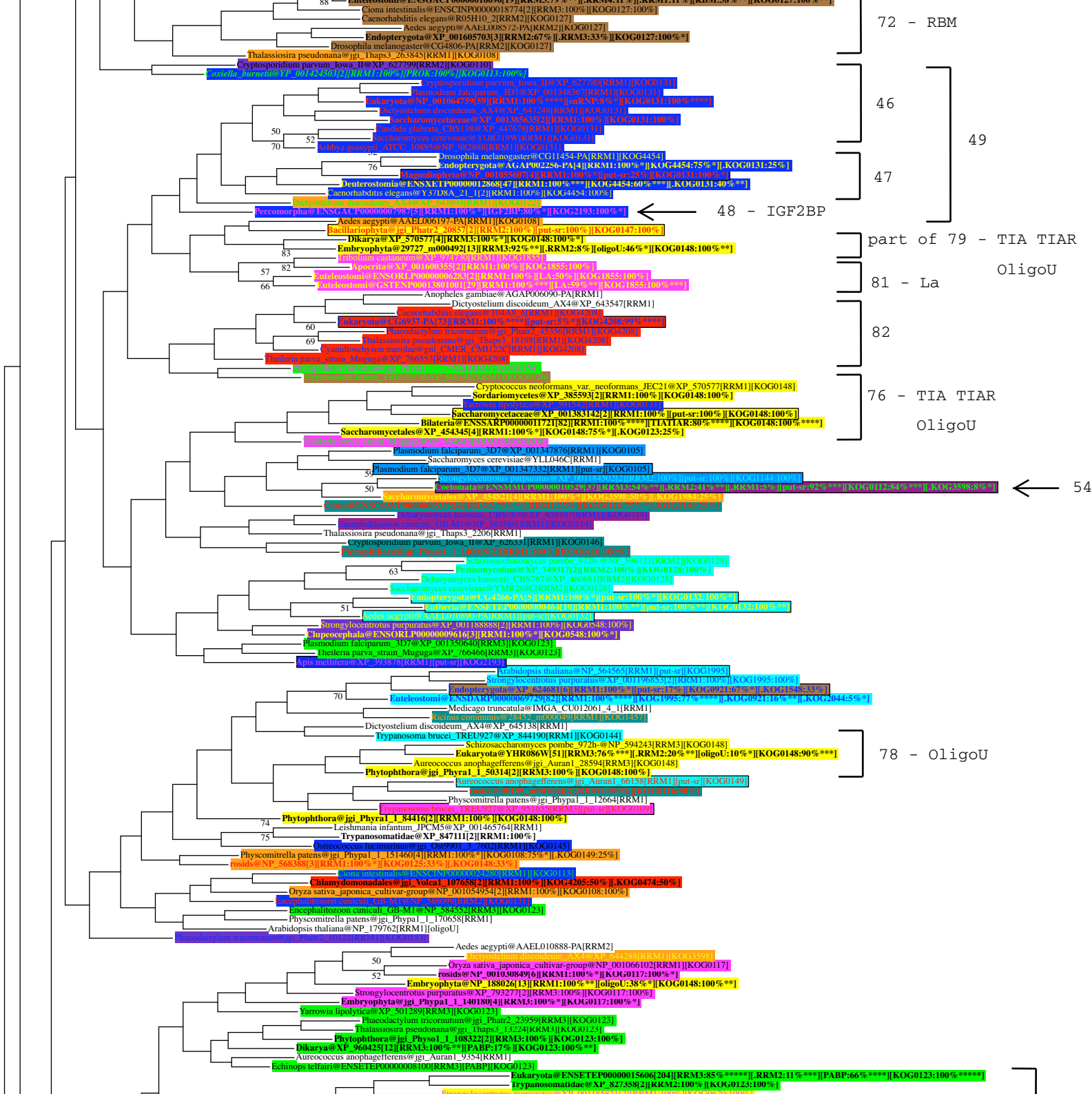


Fig. S5

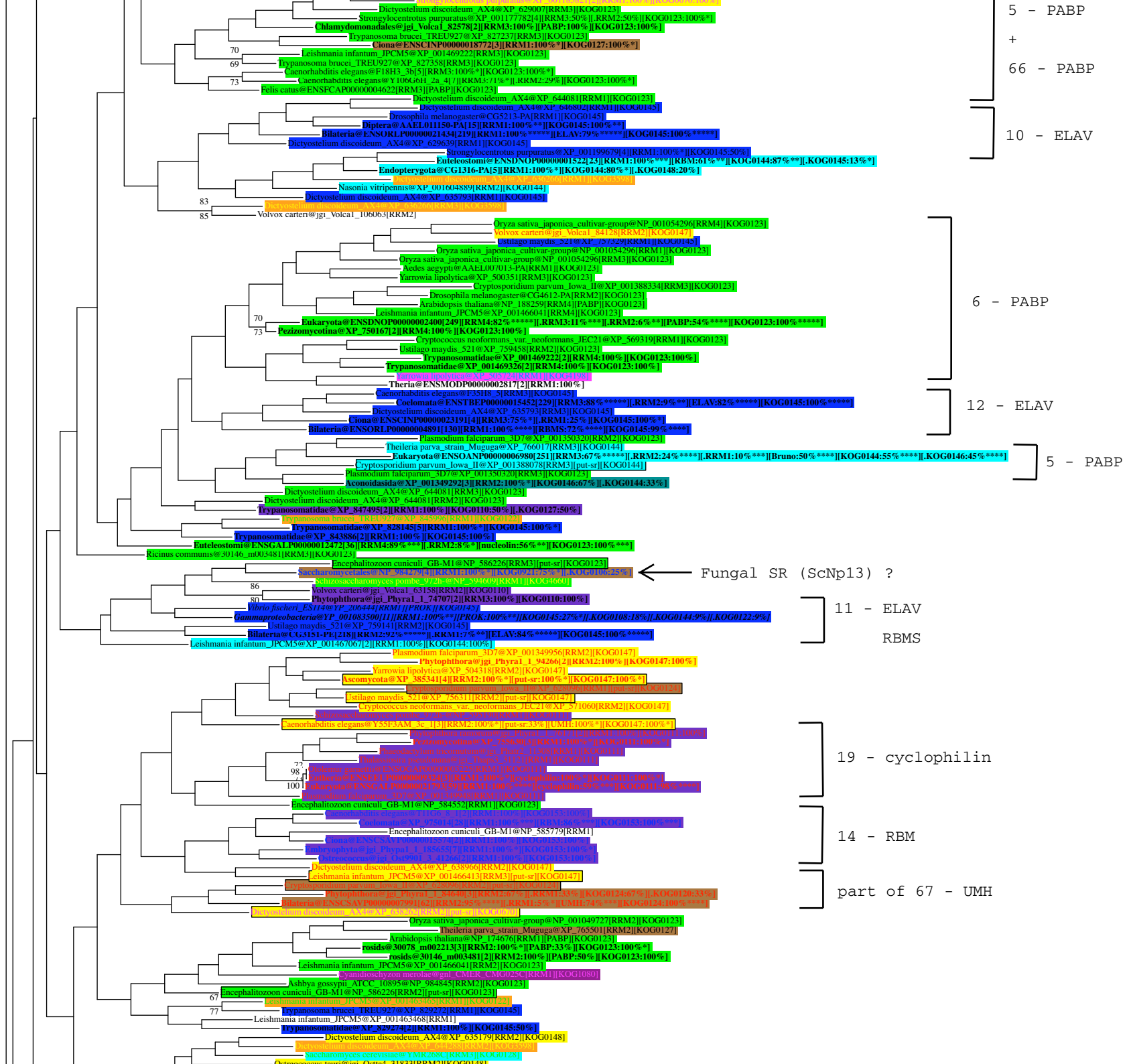


Fig. S5

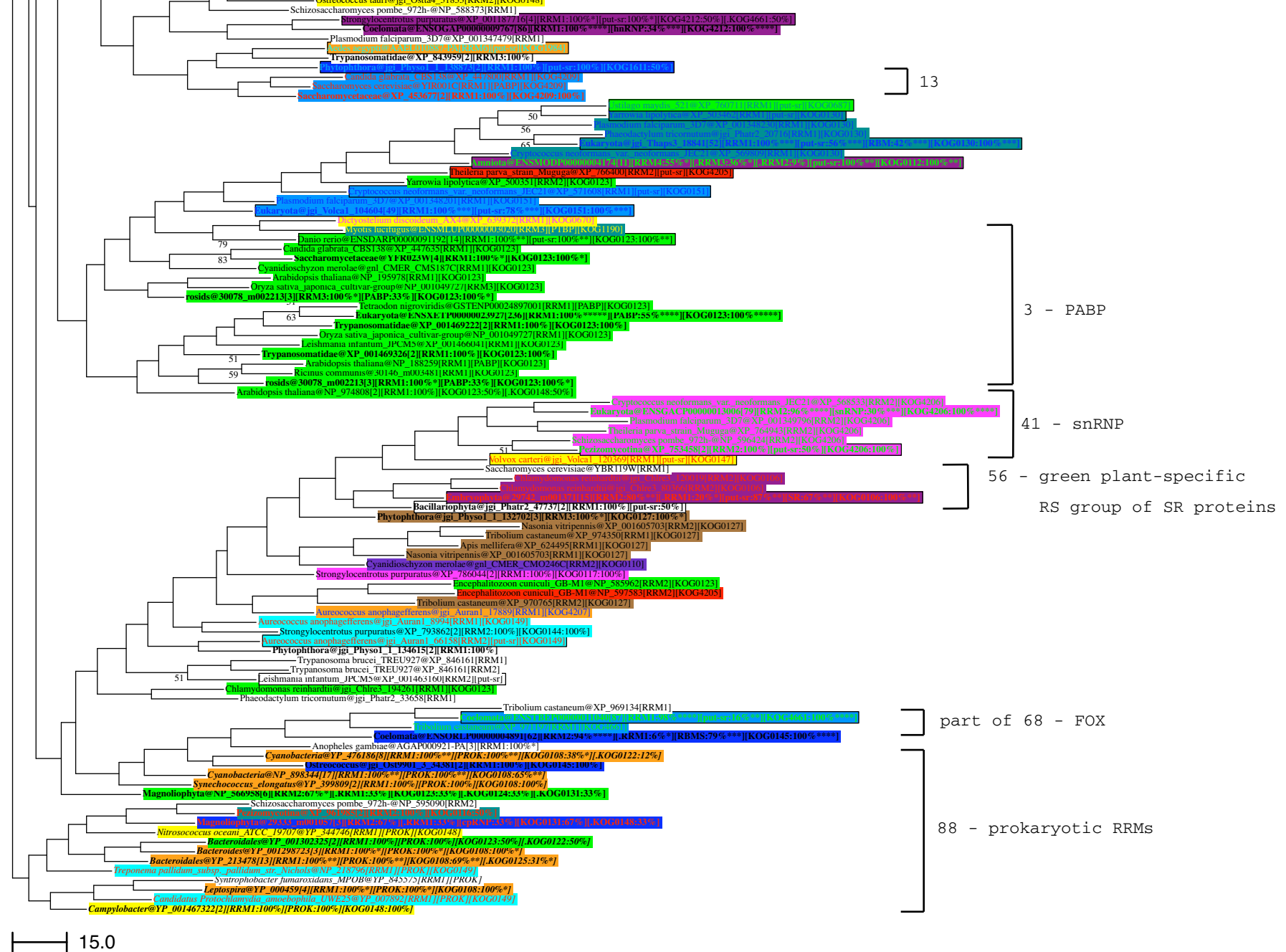
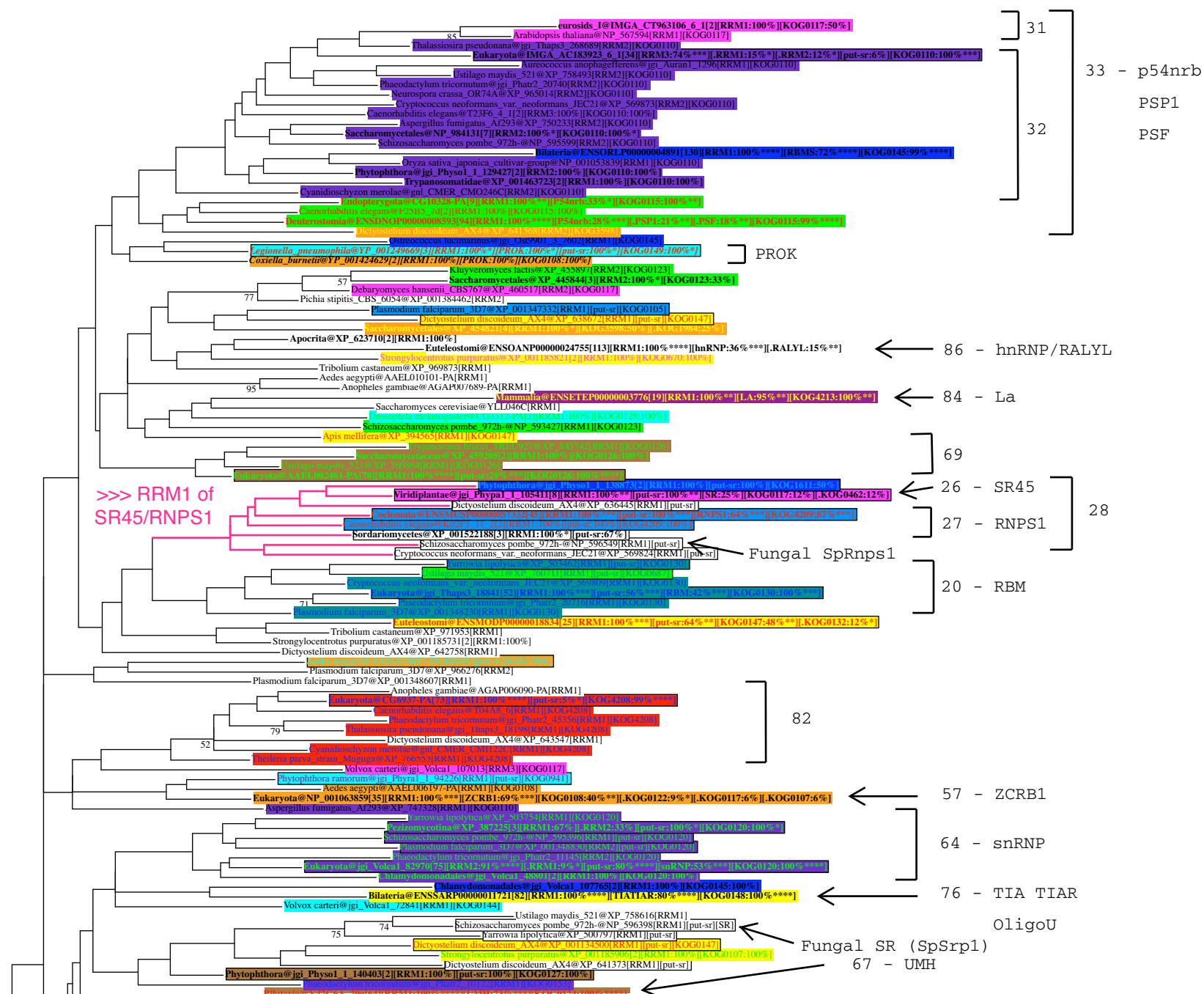


Fig. S6



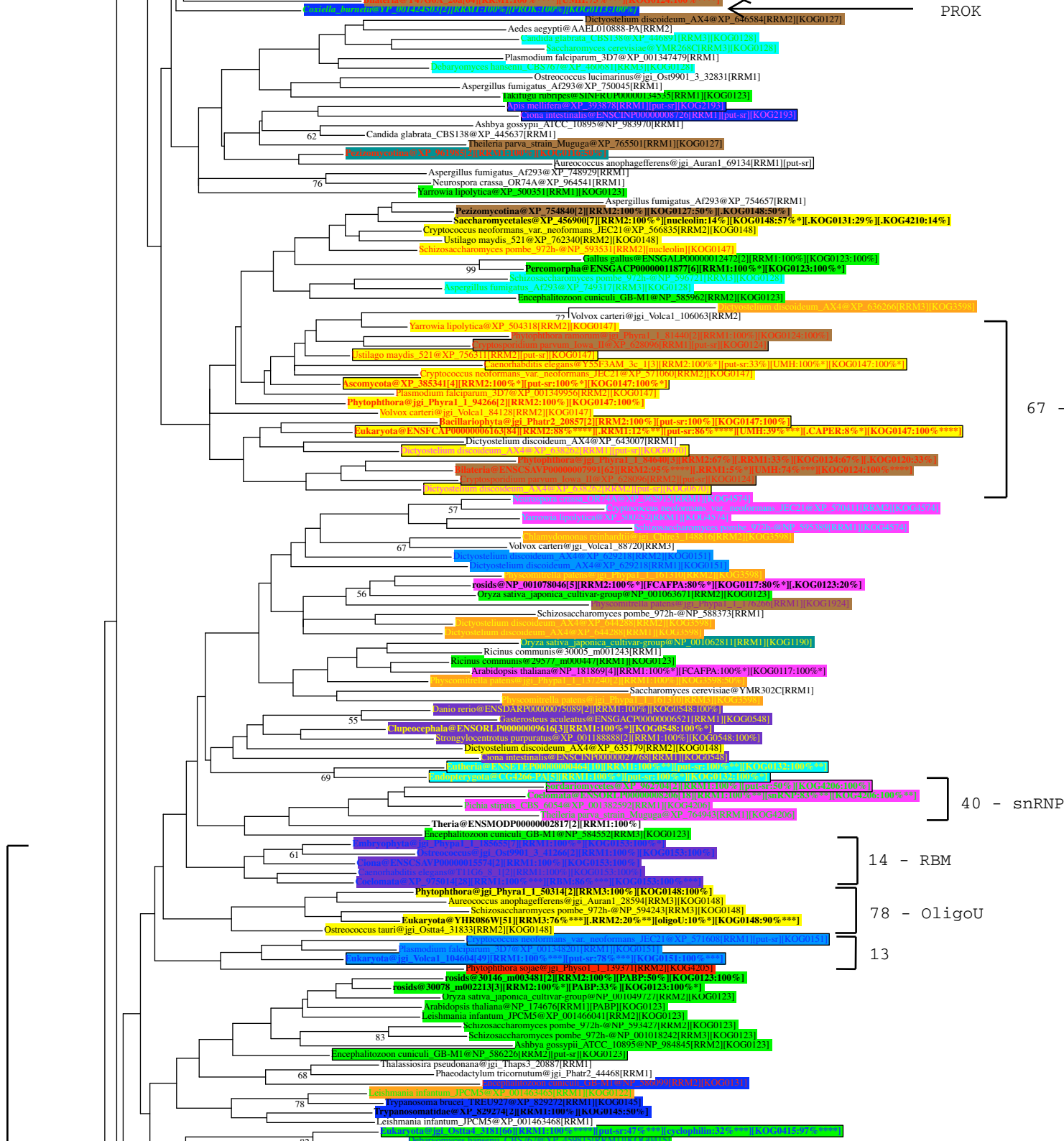


Fig. S6

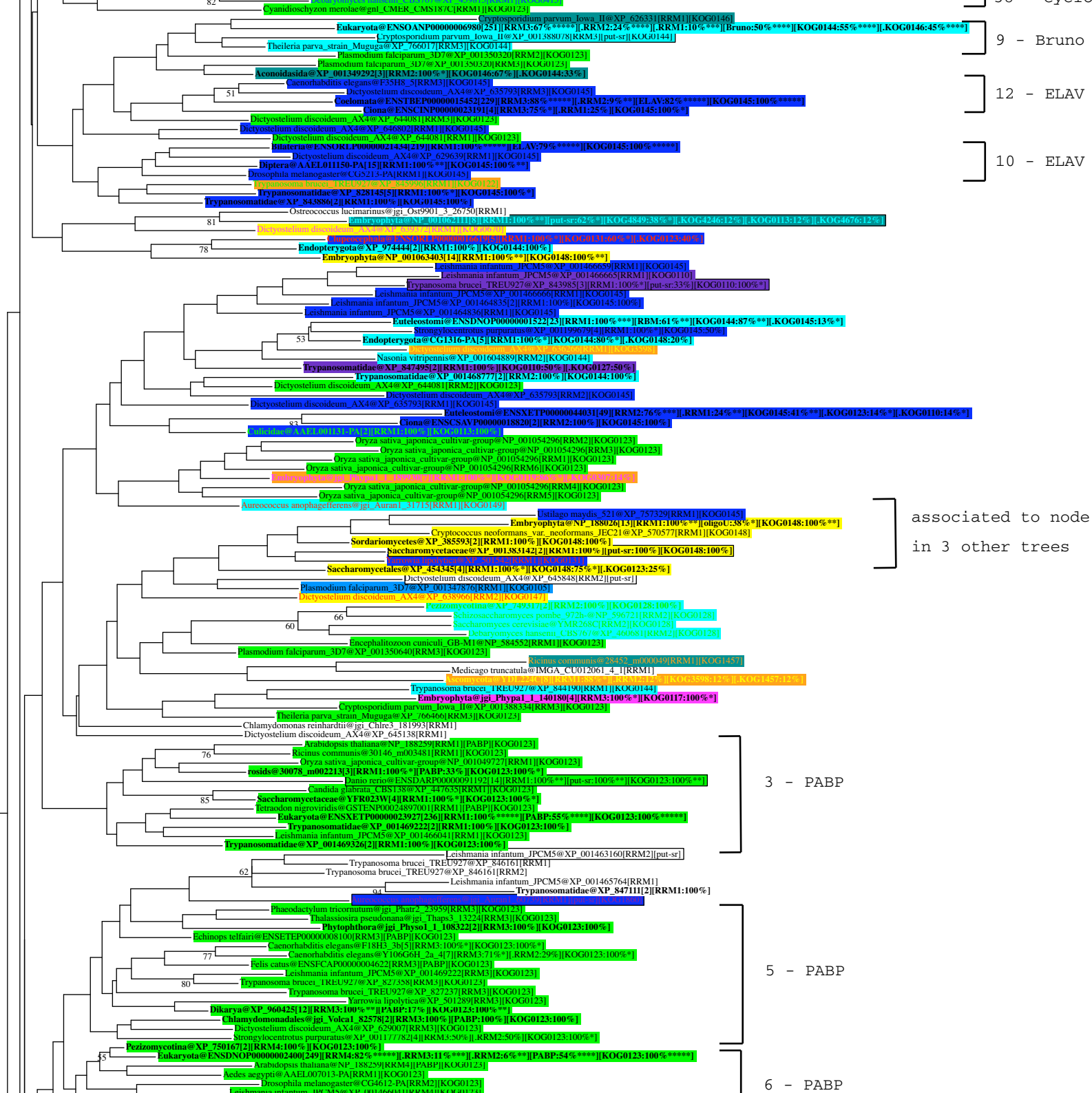


Fig. S6

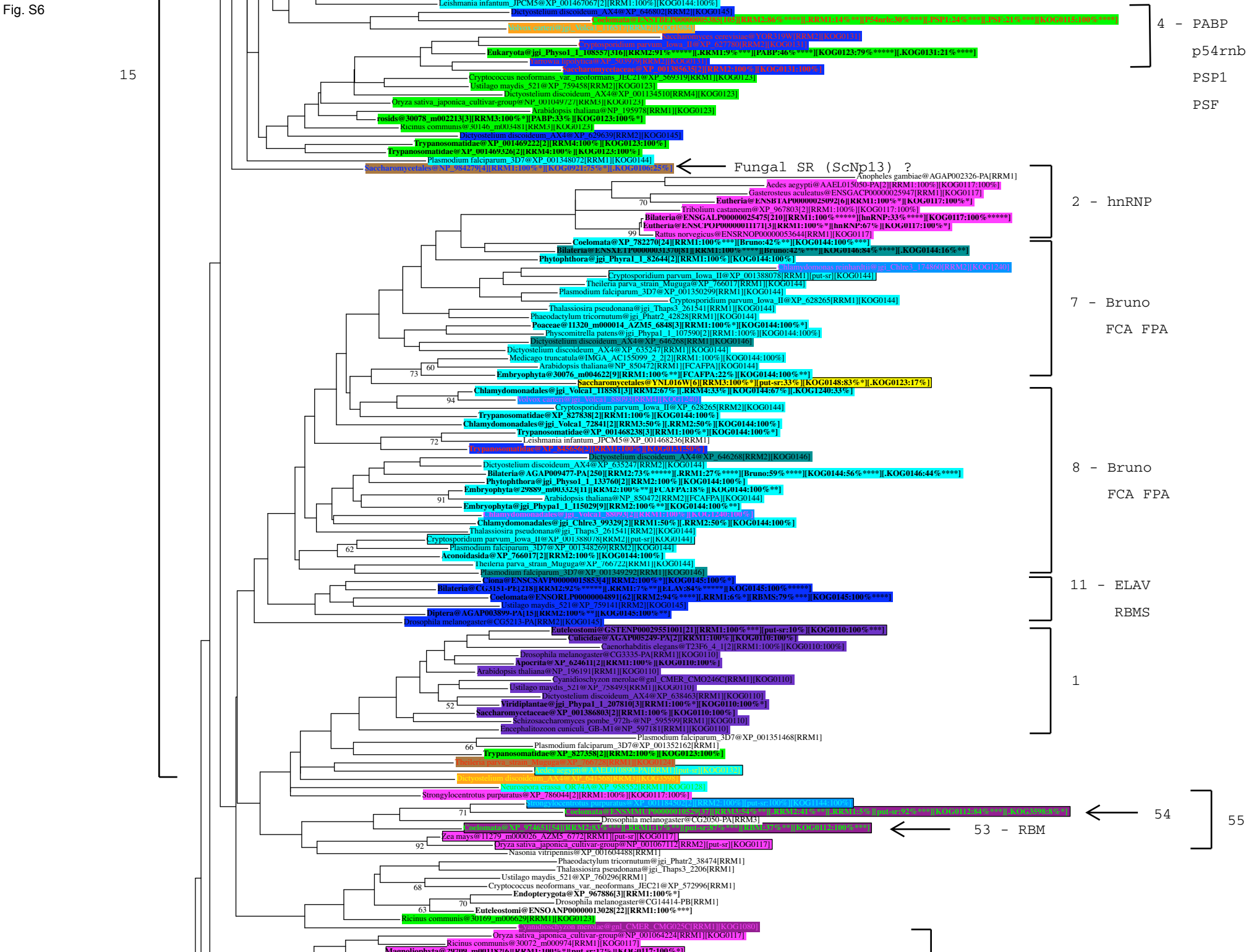


Fig. S6

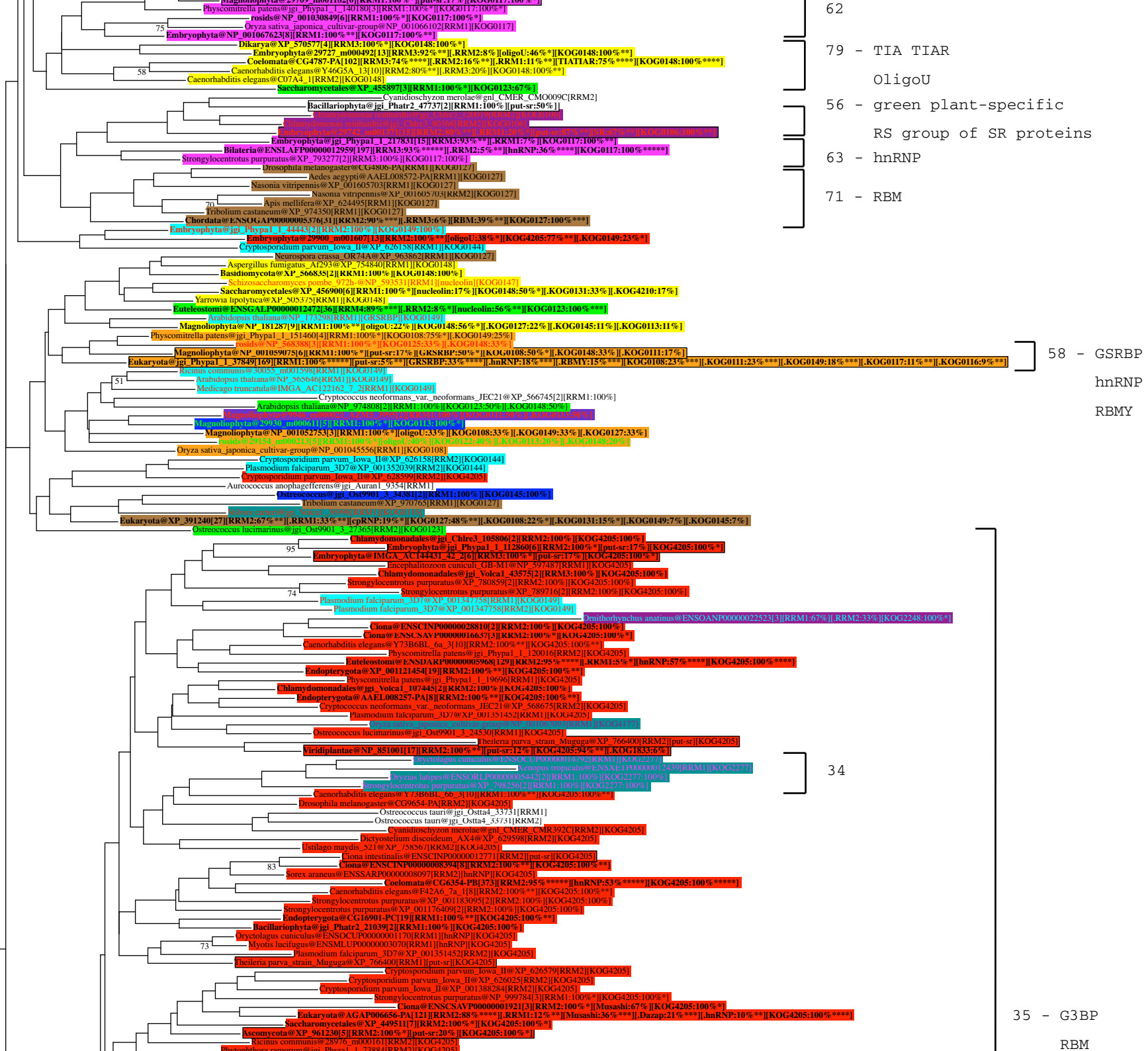
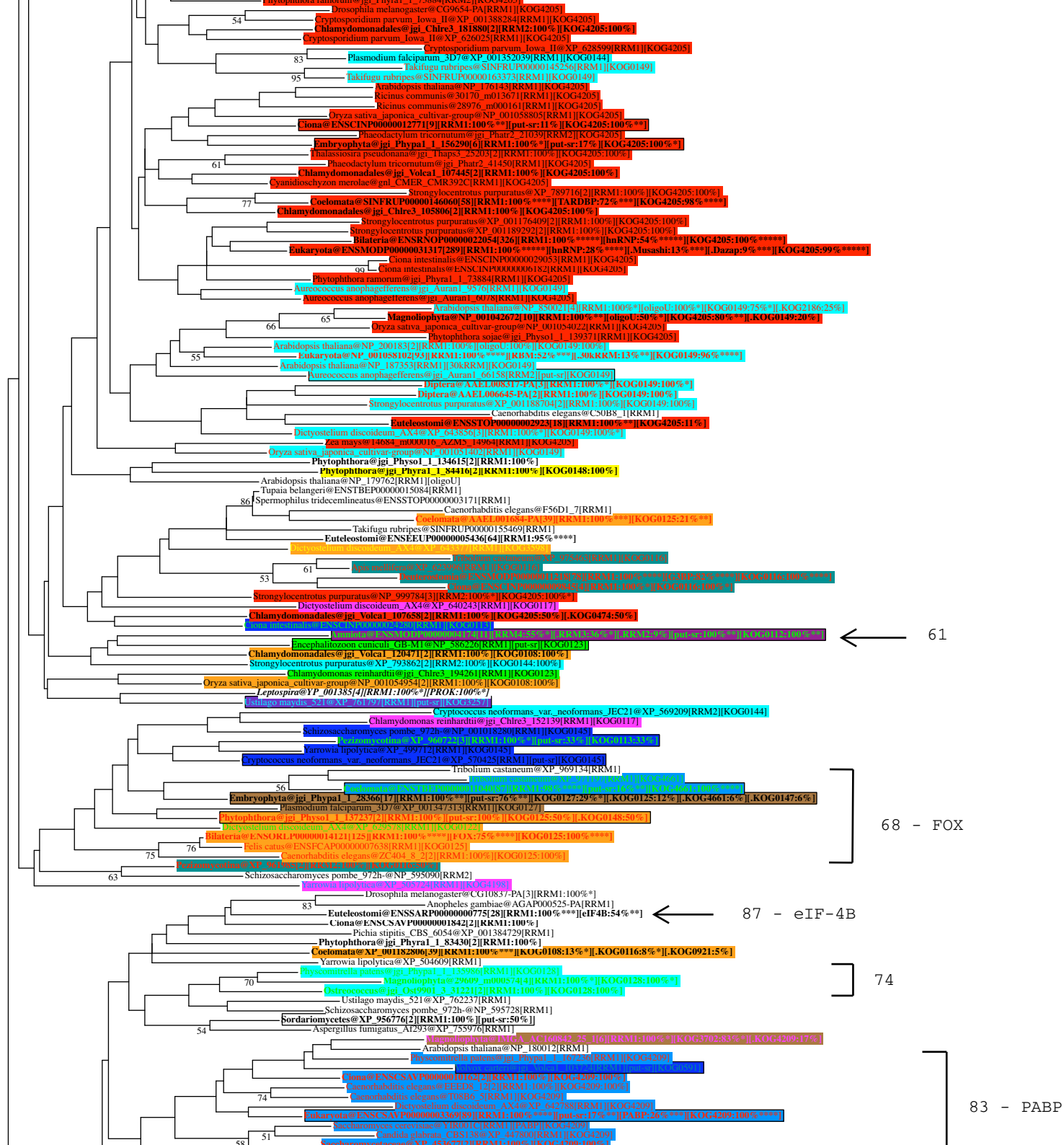


Fig. S6



30K-RRM
hnRNP
Musashi
Dazap
TARDBP
OligoU

61

68 - FOX

87 - eIF-4B

74

83 - PABP

Fig. S6

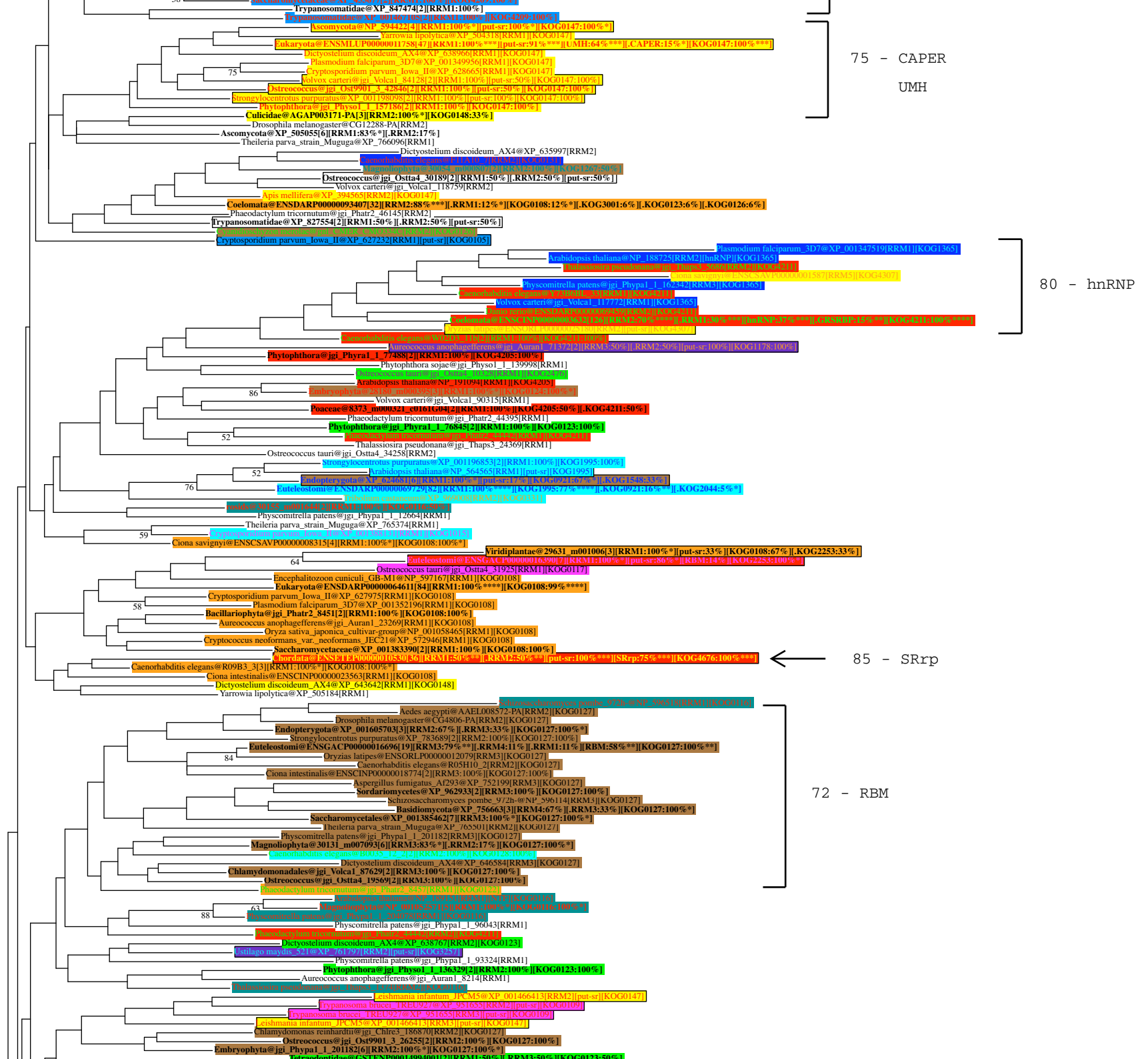


Fig. S6

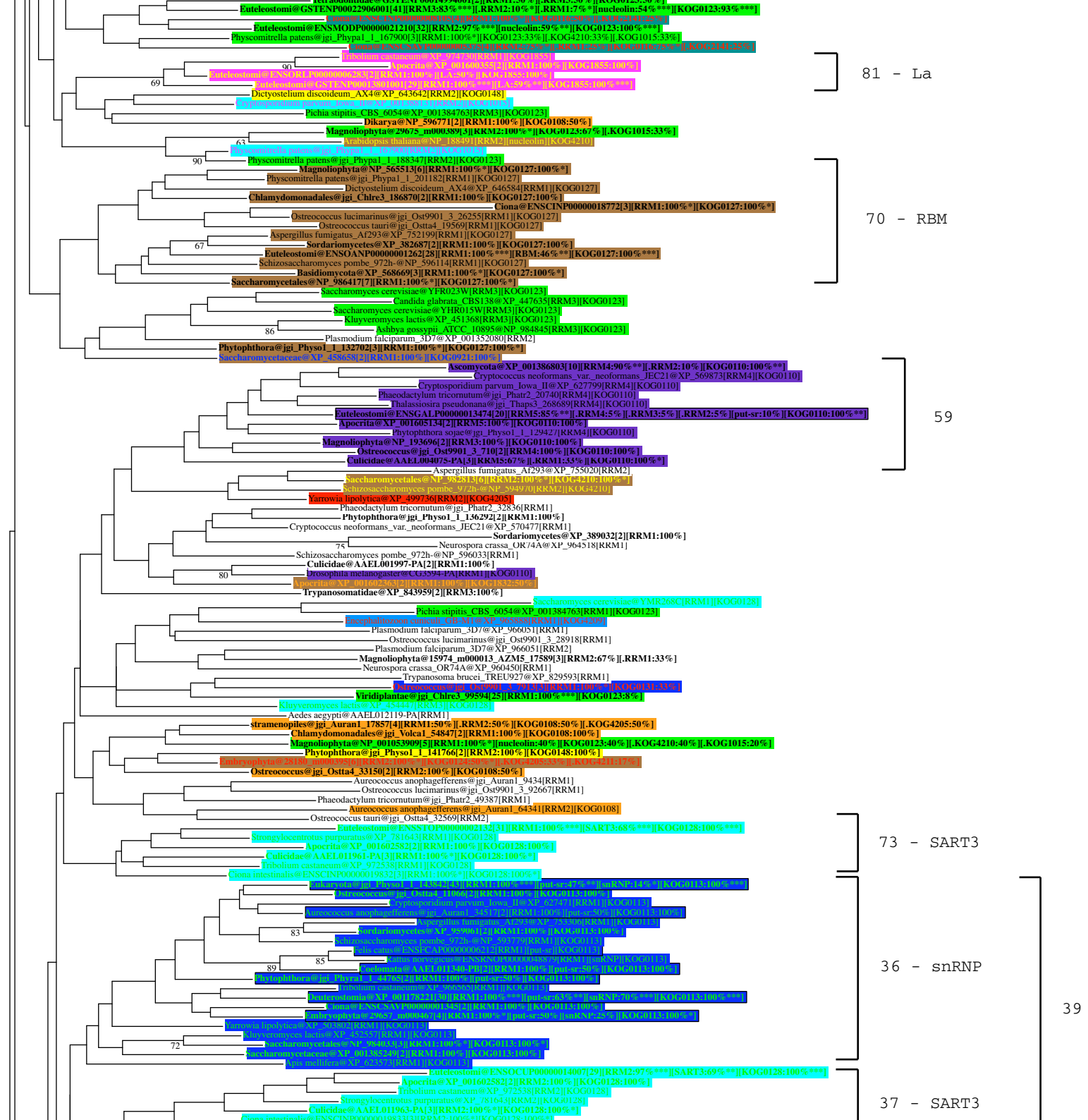


Fig. S6

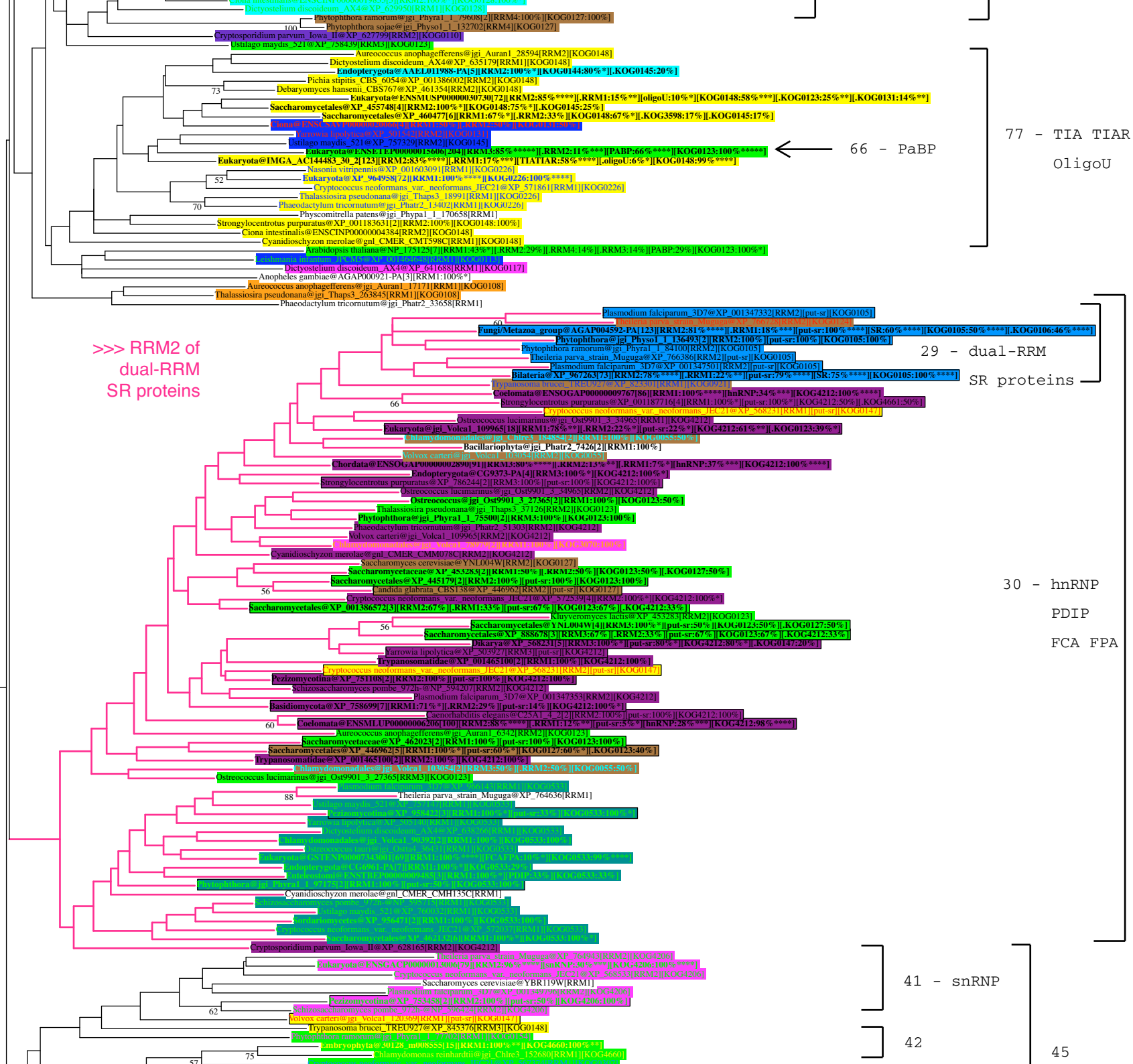


Fig. S6

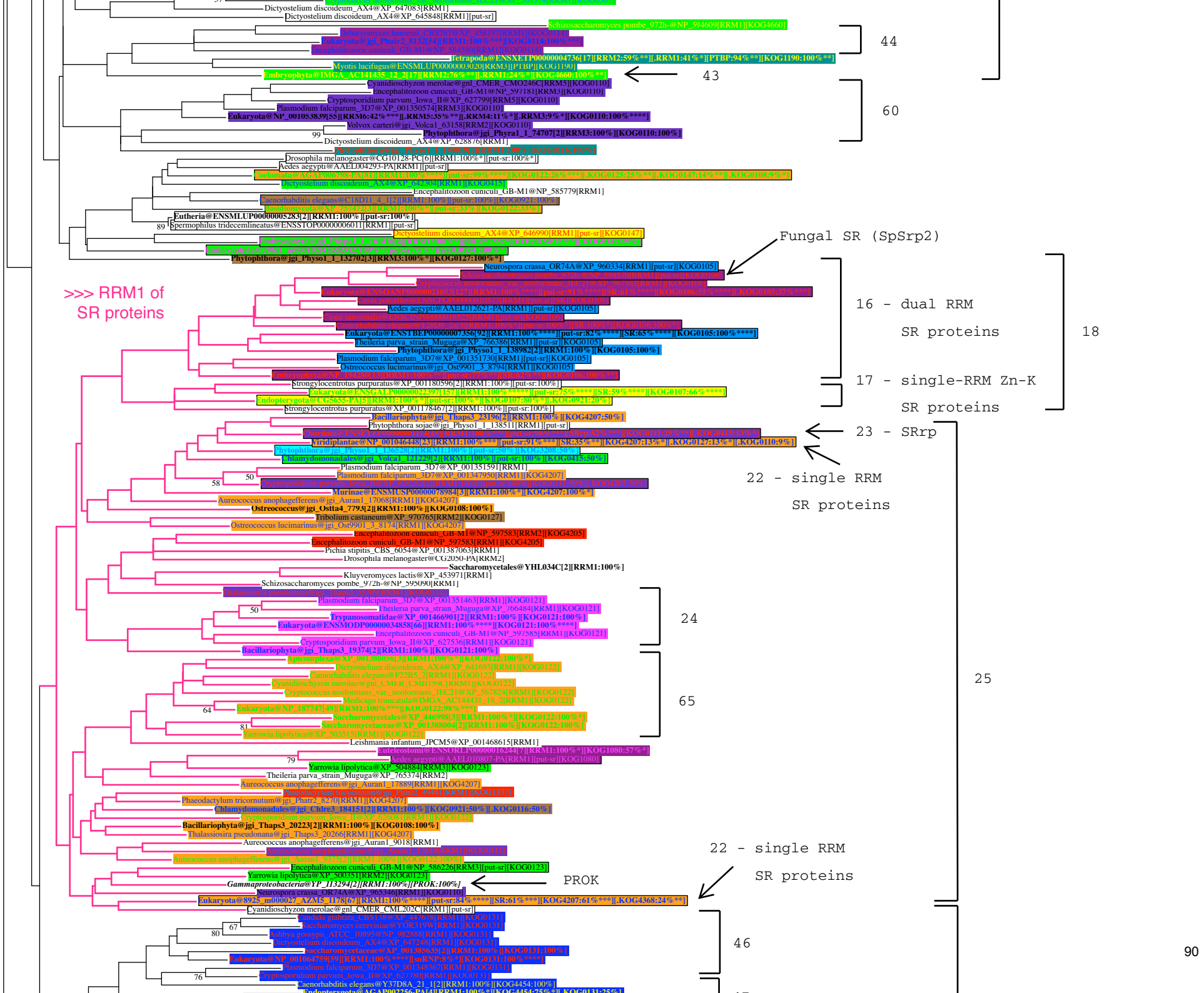


Fig. S6

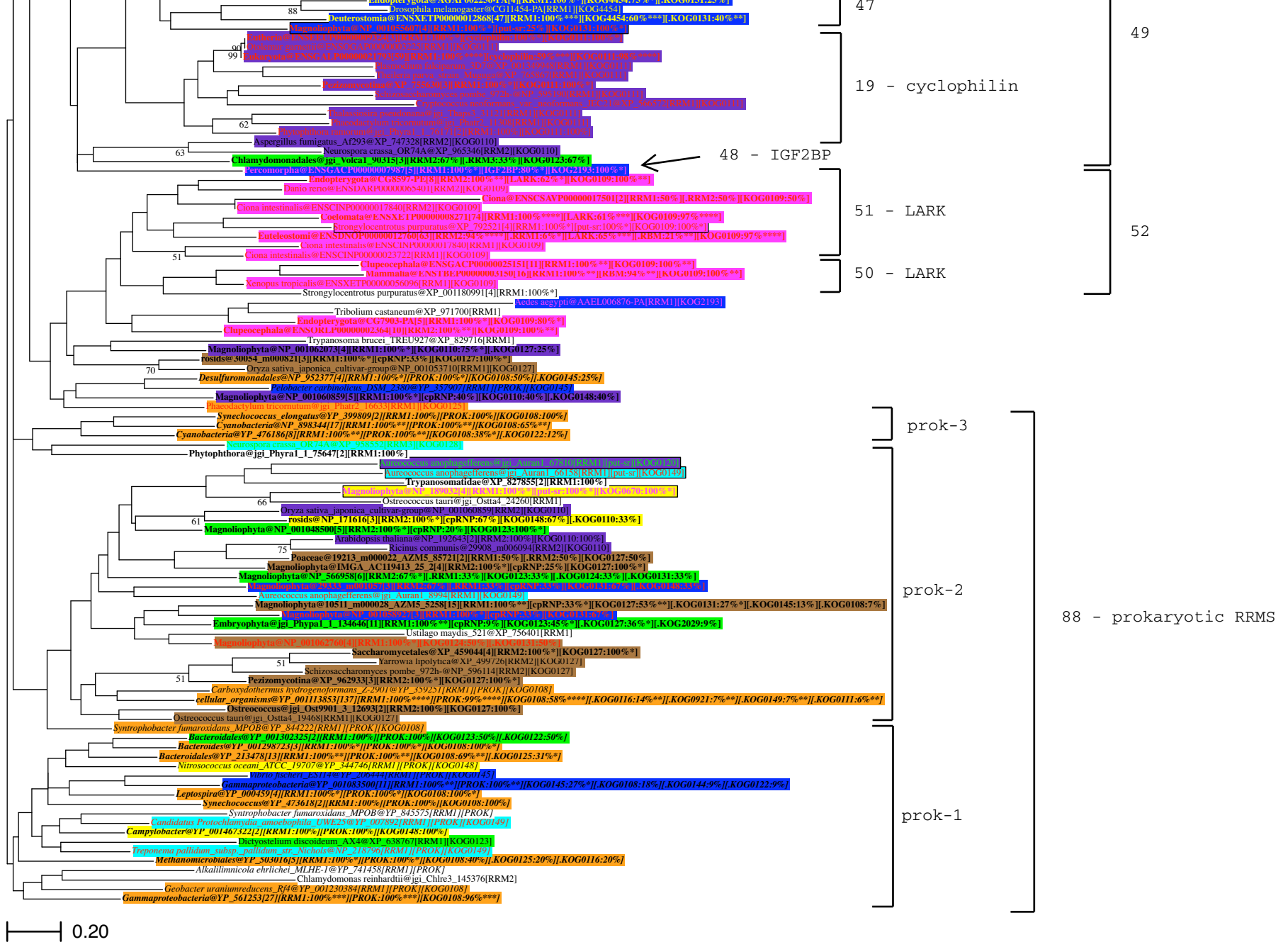


Fig. S7

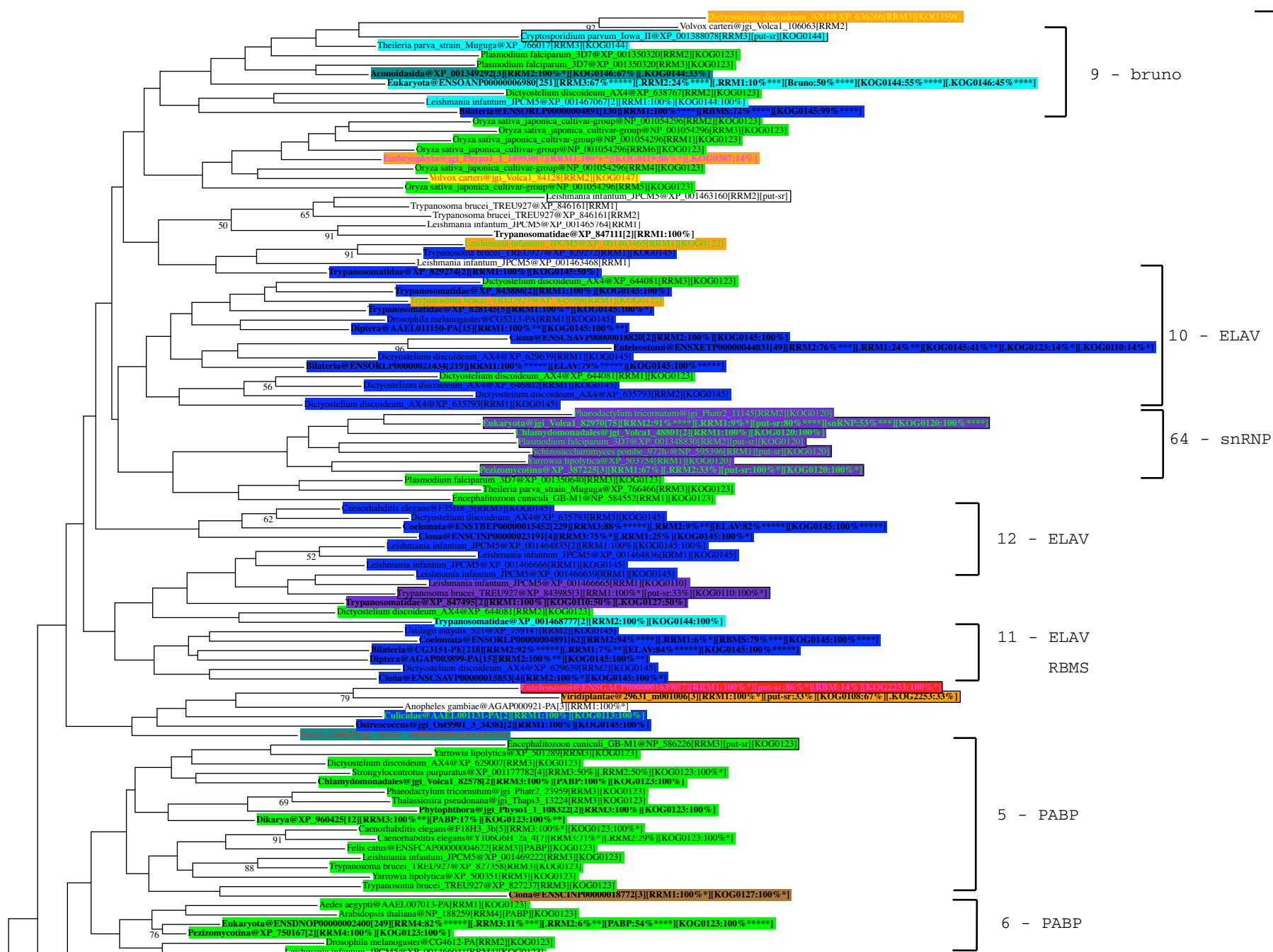


Fig. S7

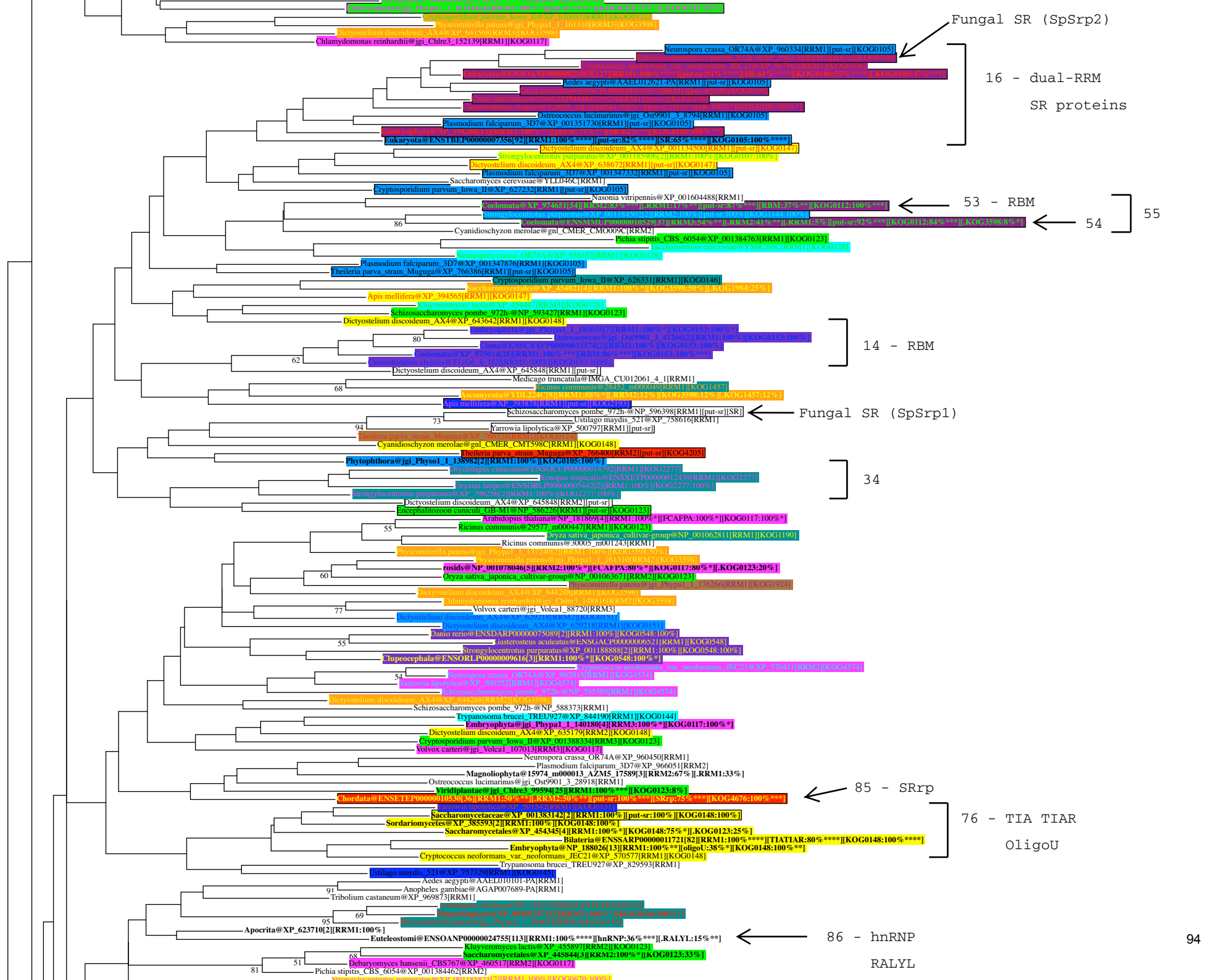


Fig. S7

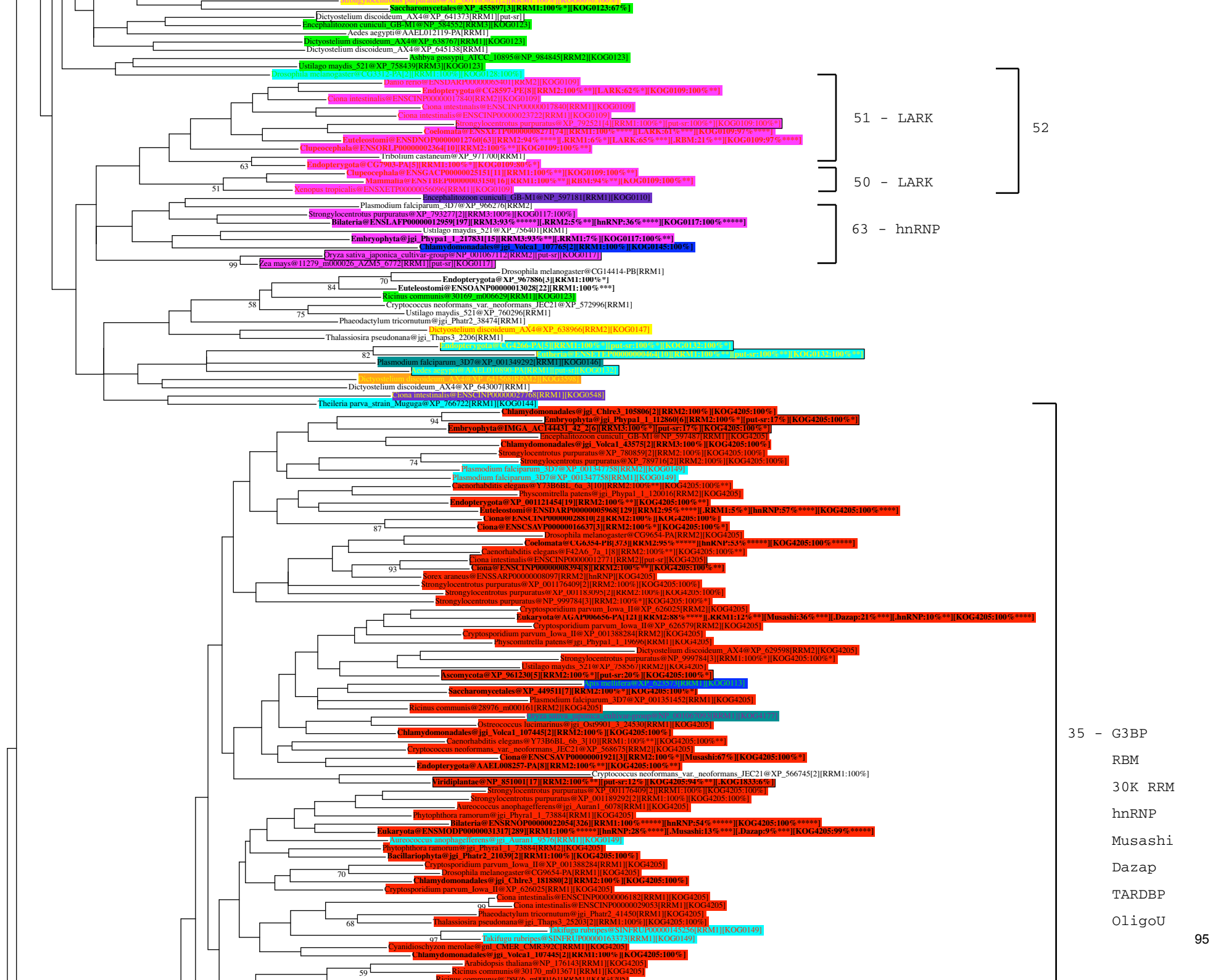


Fig. S7

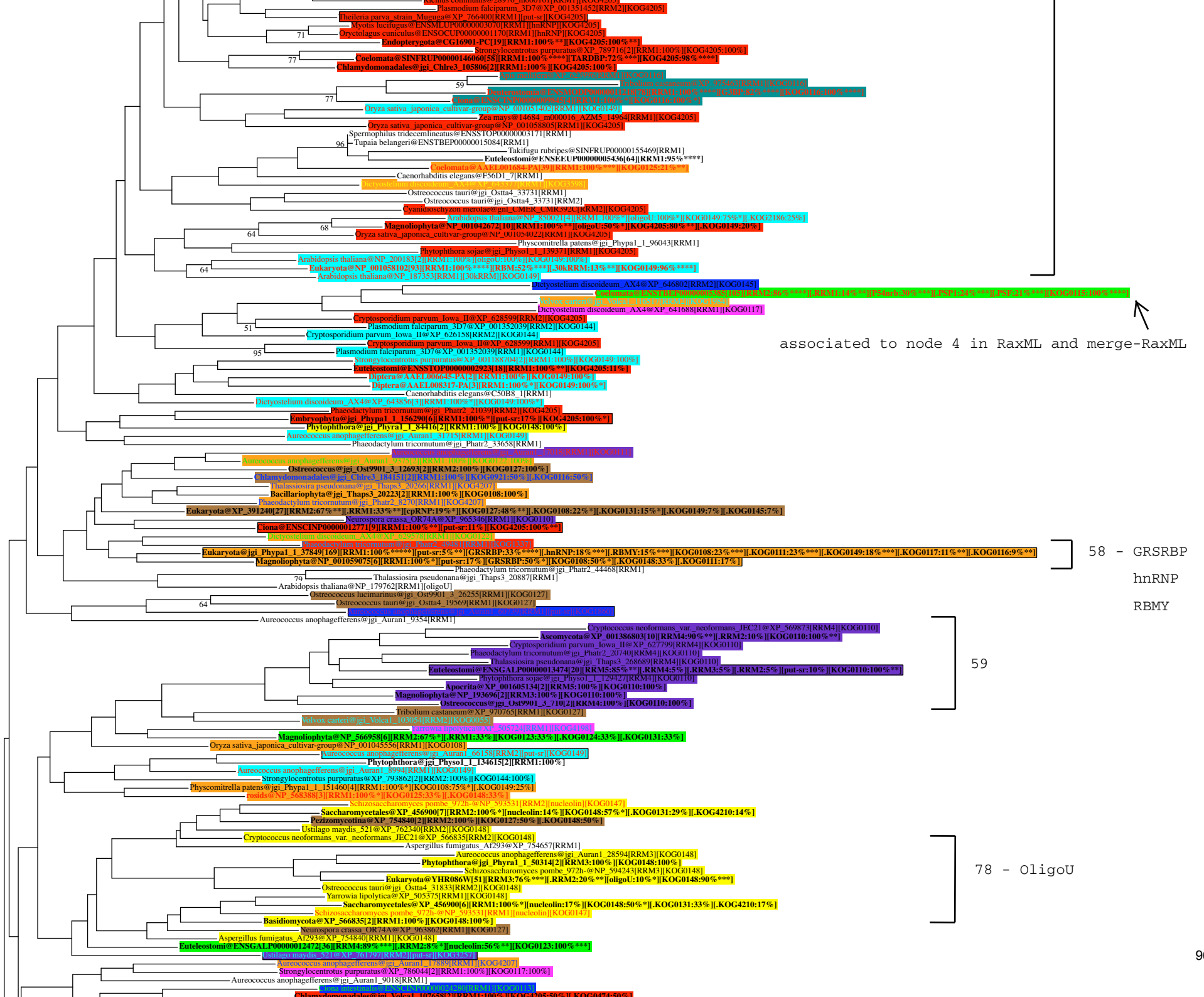
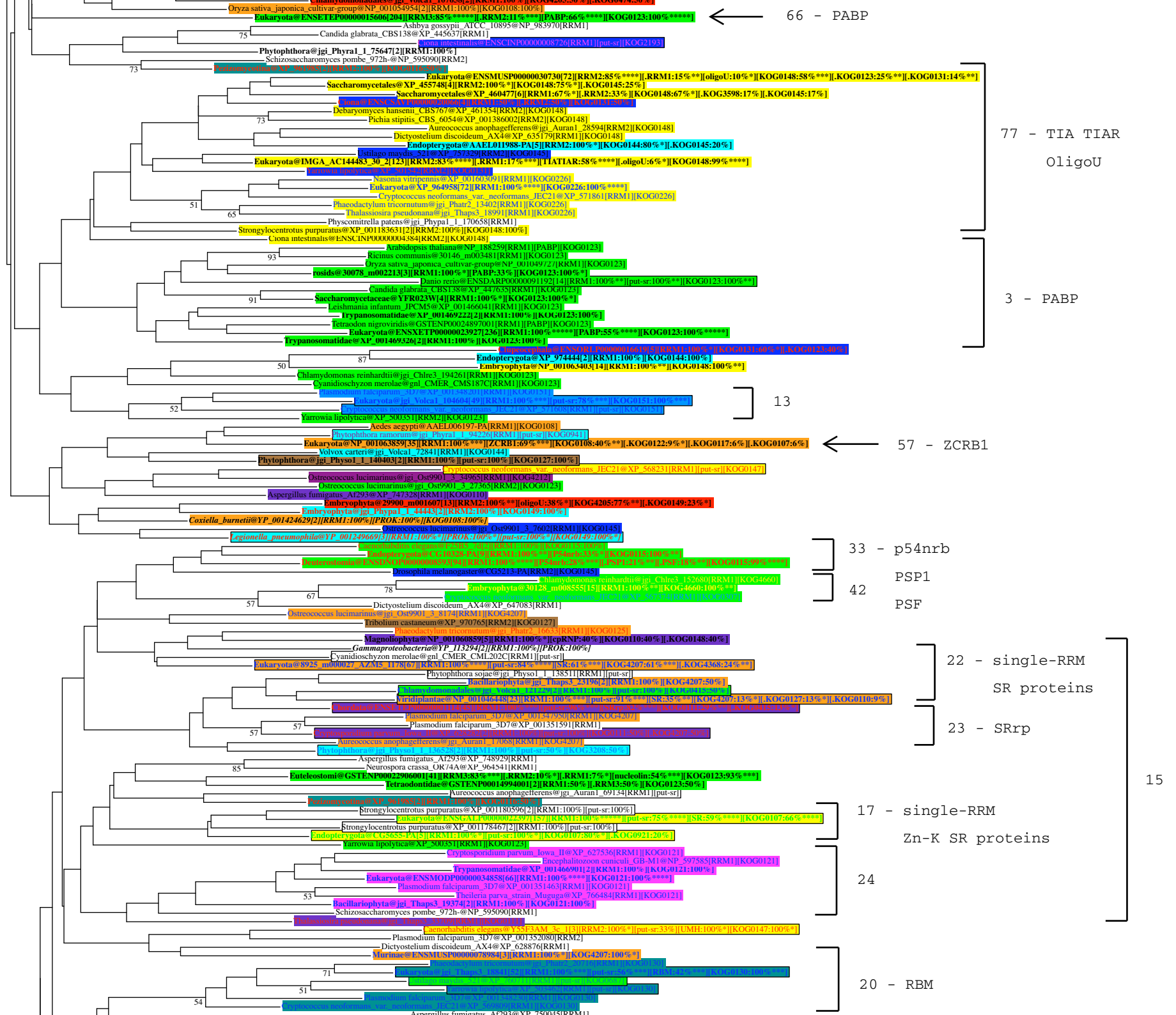


Fig. S7



[illegible]

Fig. S7

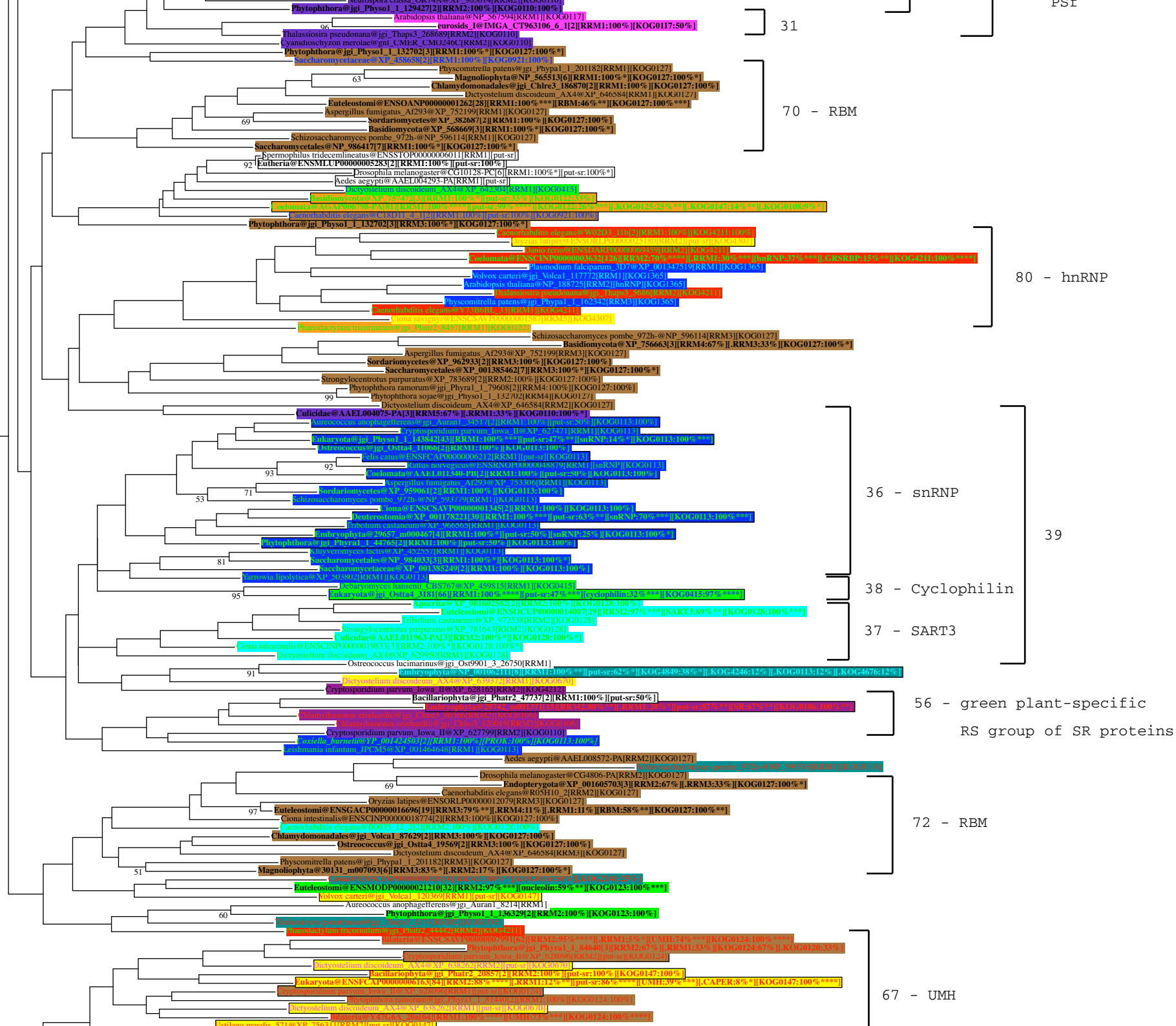


Fig. S7

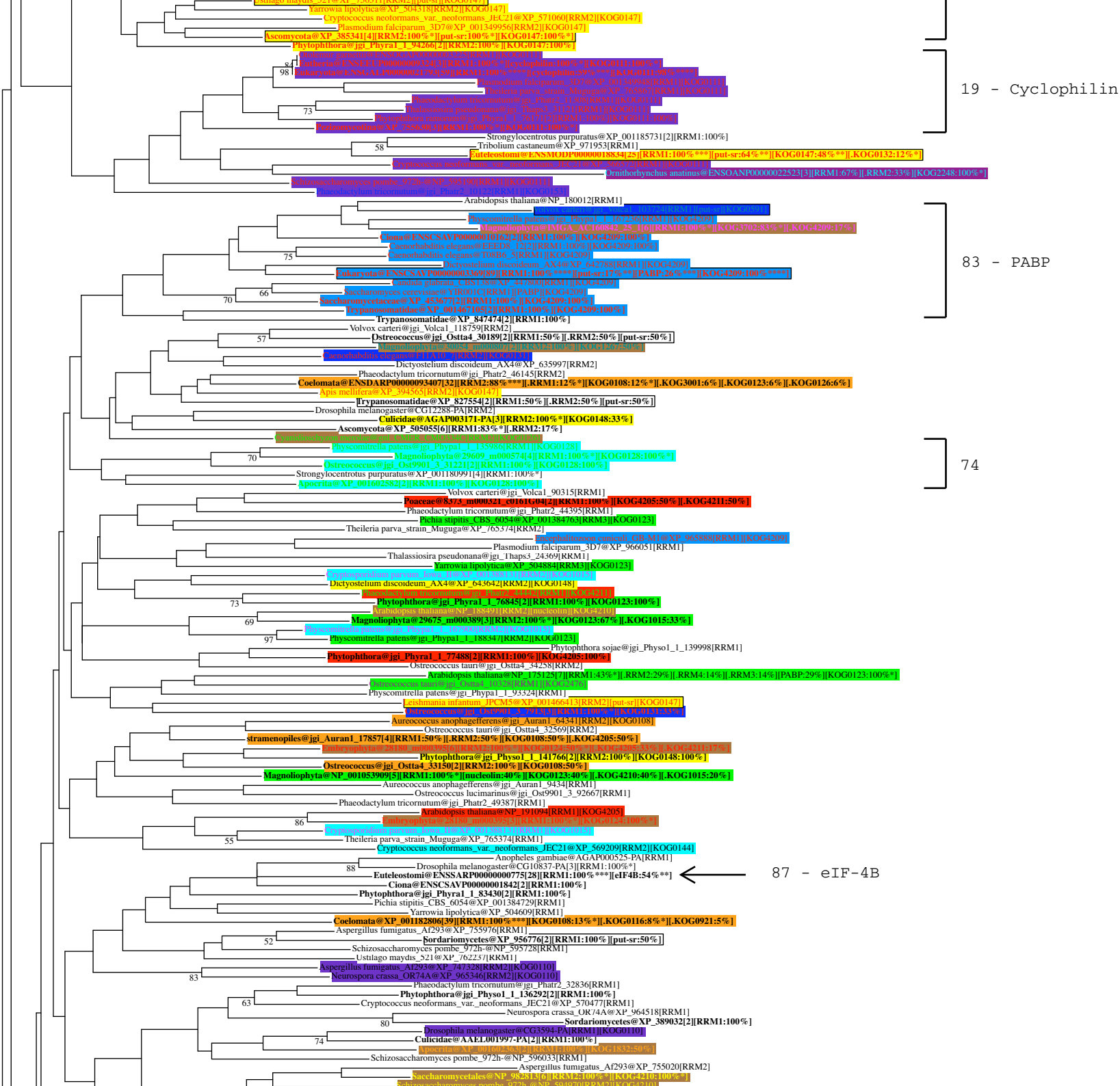


Fig. S7

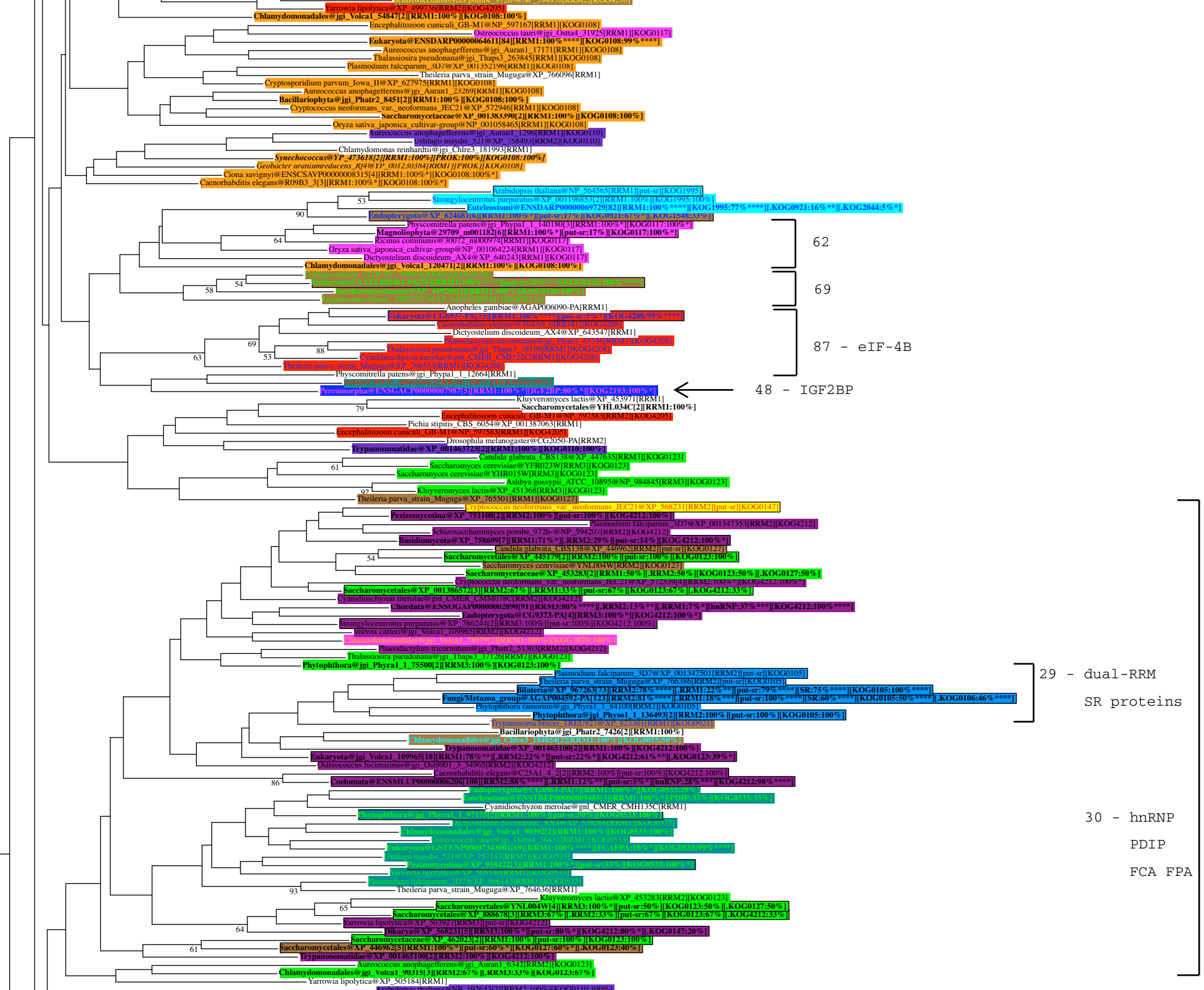


Fig. S7

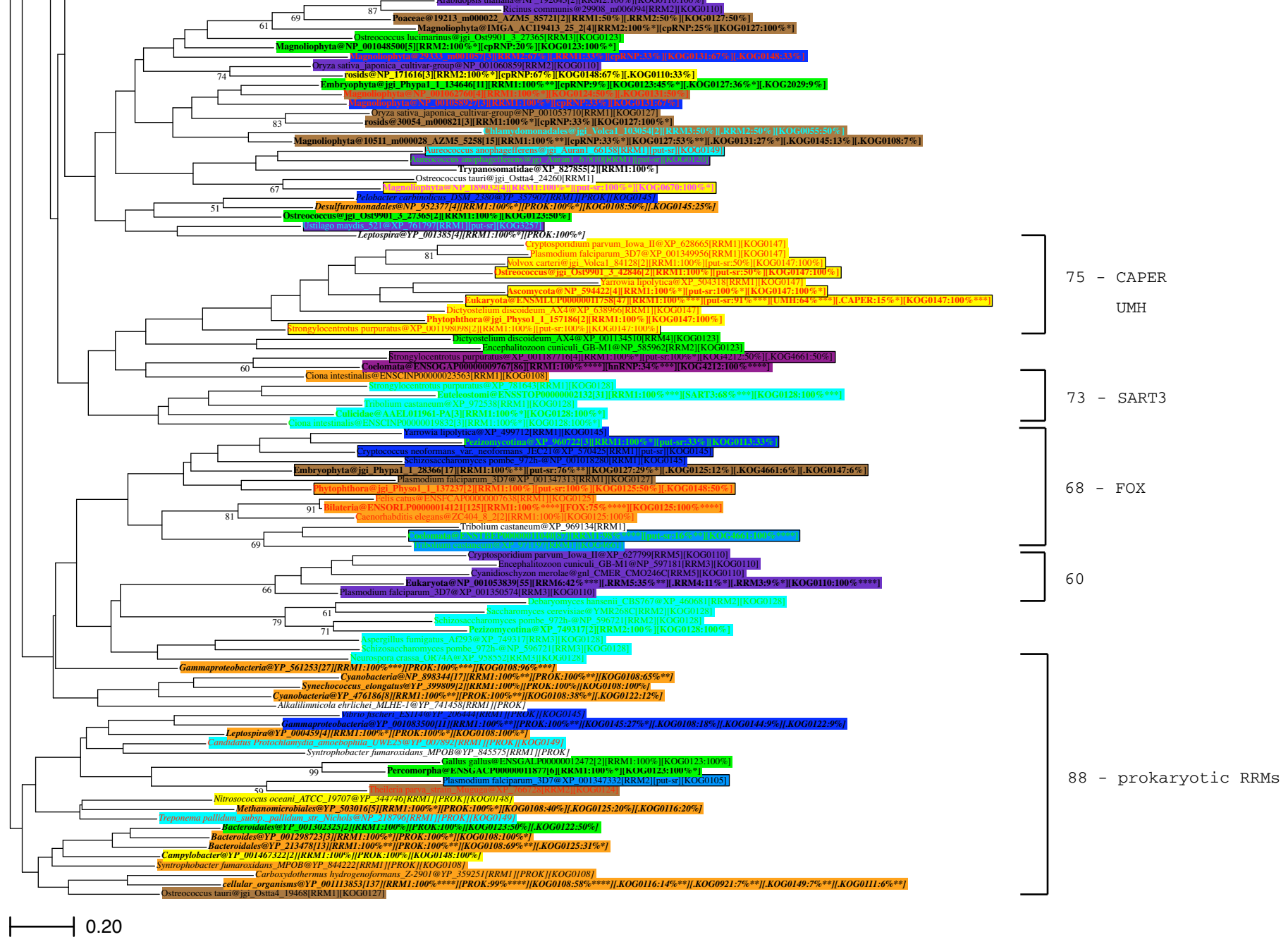


Fig. S8

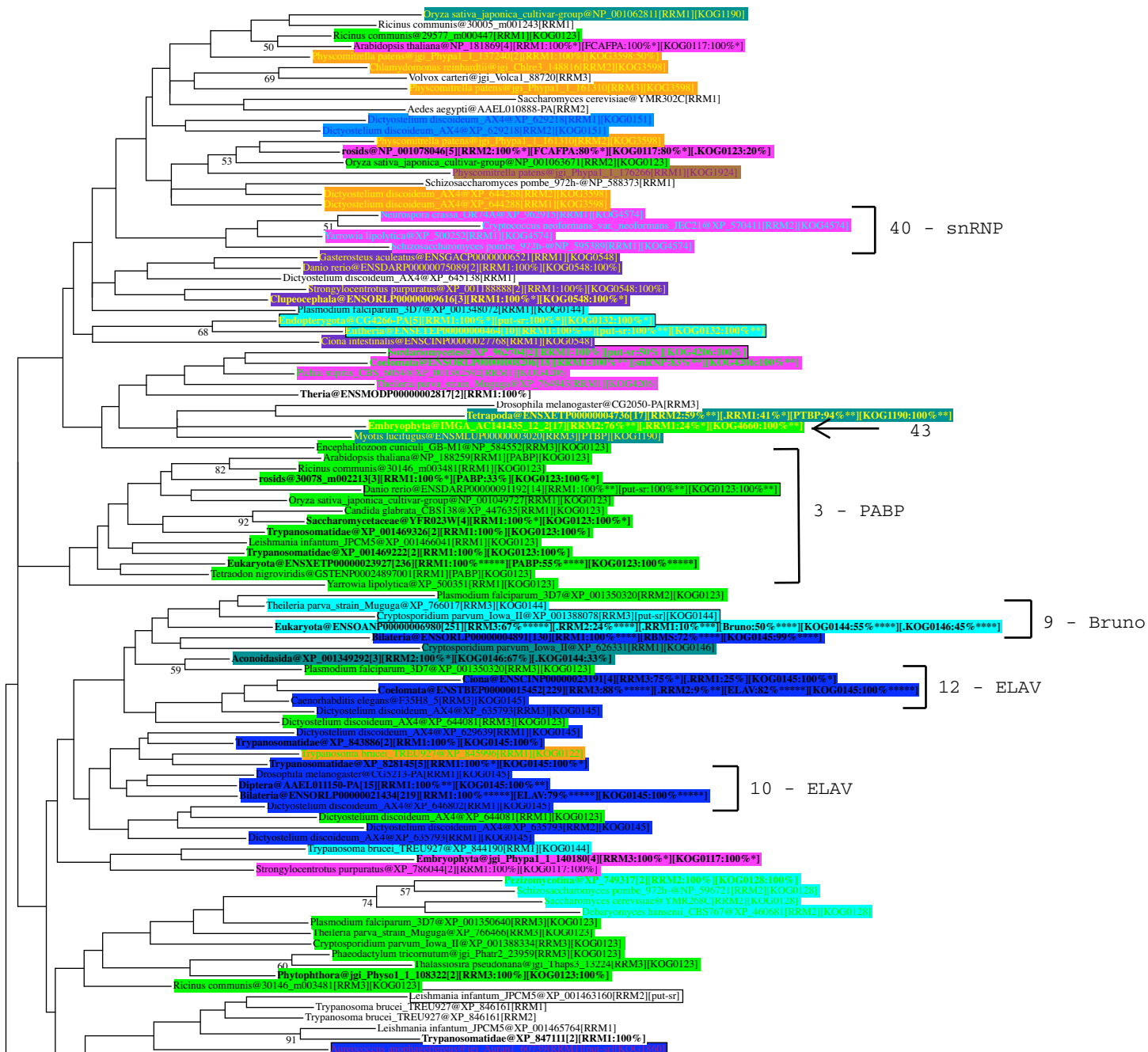


Fig. S8

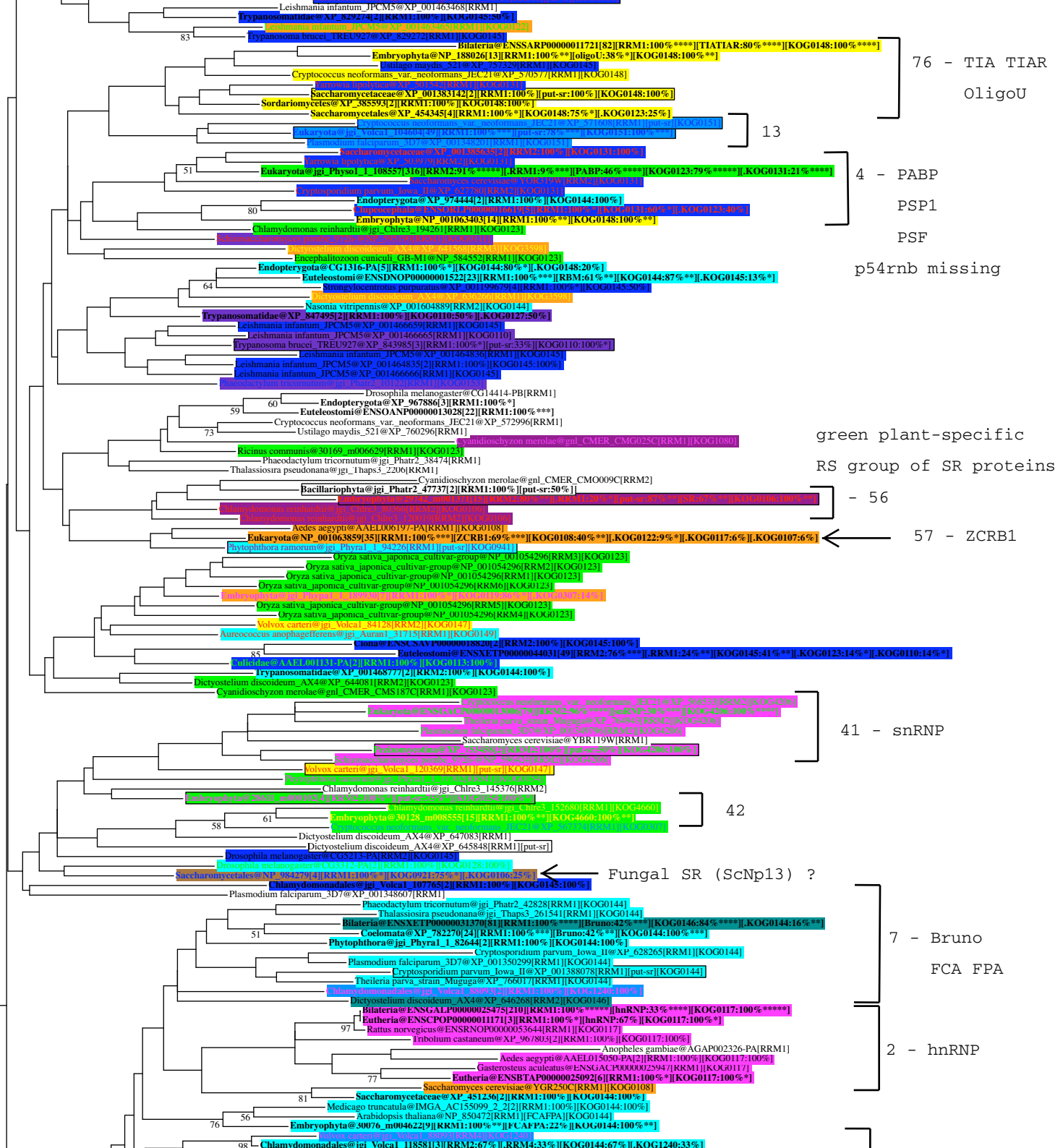


Fig. S8

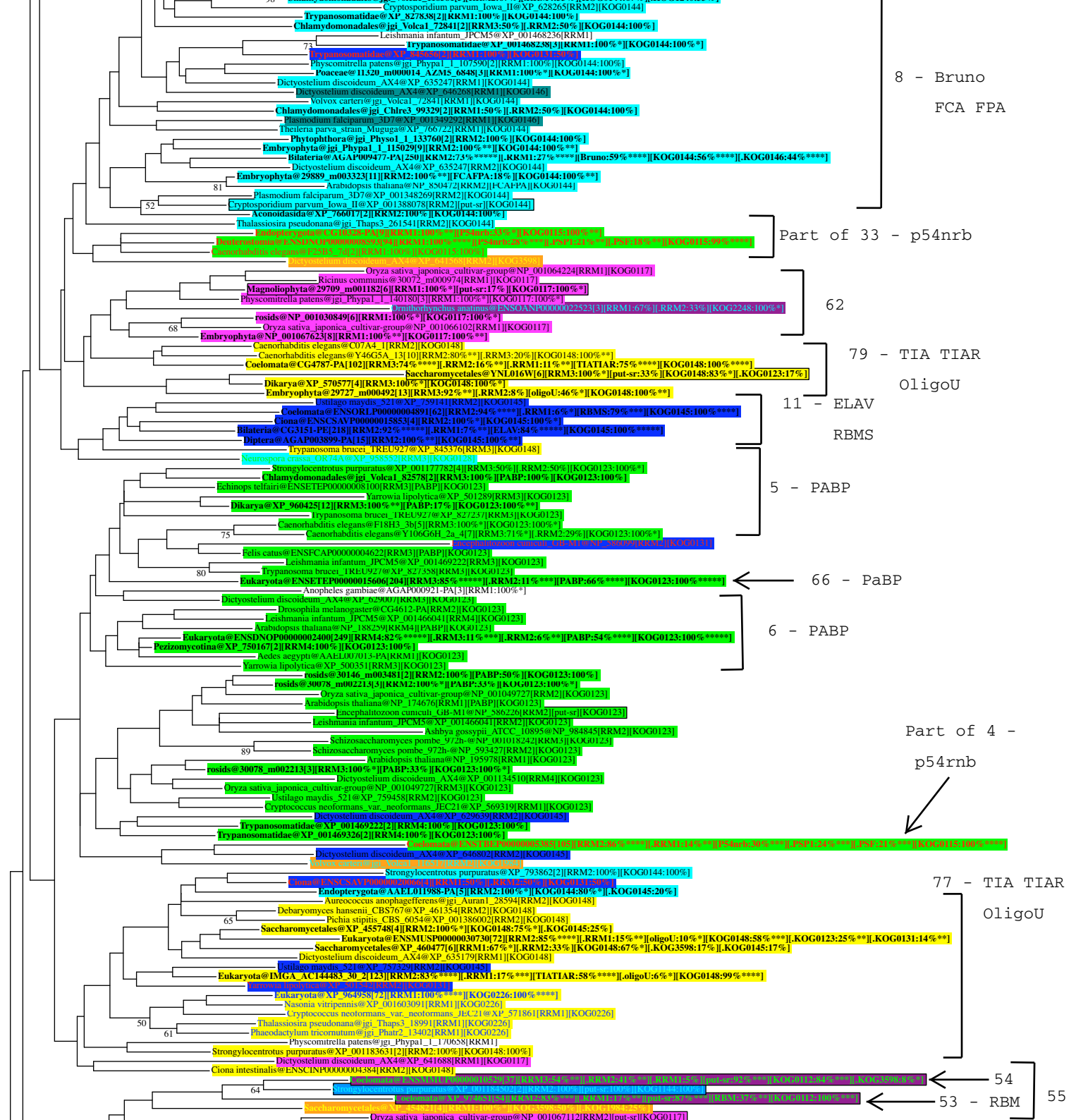


Fig. S8

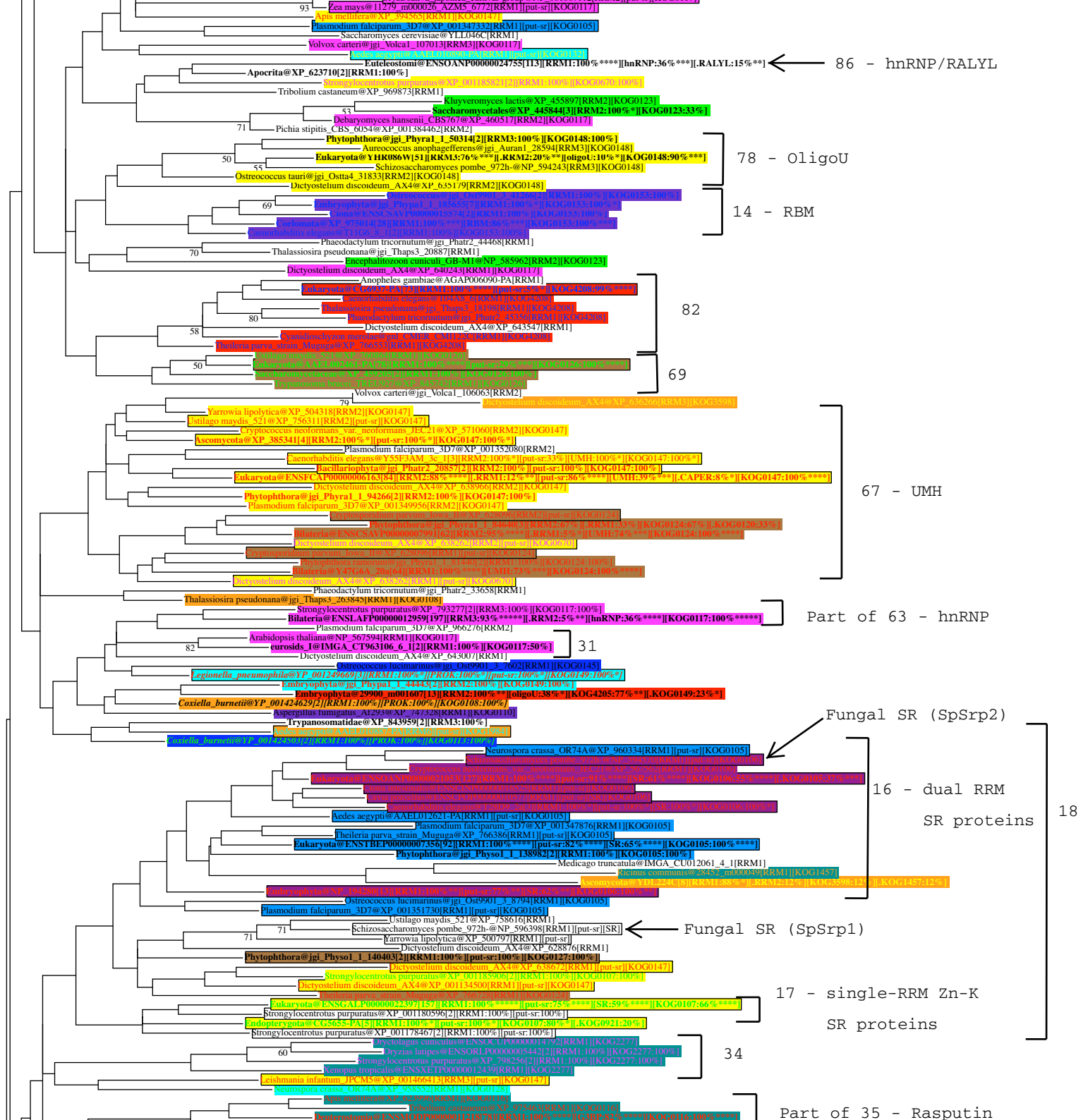


Fig. S8

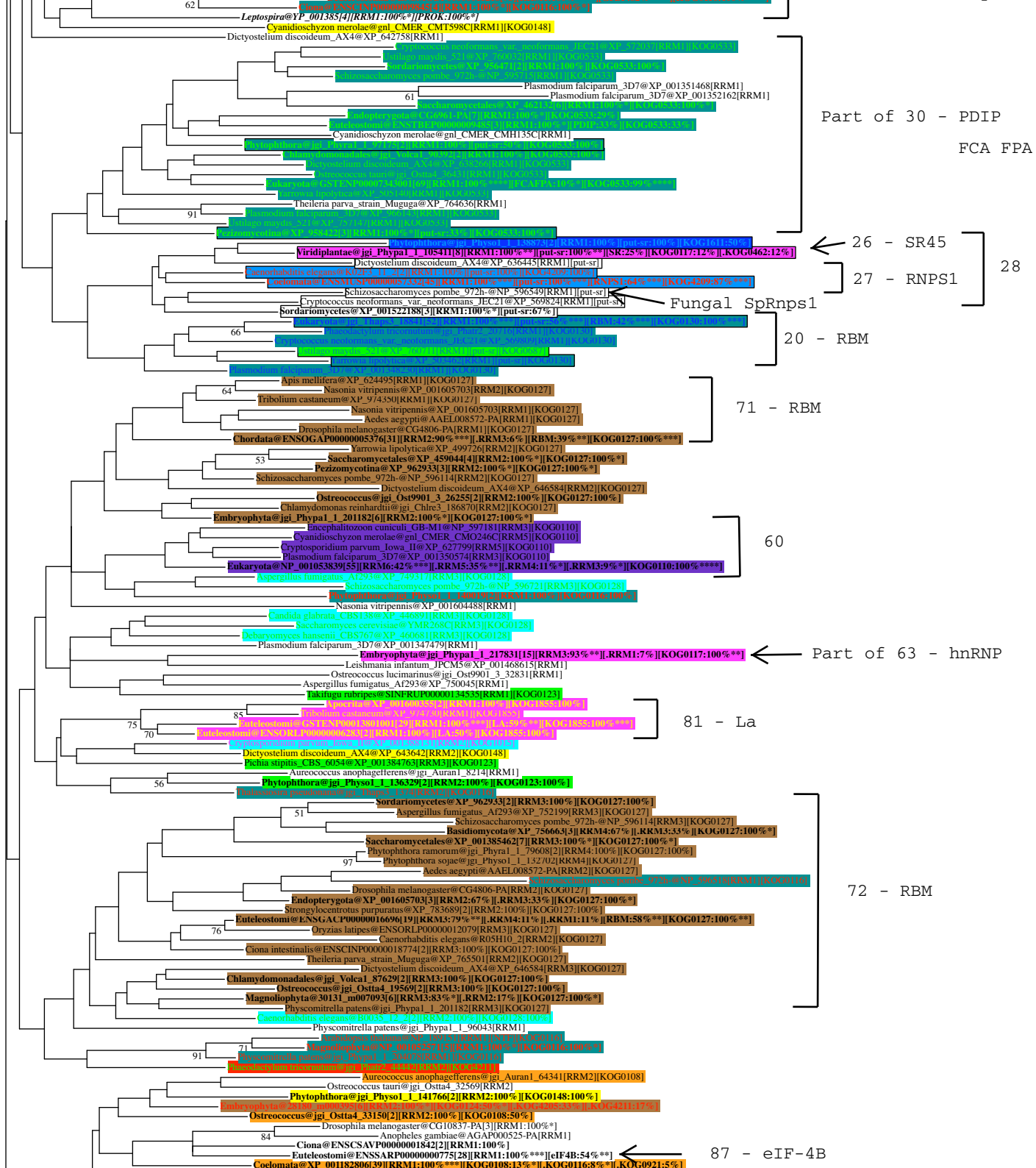


Fig. S8

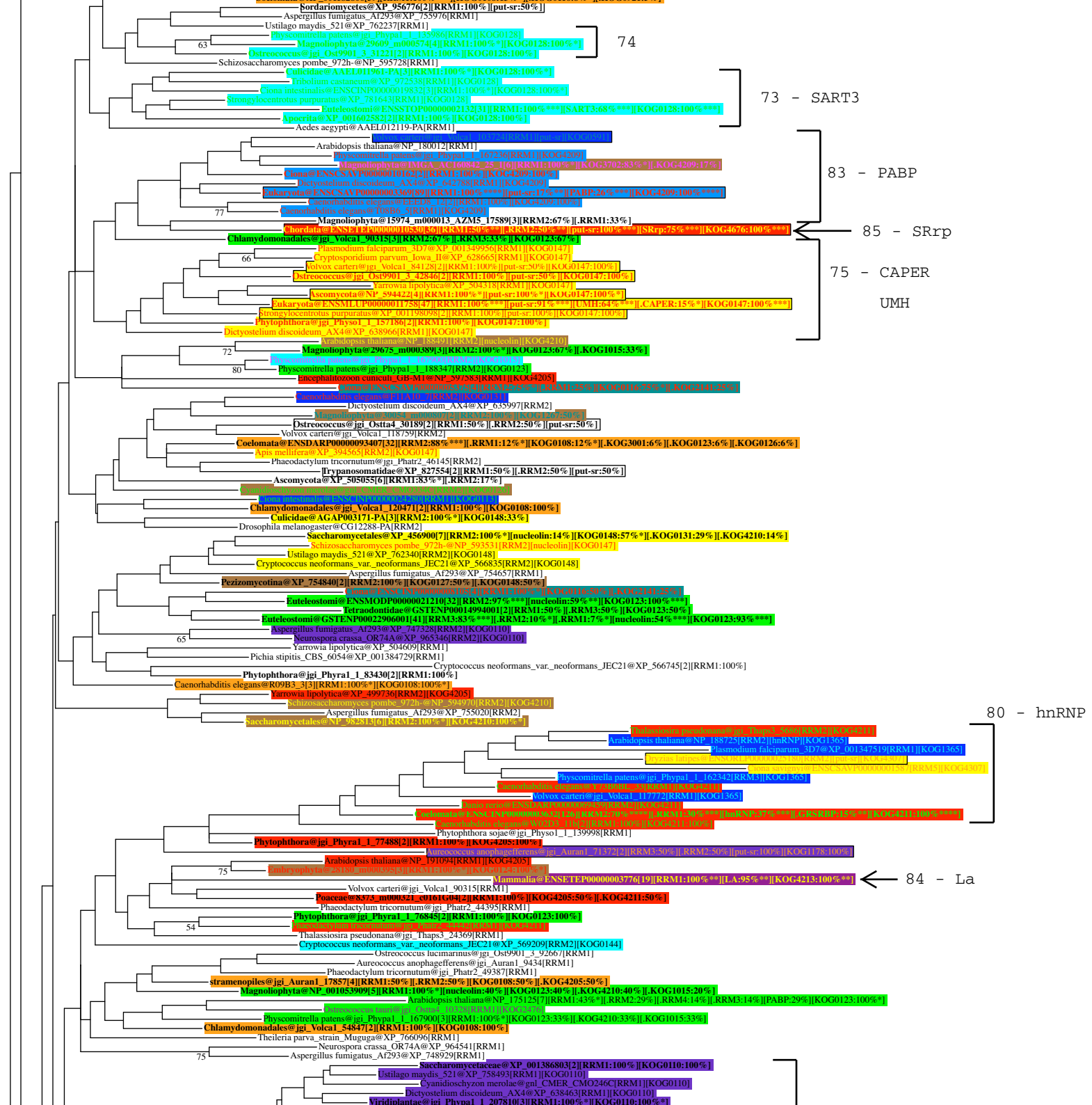


Fig. S8

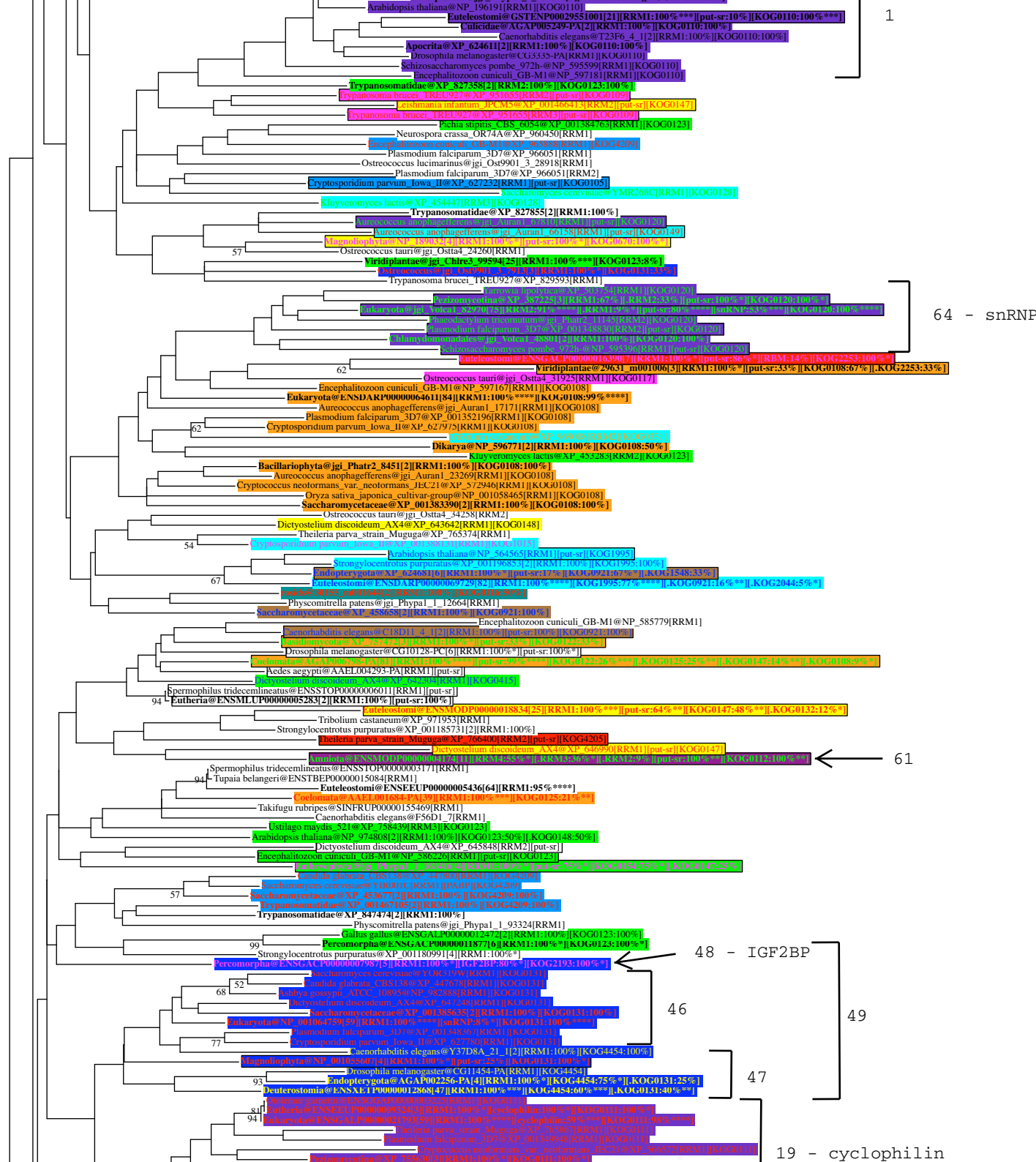


Fig. S8

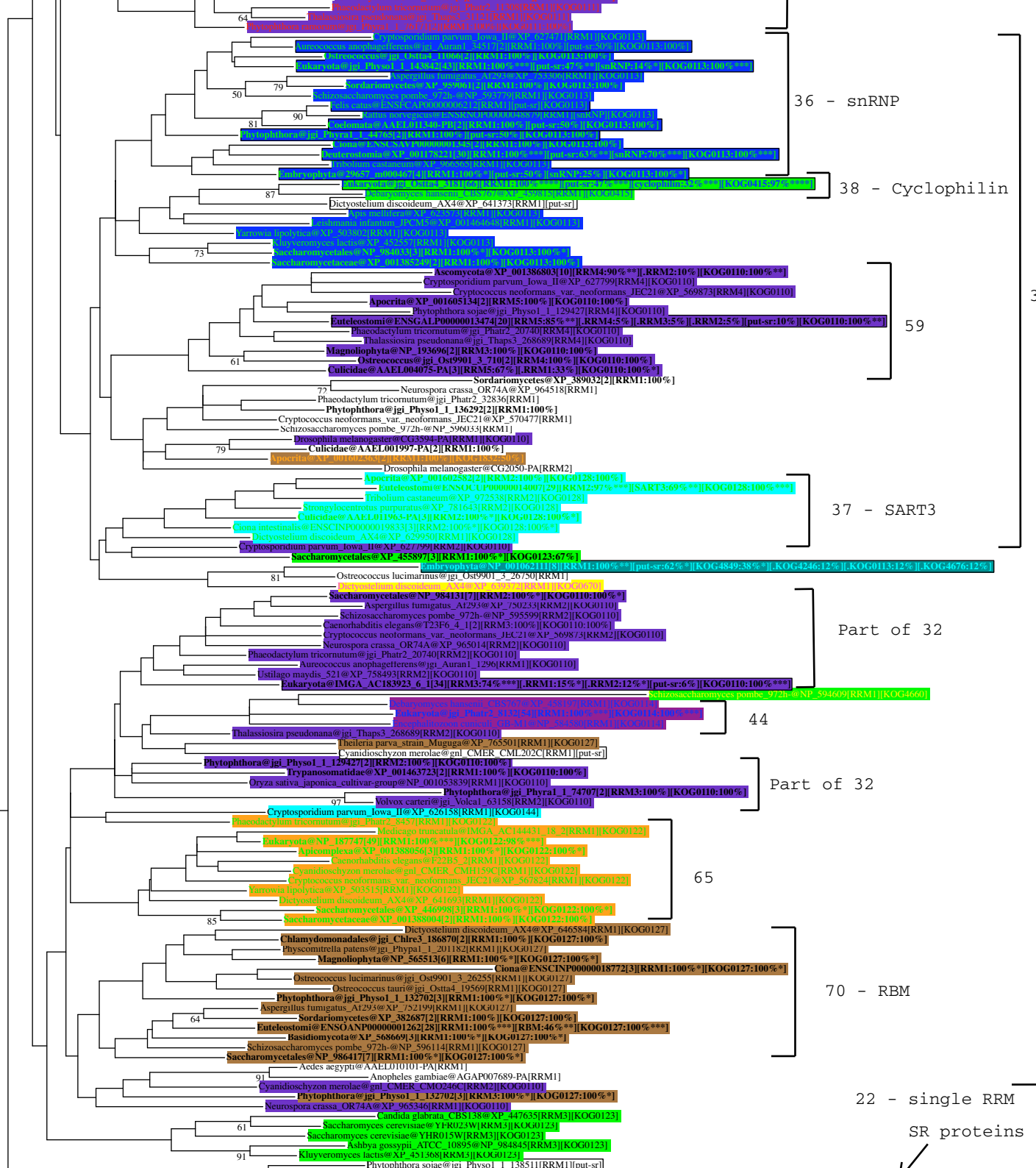
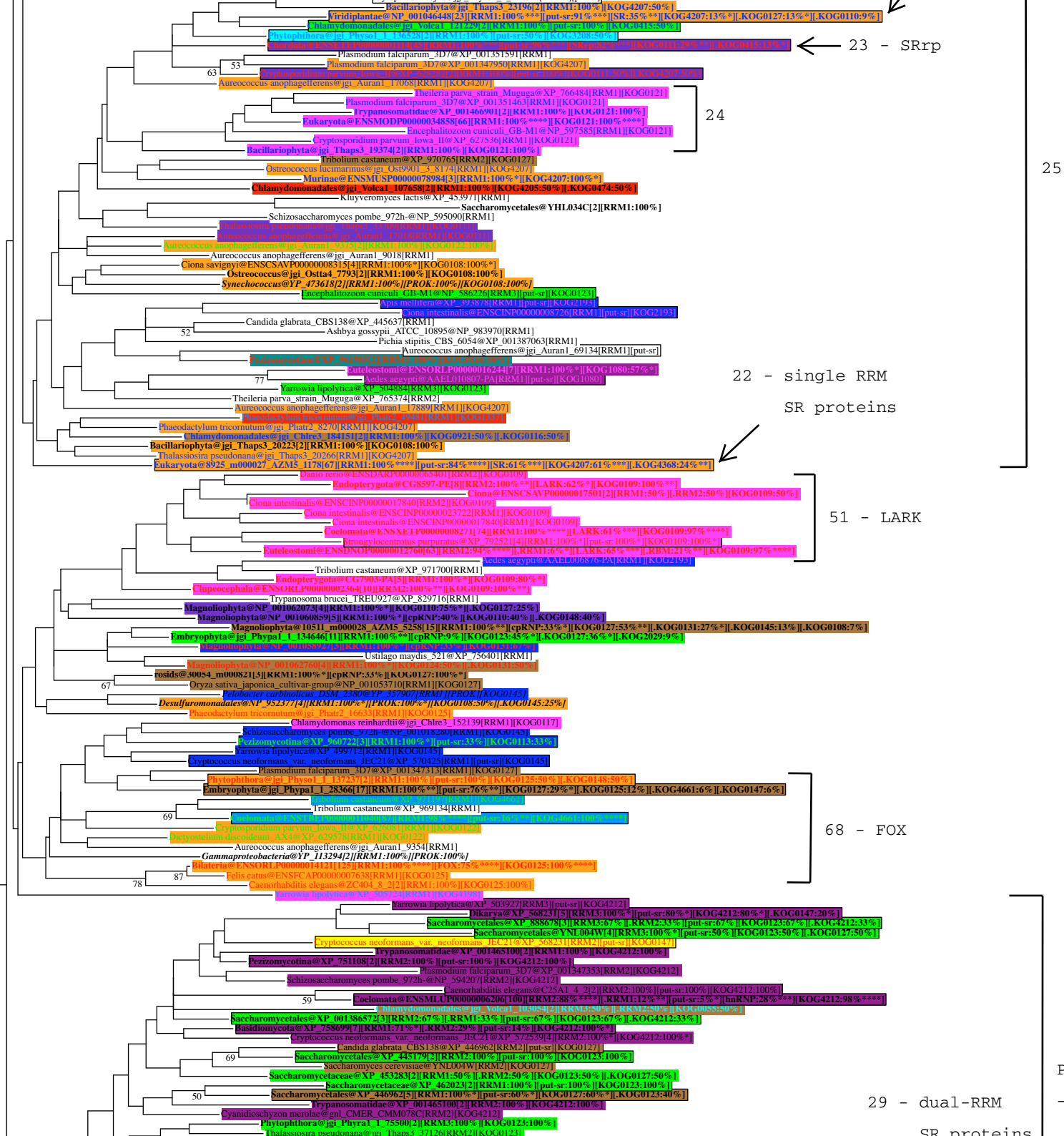


Fig. S8



25

Part of 30

Fig. S8

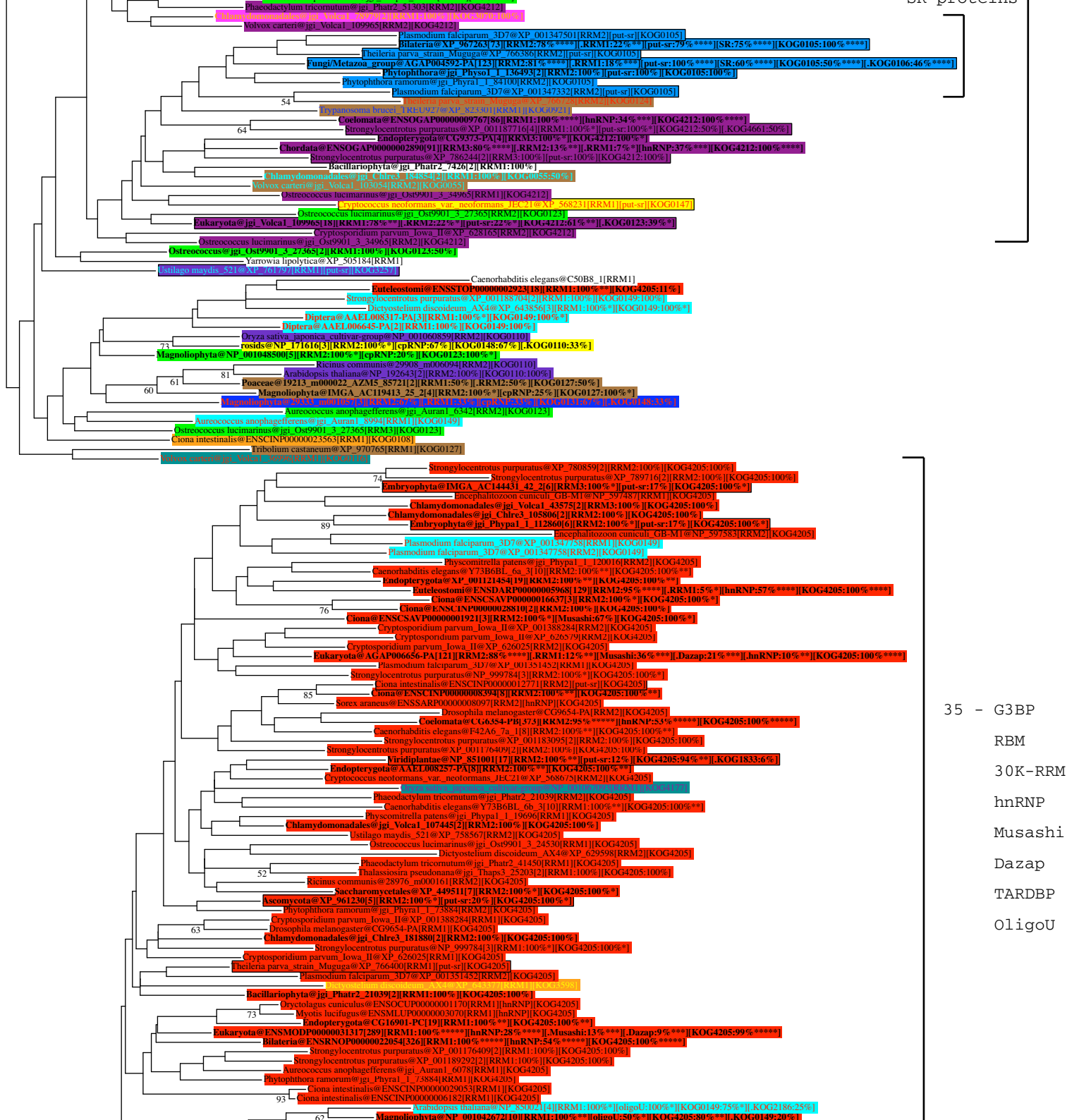


Fig. S8

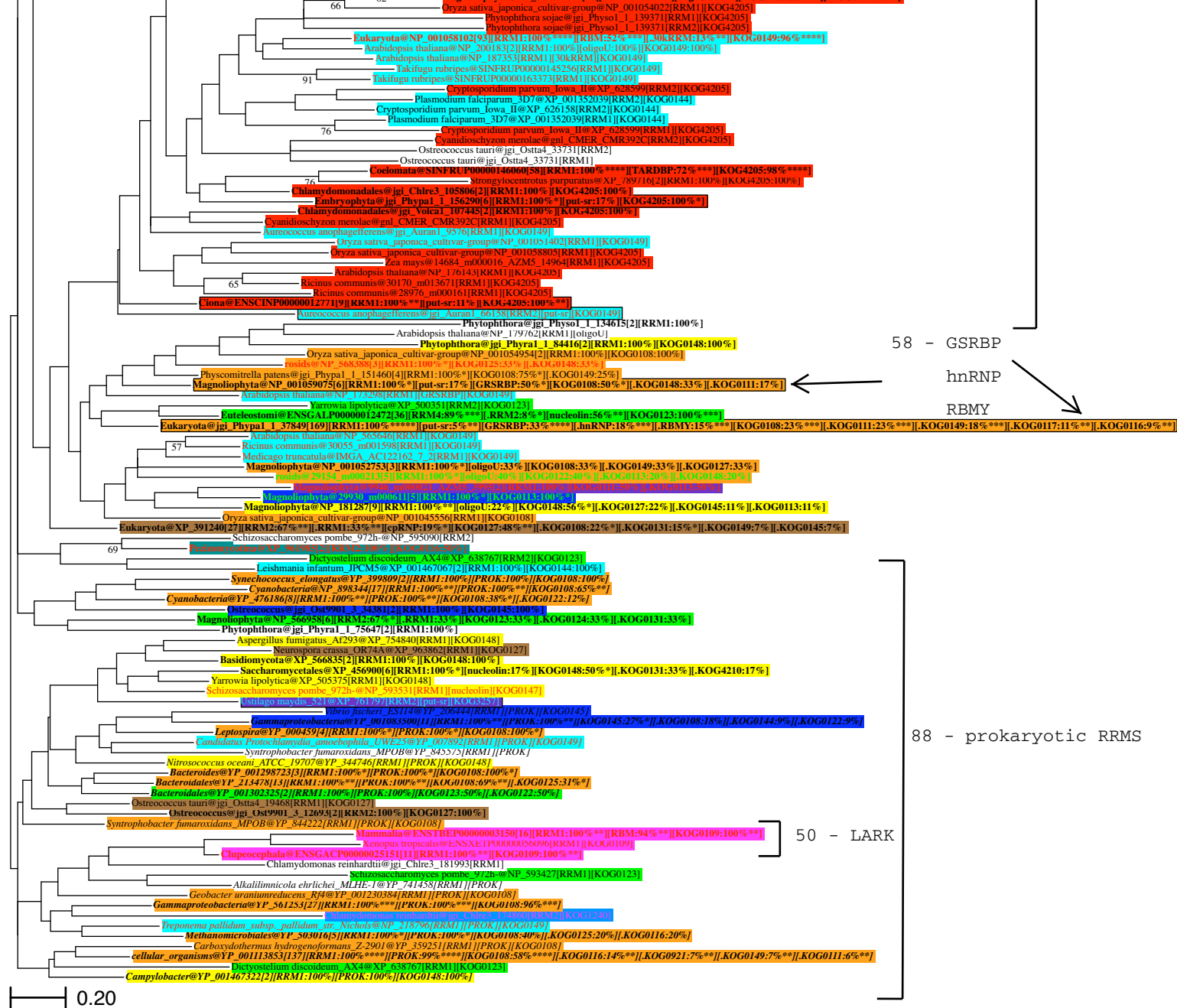
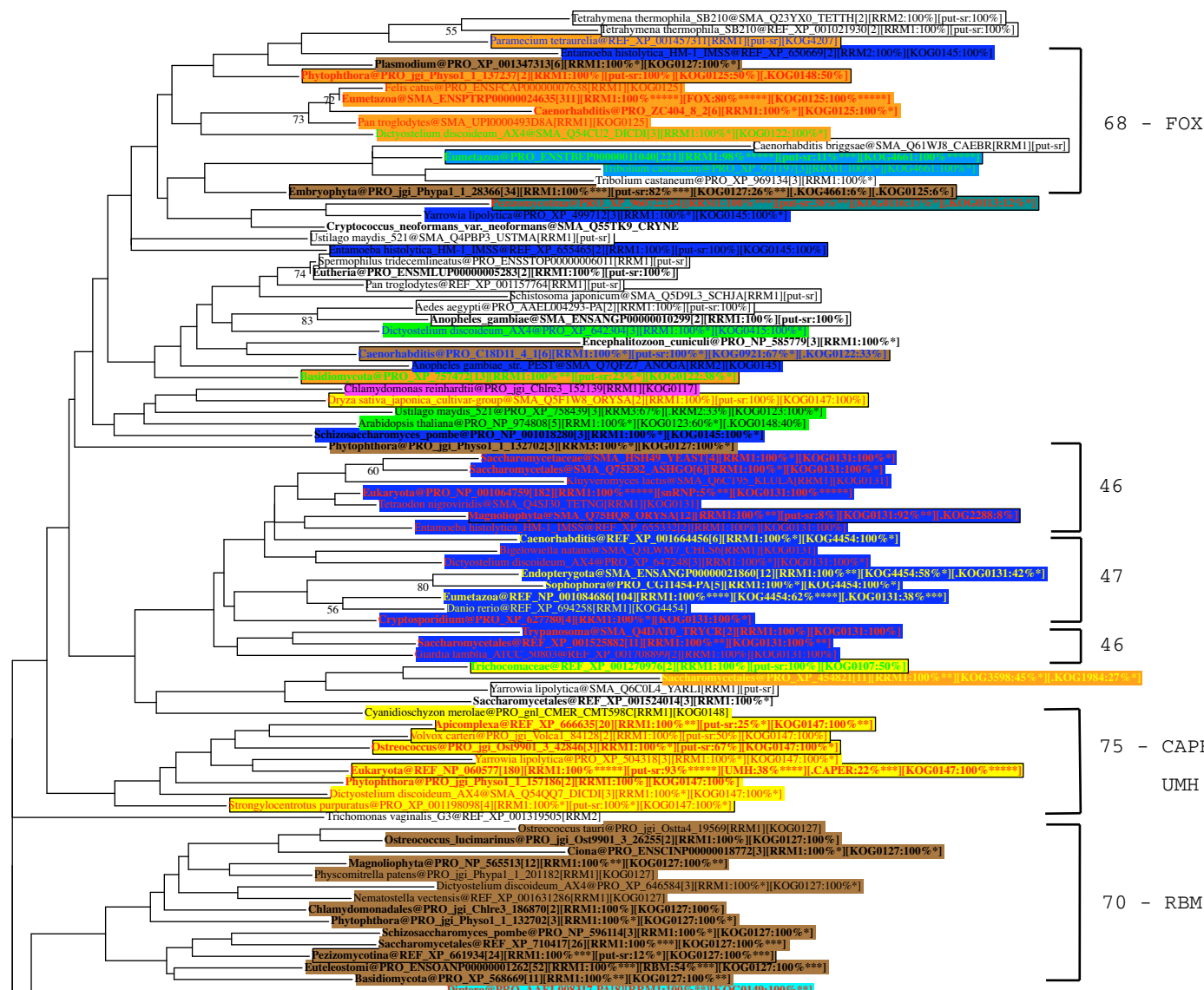
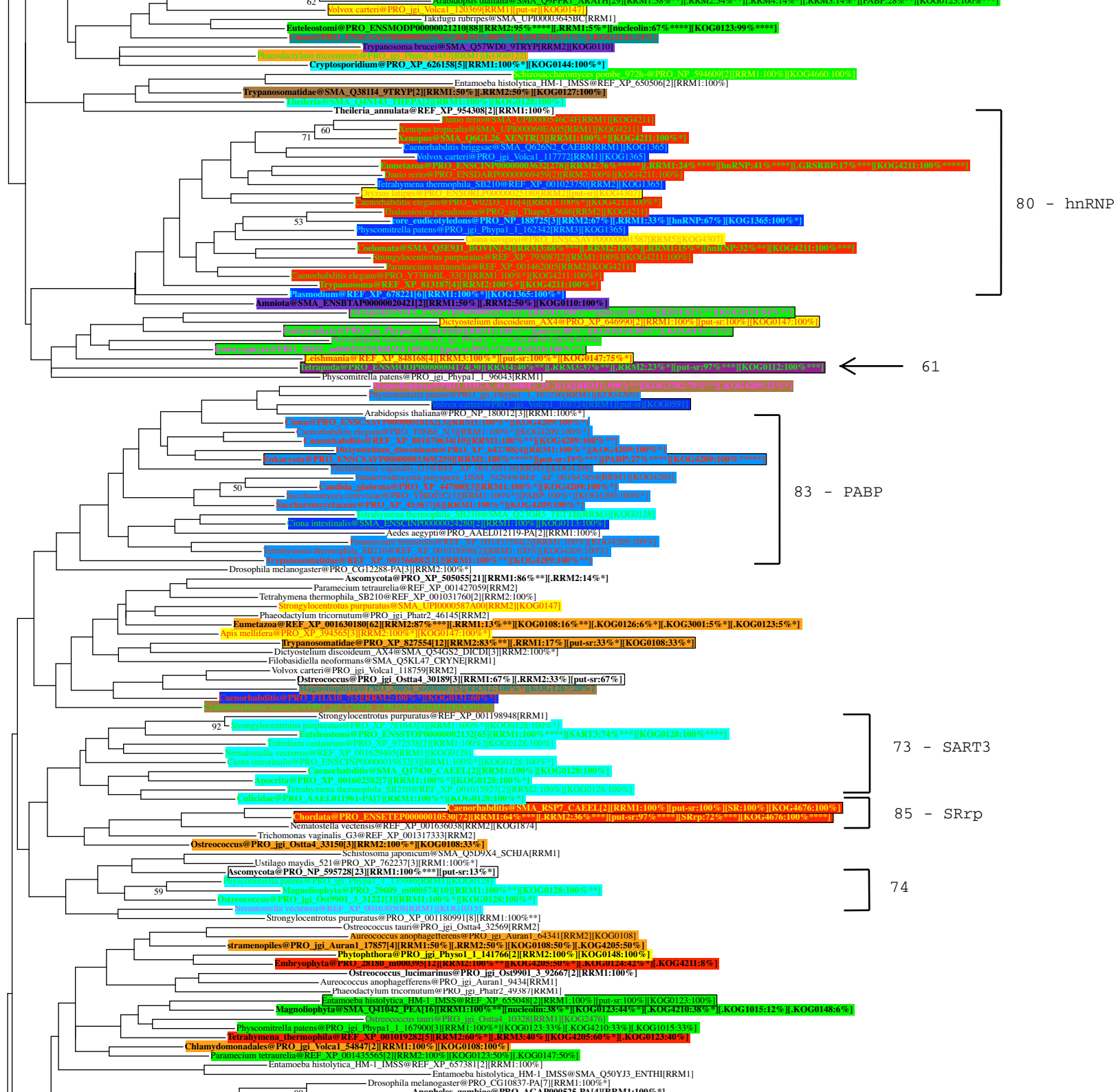


Fig. S9



[illegible]

Fig. S9



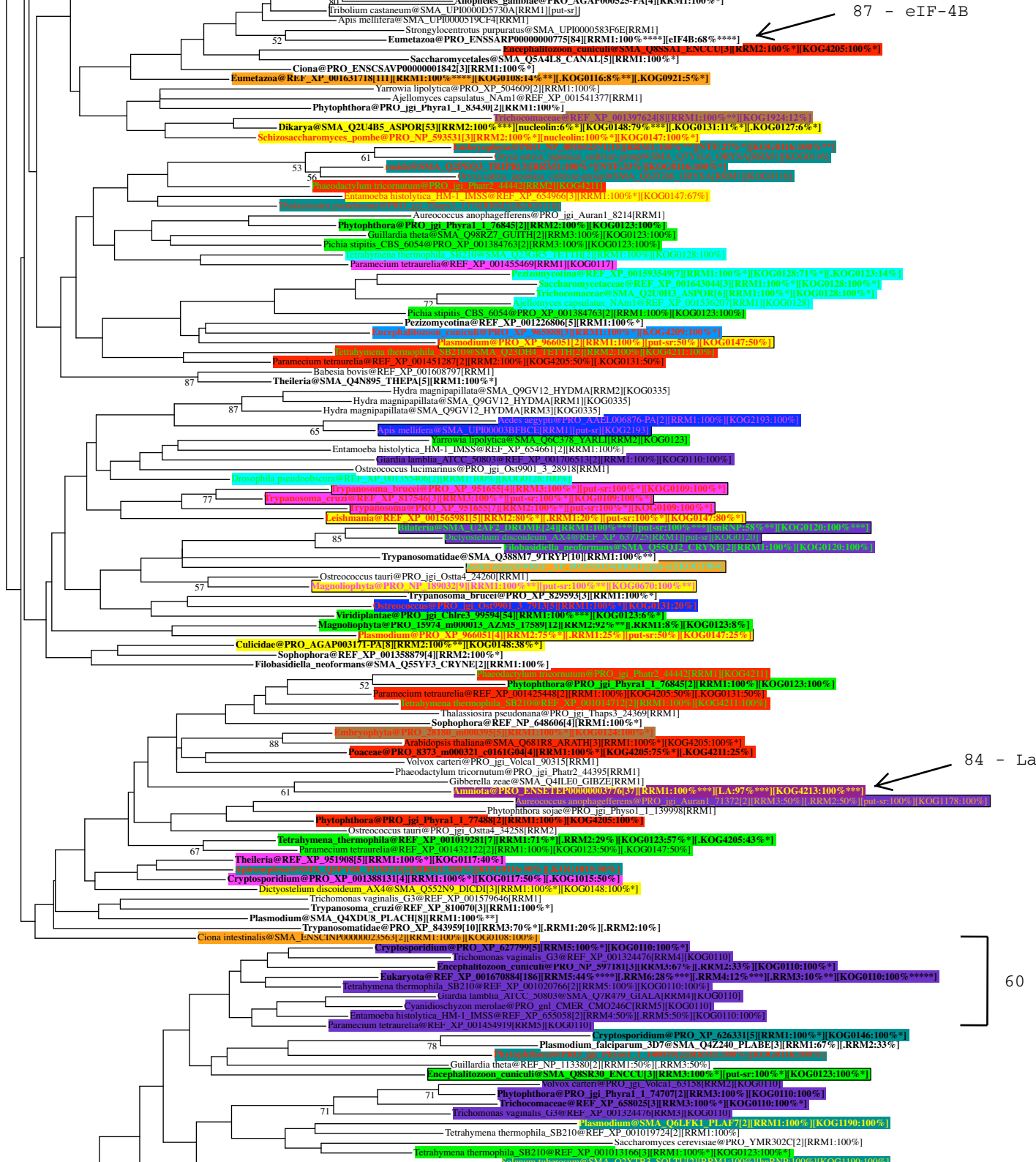


Fig. S9

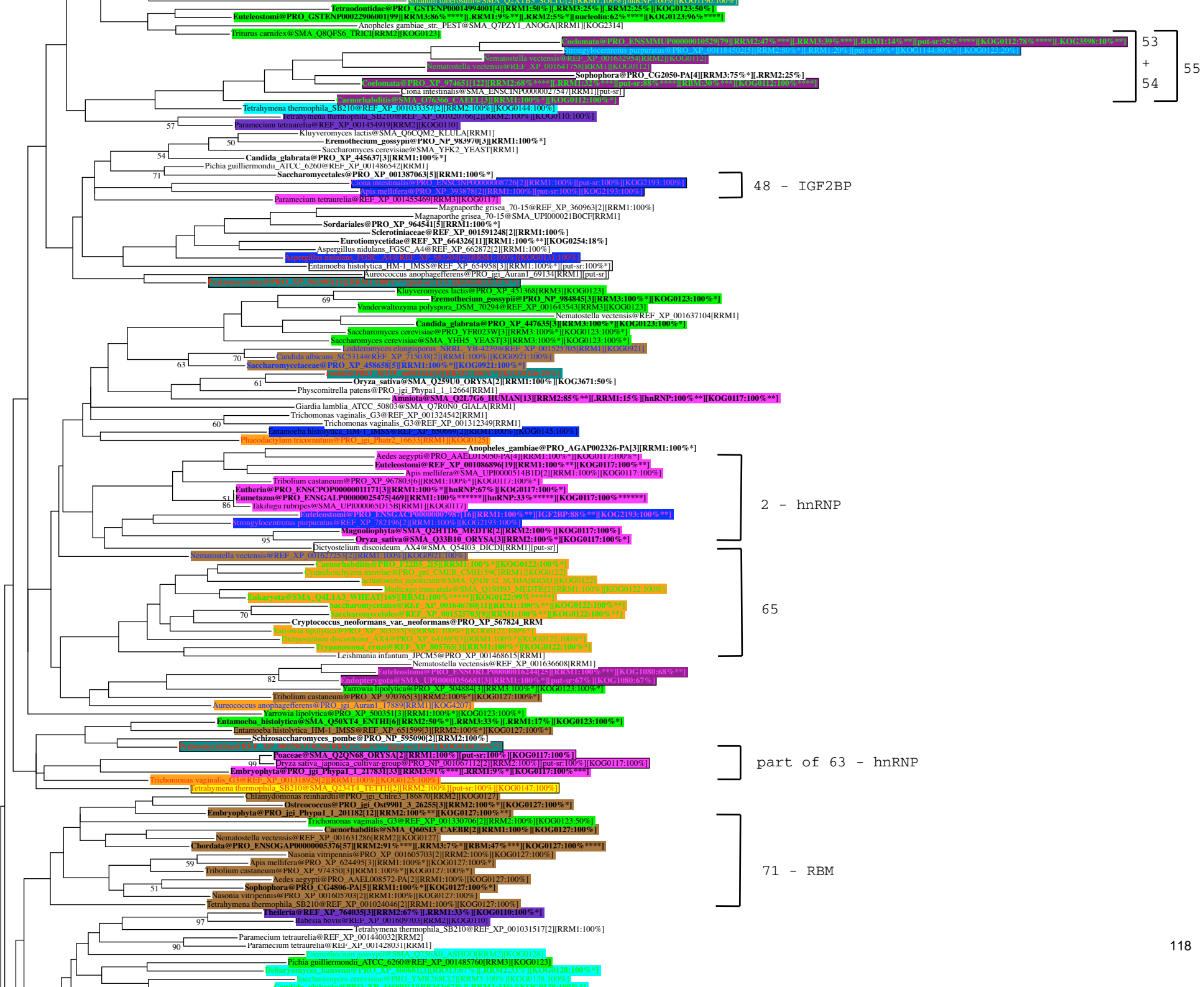


Fig. S9

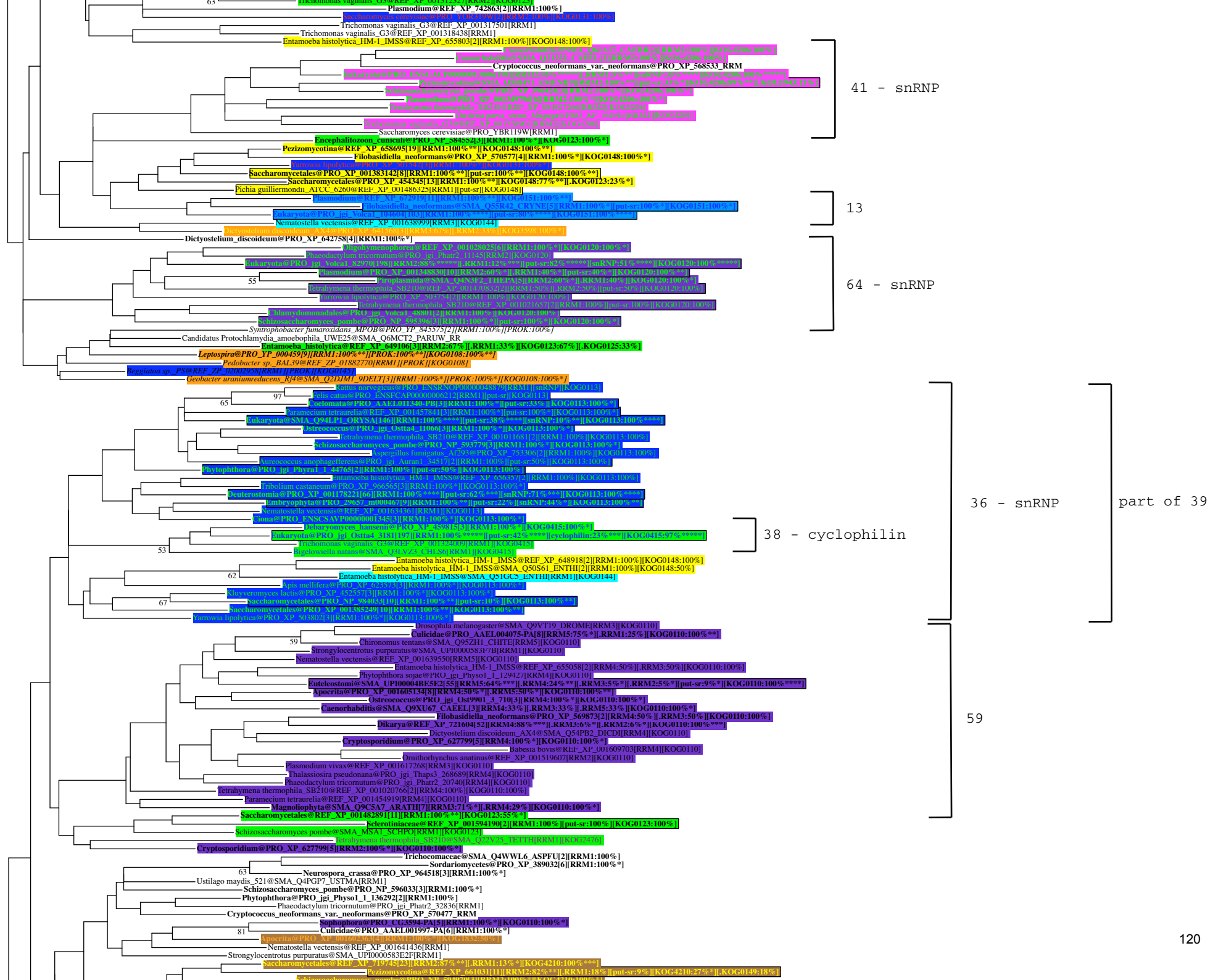
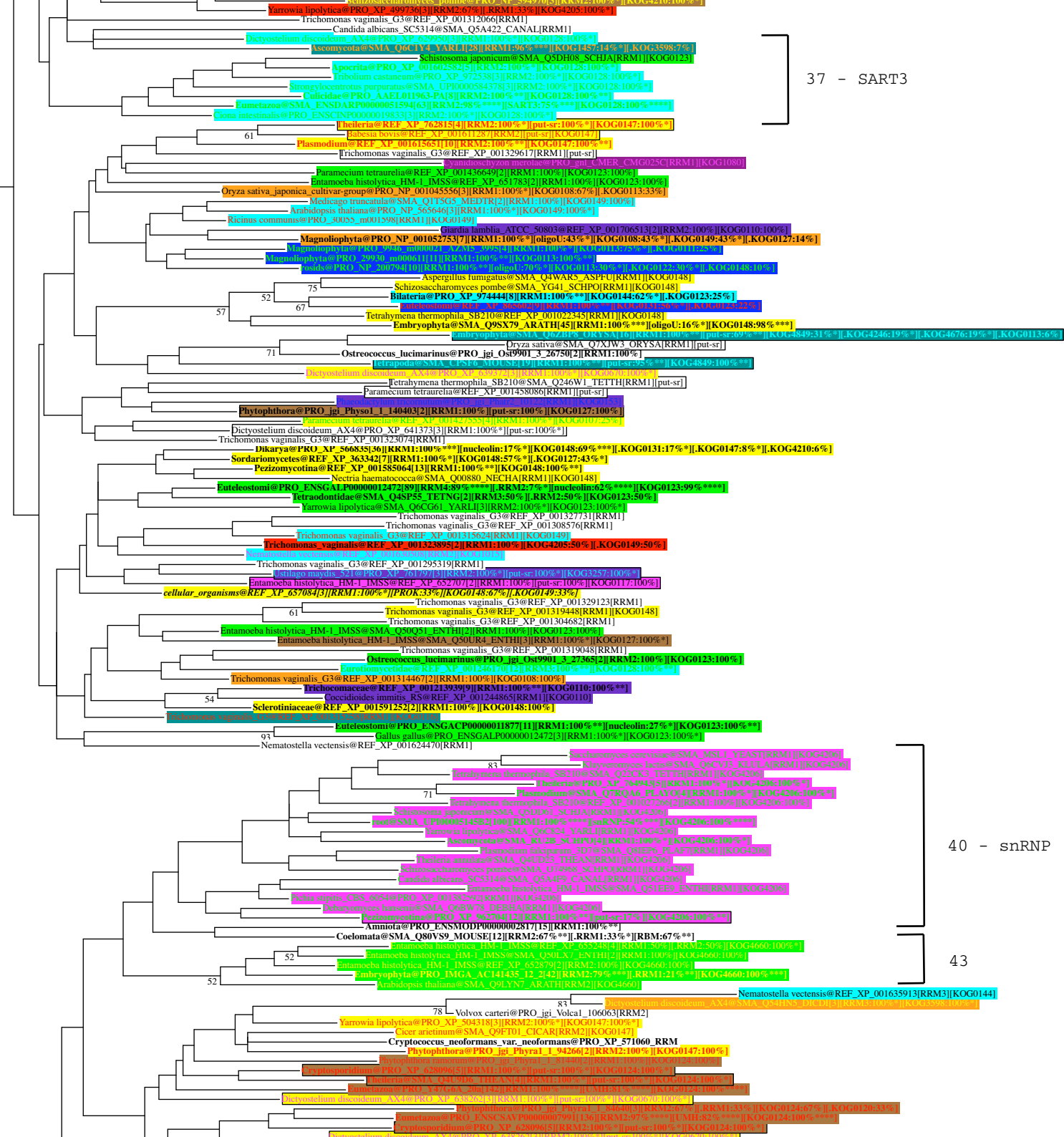


Fig. S9



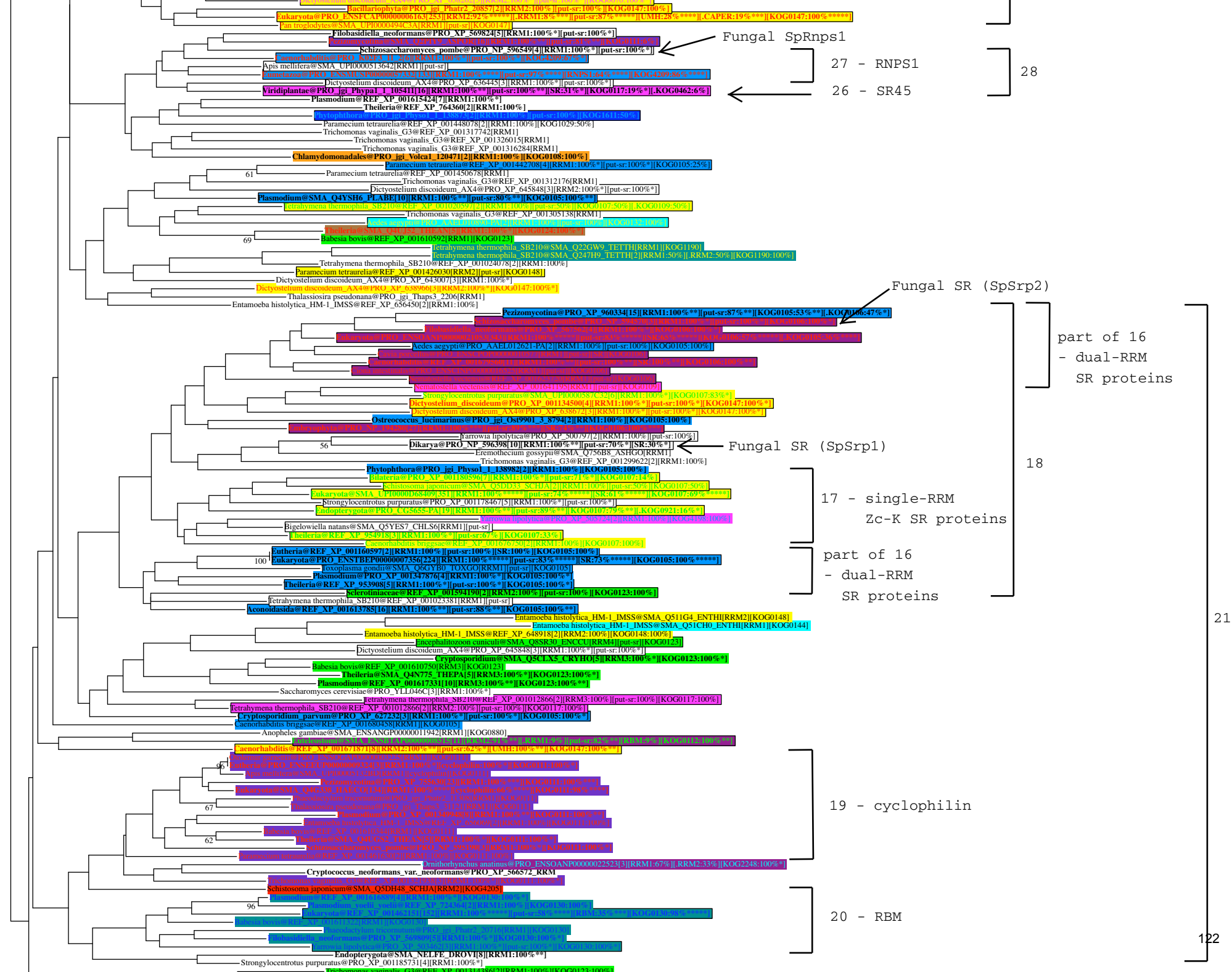
37 - SART3

part of 39

40 - snRNP

43

Fig. S9



[illegible]

Fig. S9

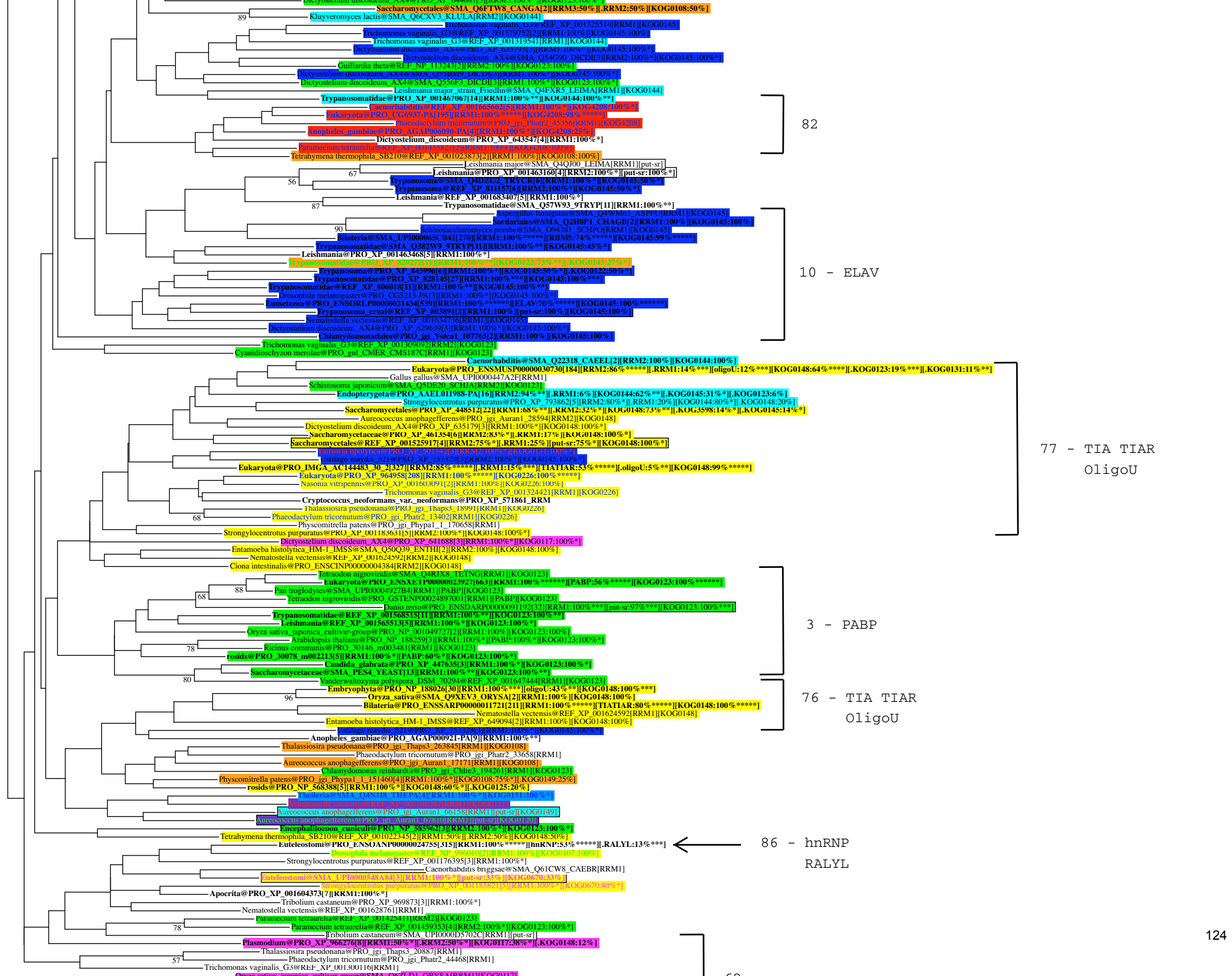


Fig. S9

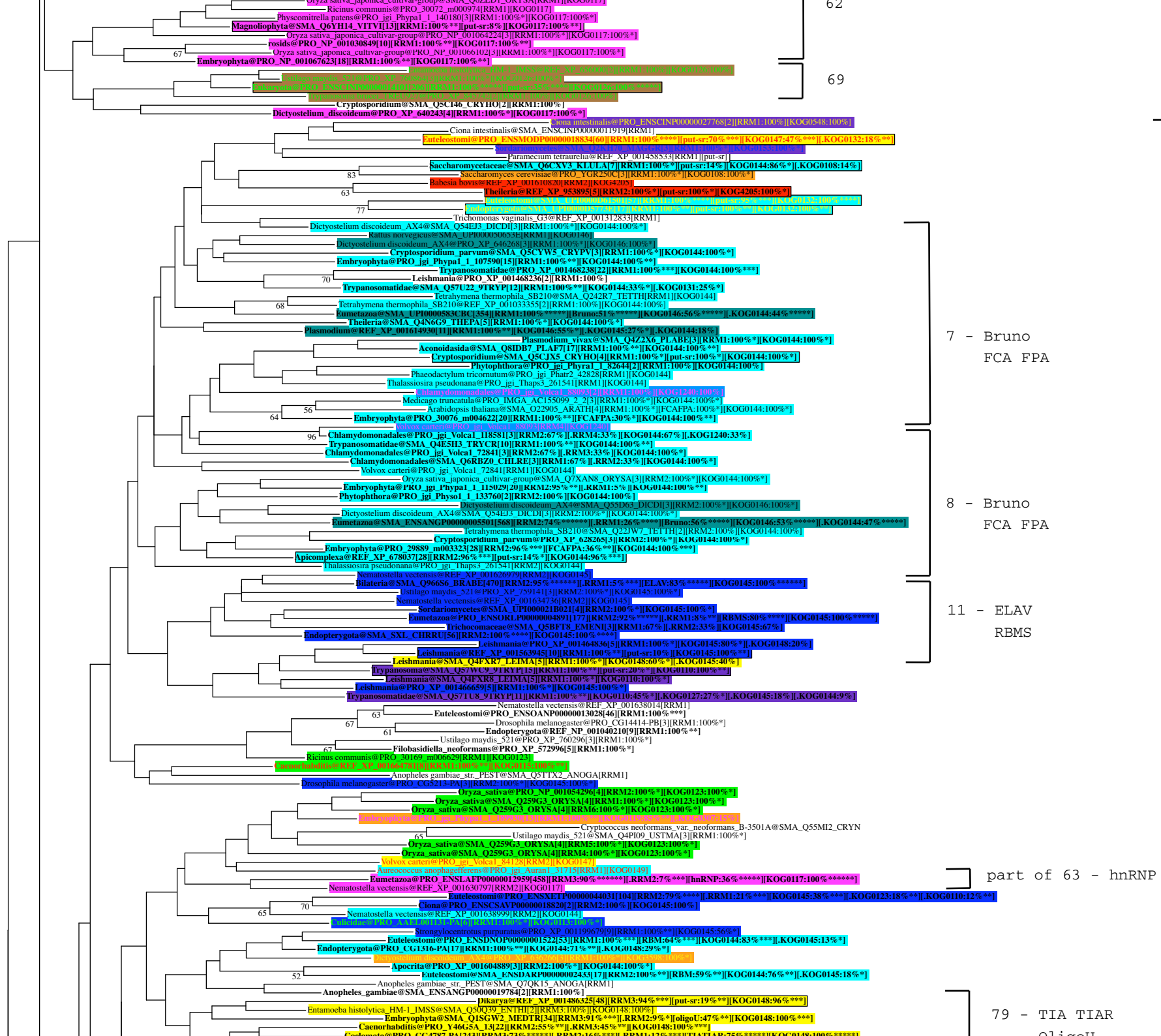


Fig. S9

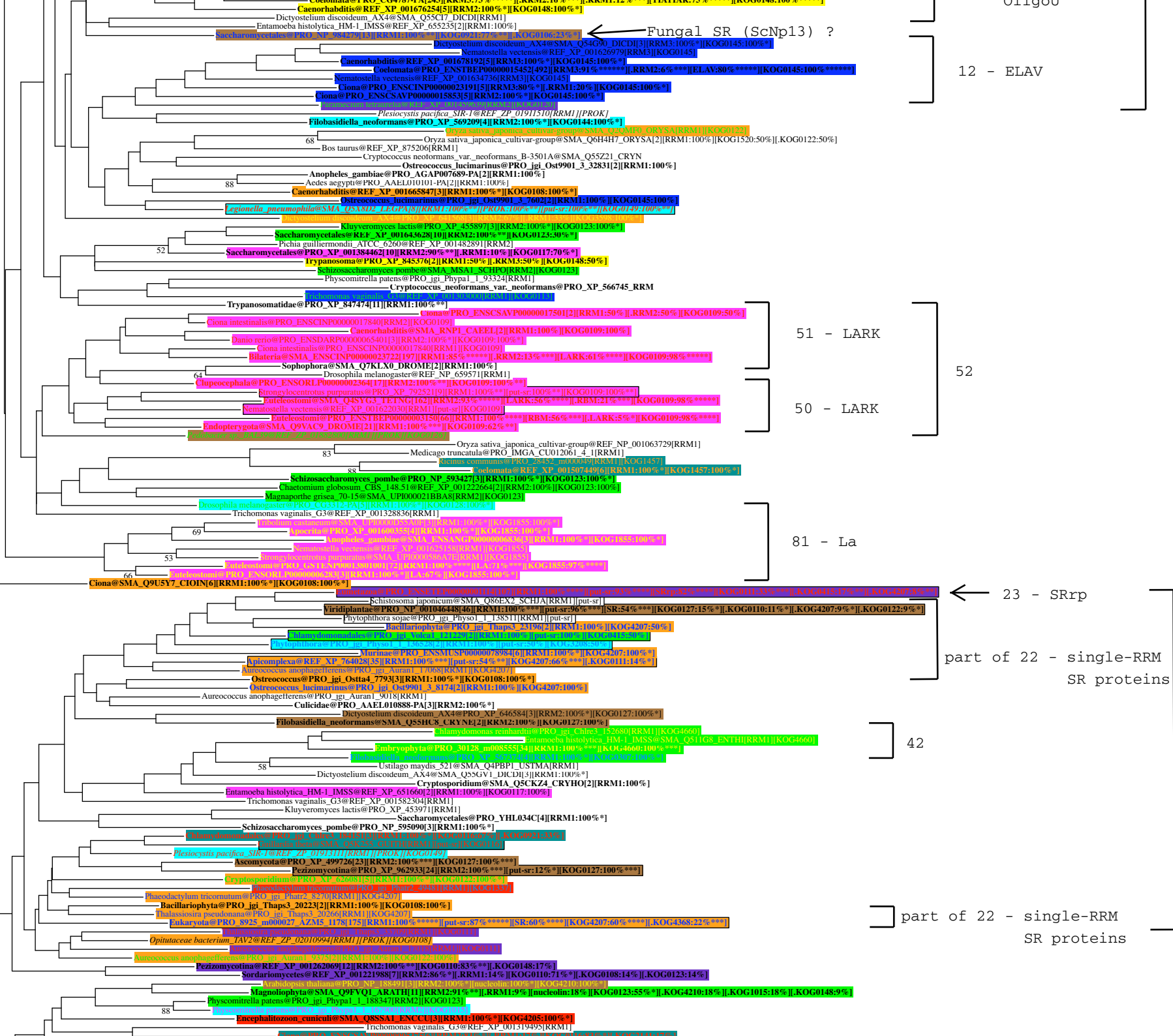


Fig. S9

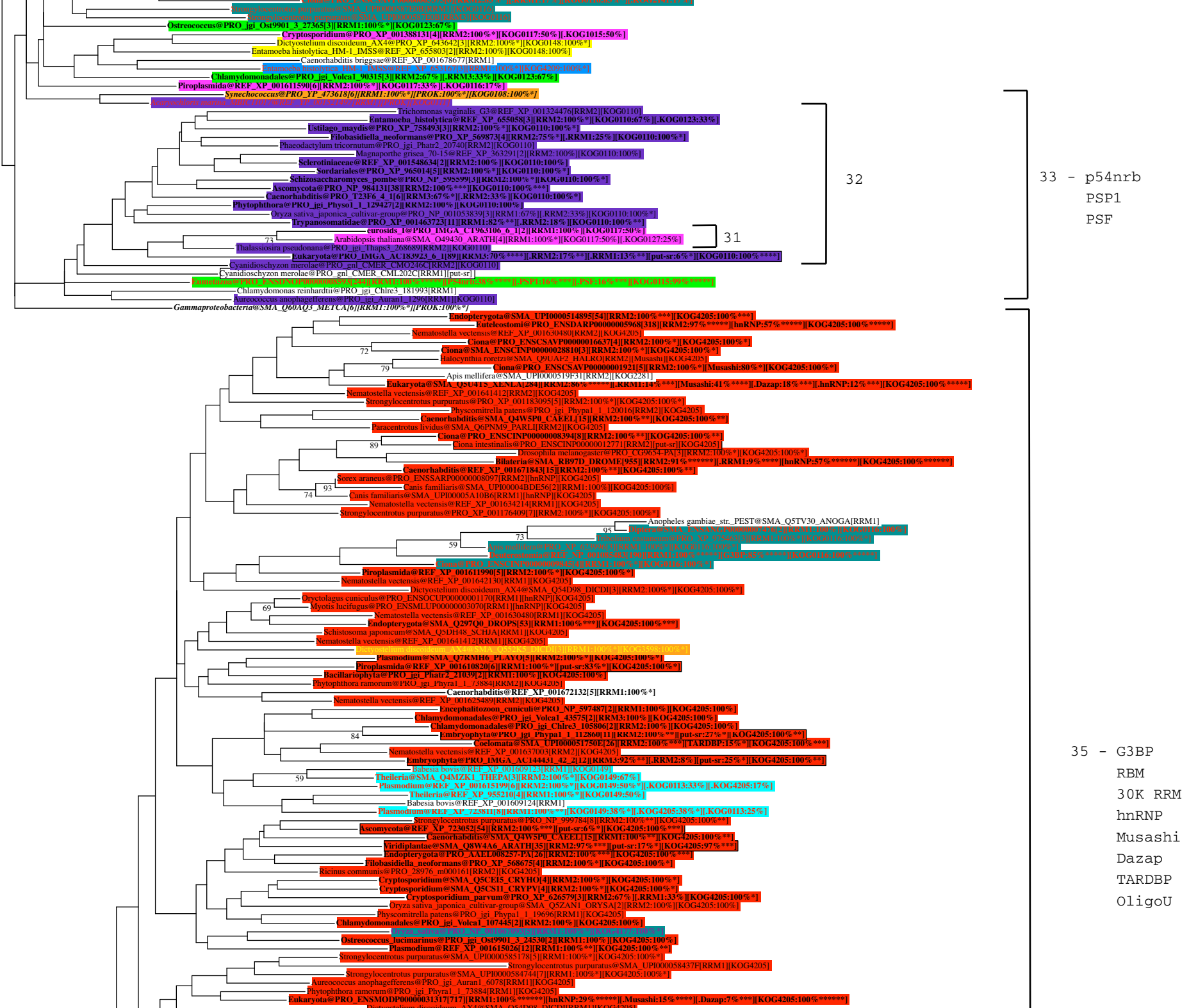


Fig. S9

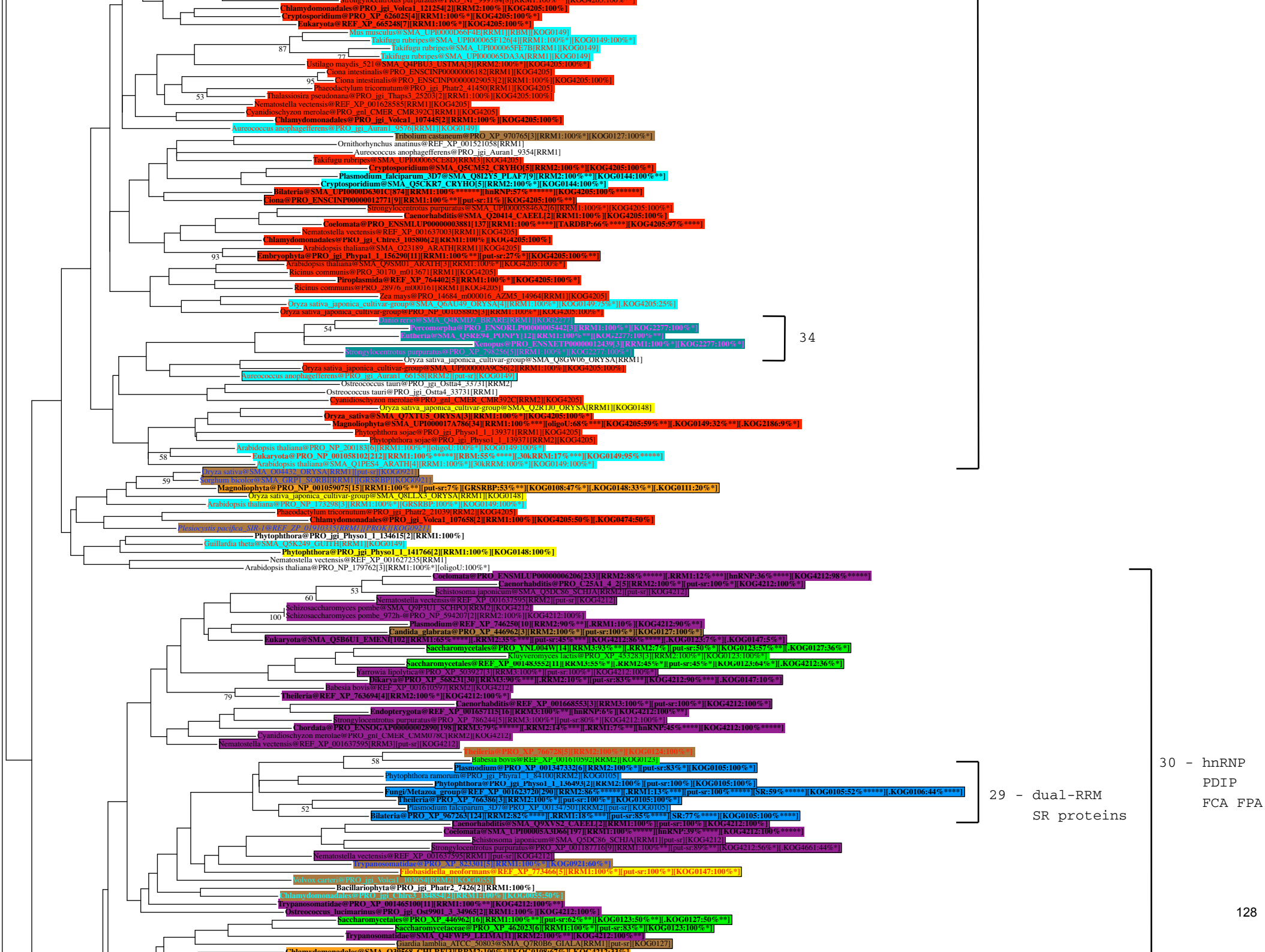
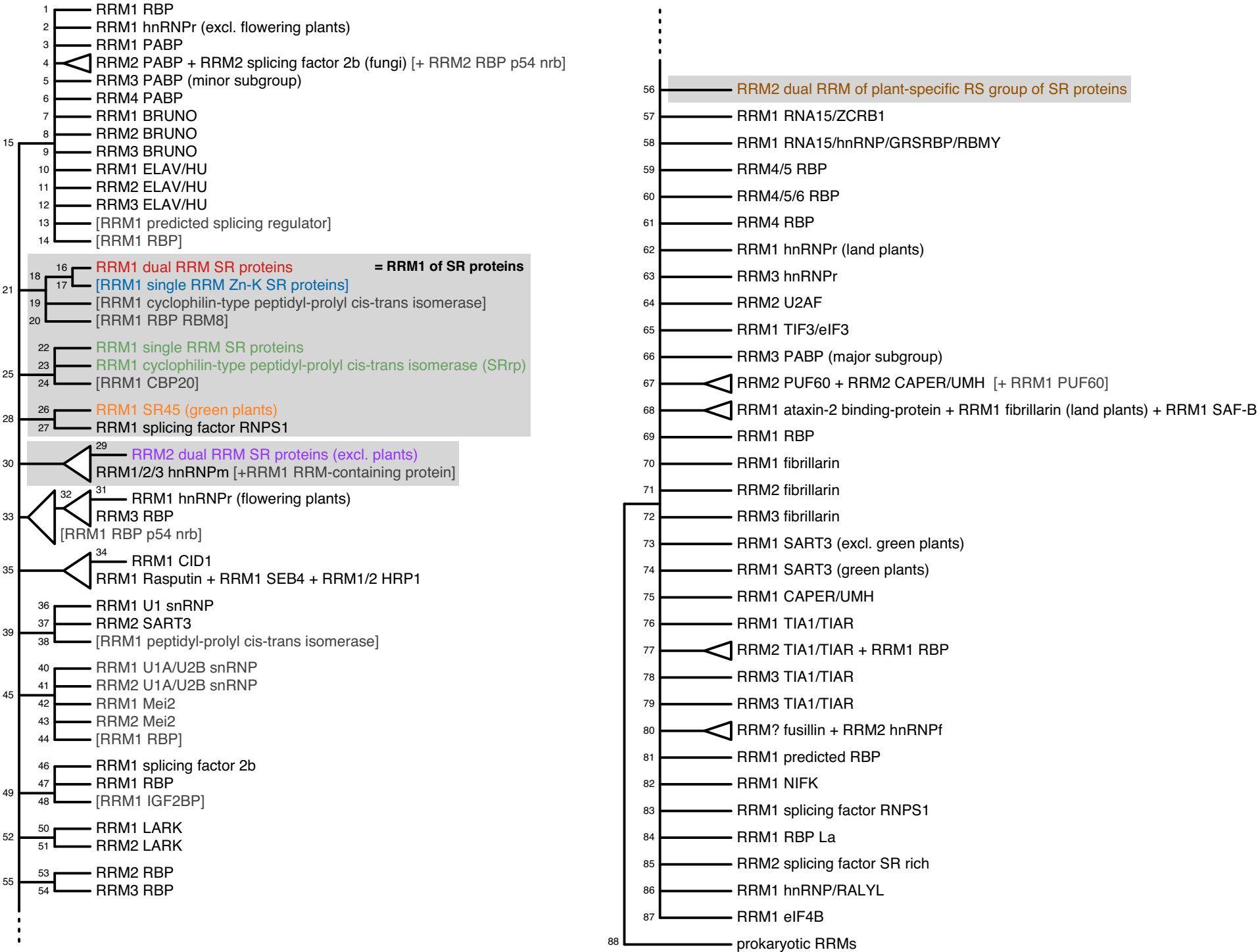


Fig. S9

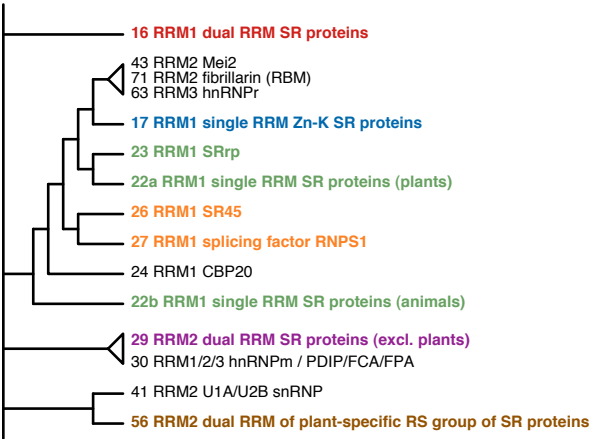


88 - prokaryotic RRM5

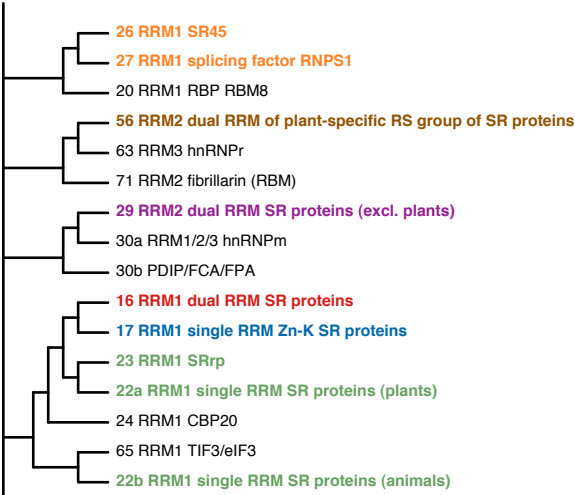
Fig. S10



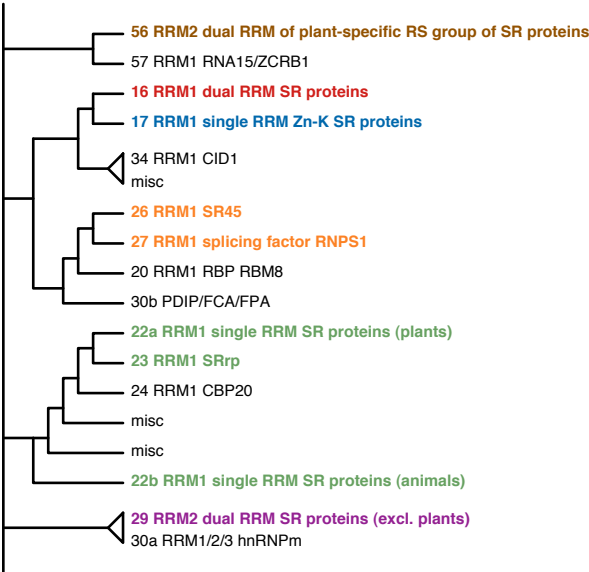
A PAUP* (MP)



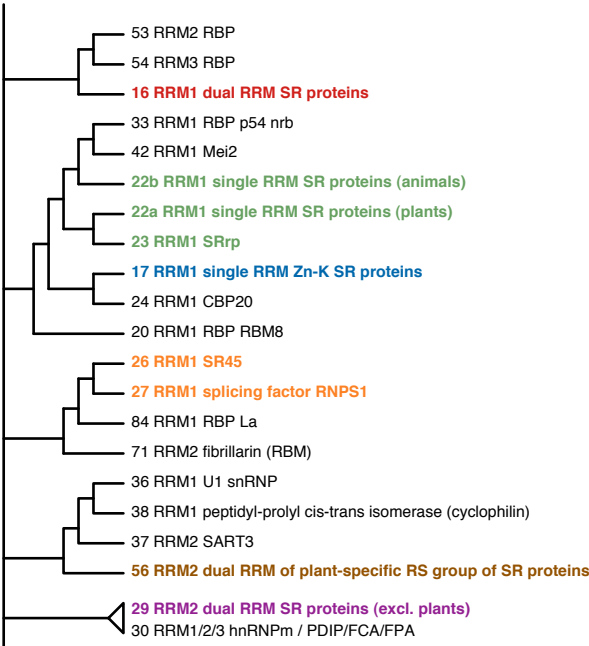
B RAXML (WAG+ Γ_4)



D RAXML (LG+F+ Γ_4)



C TREEFINDER (WAG+ Γ_4)



E large RAXML (WAG+ Γ_4)

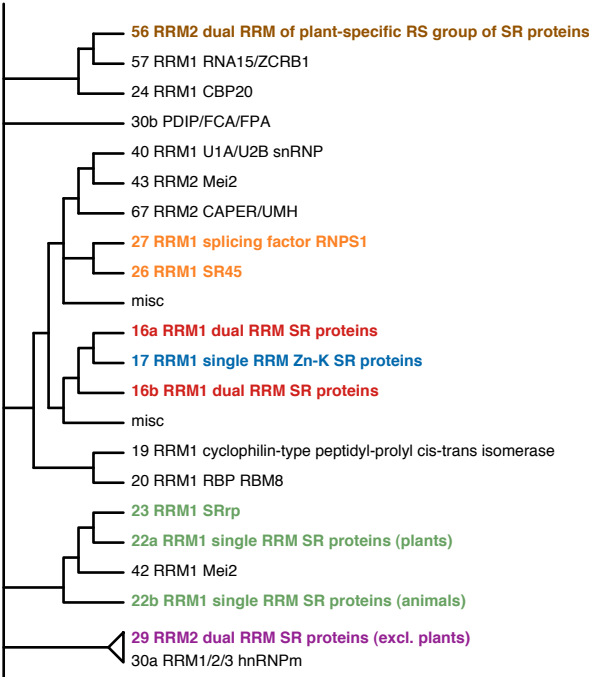


Fig. S12

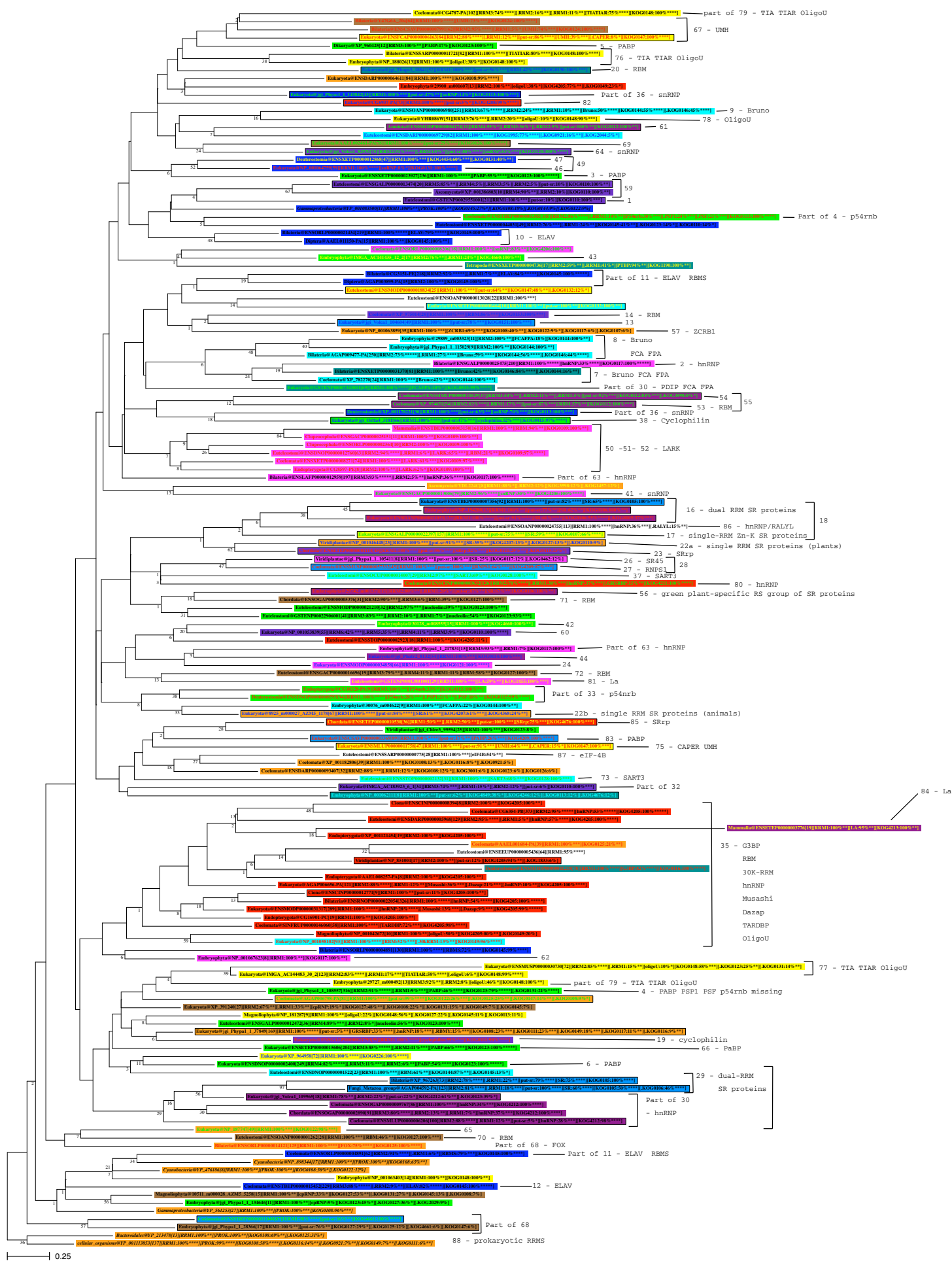


Fig. S13

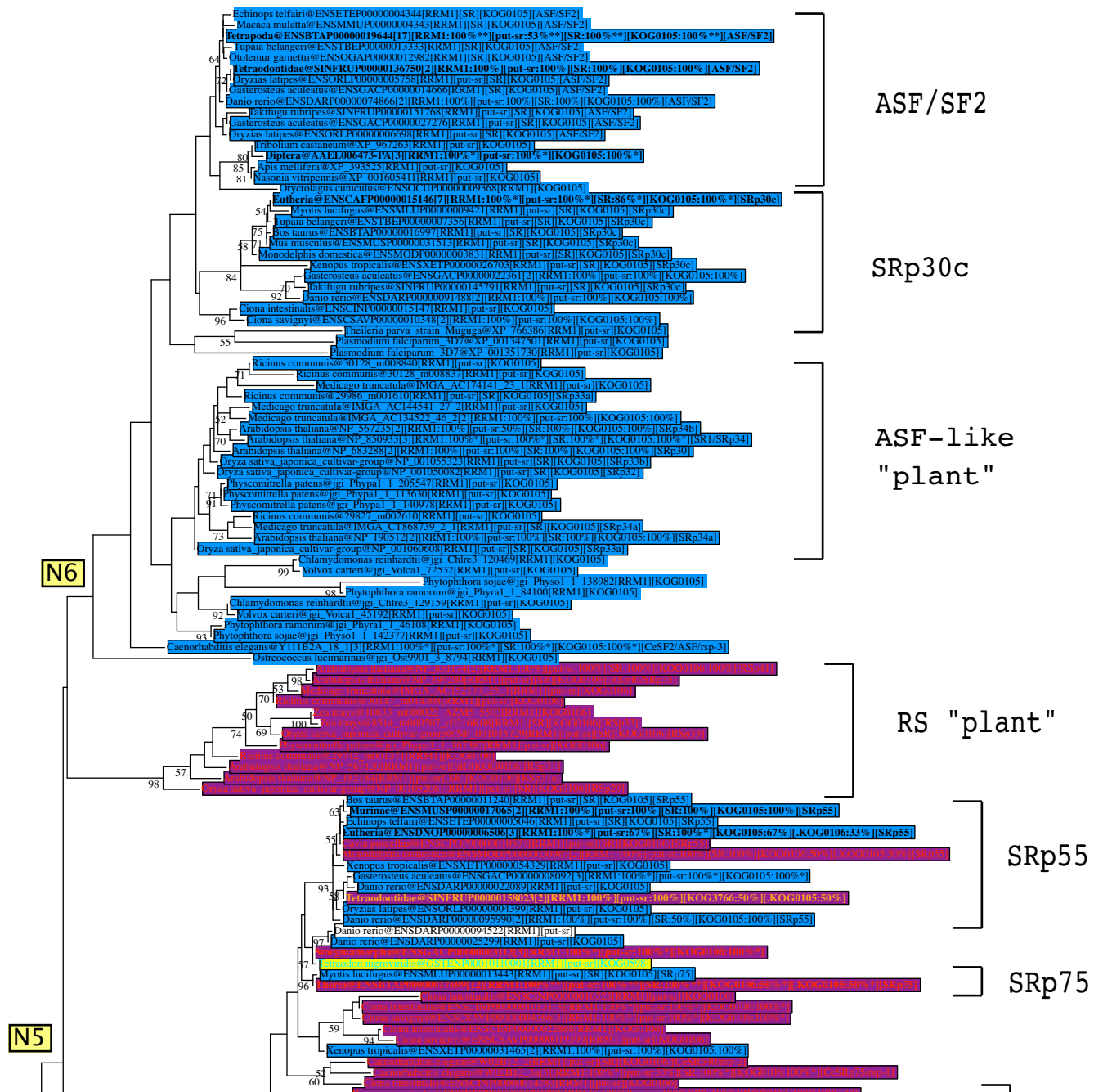


Fig. S13

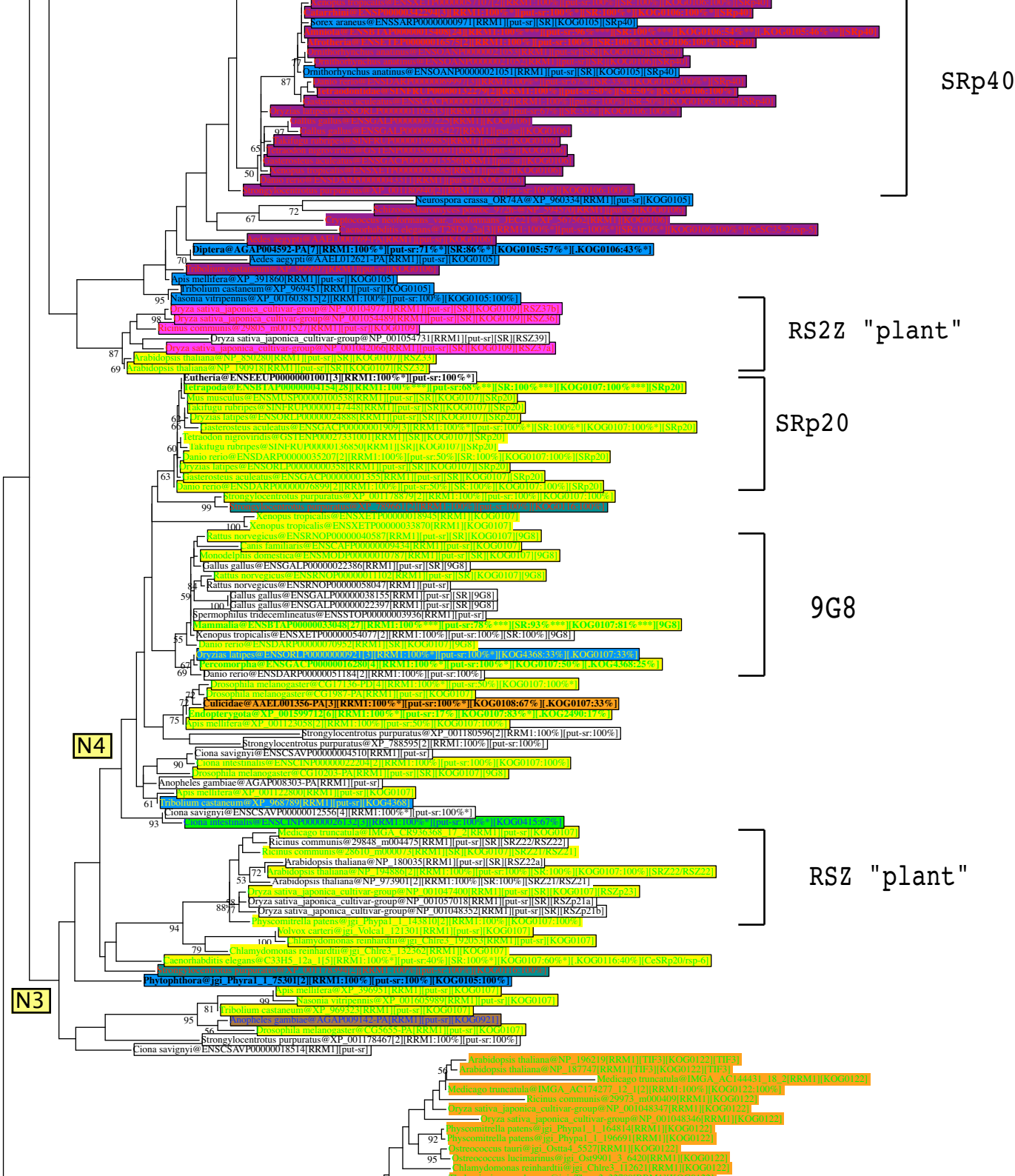


Fig. S13

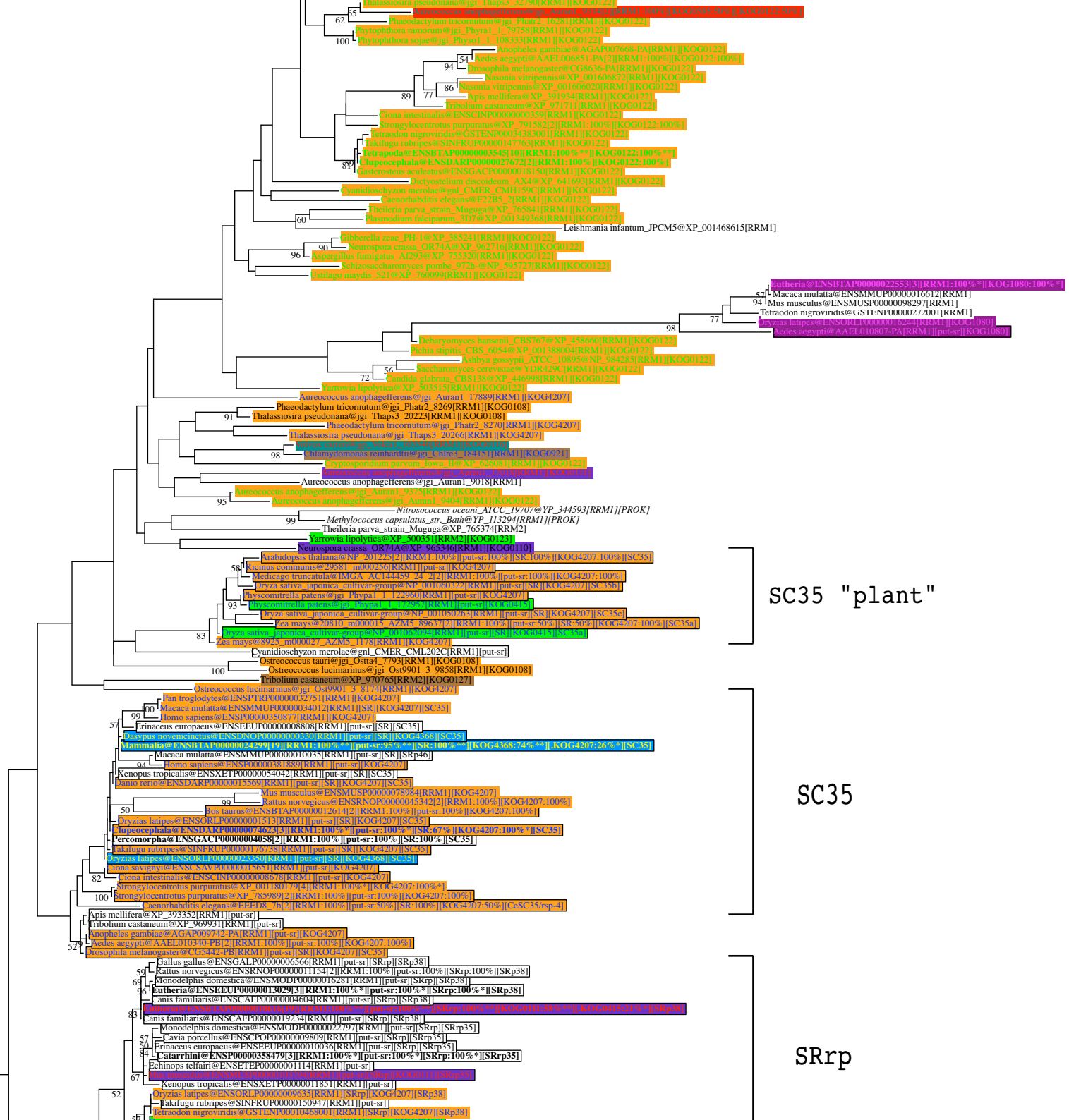


Fig. S13

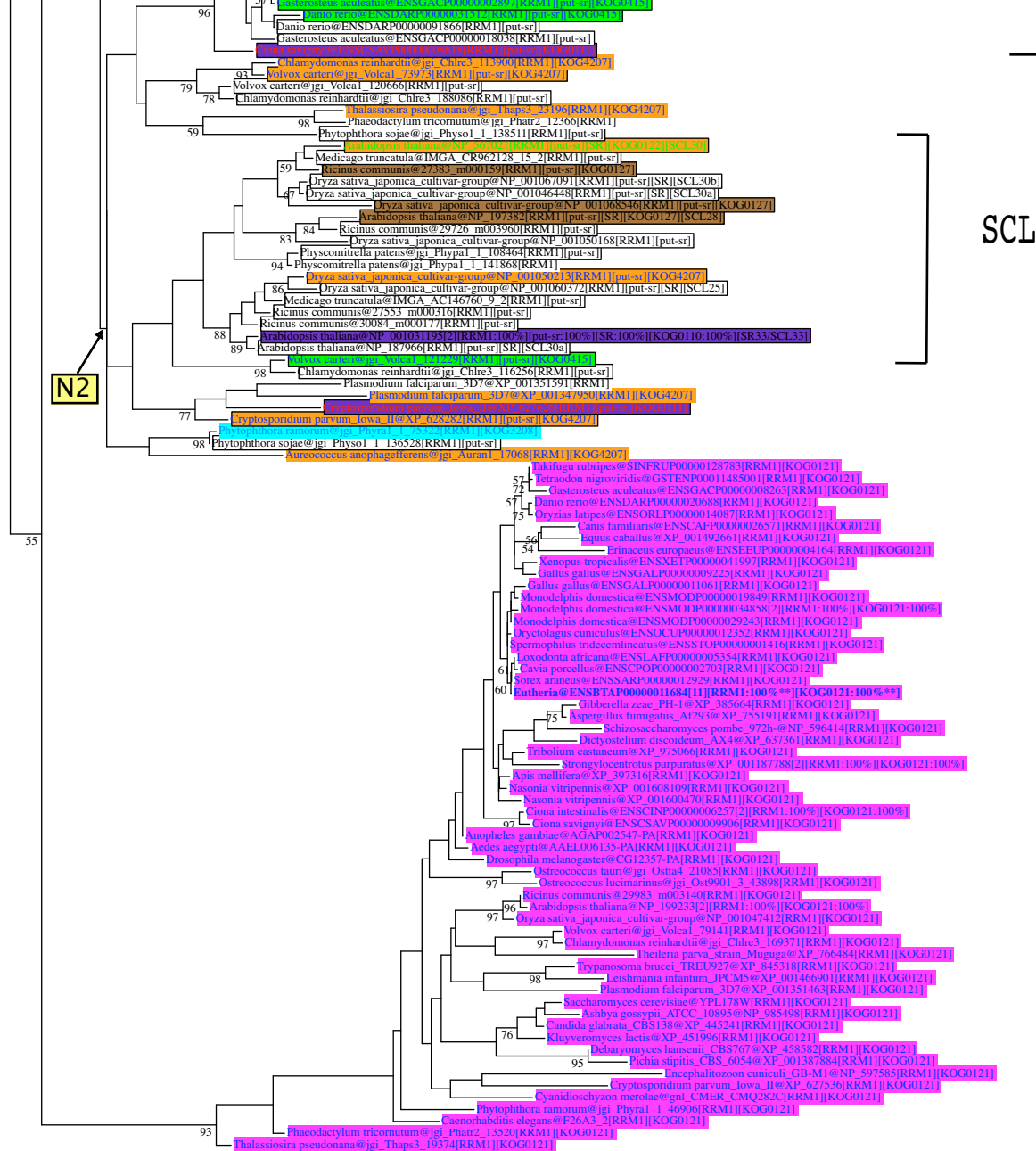


Fig. S14

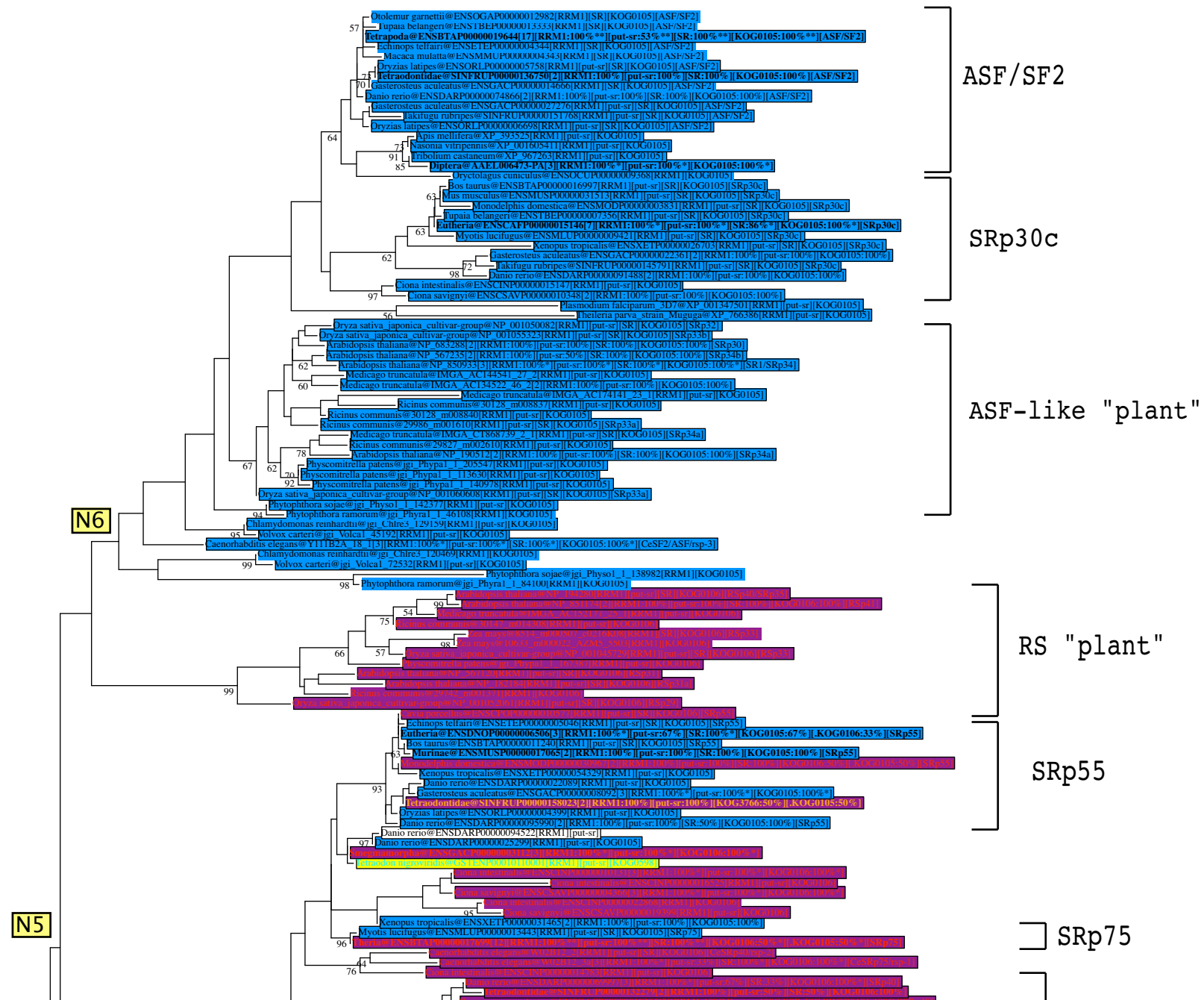


Fig. S14

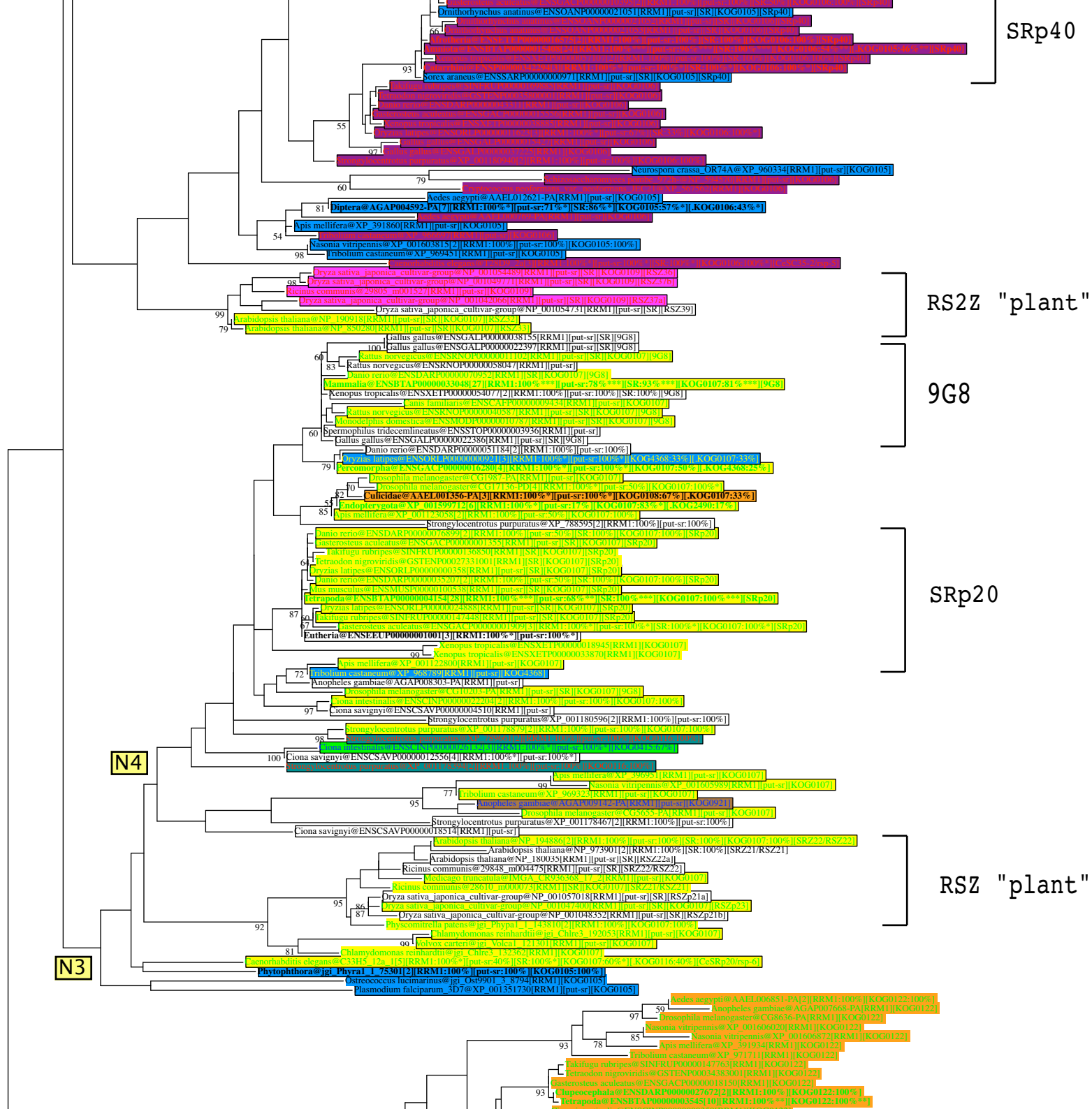


Fig. S14

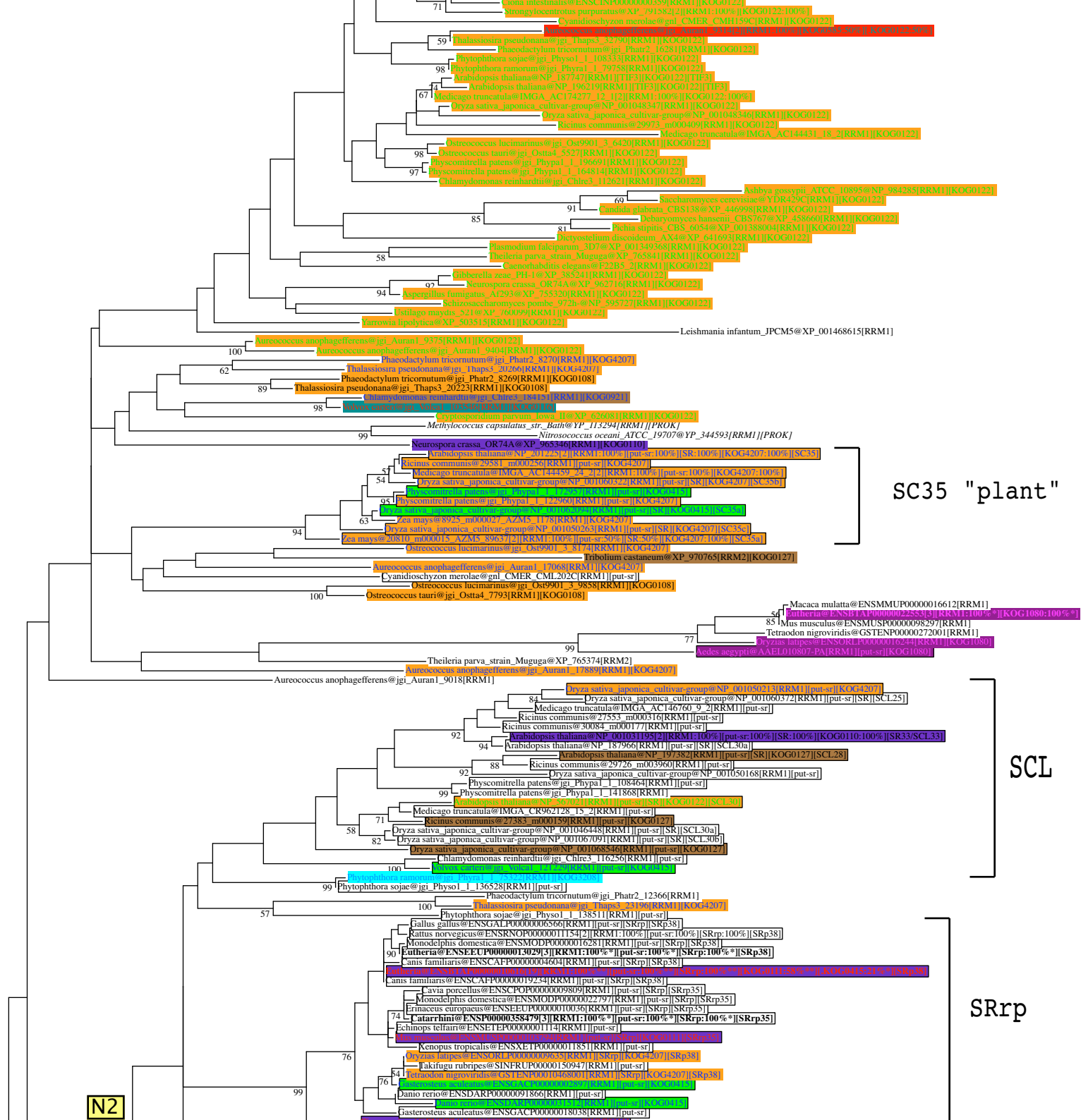


Fig. S14

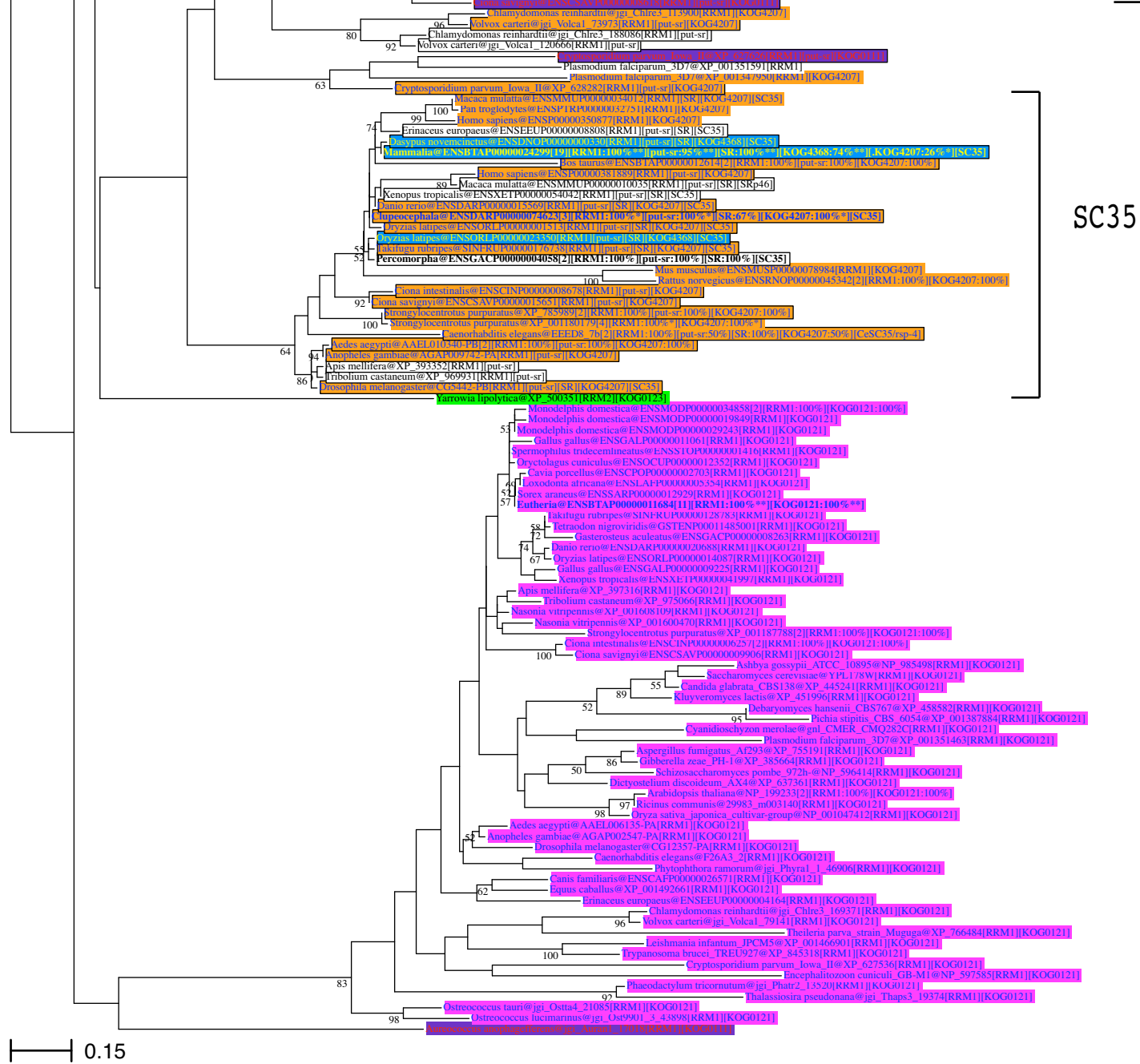


Fig. S15

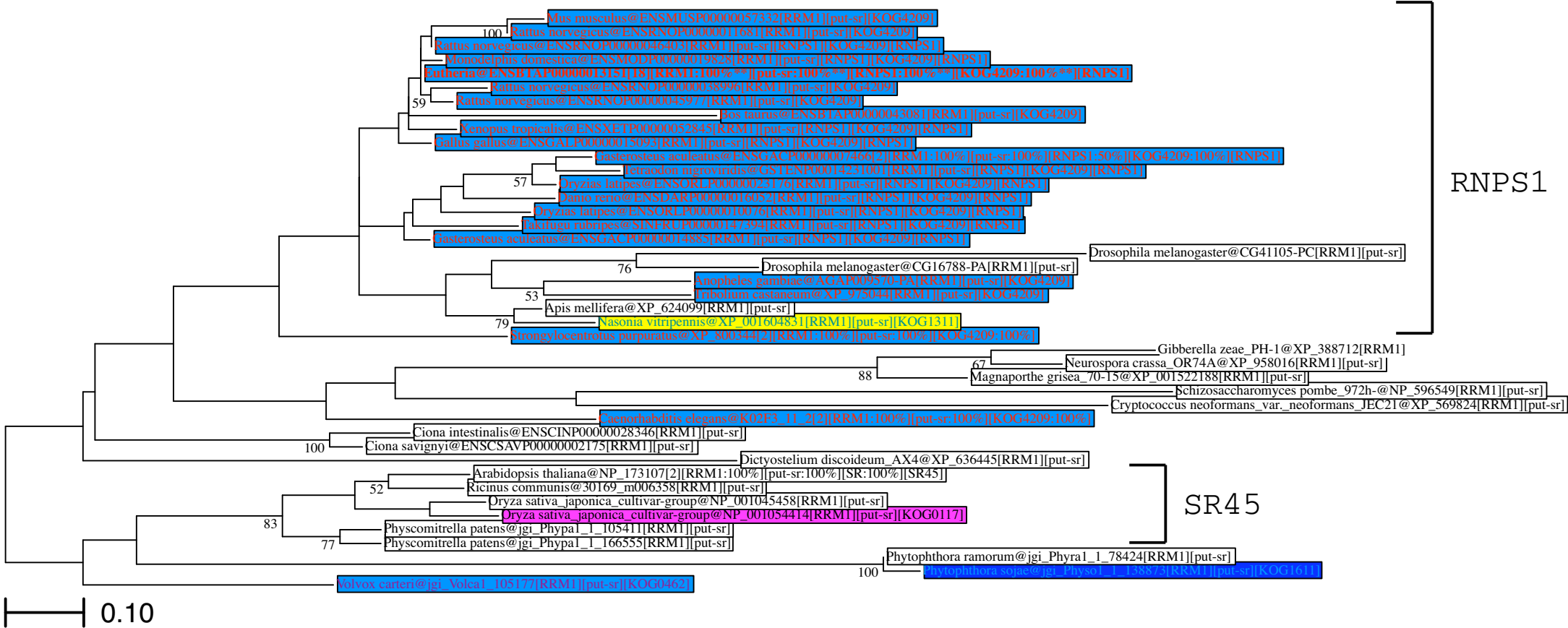


Fig. S16

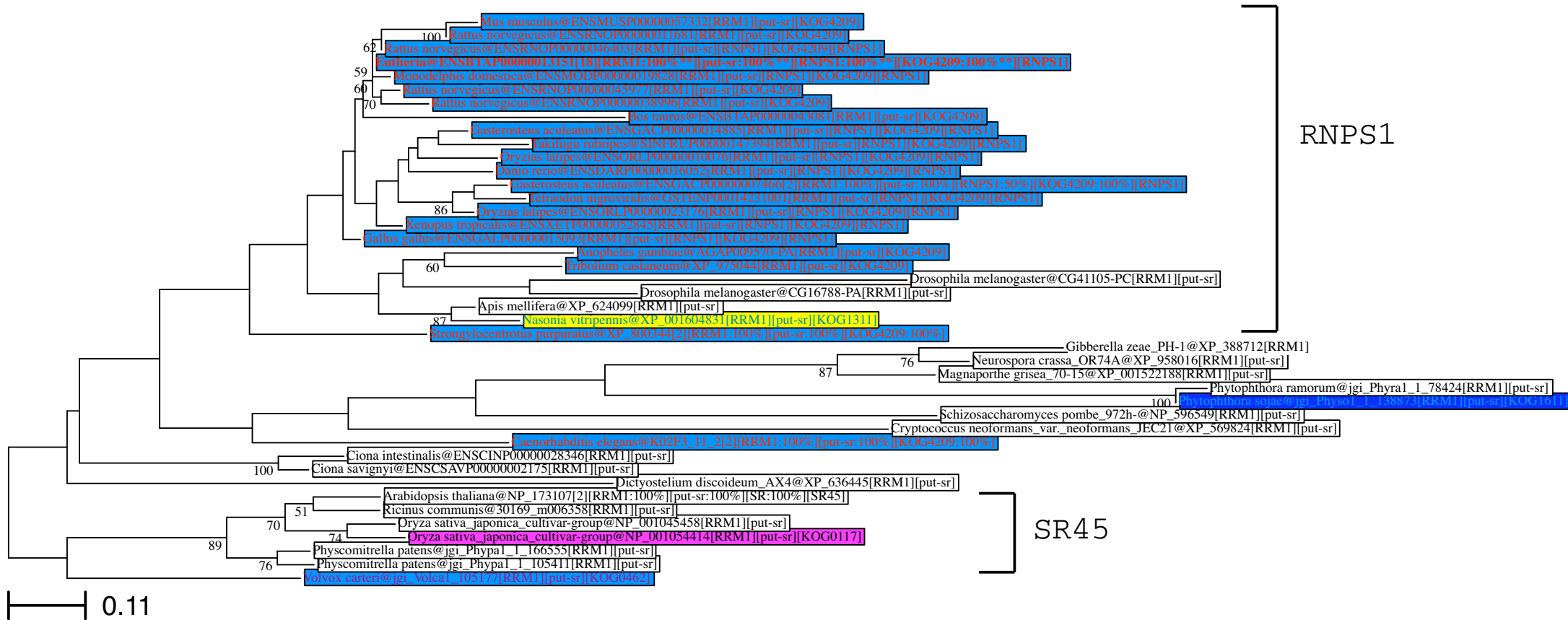


Fig. S17

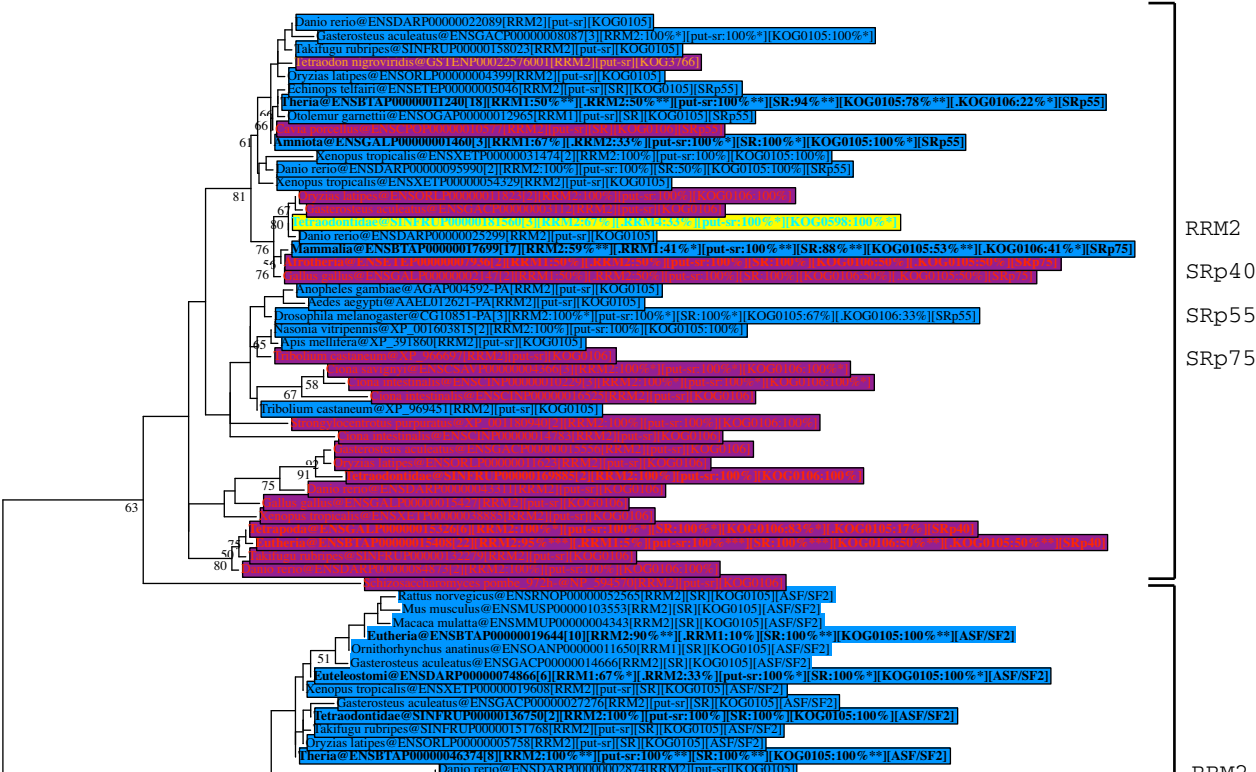


Fig. S17

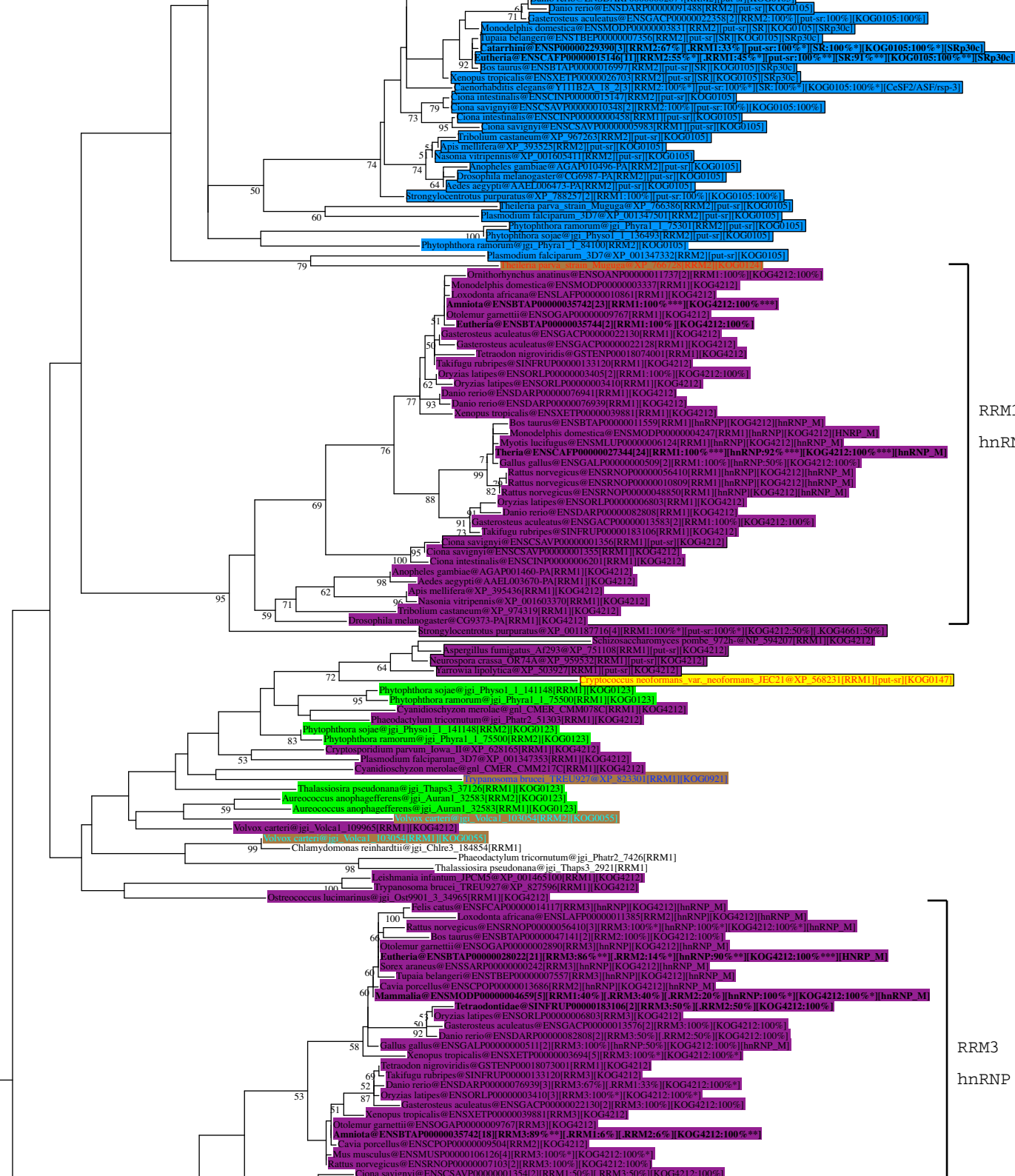


Fig. S17

Phylogenetic tree showing the relationship between RRM2 and hnRNP M domains across various species. The tree is rooted at the bottom and branches upwards. Species names are listed next to their corresponding branches, often followed by accession numbers and domain identifiers in brackets. The tree shows a clear separation between RRM2 and hnRNP M domains, with RRM2 domains generally clustering together and hnRNP M domains forming a distinct group. Bootstrap values are indicated at the nodes. The tree is color-coded: green for RRM2 domains and purple for hnRNP M domains. The RRM2 group includes species like *Candida glabrata*, *Saccharomyces cerevisiae*, and *Aspergillus fumigatus*. The hnRNP M group includes species like *Homo sapiens*, *Mus musculus*, and *Drosophila melanogaster*. The tree also shows some species with both domains, such as *Candida albicans* and *Candida glabrata*. The tree is labeled "RRM2" and "hnRNP M" on the right side.

Fig. S17

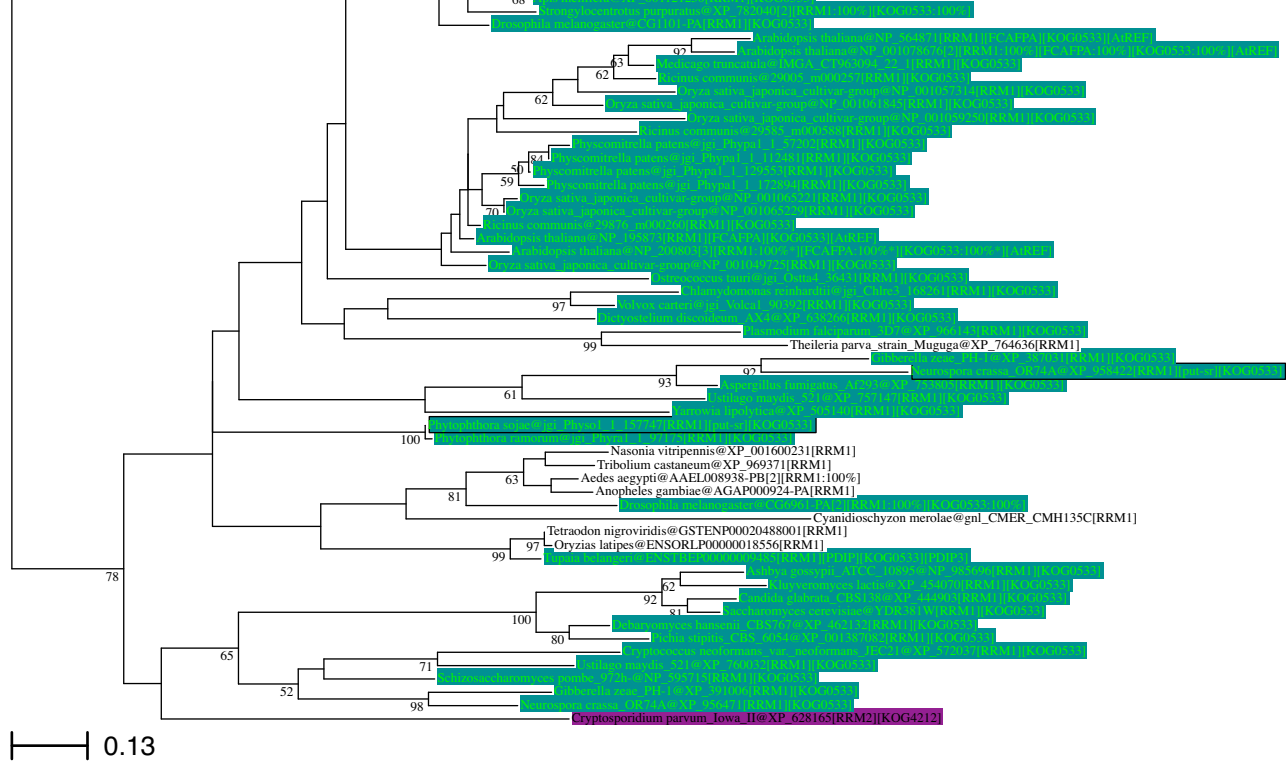


Fig. S18

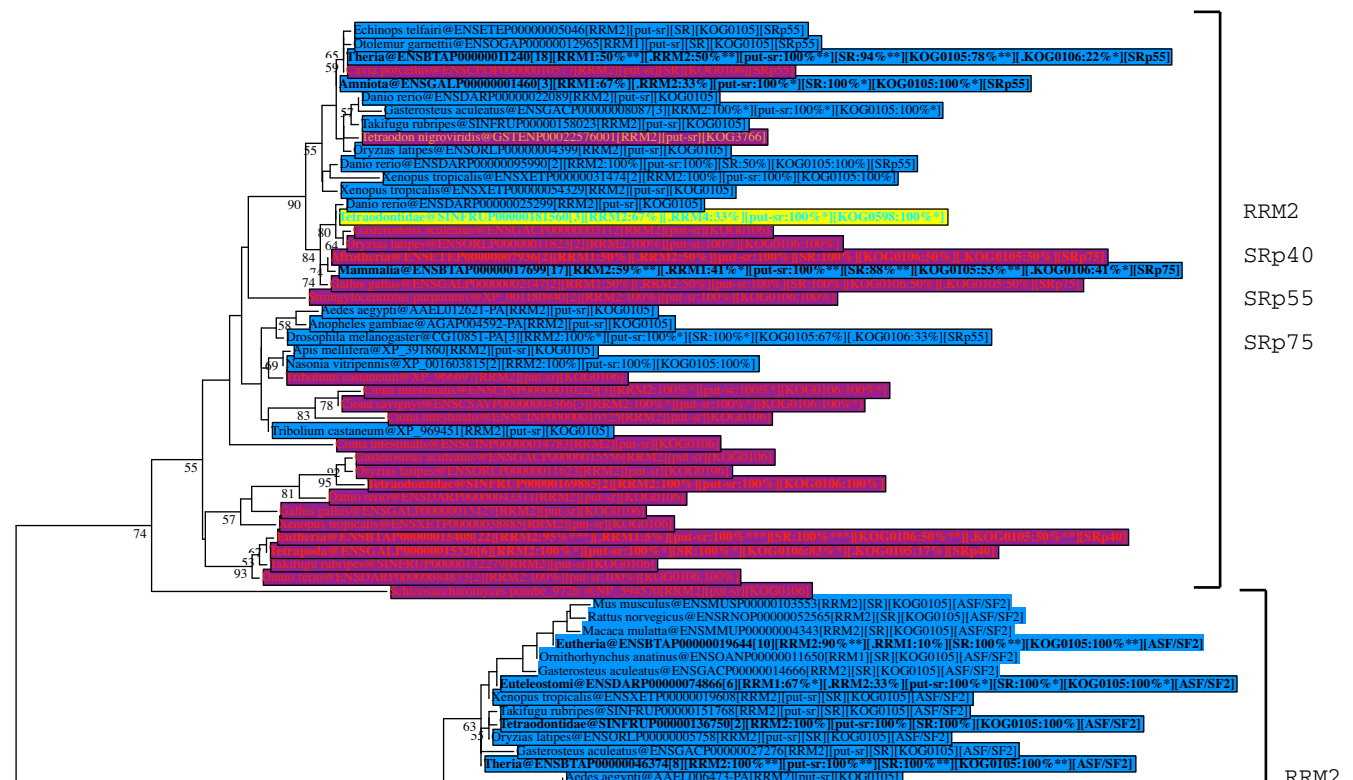


Fig. S18

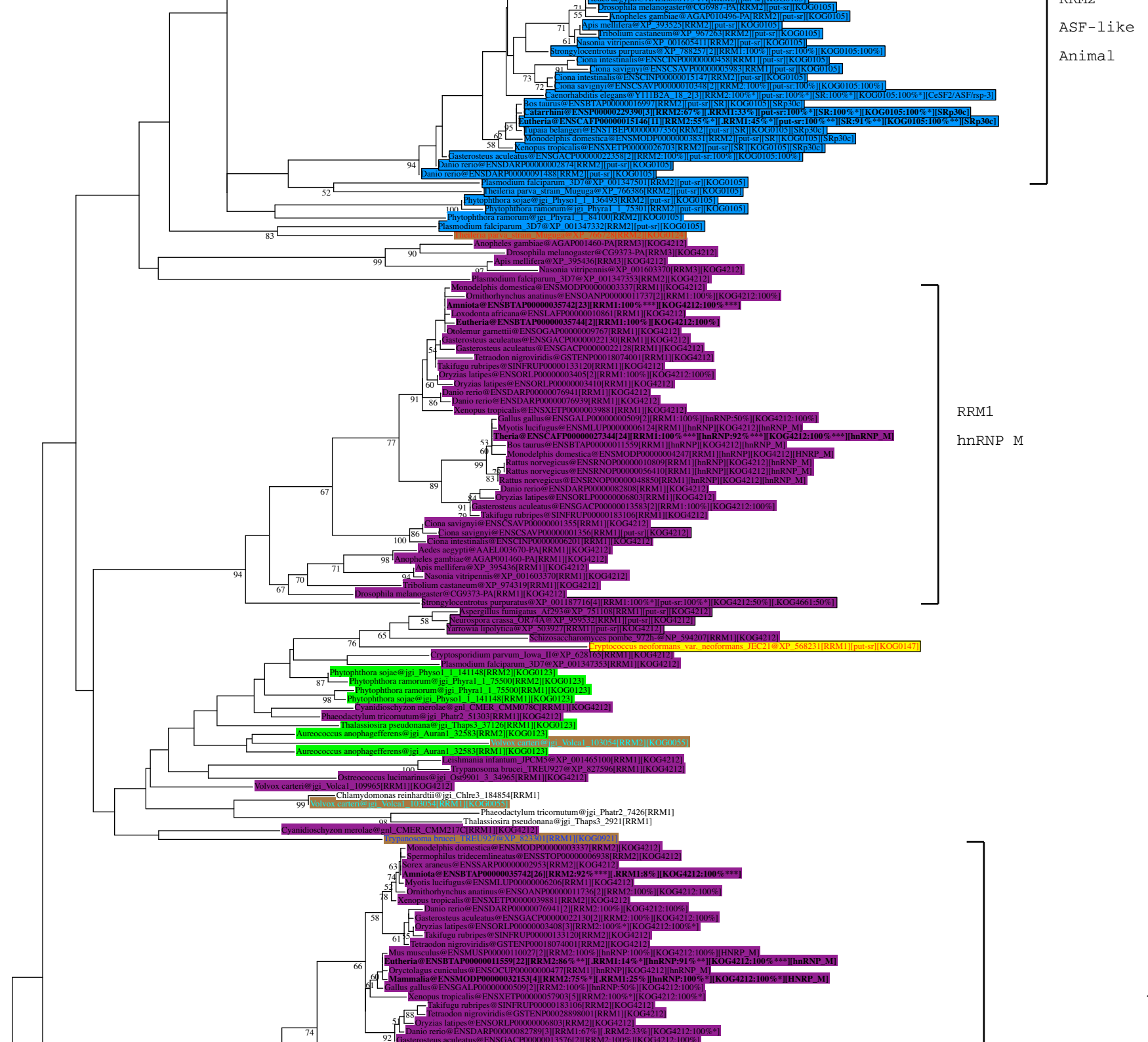


Fig. S18

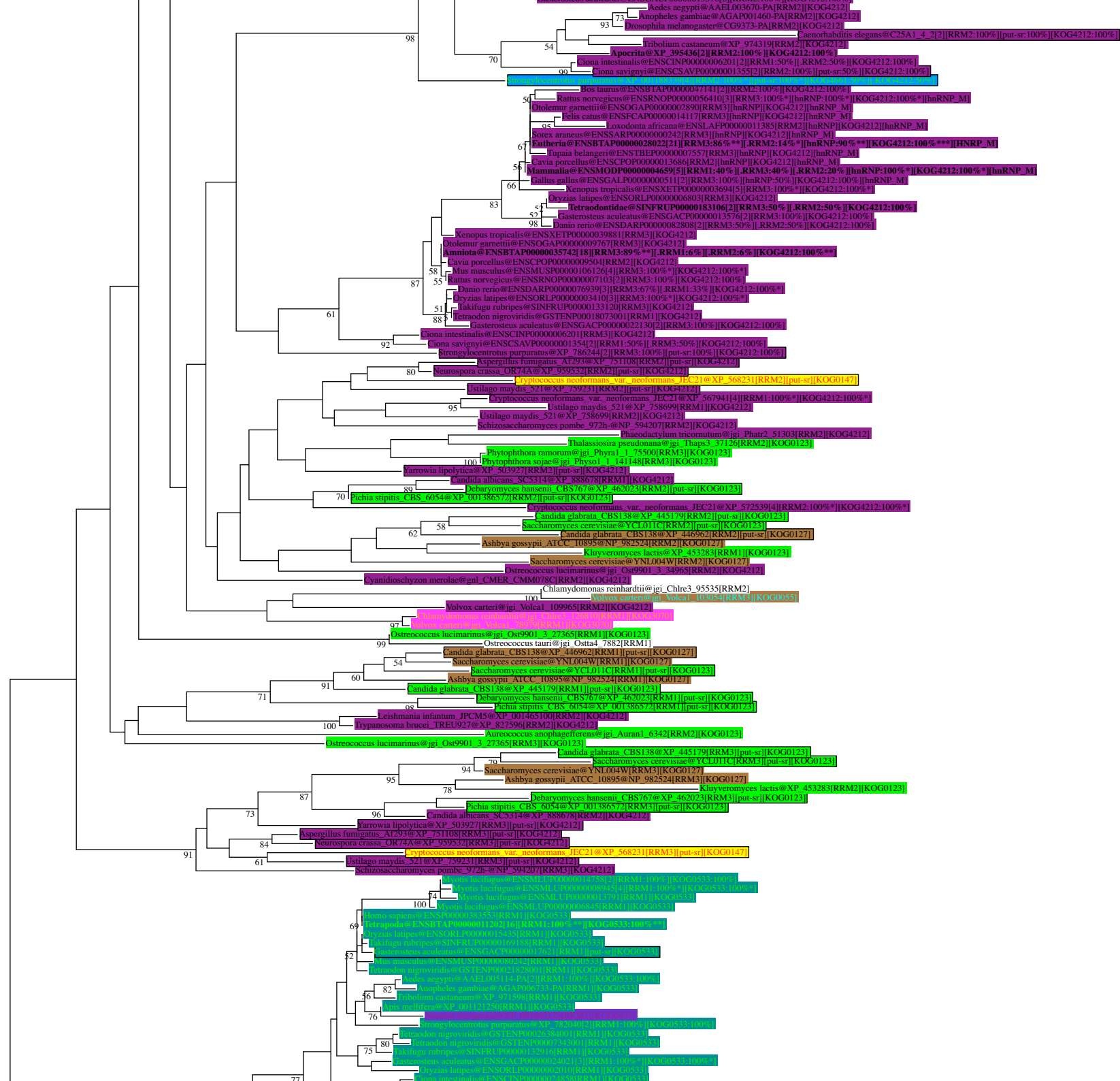
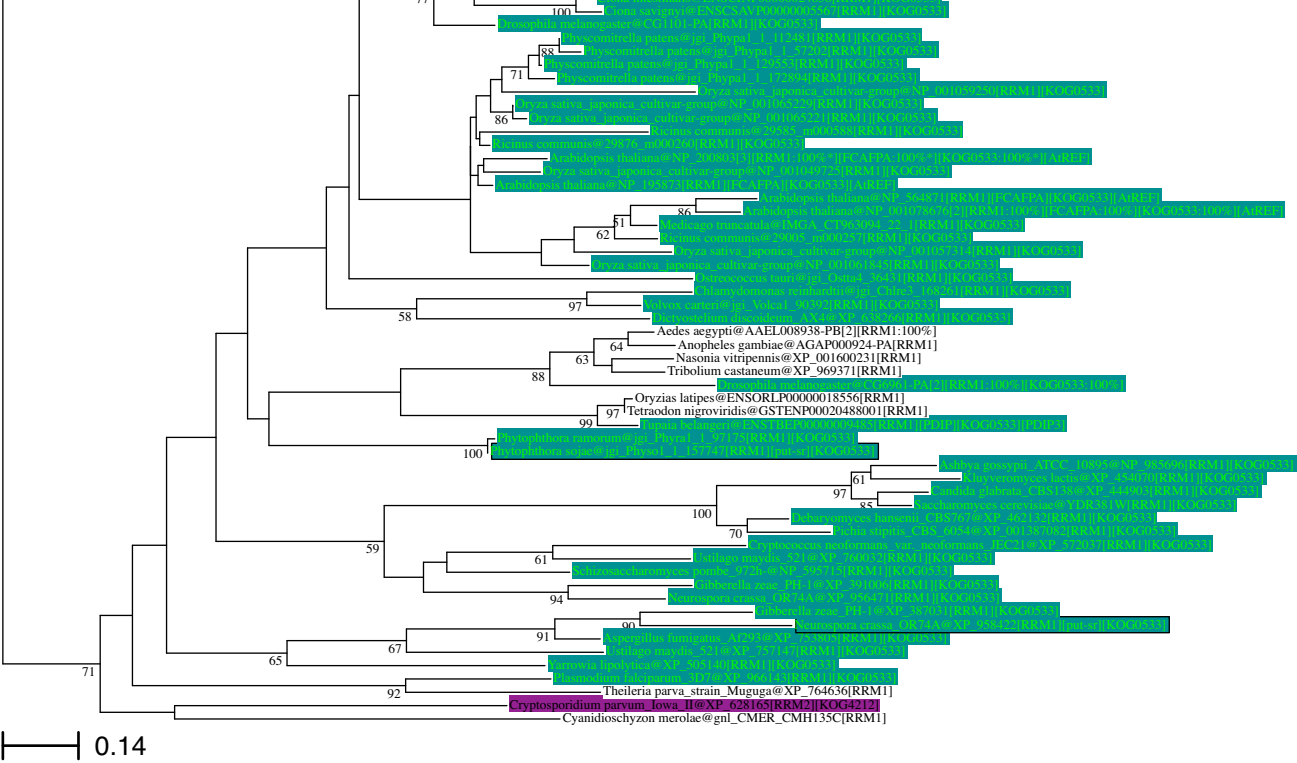
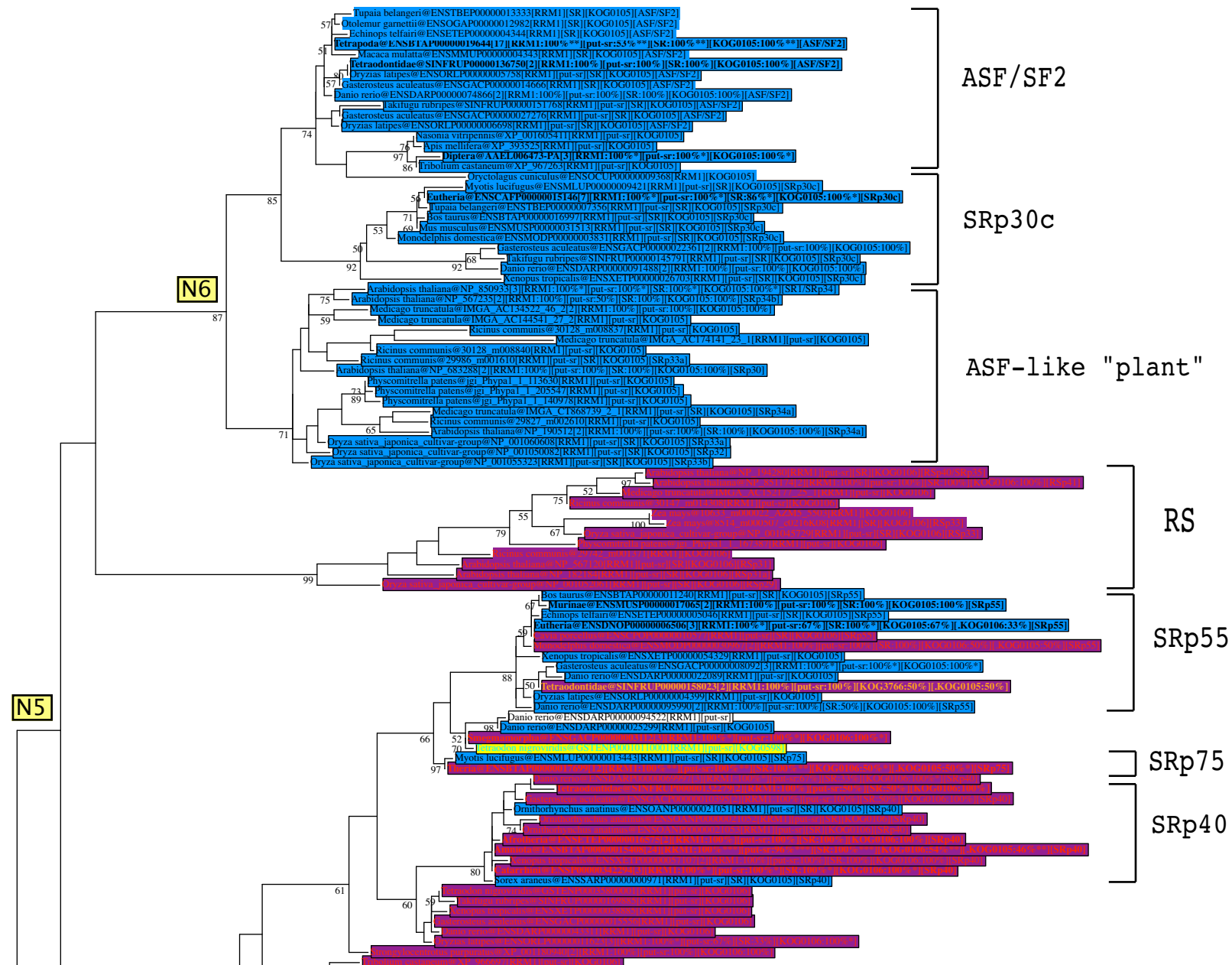


Fig. S18





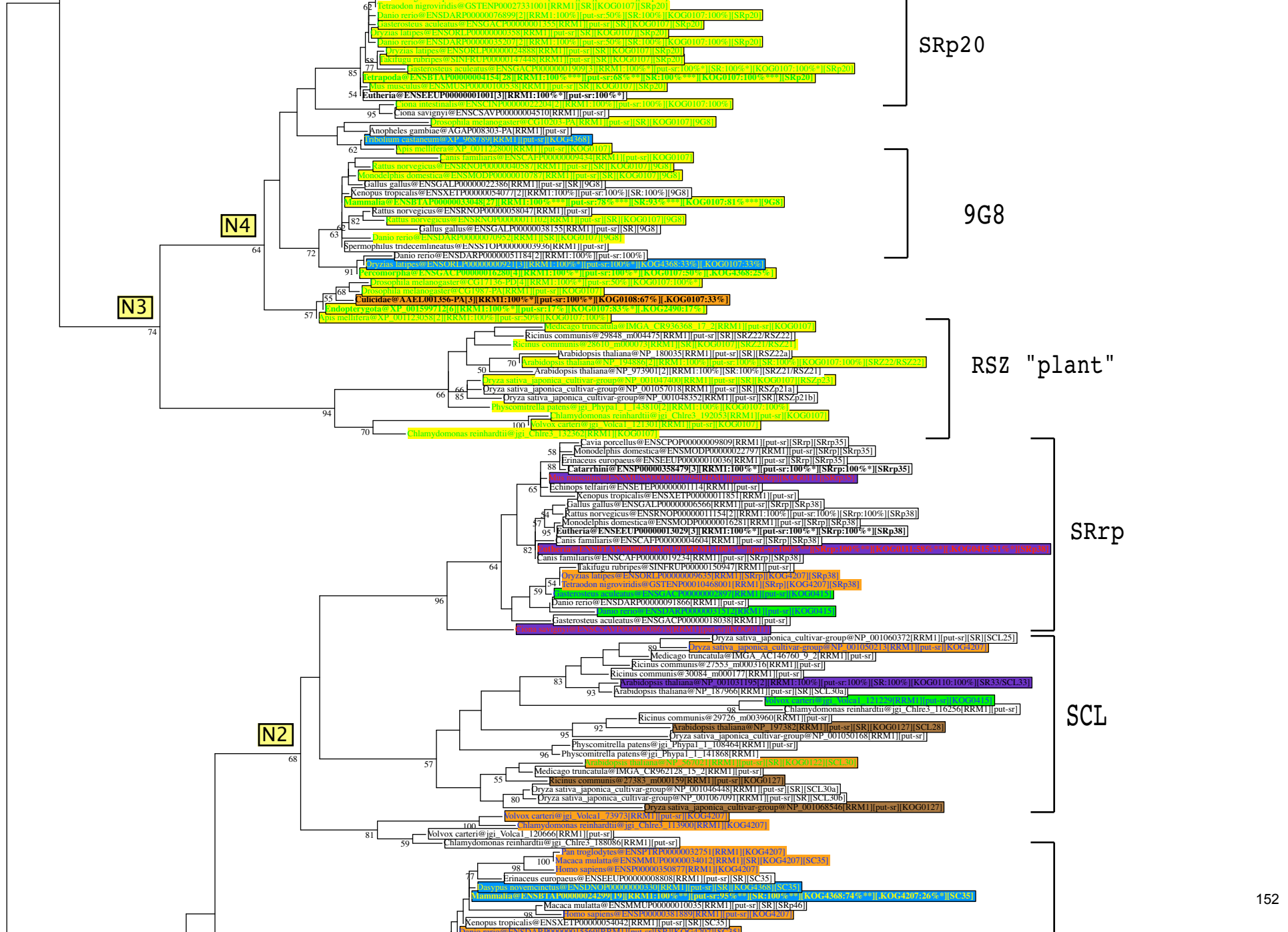


Fig. S19

0.12

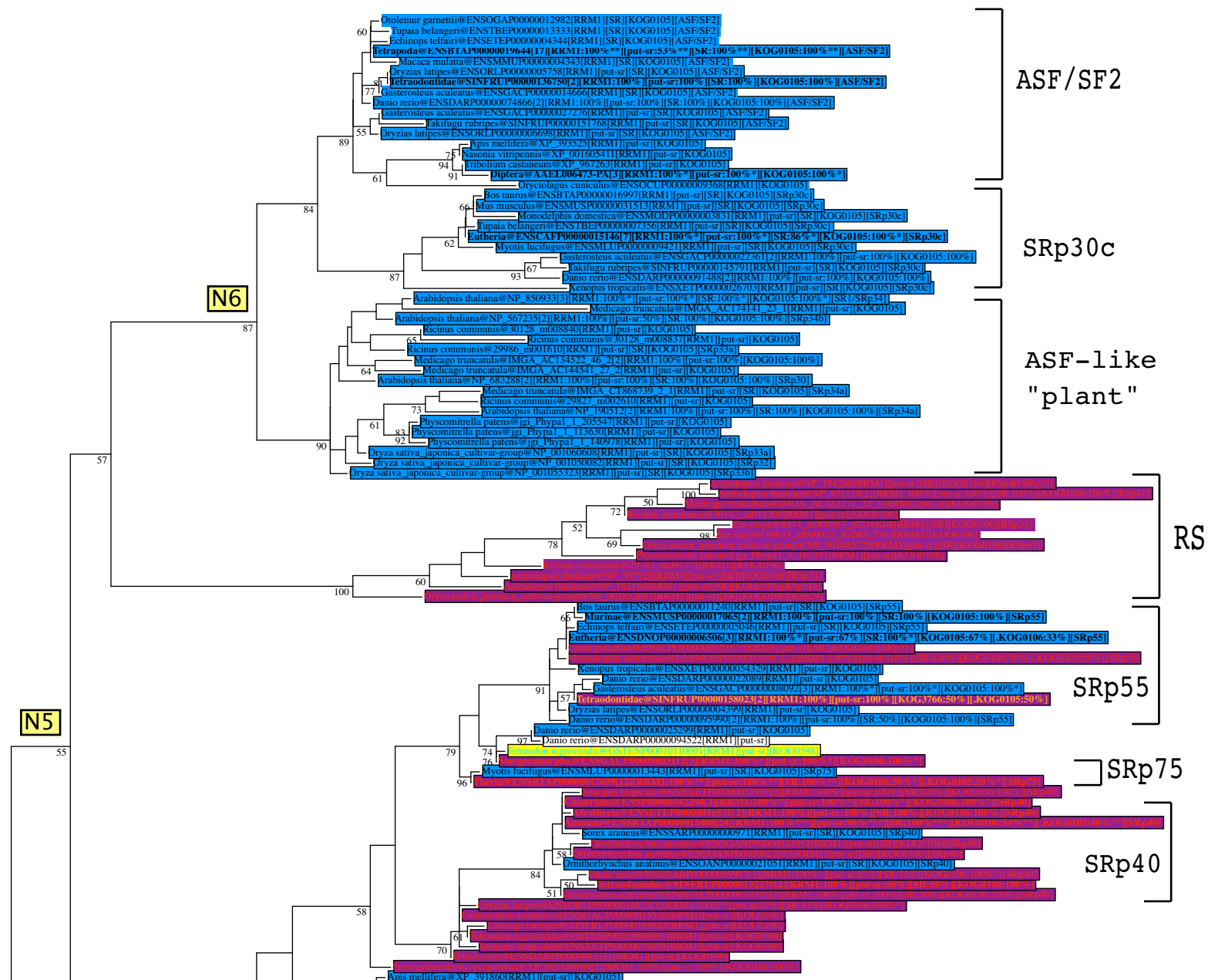


Fig. S20

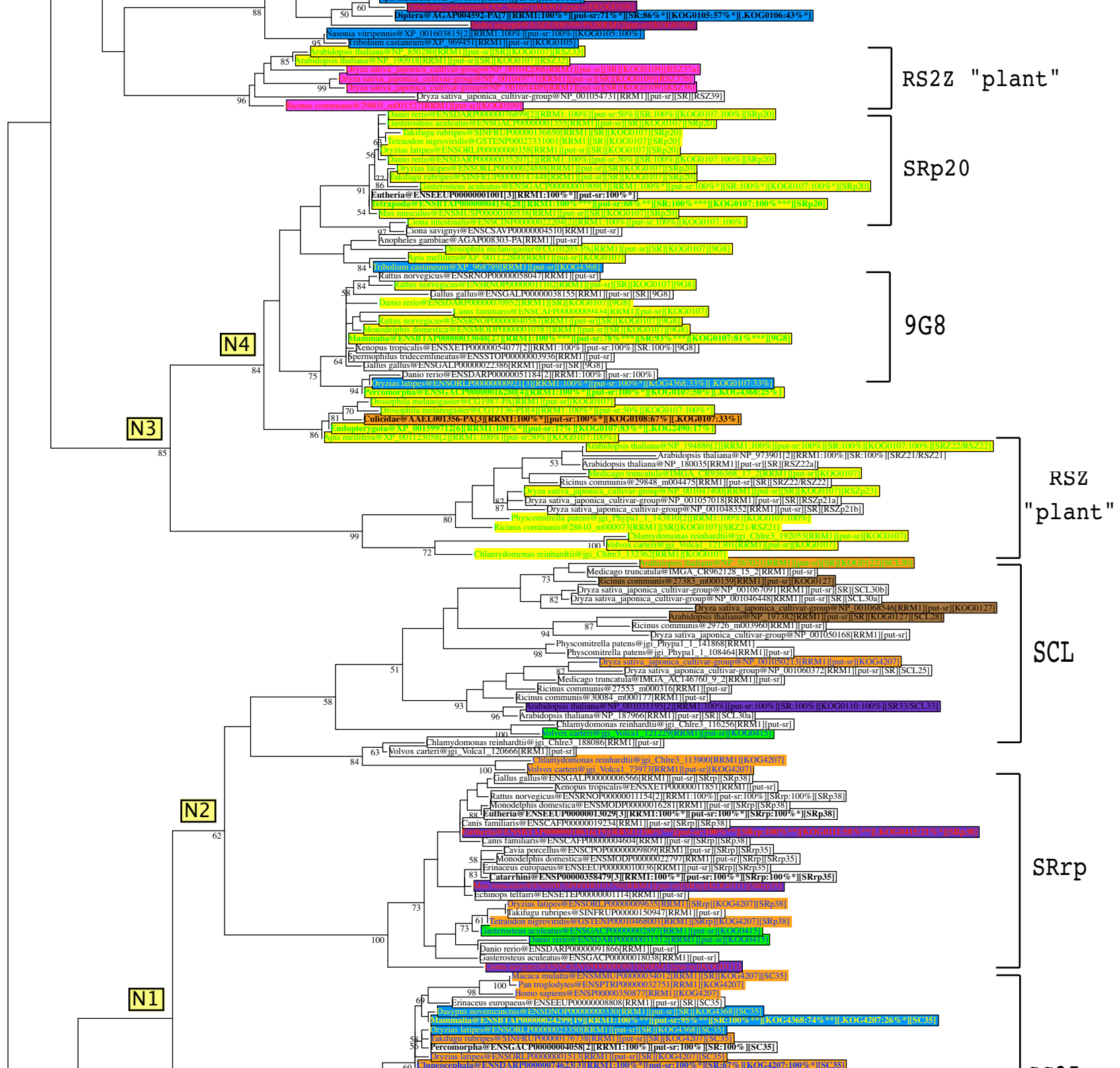


Fig. S20

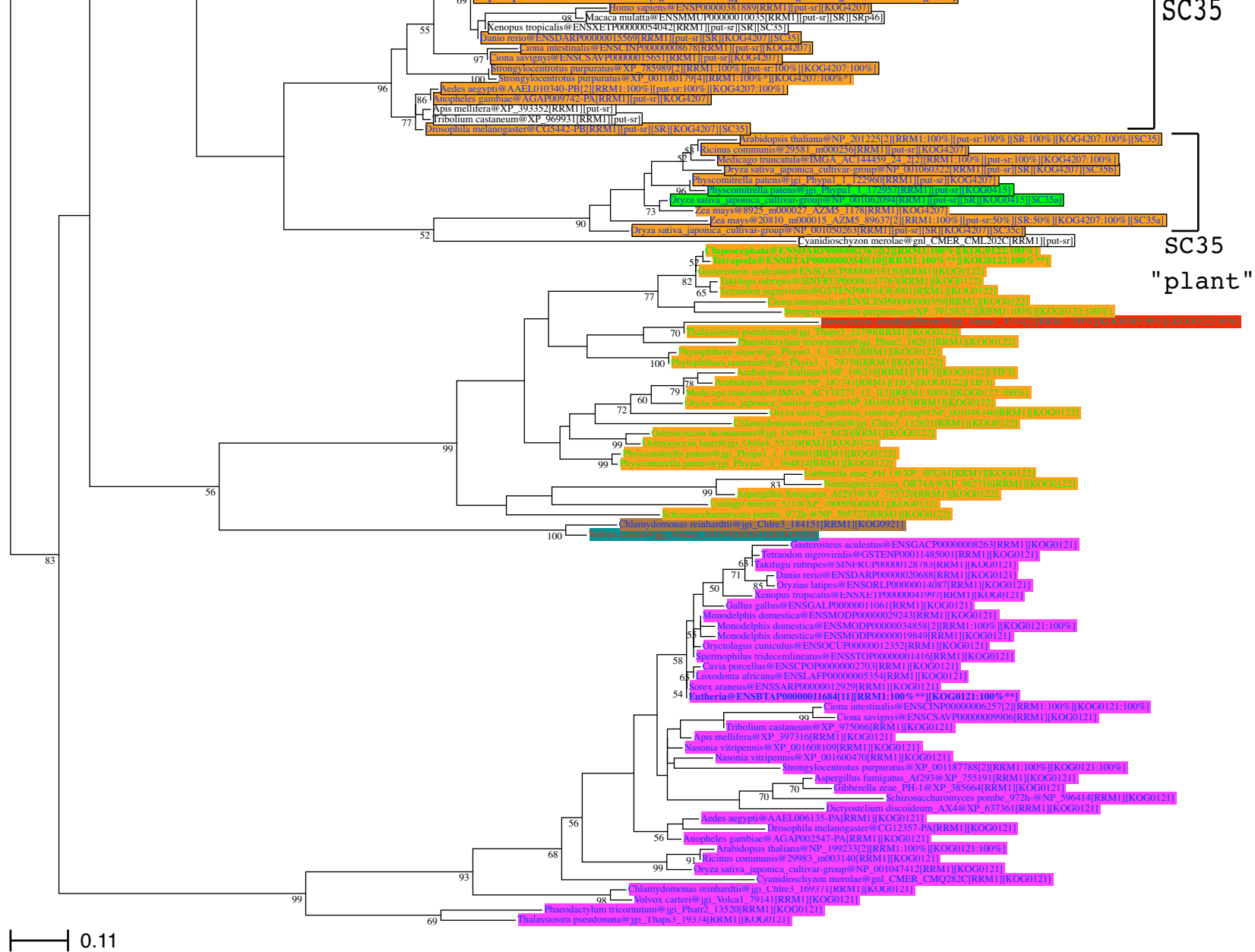


Fig. S21

A. RRM1 of Single RRM SR proteins

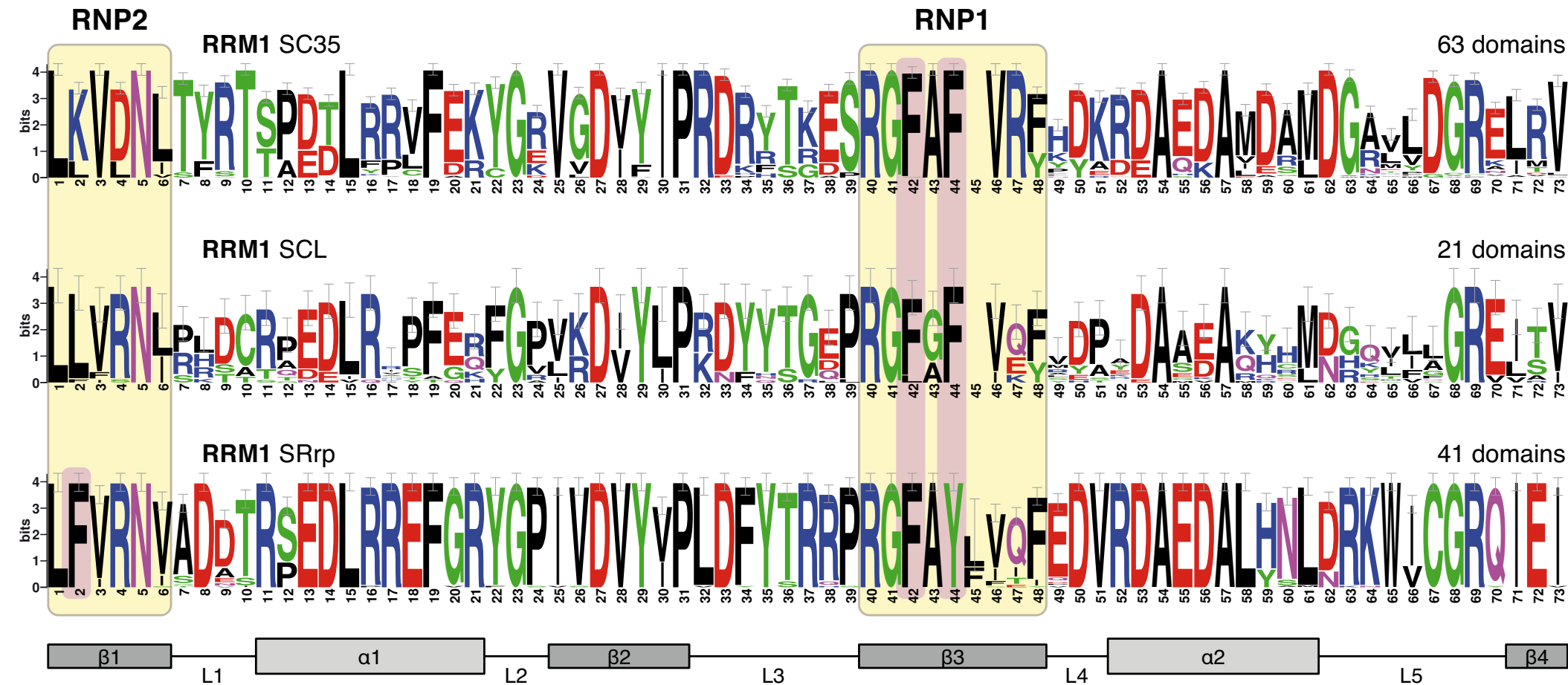


Fig. S21

B. RRM1 of Single RRM ZnK-like SR proteins

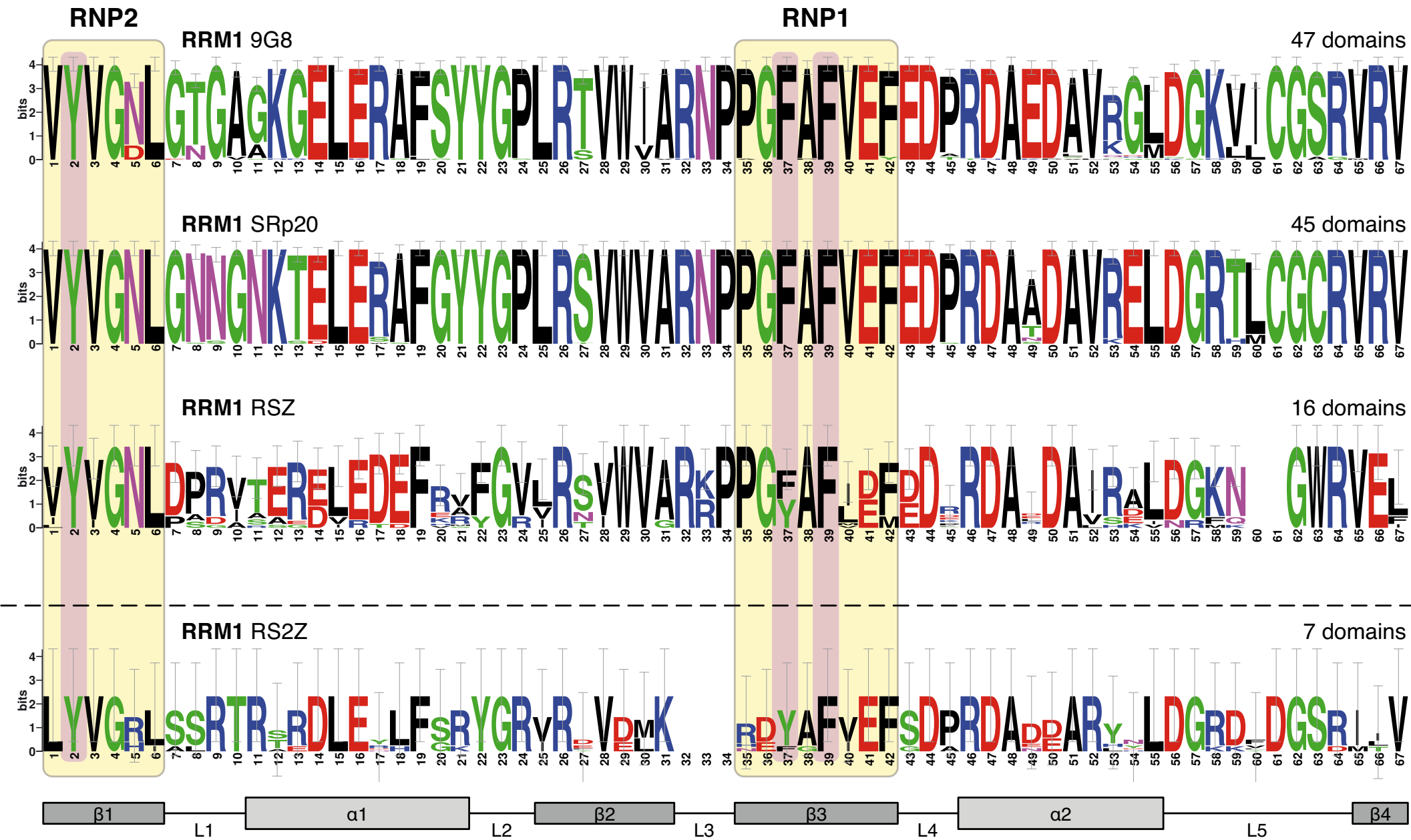


Fig. S21

C. RRM1 of Dual RRM SR proteins

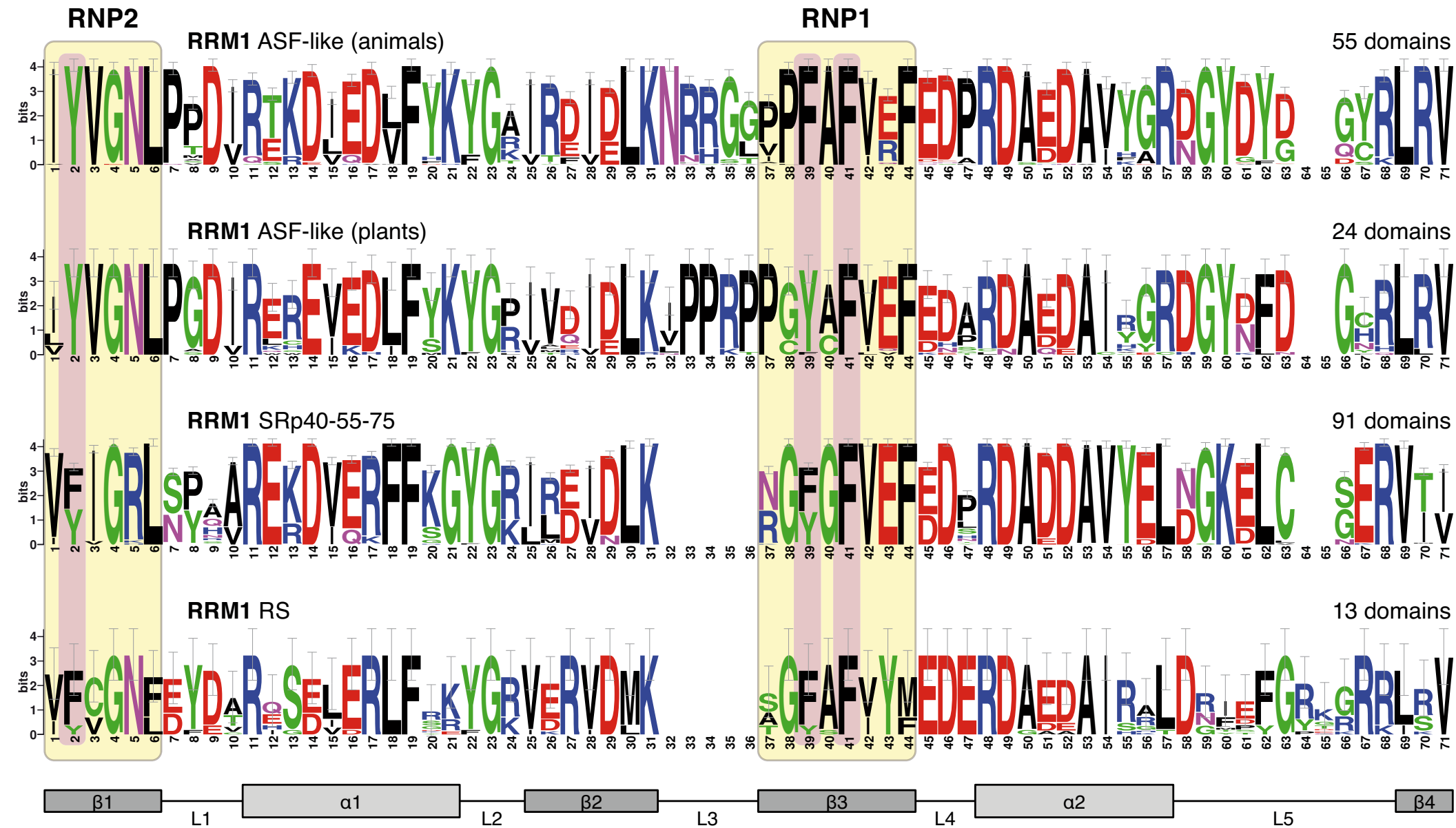


Fig. S21

D. RRM1 of RNPS1-like proteins

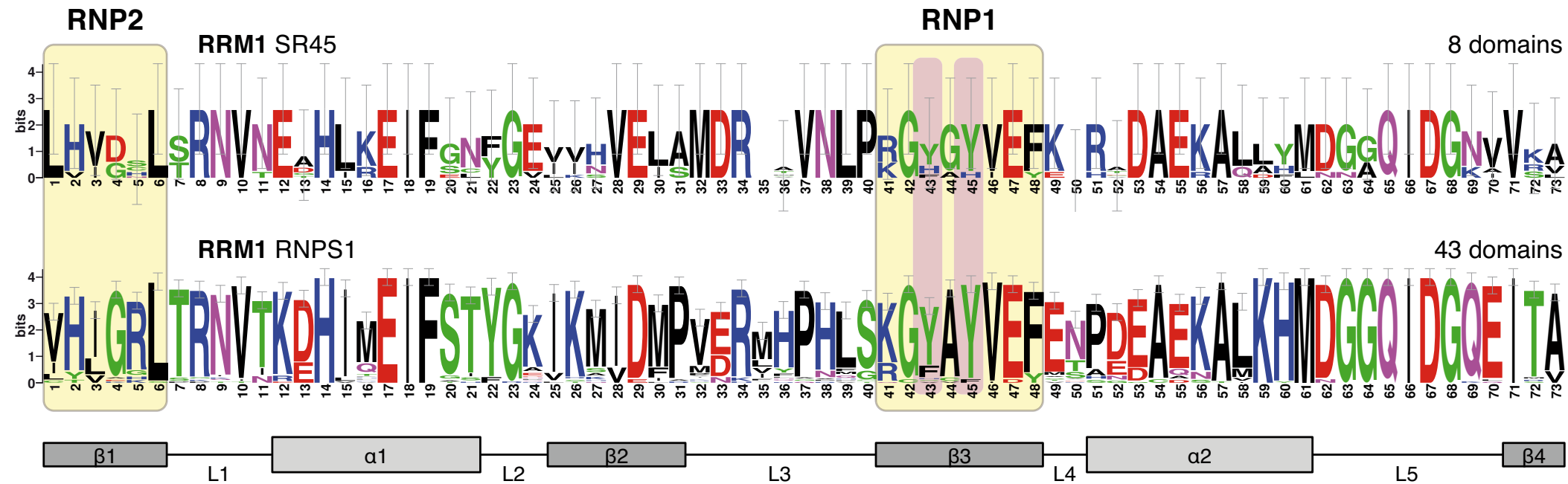


Fig. S22

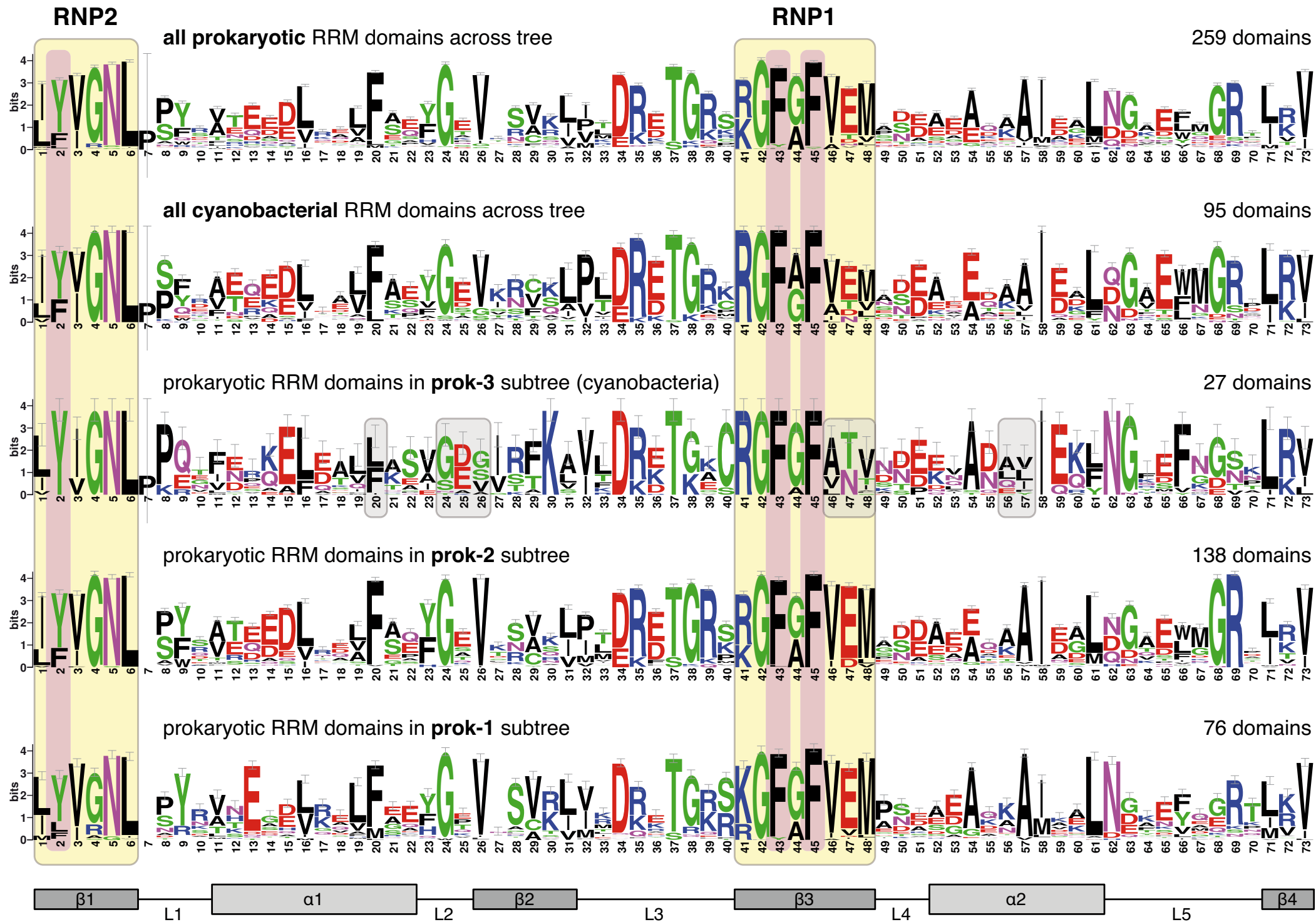
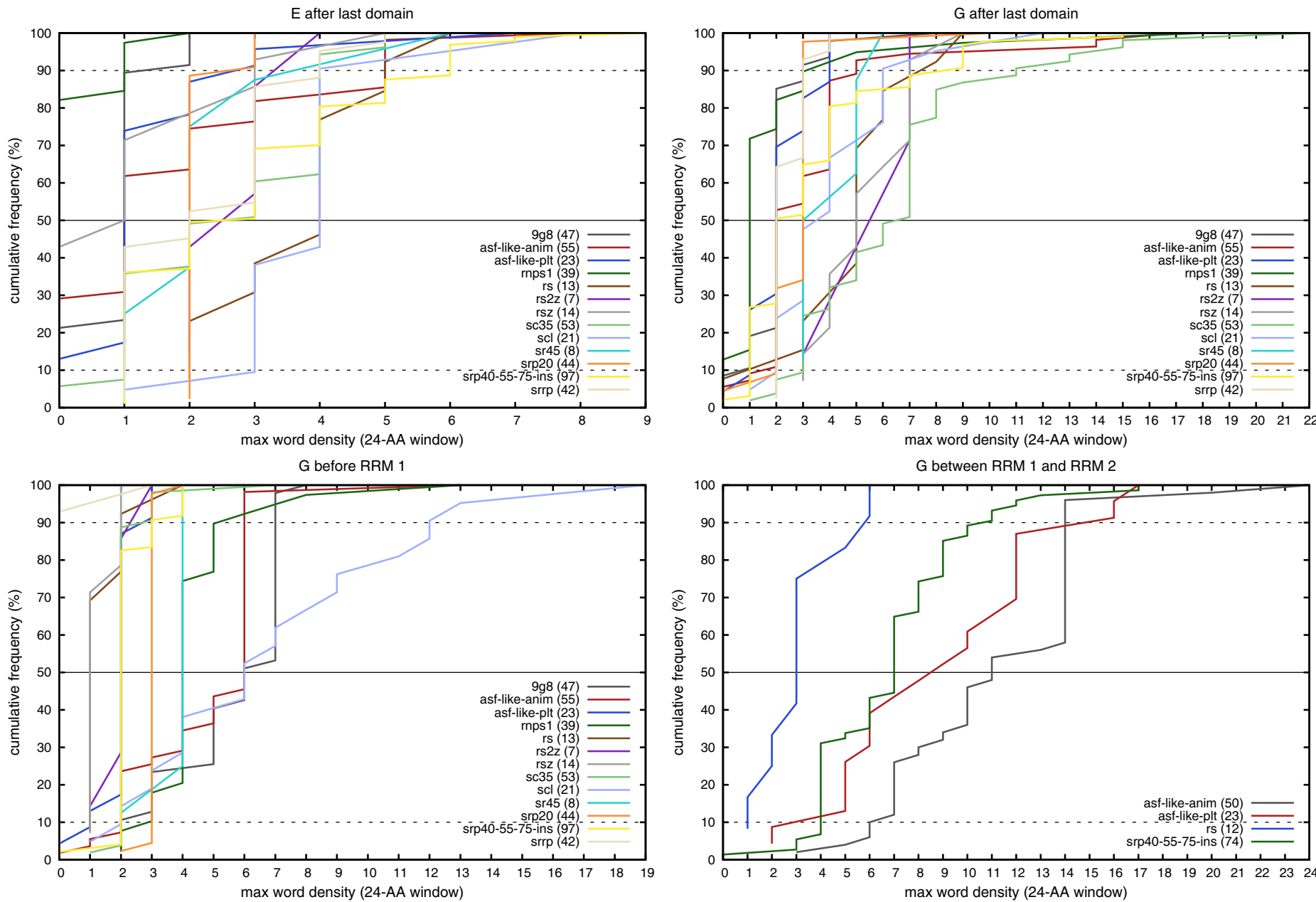


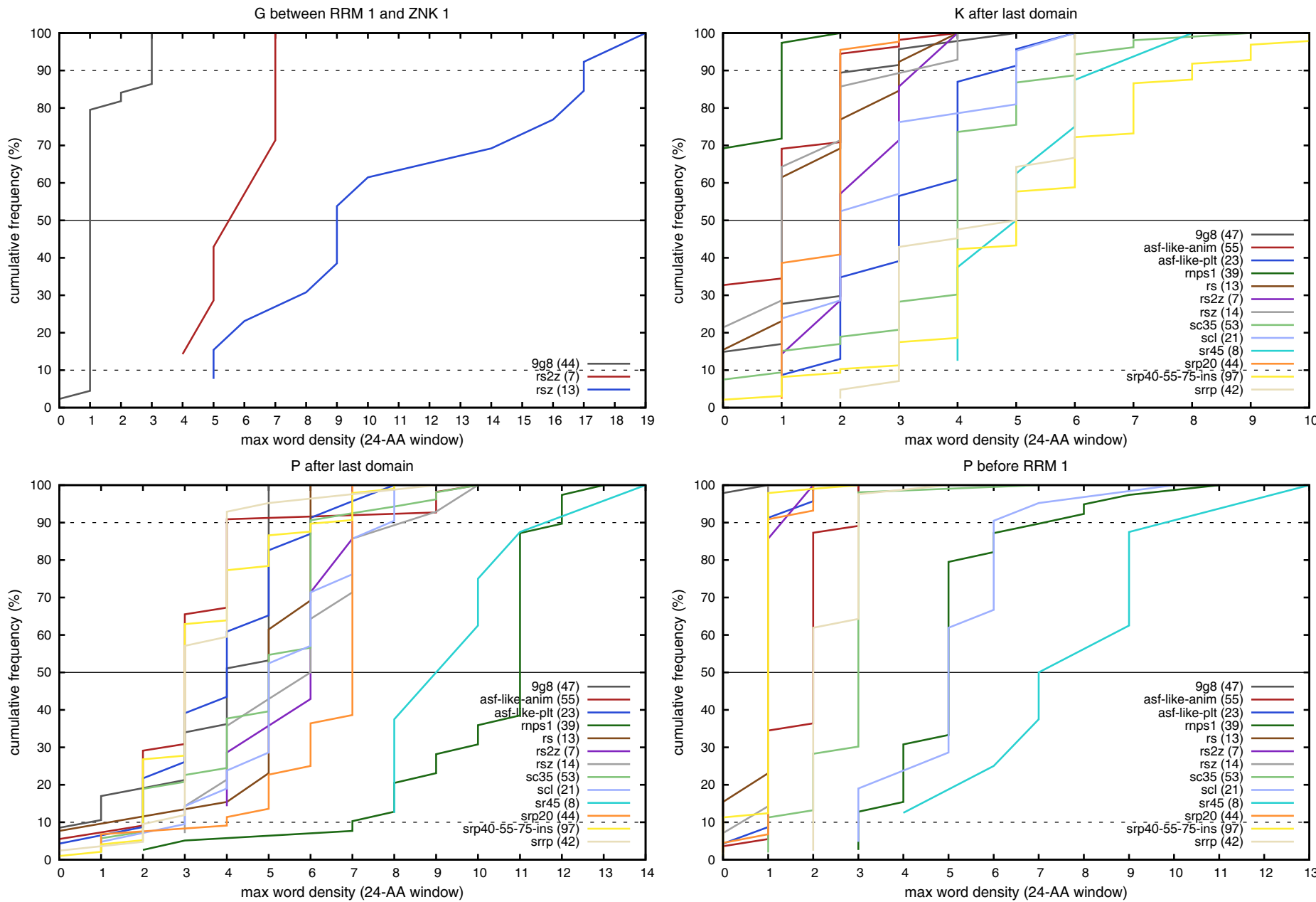
Fig. S23



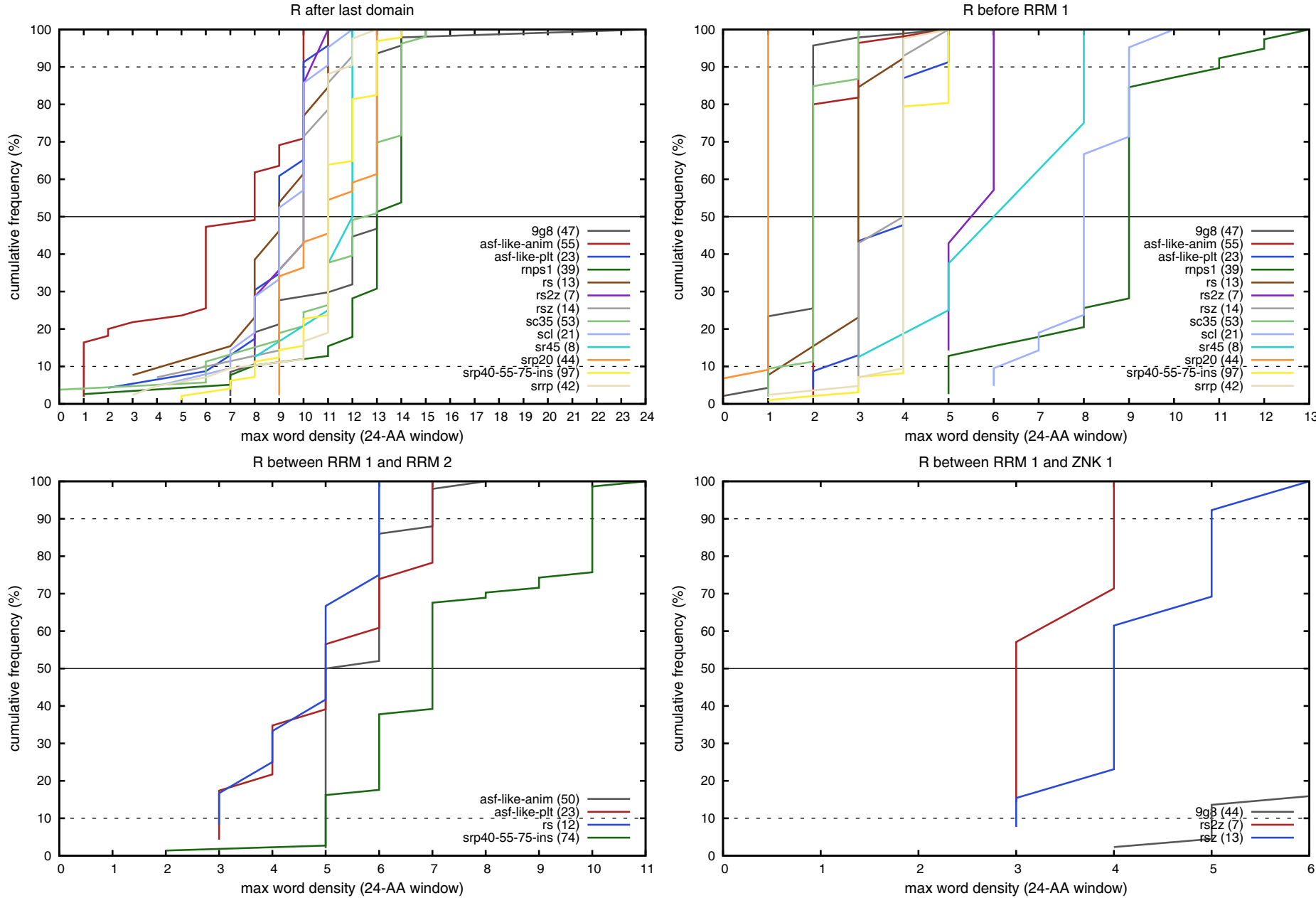
Word density cumulative distributions <plotdist> - page 1



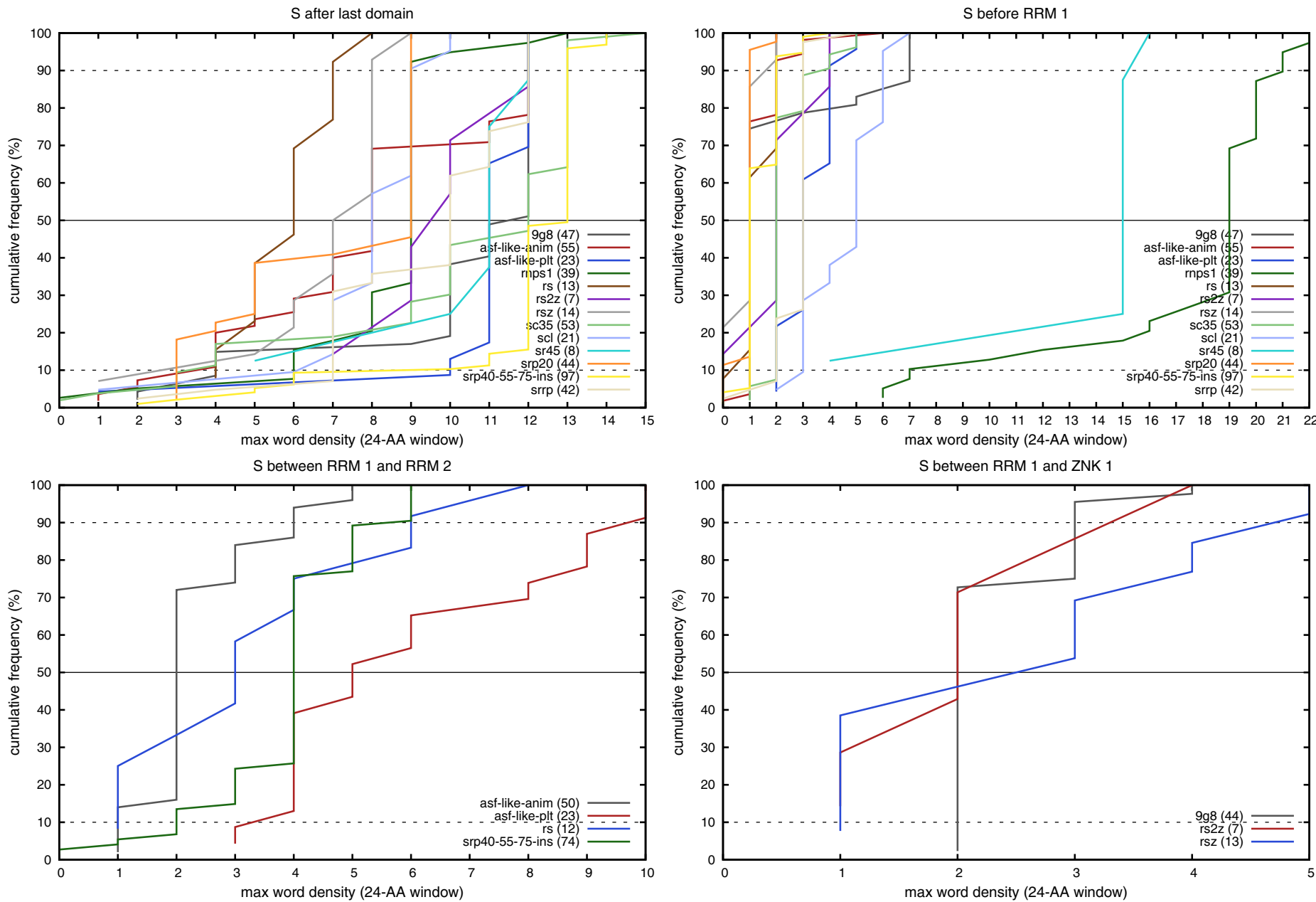
Word density cumulative distributions <plotdist> - page 2



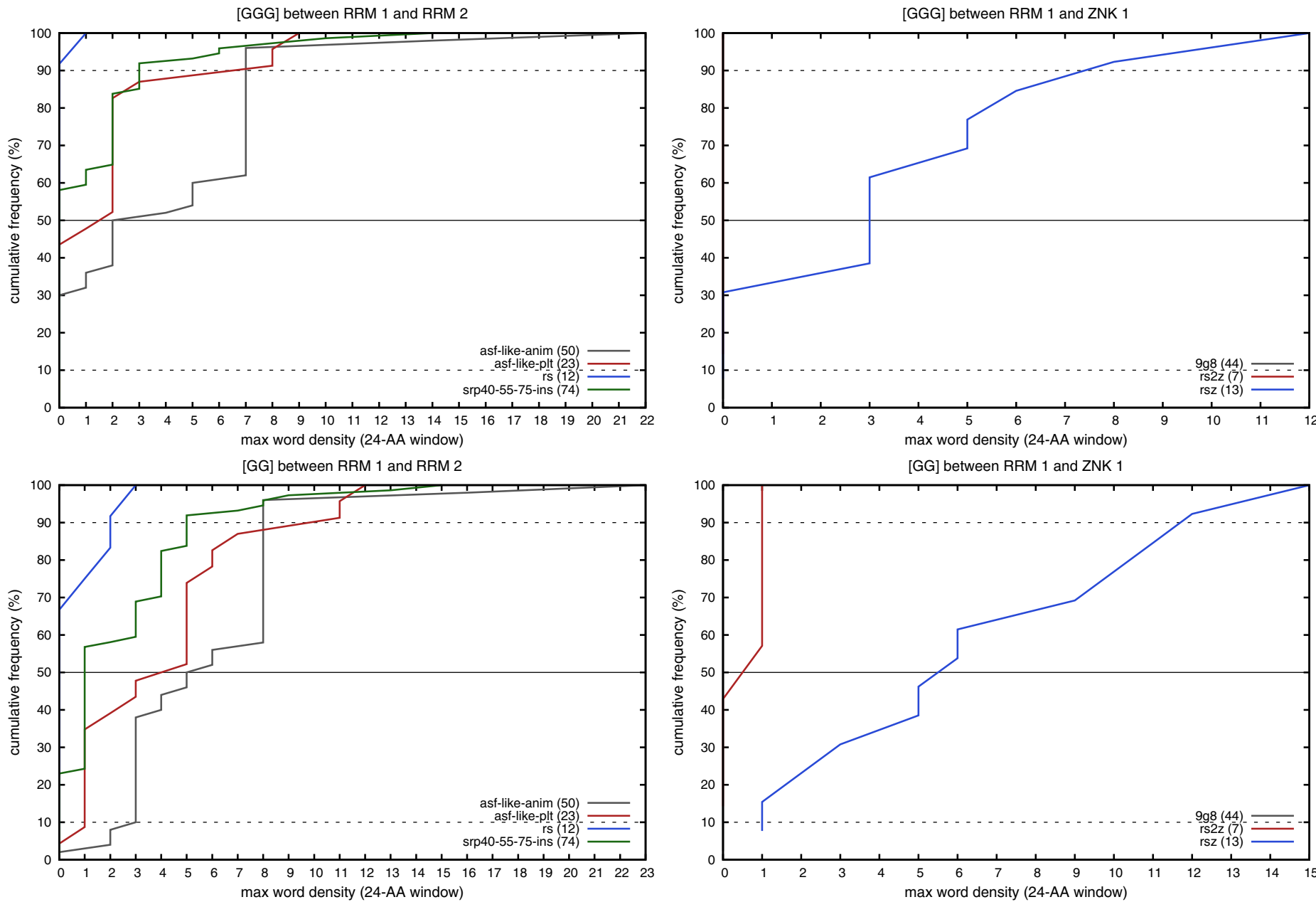
Word density cumulative distributions <plotdist> - page 3



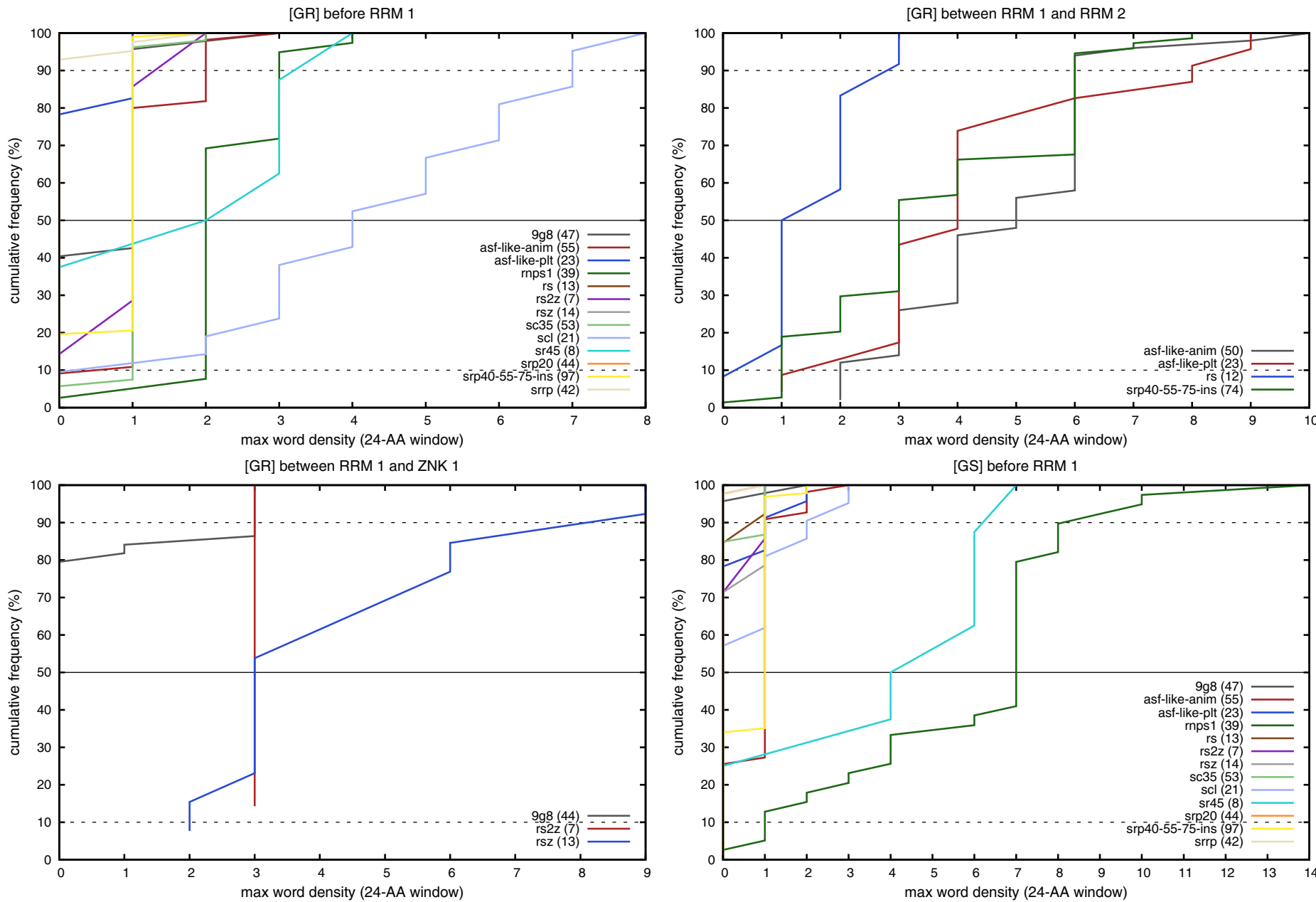
Word density cumulative distributions <plotdist> - page 4



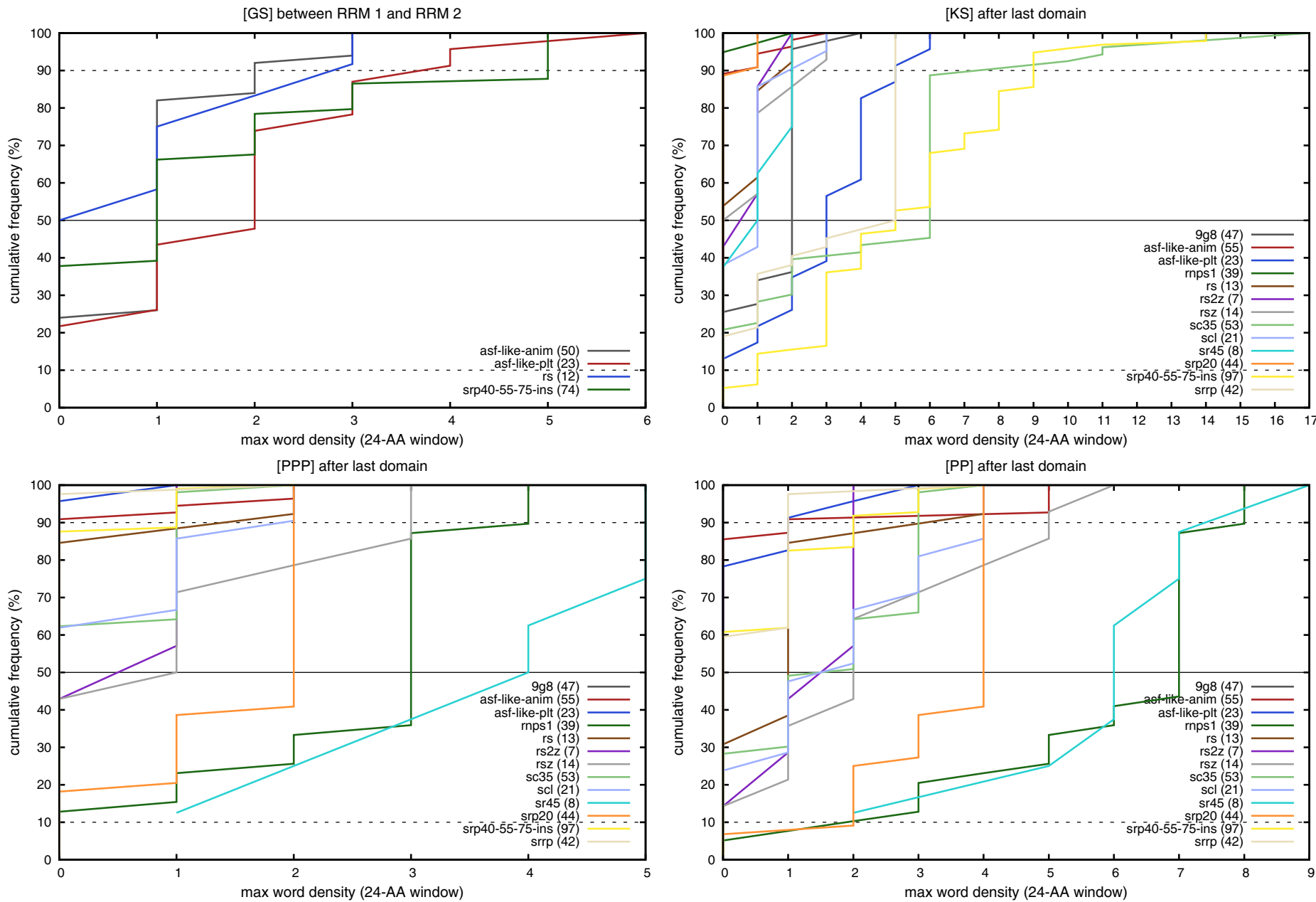
Word density cumulative distributions <plotdist> - page 5



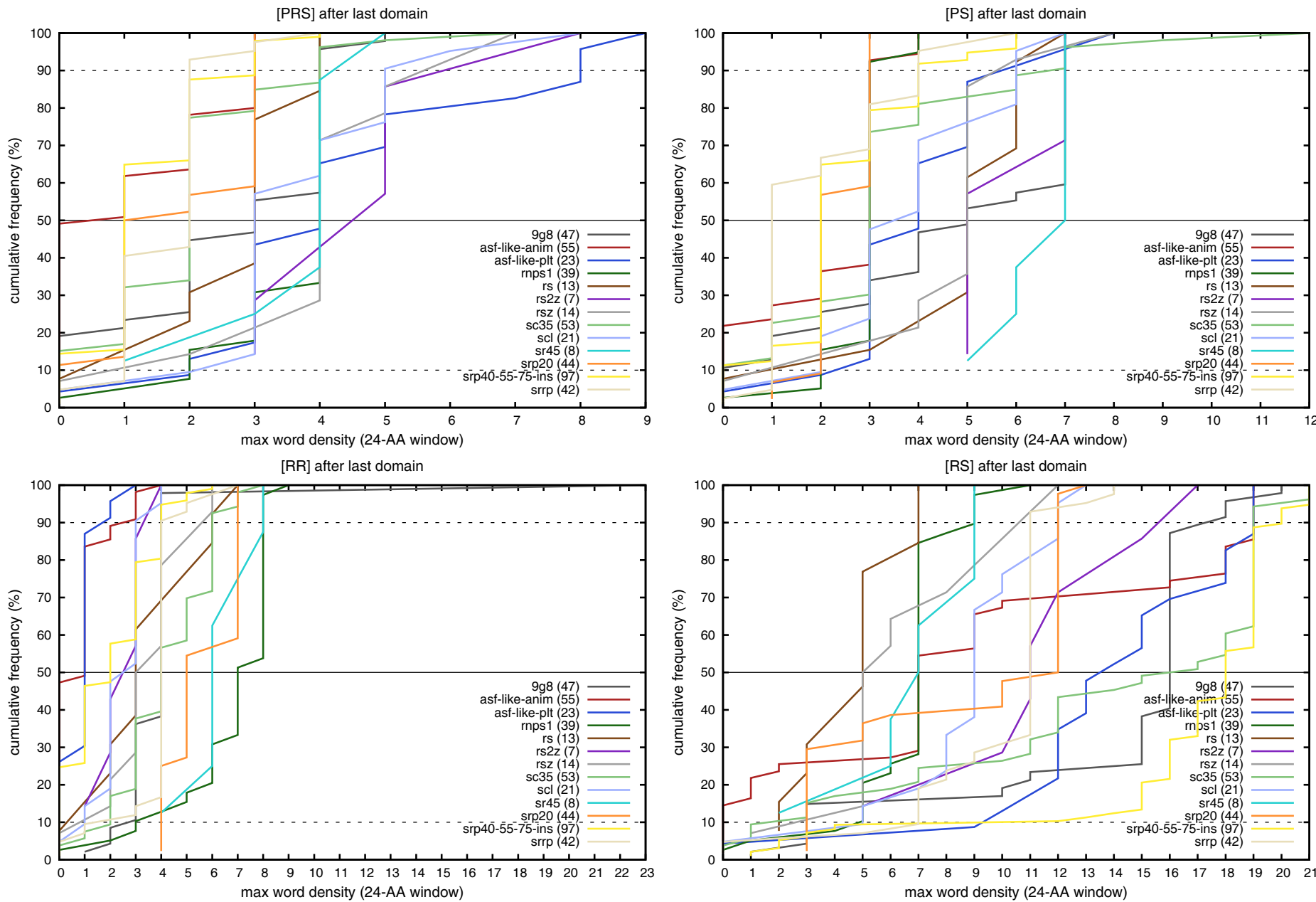
Word density cumulative distributions <plotdist> - page 6



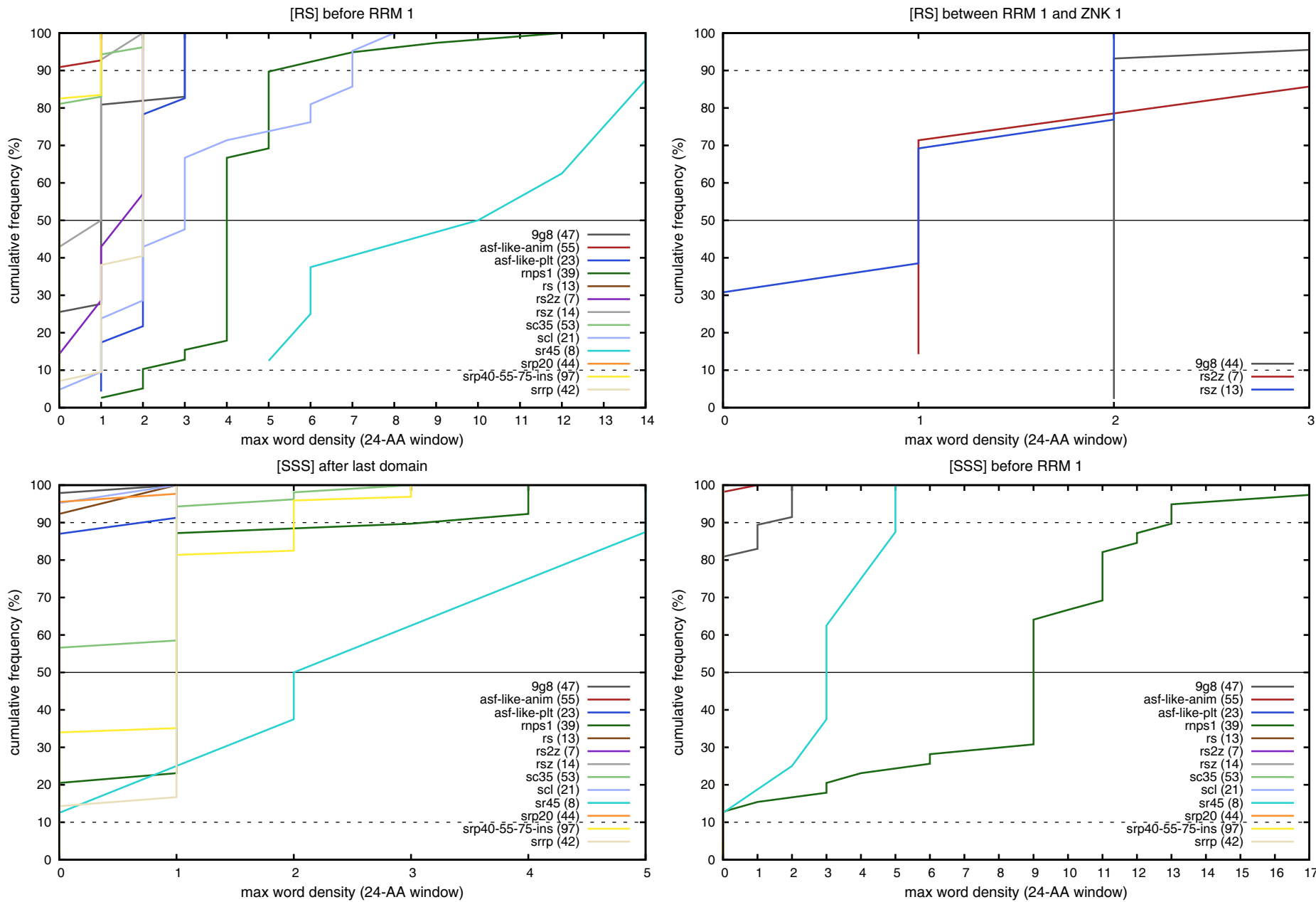
Word density cumulative distributions <plotdist> - page 7



Word density cumulative distributions <plotdist> - page 8



Word density cumulative distributions <plotdist> - page 9



Word density cumulative distributions <plotdist> - page 10

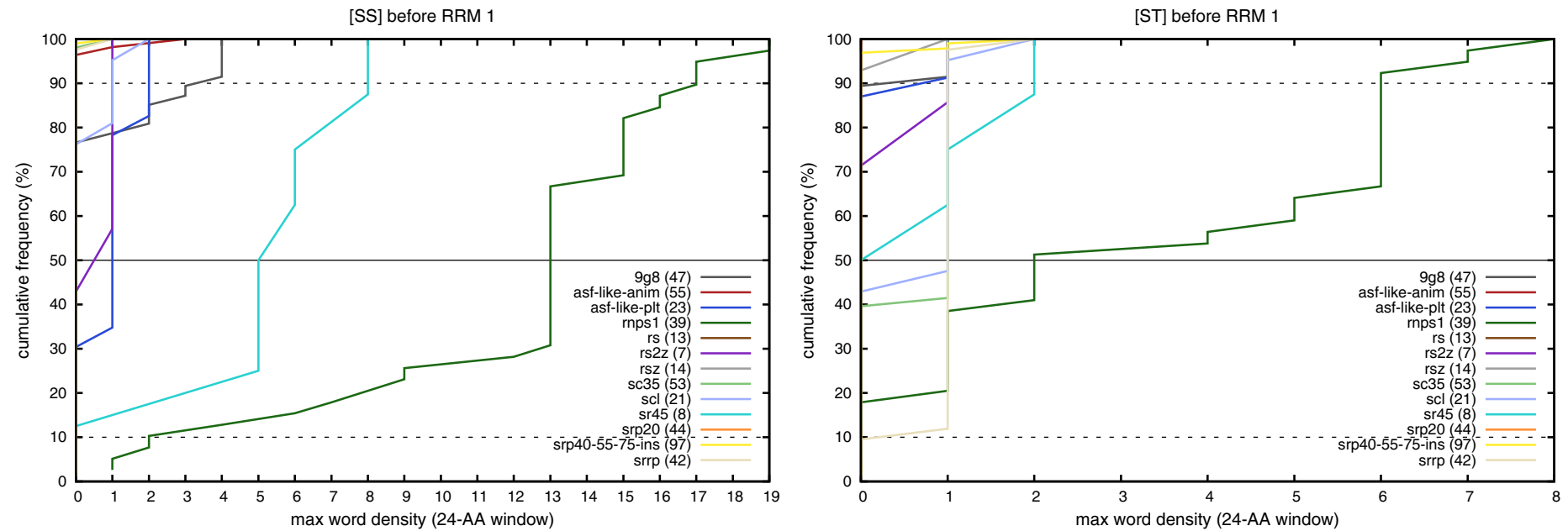


Fig. S25

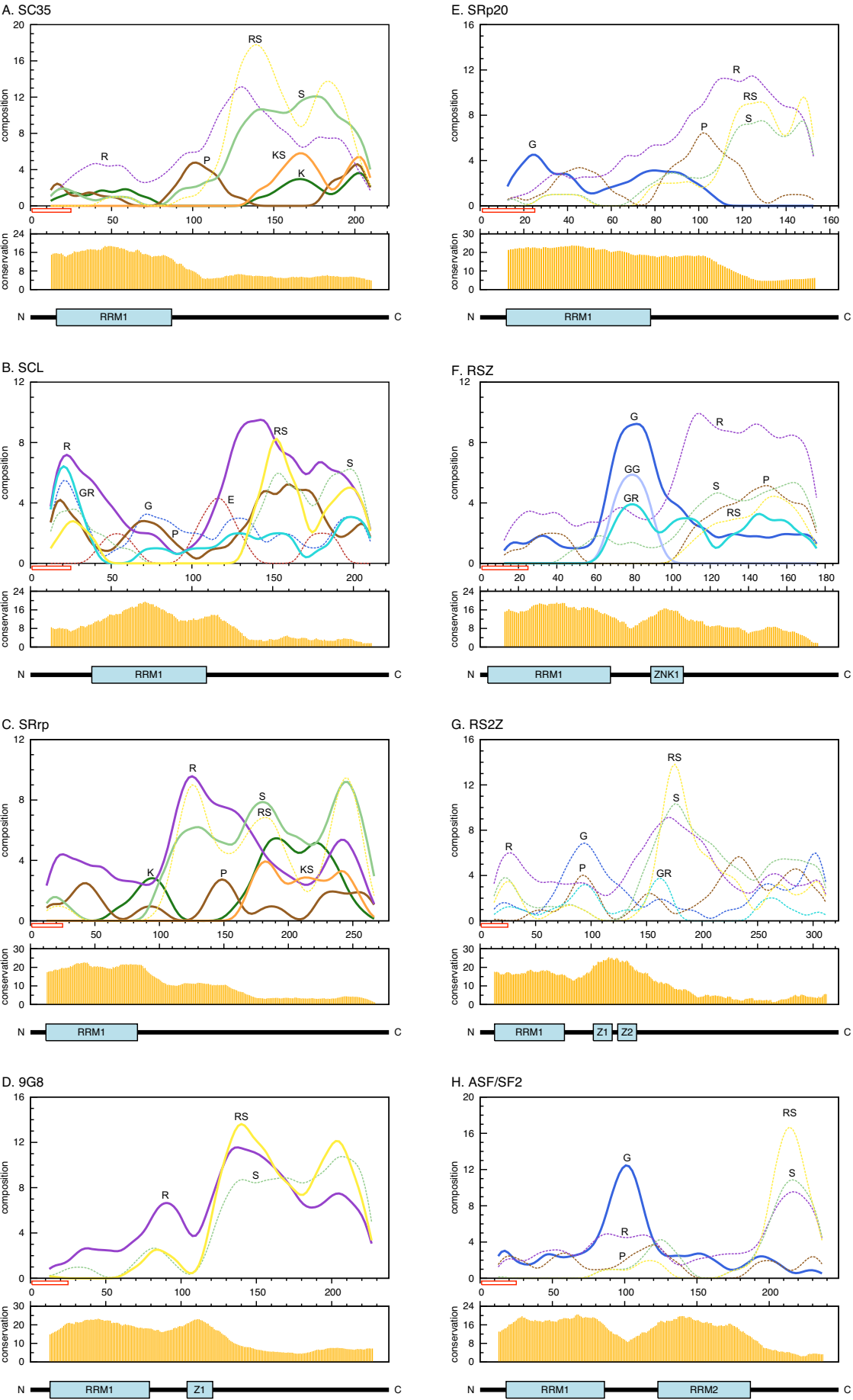


Fig. S25

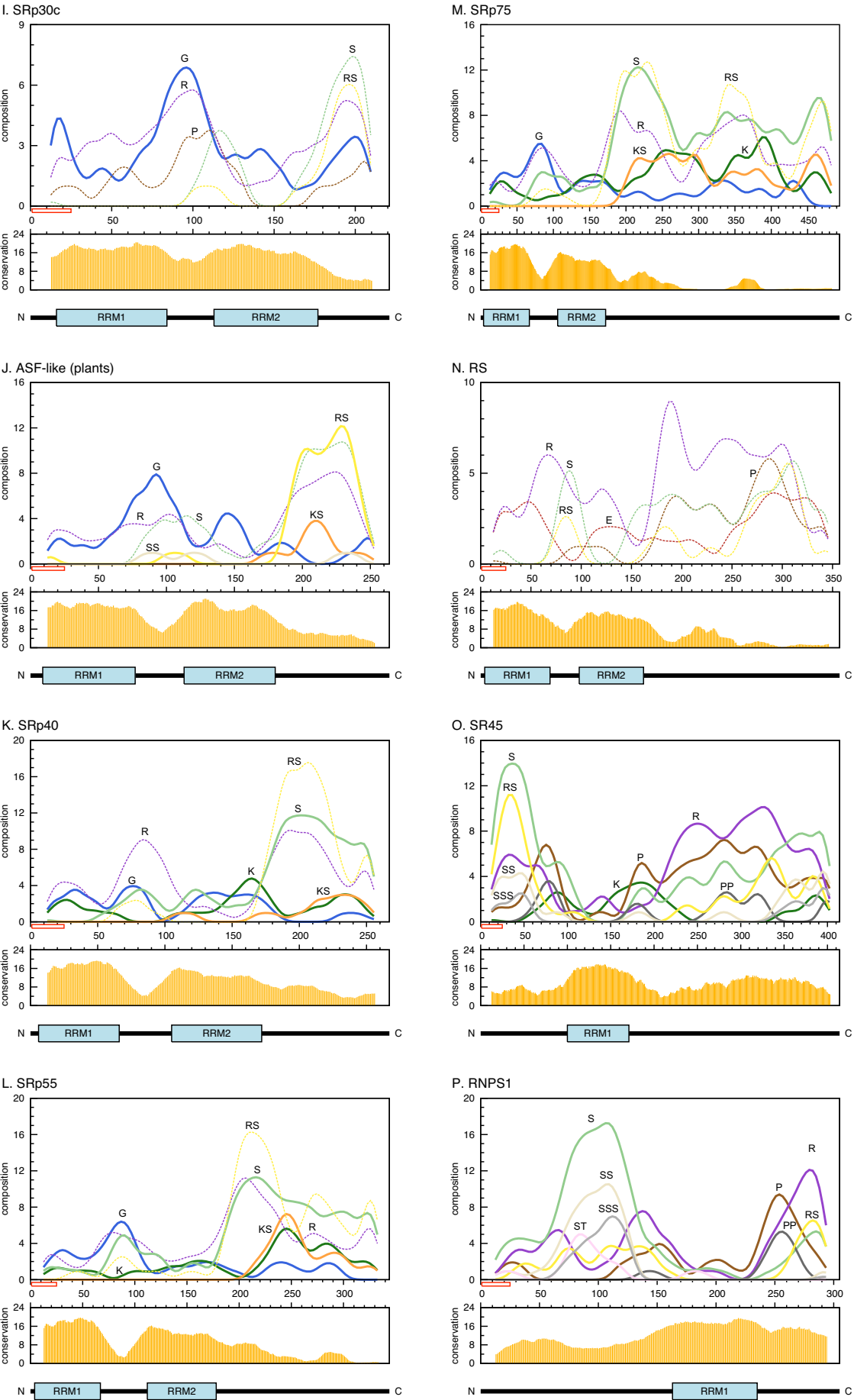


Fig. S26

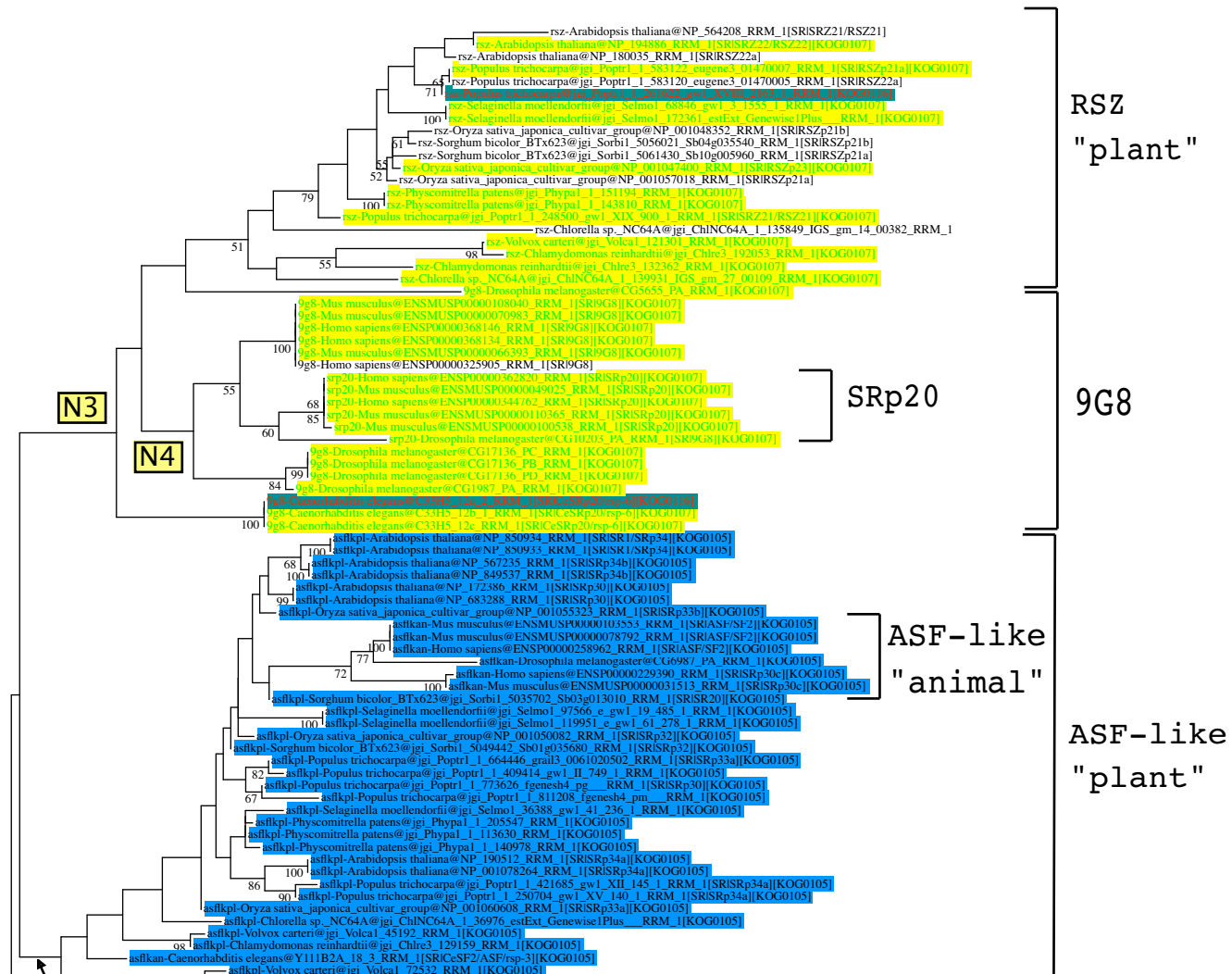


Fig. S26

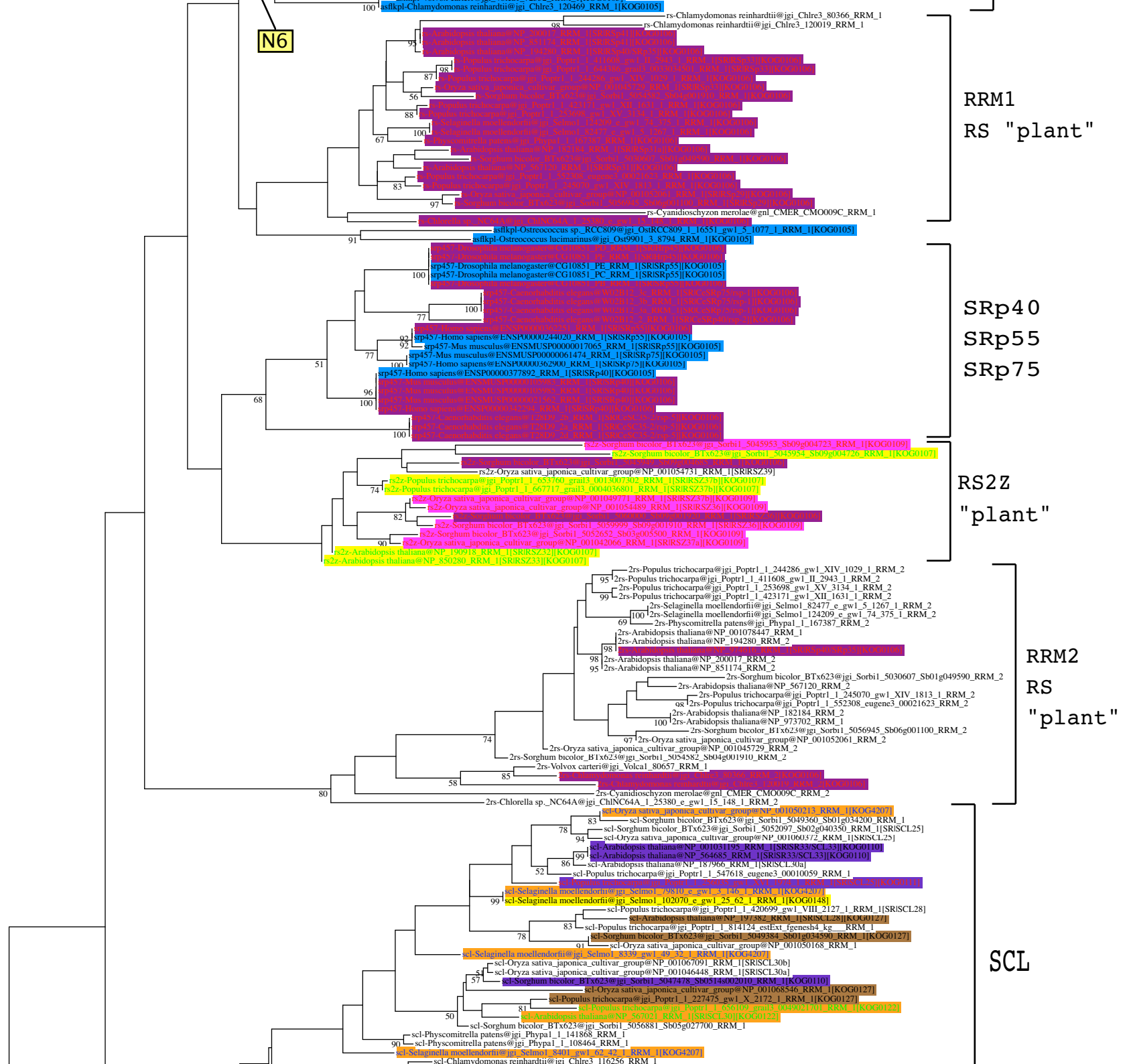


Fig. S26

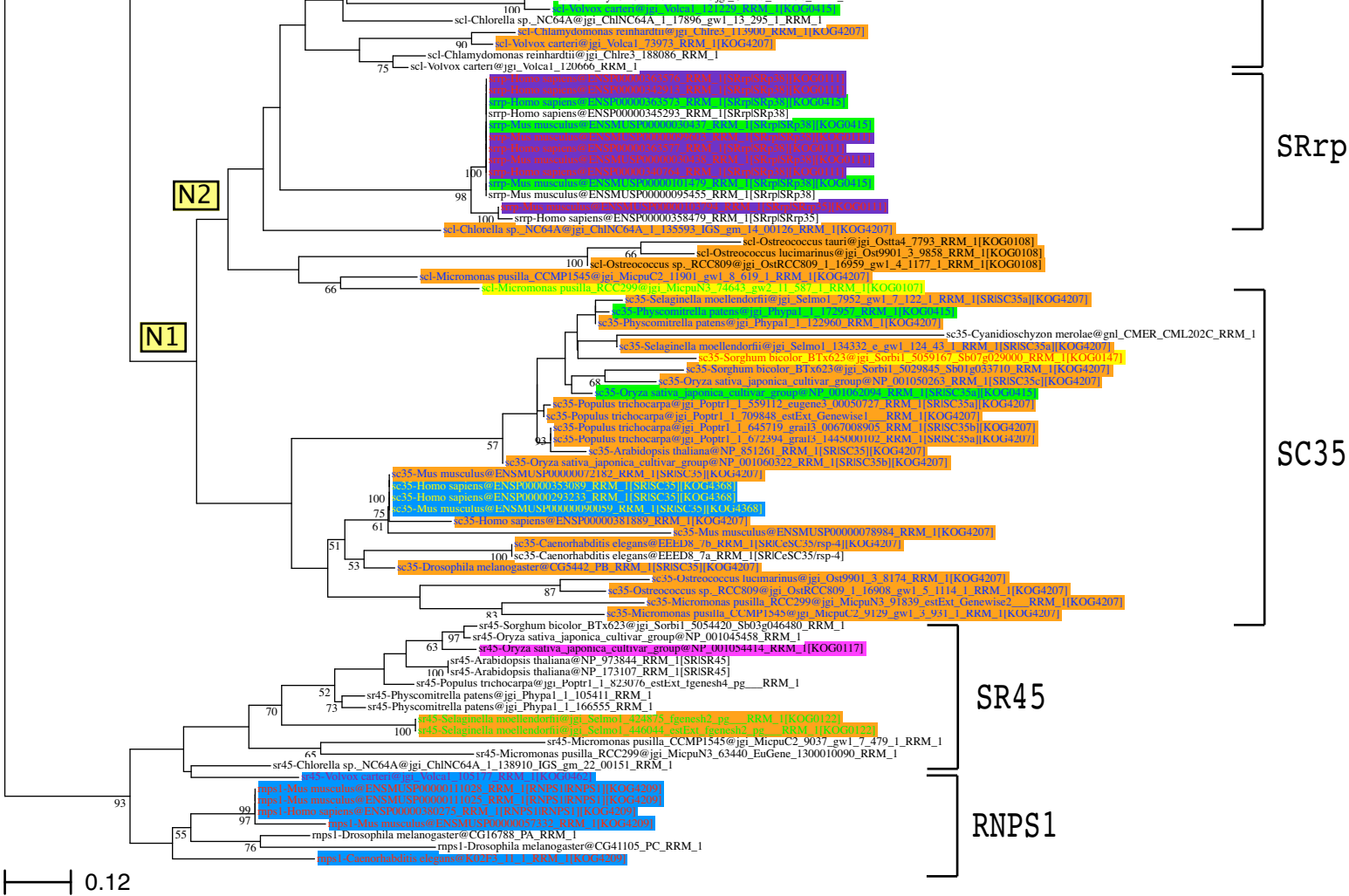


Fig. S27

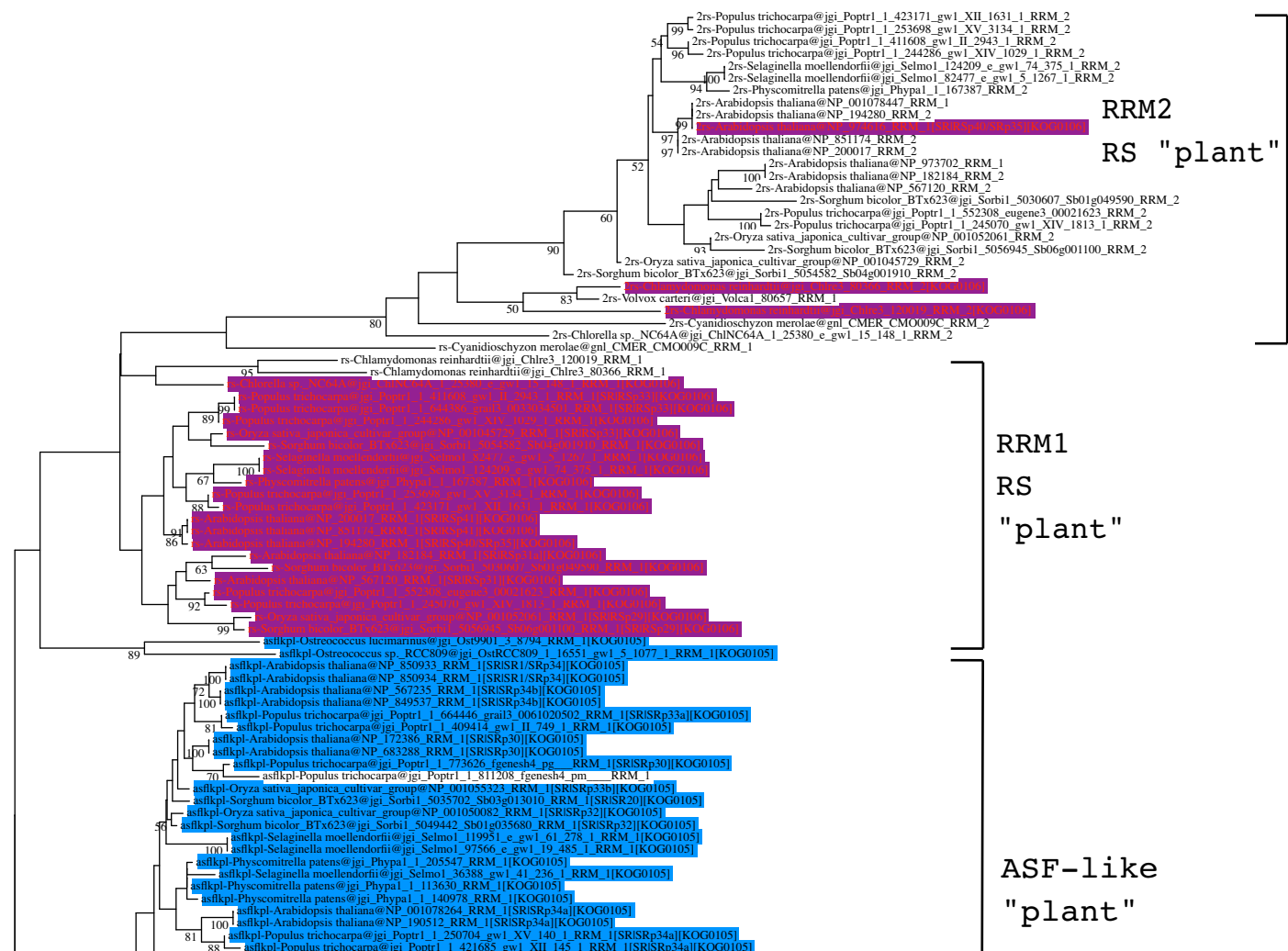
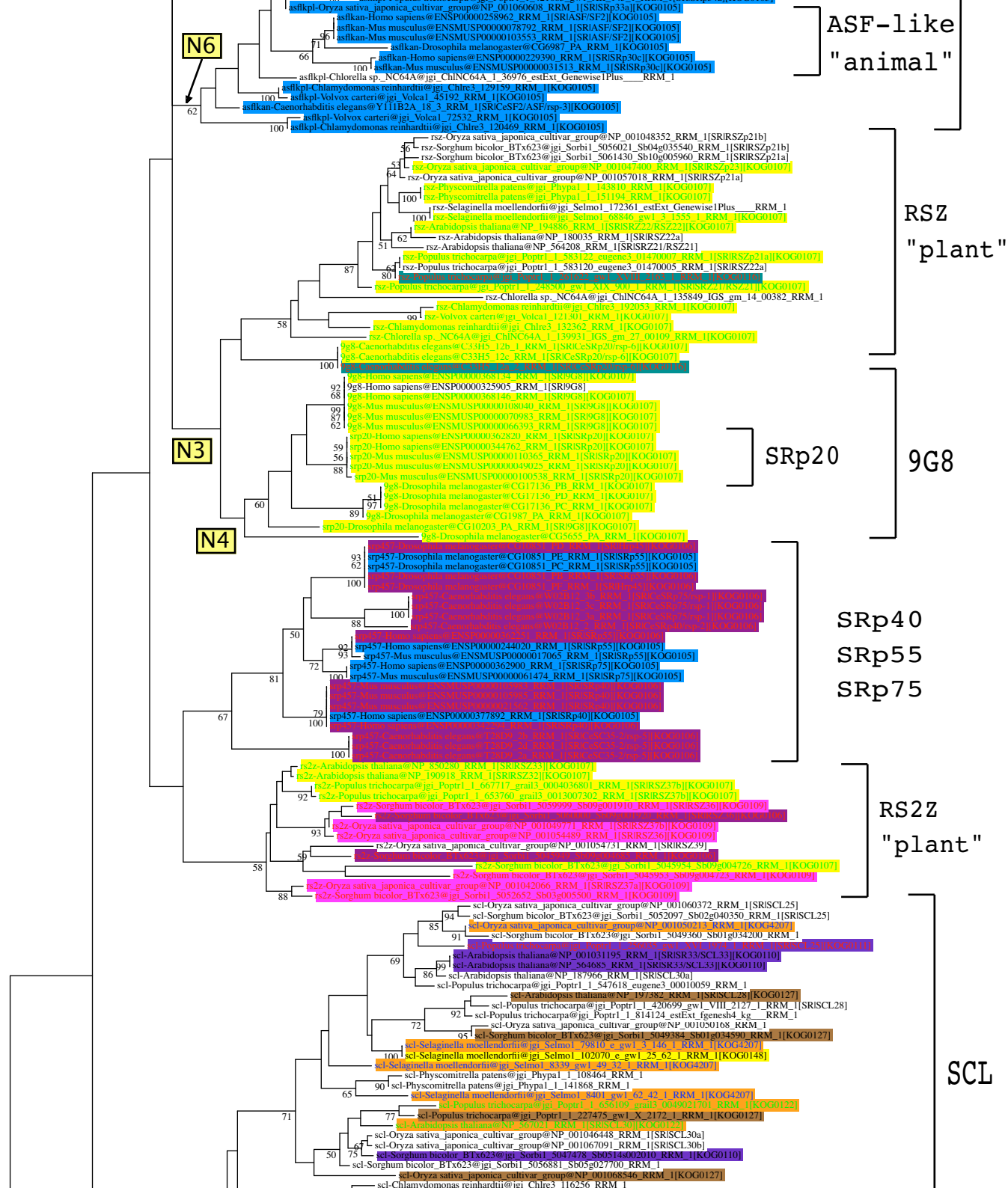


Fig. S27



Phylogenetic tree of the SR protein family, showing relationships between various species and their corresponding SR proteins. The tree is rooted at the bottom left and branches upwards. Major clades are labeled on the right: SRrp (top), SC35 (middle), SR45 (lower middle), and RNPS1 (bottom). Bootstrap values are shown at the nodes. Species names and protein IDs are listed next to the branches. Some branches are highlighted with colored boxes (green, orange, blue, purple) to indicate specific groups or relationships. A scale bar at the bottom left indicates a distance of 0.16.

SRrp

SC35

SR45

RNPS1

0.16

Fig. S28

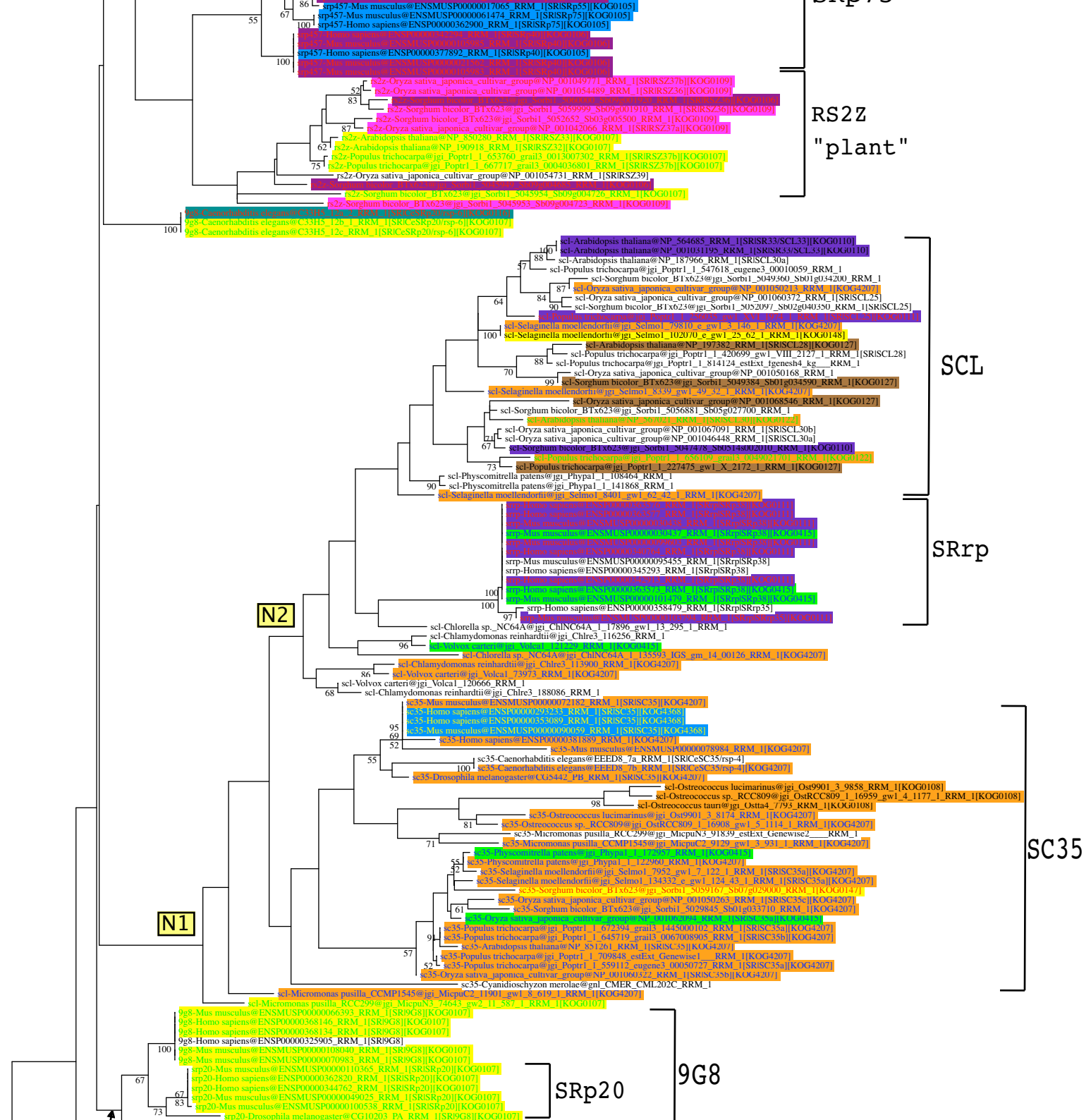


Fig. S28

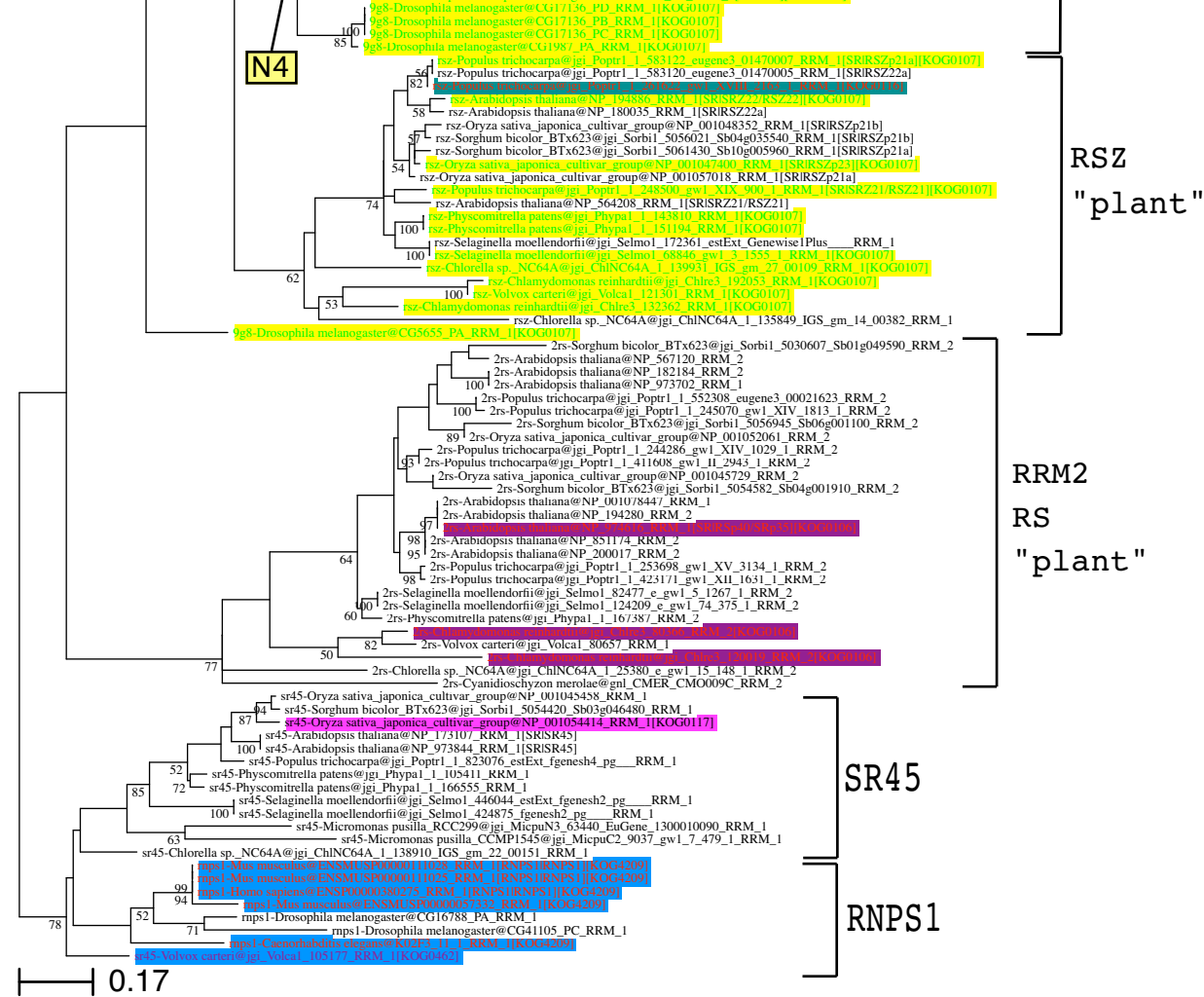


Fig. S29

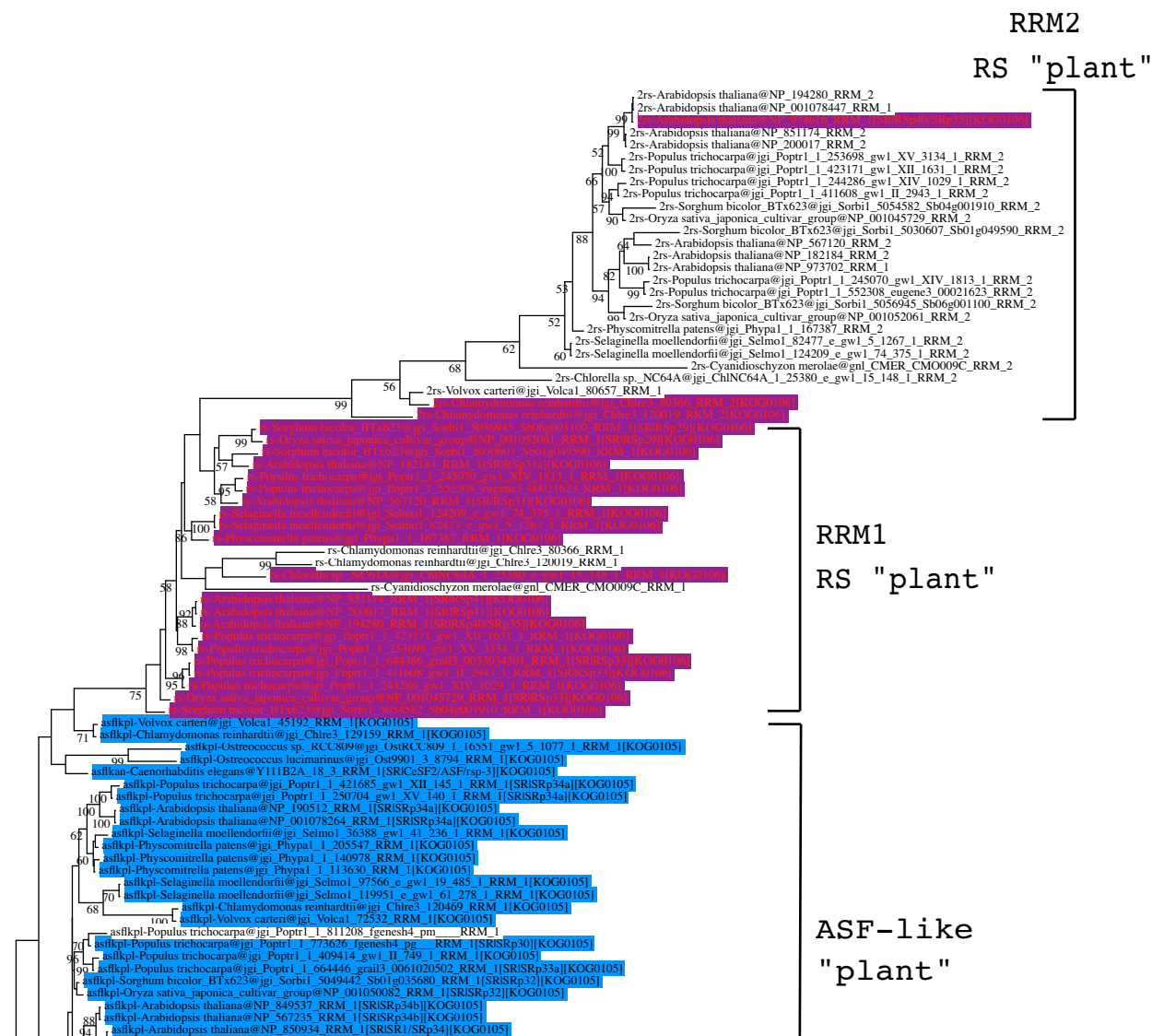


Fig. S29

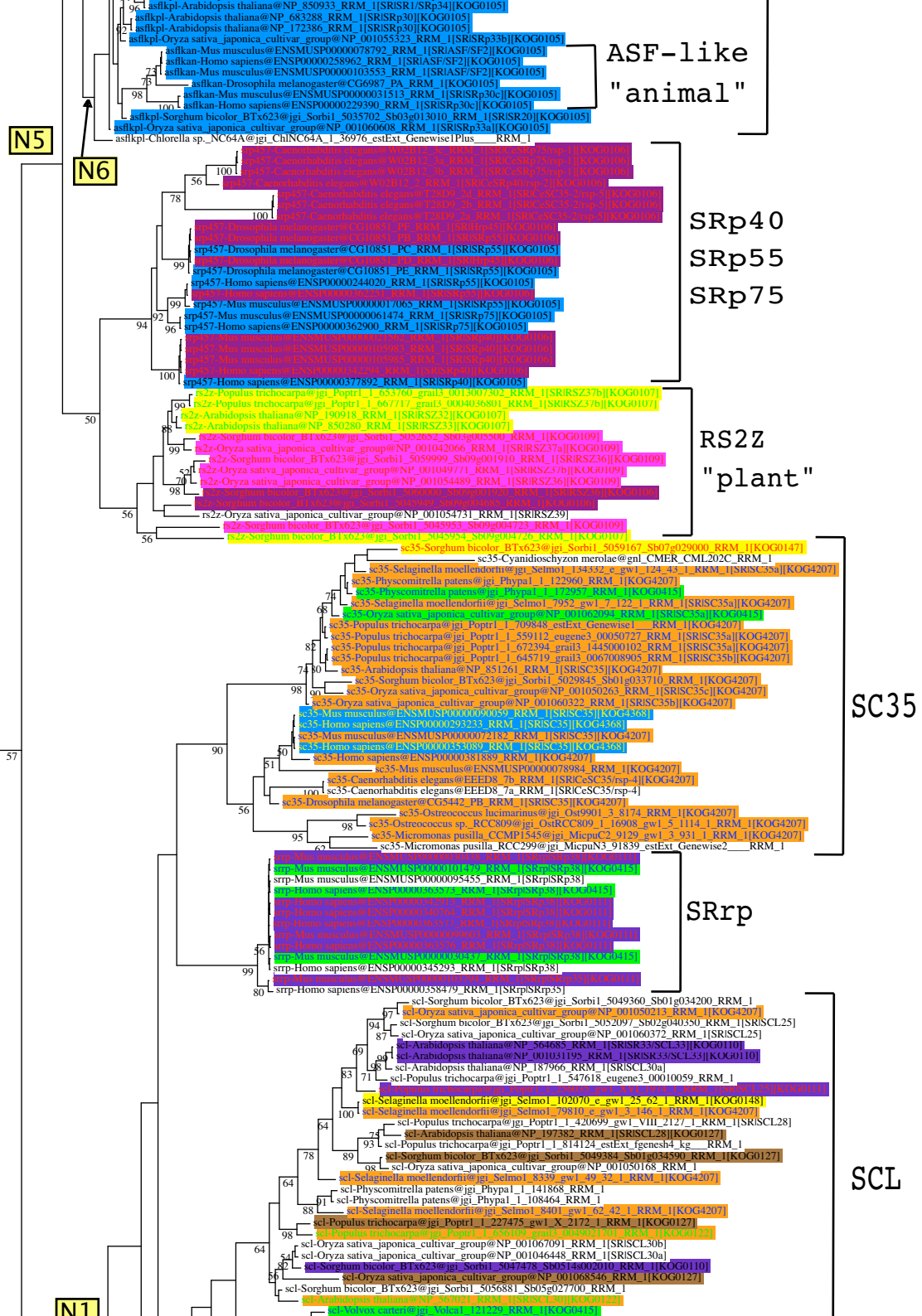


Fig. S29

