1 **Evolutionary analysis of LP3 gene family in conifers: an ASR homolog**

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Abstract

Drought has long been established as a major environmental stress for plants which have in turn developed several coping strategies, ranging from physiological to molecular mechanisms. *LP3*; a homolog of the Absciscic Acid, Stress and Ripening (*ASR*) gene was first detected in tomato; and has been shown to be present in four different isoforms in loblolly pine called *LP3-0*, *LP3-1*, *LP3-2* and *LP3-3*. While *ASR* has already been extensively studied notably in tomato, the same cannot be said of *LP3*. Like *ASR*, the different *LP3* isoforms have been shown to be upregulated in response to water deficit stress and to also act as transcription factors for genes likely involved in hexose transport. In this study we have investigated the evolutionary history of *LP3* gene family, with the aim of relating it to that of *ASR* from a phylogenetic perspective and comparing the differences in selective pressure and codon usage. Phylogenetic analyses of different *LP3* homologs compared to *ASR* show that *LP3* is less divergent across species than *ASR* and that even when comparing the different sub-sections of the gene the divergence rate of *LP3* is lower than that of *ASR*. Analysis of different gene parameters showed that there were differences in GC1% and GC2% but not in total or GC3% content. All genes had a relatively high CAI value associated with a low to moderate ENC value, which is indicative of high translation efficiency found in highly expressed genes. Analysis of codon usage also showed that *LP3* preferentially uses different codons than *ASR*. Selective pressure analysis across most of the *LP3* and *ASR* genes used in this study showed that these genes were principally undergoing purifying selection, with the exception of *LP3-3* which seems to be undergoing diversifying selection most probably due to the fact that it likely recently diverged from *LP3-0*. This study thus provides insight in how *ASR* and *LP3* have diverged from each other while remaining homologous.

Keywords: *ASR*, *ABA/WDS*, *LP3*, *drought resistance*, *pine*, *selective pressures*, *codon usage*, *GC-content*.

1. Introduction

Land colonisation by plants during the Paleozoic has forced these to adopt several adaptive strategies to survive desiccation (Edwards and Selden, 1992). These strategies led to the development of organs such as roots for taking up water and the implementation of water stress management tactics like the closure of stomata and the modulation of osmotic pressures within the plant cell in an effort to maintain the plants' water potential (Chaves et al., 2003). Today, many plants species have adapted to be able to cope with drought through millennia of evolution, yet anthropogenic climate change is expected to dramatically affect the growth conditions of most plant species, notably through increased drought occurrence and aridity around the world.

Drought is a major hazard to the survival and development of commercially important plants, from both crops to forest tree species. In recent years, there has been an observed increase in drought occurrences notably in southern Europe, sub-Saharan Africa and many other areas around the world and this trend will only increase with time as climate change continues to progress (Gudmundsson and Seneviratne, 2016; Ruosteenoja et al., 2018). In this context, it is more important than ever to understand more about the mechanisms by which plants adapt and overcome water deficit stress in an effort to potentially produce more drought resistant varieties.

Water deficiency as a major stress for plant species is detected in many ways, with the signalling component being mediated largely through the phytohormone Absciscic acid (ABA) which is involved in stress response in plants, notably via its' effects on gene expression and osmotic pressure adjustment within the plant cell (Bray, 1993). ABA is also implicated in the plant response to cold stress and the ripening process. The ABA dependent pathway has been the focus of extensive studies in a multitude of species, notably *Arabidopsis thaliana* L. and *Populus tremula* L.

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61 Since the 1990s several research projects have focused on a drought responsive gene called
62 ABA, Stress and Ripening (*ASR*), first detected in tomato leaves yet remarkably absent from
63 *Arabidopsis thaliana* (Iusem et al., 1993). This research has led to the discovery of many
64 different *ASR* orthologues and paralogs, with tomato having five different *ASR* genes, and rice
65 up to six to date (Dominguez and Carrari, 2015; Frankel et al., 2006). *ASR1* in tomato has by
66 far been the most studied *ASR* gene in tomato. Transgenic expression of the *ASR* gene in
67 *Arabidopsis* produced a phenotype similar to what is observed in *abi4* mutants in addition to an
68 increased tolerance to salt, cold and other stresses (González and Iusem, 2014; Yang et al.,
69 2005).

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71 The *ASR* gene family contains a highly conserved midsection gene domain called the
72 ABA/WDS domain (Pfam reference: PF02496), which is also highly conserved in *LP3*. The
73 ABA/WDS domain is also expressed in mushrooms of the *Fomitopsis* genus, a membrane
74 protein of *Pseudomonas* and angiotensin found in fern (Wang et al., 2002; Padmanabhan et al.,
75 1997; González and Iusem, 2014). *ASR* in its native state is a disorganised, highly hydrophilic
76 protein that requires two zinc ions to bind to lysine located in its N-terminal region to adopt its
77 functional conformation, which leads to a protein dimerization and in turn bind to the plants'
78 DNA sequence (Goldgur et al., 2007; González and Iusem, 2014). *ASR* proteins act as
79 transcription factors that induce the expression of aquaporins, cellulose synthases (*CESA*) and
80 glucanases. *ASR1*, the most studied of the *ASR* genes, is for example involved in sugar
81 metabolism in response to drought (Dominguez and Carrari, 2015).

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83 An *ASR* homolog called *LP3* was first discovered in the roots of loblolly pine (*Pinus taeda* L.)
84 whose background constitutive expression was significantly upregulated in drought conditions

(González and Iusem, 2014; Padmanabhan et al., 1997; Wang et al., 2002). For the purposes of this study, while both genes are homologous, the terms *LP3* and *ASR* will be used to describe the gymnosperm and angiosperm sequences, respectively. *LP3* differs from *ASR* in that it contains a consequent insertion of 35 amino acids between its N-terminal and ABA/WDS regions and is present as a gene family (each individual gene isoform is called *LP3*-0, *LP3*-1, *LP3*-2 and *LP3*-3; *LP3*-2 and *LP3*-3 have only been partially sequenced therefore only partial sequences are available) within pines and other gymnosperms (Chang et al., 1996; Padmanabhan et al., 1997). *LP3* transport into the nucleus is mediated by the putative C-terminal Nuclear Localisation Signal (NLS) of sequence KKESEKEEKEAEGKKHHH (Padmanabhan et al., 1997; Wang et al., 2002). Alternatively, this NLS sequence might not be necessary due to the short size of the *LP3* protein which should allow it to diffuse through the nuclear envelope. Indeed research into *ASR* has shown that the NLS sequence to the one described above is not necessary for the *ASR* protein to diffuse into the nucleus (Ricardi et al., 2012). *LP3* has not been as extensively studied as *ASR*, probably due to the difficulty of genetic studies within gymnosperms. This lack of study is the motivation for this study.

The objective of this research work is to investigate and compare the rate and mode of evolution of two orthologous genes *LP3* and *ASR* genes. To achieve our objective we have conducted the following actions: We have (i) retraced the phylogeny of *LP3* as a member of the ABA/WDS family and relate it to the *ASR* genes, (ii) estimated the GC content and Codon Usage Bias (CUB), and (iii) determined the mode of evolution of different subsections of the *ASR/LP3* genes.

2. Materials and Methods

2.1 Identification of LP3 and ASR genes

Loblolly pine LP3-0, LP3-1, LP3-2 and LP3-3 CDSs were downloaded from NCBI (*Padmanabhan et al., 1997*). Homologous angiosperm ASR and where possible gymnosperm LP3 whole gene CDSs were then extracted from NCBI using these sequences as queries via BLASTN in the NCBI database (*Boratyn et al., 2013*) with an e-value of 10^{-10} as a threshold. More complete gymnosperm homologous sequences were also extracted via BLASTN in the Gymno Plaza database(v1.0) (*Altschul, 1997*). For naming sequences in the instances where the gymnosperm sequences were uncharacterized, comparison with loblolly pine LP3 sequences via the NEEDLE alignment tool were done and whichever alignment had the highest score was used to determine to which isoform the uncharacterized sequence was most likely to be orthologous. Those sequences were then number as LP3-0-1, LP3-0-2, LP3-0-3 etc. according to the species. Since LP3 and ASR are members of the ABA/WDS induced protein superfamily (*Chang et al., 1996; González and Iusem, 2014; Padmanabhan et al., 1997*) care was taken to ensure that all sequences retrieved contained the ABA/WDS domain using PFAM v.31 (*Bateman and Finn, 2007; Mistry et al., 2007; Schaeffer et al., 2017*). Sequence names and accession numbers used in phylogenetic tree reconstruction according to species is shown in the Supplementary Table 1. Supplementary Table 2 represents majorly represented species in which three or more ABA/WDS genes are present and its use is further detailed in section 2.3.

2.2 Phylogenetic analysis

The phylogenetic history of LP3 and ASR was determined using MEGA X (Kumar et al., 2018). Firstly, this was done by looking at the whole nucleotide sequences, then by looking only at the conserved ABA/WDS region of the sequences, the conserved N-terminal zinc binding region before the gymnosperm insertion, and then finally by looking only at the variable C-terminal NLS/DNA binding region of the sequences, producing a total of four different trees called

FullSeq-tree, ABA/WDS-tree, N-tree and C-tree, respectively. The taxonomic phylogenetic tree was constructed using the Timetree software (Kumar et al., 2017).

For FullSeq-tree, sequences were aligned using the MUSCLE algorithm (Edgar, 2004), checked for errors and the multiple sequence alignment was exported for further analysis. The Maximum Likelihood (ML) Phylogenetic best fit model was determined in MEGA X by log-likelihood analysis of each model and the one with the highest AICc score was used. The resulting best fit model for the sequences used in tree FullSeq-tree was the Kimura 2 parameter model. The phylogenetic tree was created using the Maximum likelihood method combined with the Kimura 2 parameter model with a gamma parameter of 1, 30 with 1000 permutations.

ABA/WDS-tree was constructed by isolating the highly conserved ABA/WDS nucleotide domains from the MSA of *LP3* and *ASR* and exporting those for phylogenetic analysis. The ML phylogenetic model was determined in the same manner as previously described, with the resulting best model by log-likelihood analysis being the Kimura 2 parameter model. The tree was constructed using the ML method with the Kimura 2 parameter with a Gamma parameter equal to 1,0846 with 1000 permutations.

Tree N-tree was constructed by extracting the N-terminal nucleotide region of *LP3* and *ASR*. Due to the presence of incomplete sequences that did not cover this section of the gene, the following sequences were excluded from the phylogenetic analysis: *LP3-0 Cupressus sempervirens*; *LP3-1 Pinus sylvestris*; *LP3-1 Pinus hwangshenensis*; *LP3-0 Pinus massoniana*; *LP3-2 Pinus taeda*; *LP3-2 Pinus sylvestris* and all *LP3-3* sequences. The ML phylogenetic model was determined in the same manner as previously described, with the resulting best model by log-likelihood analysis result being the Kimura 2 parameter model. The

tree was therefore constructed using the ML method with the Kimura 2 parameter model with a gamma parameter equal to 1, 27 with 1000 permutations.

Tree C-tree was constructed by focusing on the C-terminal NLS/DNA binding regions of the sequences. The ML phylogenetic model was determined in the same manner as previously described, with the resulting best model by log-likelihood analysis result being the Kimura 2 parameter model. The following partial sequences were excluded from the phylogenetic analysis due to too short C-terminal sequences: *LP3-0 Cupressus sempervirens*, *LP3-0 Pinus massoniana*; *LP3-2 Pinus taeda*; *LP3-2 Pinus sylvestris* and all *LP3-3* sequences. The tree was therefore constructed using the ML method with the Kimura 2 parameter model with a gamma parameter equal to 1, 5588 with 1000 permutations. Analysis of gene duplication events and construction of the corresponding gene duplication tree was also carried out in MEGA X, using FullSeq-tree as a template on which to perform the analysis.

2.3 GC% and RCU analyses

Sequence names and accession numbers for determining GC and RCU content according to species are shown in the Supplementary Table 2

The Relative Synonymous Codon Usage (RCU) is a measure of the codon usage bias for a particular amino acid. As such codon bias is can be a measure of how efficient and accurate a given gene translation is. The RCU of the ABA/WDS genes found in majorly represented species (species in which at least three different ABA/WDS genes are present) was extracted using MEGA X. The average RCU values per amino acid were then calculated and used to determine which codon was on average the most used in a particular gene. Codons with RCU values above 1 are abundant, whilst codons with RCU values below 1 are less abundant. Codons for Methionine and Tryptophane were not included since these amino acids are encoded

by only one codon. Stop codons were not included either as they are only involved in transcription termination and therefore not in transcription efficiency.

Individual gene parameters from majorly represented species such as total GC, GC1, GC2, GC3 contents, Codon Adaptive Index (CAI), and Effective Number of Nucleotides (ENC) were computed using CAIcal (<http://genomes.urv.cat/CAIcal/>). The CAI is derived from the codon usage of highly expressed genes in organisms and is positively correlated with transcription levels. As such the CAI is often used as a proxy for expression levels (Sharp and Li, 1987). The ENC is a number corresponding to the overall codon bias in a given gene, with 20 symbolising a complete bias of only one codon per amino acid whereas a value of 61 symbolises a completely unbiased codon usage, with each available codon being used equally for a given amino acid (Wright, 1990). Statistical analyses were done in R using $p=0.05$ as the significance threshold. Gene parameters were first compared using a Levene test to ensure variance equality among the different genes, followed by either ANOVA or a Kruskal-Wallis test. If either of these indicated the presence of a significantly different group then a Tukey HSD test was performed in the case of ANOVA and a pairwise Wilcoxon test in the case of a Kruskal-Wallis. Pearson correlations between the different gene parameters were also done. For this the different ASR and LP3 genes were grouped together.

2.4 Mode of evolution of different subsections of the ASR/LP3 gene

A codon-by-codon selective pressure analysis provides insights into which amino acids in a protein are undergoing selective constraints or not. This in turn allows one to suggest which amino acids are likely to change over time. Visualisation of codon selective pressure as defined by the ratio of synonymous to non-synonymous codons $\omega = dN/dS$ on the *LP3-0* gene was done using the complete CDS of all *LP3-0* homologous sequences were uploaded to the Selecton server for selective pressure analysis using the M8 model that allows for positive

selection (Stern et al., 2007). The sequences were aligned in the server using the MUSCLE algorithm (Edgar, 2004) and the *Pinus taeda* LP3-0 CDS was set as the reference query. Statistical analysis of the calculated selective pressure was also performed using Selecton with default settings by calculating the log likelihood ratio between M8 and the null model M8a. The same procedure was repeated for LP3-1, LP3-3, ASR1, ASR2, ASR3 and ASR4. *P.taeda* LP3 and *S. lycopersicum* ASR sequences were set as references on which to visualise sites of selective pressure. There were not enough LP3-2 orthologous sequences for this analysis to be performed on it.

3. Results

3.1 Phylogenetic analysis of LP3 and ASR

On a broad level, it can be seen that LP3-1 is the most ancestral form of LP3, from which LP3-2 diverged, followed by LP3-0 and LP3-3. The ASR gene phylogeny show that ASR4 is the ancestral sequence in tomato, followed by ASR3, being ASR2 and ASR1 the result of are more recent diverge event (Figure 1). The clear distinction between the ASR and LP3 seems to

correlate with the divergence of angiosperms and gymnosperms, around 313 MYA (Supplementary Figure 1, www.timetree.org).

Figure 1: Phylogenetic tree of *Pinus taeda* LP3 and *Solanum lycopersicum* ASR sequences.

FullSeq-tree (Figure 2) shows that there is a clear divergence between the angiosperm ASR and the gymnosperm LP3 sequences. This could be to certain extent be attributed to the sequence insertion present between the N-terminal zinc binding domain and ABA/WDS regions in gymnosperm. Low bootstrap values within the gymnosperm nodes could be explained by the general high similitude between sequences which would result in them easily swapping positions during different bootstrap analyses. It can be observed that the LP3 sequences cluster together according to genus and isoform. There is also perfect clustering of LP3-1 and LP3-2 sequences within the *Pinus* cluster, however this is not the case when observing the LP3-3 cluster. In that instance, clustering of LP3-3 occurs with LP3-0-2 and LP3-0-3 of *Pinus sylvestris*. This might be indicative of orthology between LP3-3 and the *Pinus sylvestris* sequences shown. The grouping together of *Pinus taeda* LP3-3 and *Pinus taeda* LP3-0-2 with a very high bootstrap score could suggest that LP3-0-2 (PITA_00002958) might be actually a complete sequence of LP3-3. In *Picea* most of the sequences were annotated as LP3-0, except

243 one sequence that was annotated as LP3-1 (MA45729). No *LP3-2* and *LP3-3* were available.

244 The *ASR* sequences also show clear clustering together of *ASR1*, *ASR2* and *ASR3* sequences.

245 The *ASR1* of *Oryza sativa*, *ASR3* of *Zea mays*, *ASR2* of *Vitis vinifera* and *ASR3* of *Populus*

246 *trichocarpa* show signs of divergence from the other *ASR* sequences. There are big genetic

247 distances between the different *ASR* clusters, indicative of substantial divergence between the

248 *ASR* genes in the angiosperms.

Figure 2: FullSeq-tree corresponding to the entirety of available CDS of ASR/LP3 sequences. Constructed in MEGAX using the ML method and the K2 model + gamma =1,2882. Genetic distance is given in number of substitutions per site. Bootstrap values are

Looking at ABA/WDS-tree (Figure 3) which focuses on the central ABA/WDS domain, there is yet again another clear grouping of angiosperm and gymnosperm sequences together. Within the gymnosperm grouping one can observe the sub-grouping of *LP3-1* and *LP3-2* together, while similarly to FullSeq-tree, the *LP3-3* sequences are again broadly grouped together with some *LP3-0* sequences grouped alongside them. The angiosperm sequences also show clear clustering of *ASR1*, *ASR2* and *ASR3* sequences with the *Oriza sativa ASR1* and *Zea mays ASR3* seeming to diverge from the other *ASR* sequences. As in FullSeq-tree, there is also a clear clustering according to genus, with *Picea* and *Pinus* sequences clustering together, respectively.

Figure 3: ABA/WDS-tree focusing on the conserved ABA/WDS domain within each gene. Constructed in MEGAX using the ML method and the K2 model with gamma=1,0846. Genetic distances are in number of substitutions per site. Bootstrap values are shown next to each node

N-tree focuses on the N-terminal region of *ASR* and *LP3*, to which zinc ions are theorised to bind (Figure 4), here it can be observed that there is not a definite separation between angiosperm and gymnosperm sequences, with *ASR2* from *Vitis vinifera* and *ASR4* from *Solanum tuberosum* being the most divergent sequences when focusing on the N-terminal region. *LP3-1* sequences in *Pinus* formed a different cluster although with low support. After this node, *ASR* and *LP3* sequences mostly segregate according to their order. Like the trees previously analysed, the *ASR* sequences cluster according to *ASR1*, *ASR2* and *ASR3*, with the *Oriza sativa ASR1* and *Zea mays ASR3* diverging together. In contrast to previous trees, there is a less clear clustering of *LP3* sequences according to genus. There remains however a very short genetic distance between each of the *LP3* sequences, indicative yet again of a high level of conservation between the sequences.

Figure 4: N-tree focusing on N-terminal of ASR and LP3 genes. Constructed with MEGAX and using the ML method and K2 model with gamma =1,3701. Genetic distances are in number of substitutions per site. Bootstrap values are shown next to each node.

C-tree, which focuses on the variable C-terminal regions of ASR and LP3 which contains the NLS/DNA binding domain (Figure 5), again shows partial segregation of ASR and LP3 sequences. Here the tree is rooted by the ASR4 of *Solanum tuberosum*, LP3-0-3 *Pinus pinaster* and *Picea abies* LP3-0-2 and LP3-0-3 sequences, indicative that these sequences are the most divergent in the C-terminal NLS region. Subsequently, the ASR and LP3 sequences do segregate according to their order (similar to what can be observed for the other trees). Within the ASR cluster the ASR1, ASR2 and ASR3 groups show low genetic distances, which suggests that the C-terminal region of those sequences are well conserved. The LP3 C-terminal sequences also do not show much divergence between them as seen by the small genetic distances between the sequences. The exception are LP3-0-3, LP3-0-4 and LP3-0-2 sequences of *Picea abies*, which show a high level of divergence from the other LP3 sequences. The segregation within the LP3 sequences showed a similar clustering mostly according to the genus.

Figure 5: C-tree focusing on the C-terminal region of ASR and LP3 genes. Constructed with MEGA X and using the ML method with K2 model and gamma= 1,5588. Genetic distances are in number of substitutions per site. Bootstrap values are shown next to each node

3.2 Gene parameters and RSCU analyses

There appear to be differences in average preferential codon usage between the different ABA/WDS genes (Table 1, Figure 6). Both LP3_0 and LP3_3 have the same most highly used codon AGG, encoding arginine, at RSCU values 3,71 and 6 respectively. LP3-2 and ASR2 both preferentially use CCA, encoding proline, at RSCU values 4 and 2,77 respectively. Furthermore, ASR2 has a second codon AGC, encoding serine, at RSCU 2,77. LP3_1, ASR3 and ASR4 have all got codons encoding for serine as their most used codons with codons UGC, AGC and AGU at RSCU values 3,86 , 3,27 and 2,8 respectively. There were similarities in least used codons, such as the arginine encoding CGG and leucine encoding CUA.

Gene	AA	Codon	RSCU
ASR1	Leucine	CUC	2,63
ASR2	Proline, Serine	CCA, AGC	2,77
ASR3	Serine	AGC	3,27
ASR4	Serine	AGU	2,8
LP3_0	Arginine	AGG	3,71
LP3_1	Serine	UGC	3,86
LP3_2	Proline	CCA	4
LP3_3	Arginine	AGG	6

Table 1: Average most used codon in ABA/WDS genes.

Figure 6: Heatmap of average codon usage per ABA/WDS genes. Codons separated according to whether they are AU or GC ended. Average codon usage above 1,5 are indicated in red while codon usage lower than 0,5 are indicated in blue. Produced in R.

In all cases, the average GC2% of the ABA/WDS genes was lower than both average GC1% and GC3%. With the exception of ASR1, all ABA/WDS genes had on average higher GC1% than GC3% (Table 2). Levene test results showed that only GC1 and GC2 respected the equal variance among groups assumption for ANOVA ($p > 0,05$). Total GC, GC3, ENC and CAI were thus tested using a Kruskal-Wallis test. GC1, GC2 and CAI had significant differences between the ABA/WDS genes ($p < 0,05$) whereas total GC, GC3 and ENC showed no significant difference between the ABA/WDS genes ($p > 0,05$).

Gene	Length(bp)	CAI	GC%tot	GC1%	GC2%	GC3%	ENC
ASR1	323,25	0,8428	56,825	71,25	27,2	72,05	44,775
ASR2	336	0,852	55,9	69,125	31,8	66,7	37,725
ASR3	337,5	0,866	56,425	69,05	33,1	67,175	41,9
ASR4	629	0,8217	43,46666667	56,5	36,6	37,33333333	50,03333333
LP3_0	435,7	0,8472	50,69333333	64,76333333	30,43666667	56,89	51,02333333
LP3_1	300,75	0,8528	51,25	68,975	27,875	56,975	42,4
LP3_2	306	0,8435	51,6	71,95	29,35	53,5	53,9
LP3_3	272	0,9073	52,83333333	67,73333333	35,43333333	55,43333333	37,33333333

Table 2: Average gene parameters of ABA/WDS genes.

Analysis of GC1 (Figure 7) suggests that on average ASR1 and LP3_2 have a higher GC1% than LP3_0, which itself has a higher GC1% than ASR4. ASR2, ASR3, LP3_1 and LP3_3 do not have significantly different GC1% from ASR1, LP3_2 and LP3_0.

Figure 7: Comparison of the average GC1% per ABA/WDS gene, done in R, using a one-way ANOVA followed by Tukey HSD test.

Analysis of GC2% (Figure 8) suggests that ASR4 has on average a significantly higher GC2% than ASR1, LP3_0, LP3_1 and LP3_2. In turn, this analysis suggests that on average LP3_3 has a significantly higher GC2% than LP3_0. By contrast, ASR2, ASR3 and LP3_2 do not appear to have significantly different GC2% from each other.

336

337 Figure 8: Comparison of the average GC2% per ABA/WDS gene, done in R, using a one-way ANOVA followed
 338 by Tukey HSD test.

339 There is also variation in the average CAI of ABA/WDS genes between the different majorly
 340 represented species (Figure 9). *Picea abies*, *Picea glauca*, *Populus trichocarpa*, *Solanum*
 341 *lycopersicum* and *Solanum tuberosum* have similar CAI levels to each other and are
 342 significantly lower than *Oryza sativa*, *Picea sitchensis*, *Pinus pinaster*, *Pinus sylvestris*, *Pinus*
 343 *taeda* and *Zea mays*. *Oryza sativa* appears to have a significantly higher CAI than all other
 344 species apart from *Picea sitchensis*, *Pinus pinaster* and *Zea mays*. Finally, *Pinus sylvestris*
 345 appears to have a significantly lower average CAI than *Pinus pinaster*, *Zea mays* and *Oryza*
 346 *sativa*, but is significantly higher on average than *Picea abies*, *Picea glauca*, *Populus*
 347 *trichocarpa*, *Solanum lycopersicum* and *Solanum tuberosum* yet is not significantly different
 348 from *Picea sitchensis* and *Pinus taeda*.

Figure 9: CAI per species of the ABA/WDS genes obtained from the values of majorly represented species, done in R, using a Kruskal-Wallis test followed by a pairwise Wilcoxon test.

Significant correlations were found between the different gene parameters in ASR and LP3 (Table 3; Table 4). In both ASR and LP3, gene length was negatively correlated with total GC%, GC1% and positively correlated with ENC. CAI was positively correlated with total GC% and GC3% in ASR and was positively correlated with GC1%. CAI was also negatively correlated with ENC in both cases. Total GC% was in turn positively correlated with GC1% and GC3% in both ASR and LP3 genes however total GC% was correlated with ENC in ASR only. GC1% was negatively correlated with GC2% in both ASR and LP3 and positively correlated with GC3% in ASR only. GC3% was negatively correlated with ENC in ASR but displayed no significant correlation with ENC in LP3.

	Length	CAI	GC_tot	GC_one	GC_two	GC_three	ENC
Length		0.5806	0.0413	0.0000	0.0294	0.0602	0.5827
CAI	-0.14		0.0001	0.4982	0.1384	0.0000	0.0000
GC_tot	-0.50	0.80		0.0182	0.5516	0.0000	0.0000
GC_one	-0.89	0.18	0.56		0.0048	0.0263	0.4806
GC_two	0.53	0.37	0.16	-0.65		0.5729	0.0572
GC_three	-0.46	0.81	1.00	0.54	0.15		0.0000

ENC | 0.14 **-0.90** **-0.84** -0.18 -0.47 **-0.84**
 Table 3: Pearson correlation matrix of ASR genes. Correlation values indicated below diagonal and p-values indicated above diagonal. Significant correlations shown in bold.

	Length	CAI	GC_tot	GC_one	GC_two	GC_three	ENC
Length		0.5357	0.0284	0.0020	0.7432	0.6149	0.0018
CAI	-0.10		0.1385	0.0431	0.7252	0.6568	0.0004
GC_tot	-0.35	0.24		0.0000	0.8198	0.0000	0.3053
GC_one	-0.48	0.33	0.58		0.0110	0.9112	0.1220
GC_two	-0.05	0.06	0.04	-0.40		0.1903	0.5746
GC_three	0.08	-0.07	0.65	-0.02	-0.21		0.5214
ENC	0.48	-0.54	-0.17	-0.25	-0.09	0.11	

Table 4 Pearson correlation matrix of LP3 genes. Correlation values indicated below diagonal and p-values indicated above diagonal. Significant correlations shown in bold.

3.3 Mode of evolution of different subsections of the ASR/LP3 gene

The reference sequences of *LP3-0*, *LP3-1*, *ASR1*, *ASR2*, *ASR3* and *ASR4* show signs of purifying selection, mainly focused on K, H and E residues, and no sites of positive selection (Figure 10, Figure 11, Figure 13, Figure 14, Figure 15, Figure 16; Supplementary Table 3,4,6,7,8,9). In contrast, *LP3-3* presents signs of positive selection on residues N, S and T at positions 34, 37 and 61, respectively (Figure 12,). These residues tend to turn into E, T and A, respectively (w-values = 2,8; 2,9; 2,9; p-values= 2, 1×10^{-14} ; 1, 2×10^{-19} ; 1, 4×10^{-19} , Supplementary Table 5). On average, the ABA/WDS genes investigated here are all undergoing purifying selection, and all tend to similar amino acid sequences and codon usage as shown by the low Ka/Ks values between gene pairs (Table 5).

		LP3-0	LP3-1	LP3-2	LP3-3
U67135	LP3-0				
U52865	LP3-1	0.21			
U59451	LP3-2	0.74	0.53		
U59424	LP3-3	0.35	0.28	0.74	

		ASR1	ASR2	ASR3	ASR4
NM001247208	ASR1				
NM001320991	ASR2	0.15			
NM001309371	ASR3	0.25	0.06		
NM001282319	ASR4	0.16	0.10	0.21	

Table 5: 1 Ka/Ks estimates between (a) LP3 genes in *Pinus taeda*, and (b) ASR genes in tomato.

Legend:

The selection scale:

Positive selection Purifying selection

Figure 10: Selective pressures on LP3-0. Yellow colours indicate sites of positive/diversifying selection; purple colours indicate sites of purifying selection. Figure produced using Selecton.

Legend:

The selection scale:

Positive selection Purifying selection

Figure 11: Selective pressures on LP3-1. Yellow colours indicate sites of positive/diversifying selection; purple colours indicate sites of purifying selection. Figure produced using Selecton.

Legend:

The selection scale:

Positive selection Purifying selection

Figure 12: Selective pressures on LP3-3. Yellow colours indicate sites of positive/diversifying selection; purple colours indicate sites of purifying selection. Figure produced using Selecton.

1 11 21 31 41
M E E E K H H H H L F H K D K A E E G P V D Y E K E I K H H K H L E Q I G K L G T V A A G A Y A
51 61 71 81 91
L H E K H E A K K D P E H A H K H K I E E E I A A A A V G A G G F A F H H H E K K D A K K E E K
101
K A E G G H H H L F

Legend:

The selection scale:

Figure 13: Selective pressures on ASR1. Yellow colours indicate sites of positive/diversifying selection; purple colours indicate sites of purifying selection. Figure produced using Selecton.

1 11 21 31 41
M A E E K H Q H H H L F H H K N K E D E G G P V D Y E K E V H H S H L E K I G E L G A V A A G A
51 61 71 81 91
L A L H E K H K A K K D P E H A H K H K I E E E I A A V A A V G A G G F A F H H H H Q K K D A K K E
101 111
K K E V E G G H H H H H H Y

Legend:

The selection scale:

Figure 14: Selective pressures on ASR2. Yellow colours indicate sites of positive/diversifying selection; purple colours indicate sites of purifying selection. Figure produced using Selecton.

1 11 21 31 41
M A E E K Q H H R L F H H K N R E E G G P V D H K K V K H H S H L Q K I G E L G A V A A G A Y A
51 61 71 81 91
L H E K H K A K K D P E N A H K H K I K Q E I A A V A A V G A G G F A F H H H Q K K E A K K E K K
101
A A E K G R H H

Legend:

The selection scale:

Figure 15: Selective pressures on ASR3. Yellow colours indicate sites of positive/diversifying selection; purple colours indicate sites of purifying selection. Figure produced using Selecton.

```

1      11      21      31      41
MAEEKKHHFG GLFNHHKNKE EDTPIEKTTY EETTYEDSEK TSTYGDNTYG
51     61     71     81     91
EKTSYGDDTY GKKTTTYGDD NKYSEKTSYG DDTYDEKNT YGDENKYGEK
101    111    121    131    141
TSYSEGGDNK YGEKTSYGGD TYGEKPTSYG GDNTYGEKTS YGGGDENKYG
151    161    171    181    191
EKTSYGEKAS YGGGDDNKYG EKTSYGNEEG GYGGGVGAYS SETTTNYEEN
201    211    221    231    241
DDSGTKTSE D YKEEKKEKKH LLELGGLGAV AAGAFALHEK HKAEEKDEEHA
251    261    271    281    291
HKKKIEEEIA AVAAVGAGEE AEEHHHQQKE AKEEEEAEK KKKHEEE

```

Legend:

The selection scale:

Figure 16: Selective pressures on ASR4. Yellow colours indicate sites of positive/diversifying selection; purple colours indicate sites of purifying selection. Figure produced using Selecton.

4. Discussion

4.1 LP3 genes are less divergent than ASR genes

While there is ample evidence that *ASR* and *LP3* belong to the same gene family (González and Iusem, 2014), it is quite interesting that the nucleotide phylogeny reveals a clear segregation between the gymnosperm and angiosperm sequences, even within a highly conserved domain like the ABA/WDS domain. The separation between *LP3* and *ASR* sequences are consistent with previous phylogenetic knowledge that angiosperms and gymnosperms diverged around 313 MYA (Barbara-Montoya et al 2018), between the Pennsylvanian and Permian periods, thereby giving the *ASR* and *LP3* genes within both orders ample time to diverge (Hedges et al., 2015; Kumar et al., 2017).

The FullSeq-tree is corroborated by a previous study on *ASR* genes (Frankel et al., 2006). The phylogenetic analyses of different sub-sections of the *ASR/LP3* genes provide insight into the different divergence rates occurring within each of them. The ABA/WDS-tree, which focuses on the ABA/WDS subsection, shows that there is very little divergence between the *LP3* sequences, unlike the *ASR* sequences. This is indicative of a high level of similarity of the

ABA/WDS domain within *LP3* that is not seen in *ASR*. This can be explained by the action of negative selection acting on the *LP3* sequences, or that the rate of substitutions in gymnosperms is lower than in angiosperms (Palmé et al 2009; Buschiazzi et al 2012; De La Torre et al., 2017).

This low level of phylogenetic divergence within *LP3* can also generally be observed in the other two domain-based trees (N-terminal tree and C-terminal tree). The N-terminal tree focused on the putative zinc binding domains in the N-terminal region of *ASR/LP3* genes, therefore it would make sense that there is a low level of divergence occurring since *ASR/LP3* requires Zinc ions to adopt their functional conformation (Dominguez and Carrari, 2015; González and Iusem, 2014). A lack of clear segregation between *ASR* and *LP3* can also be indicative of high purifying selective pressures thereby favouring a conserved nucleotide sequence. The lack of a definite separation between angiosperm and gymnosperm sequences is another argument in support of the essential and possibly similar role of the N-terminal domain in both clades.

C-tree, which focused on the putative NLS/DNA binding region of *ASR/LP3*, reveals similar topological properties as the N-tree but with a lower support to the branches discerning the different *ASR* gene family members. Both *ASR* and *LP3* encode relatively small proteins and in the case *ASR1* it has been previously shown that it does not require its putative NLS to enter the nucleus (Ricardi et al., 2012; Rom et al., 2006). This low level of divergence might indicate that the selective pressures focusing on these parts of the genes stem mostly from their role as transcription factors. Following this reasoning, it could be suggested that the sequence corresponding to *lp3-0-3 Picea abies* targets a different gene somewhere along the genome other than the *LP3* gene family.

In all cases, it was observed that the *LP3* genes had much lower divergence between them than the *ASR* genes. This is in line with previous research that found that coniferous genes have a

low divergence rate among themselves when compared with angiosperm (Buschiazzo et al., 2012). In addition to all the individual reasons listed previously, previous transcriptomic analyses of homologous genes have shown that angiosperm genes tend to diverge much more strongly than coniferous genes (Li et al., 2010). Our phylogenetic analyses are therefore in line with previous known research.

4.2 Differences in GC1% and GC2% between genes, differences in CAI between species

While no significant difference was observed in total GC or GC3 content between the ABA/WDS genes, there were differences in the GC1 and GC2 contents between genes. In all cases the GC2 was lower than both GC1 and GC3, a pattern which has been observed in other gene analyses (Song et al., 2017, 2018). In all the major species investigated, CAI was on average highest in *Oryza sativa*, which in turn can be used to predict that ABA/WDS expression levels are highest within *Oryza sativa* (Sharp and Li, 1987). Previous research on ASR expression in rice has shown that it responds strongly to drought stress (Pérez-Díaz et al., 2014), so this high CAI is further indicative of high expression, which in turn lends credence to the other average CAI of ABA/WDS of the other investigated species being indicative of gene expression. It was interesting to see variations in CAI levels between the coniferous species, especially between the *Picea* and *Pinus* genera, with *Pinus* species exhibiting higher CAI than *Picea* (except for *Picea sitchensis*). This in turn may be indicative that the ABA/WDS expression is higher in *Pinus* than in *Picea*, although a more thorough gene expression analysis within more species of each genus is required to confirm this hypothesis.

Previous gene studies have focused on the correlations of CAI with various other factors such as gene length, GC content and ENC (Gun et al., 2018; Song et al., 2017, 2018; Zhou and Li, 2009). Our study however showed no significant correlation between sequence length and CAI. CAI is often correlated with GC3% yet this correlation was only significant when concerning ASR genes and not the LP3 genes. Instead CAI was positively correlated with GC1% in LP3,

which contrasts with previous gene studies (Gun et al., 2018; Song et al., 2017, 2018). Our study does reflect significant correlations between CAI and ENC within the ABA/WDS genes, indicative of a high translation efficiency found in many highly expressed genes (Sharp and Li, 1987; Wright, 1990)

4.3 ASR has a different codon usage than LP3

Another factor that contributes to differentiate ASR and LP3 gene families is the RSCU. Differences in codon usage were observed for several amino acids. Yet it was interesting to see that the amino acid with the highest codon bias was serine, although the individual codon with the highest bias was different among different genes. It has already been established that monocots and dicots differ in their codon usage for the homologous genes (Campbell and Gowri, 1990), therefore it is not improbable that gymnosperms would have different codon usages than angiosperms for homologous genes. Highly expressed genes have been shown to have both a more pronounced codon bias and higher overall GC content compared to lowly expressed genes (De La Torre et al., 2015; Song et al., 2017; Kuzniar et al., 2008), however no significant differences in overall average GC content between the ABA/WDS genes were observed in this study.

After gene duplication the original and new copies can go down multiple evolutionary paths (Innan, Kondrachov, 2011). While LP3-3 and LP3-0 genes have seemingly diverged recently they are affected by different modes of gene-duplication evolution. LP3-3 presents signs of positive selection on three residues and the rest are evolving either under neutral or purifying selection, whereas LP3-0 is only affected by purifying selection.

In LP3-3 those three residues (mutation) may have introduced new beneficial functional aspects to the original LP3 copy resulting in their fixation and maintenance through positive selection. This mode of gene-duplication evolution would suggest the acquisition of a novel function for LP3-3 gene. Notably purifying selection is acting on Lysine (K), Histidine (H) and Glutamate (E). LP3 and ASR, both belonging to the ABA/WDS gene family, are both highly

hydrophilic protein groups therefore the presence of charged, polar amino acids is important in attaining their functional conformations (González and Iusem, 2014; Rom et al., 2006). It has also been suggested that Zinc ions bind to lysine residues in the N-terminal region of both sets of genes, this binding being required for the proteins to finally obtain their functional conformation, thereby further explaining why mutations affecting Lysine are purified. Evidence of purifying selection can also be observed in both the ABA/WDS domain and C-terminal containing a putative NLS/DNA binding amino acid sequence, implying that both are important for the overall functioning of the genes. This is logical when considering that expressions of both *LP3* and *ASR* are upregulated in presence of ABA and that both act as transcription factors in response to water-deficit stress (Padmanabhan et al., 1997; Wang et al., 2002).

4.4 Conclusion and future perspectives

Overall, this study highly suggests that while *ASR* and *LP3* may have originated from the same common ancestor, they have undergone significant shifts in codon usage, maybe due to different evolutionary constraints. Different *ASR* genes have already been studied in depth, with *ASR1* being the most substantially studied of them. This is not the case for *LP3* for which more research opportunities are available. Further studies into *LP3* mutants could produce similar phenotypes as observed in *ASR* mutants. Precise functions and genomic targets of *LP3* could be hypothesized by homology with genes targeted by *ASR*. Precise mapping of the *LP3* genes onto the *Pinus taeda* genome should also be done. Further research could establish the presence of paralogous genes of *LP3* within *Pinus taeda* and their precise role in drought response. Since the responses of plants to cold stress are similar to their responses to drought stress, research into how *ASR* and *LP3* are affected in terms of expression and cellular function in conditions of cold stress would also be an interesting research objective. Finally, a precise expression network between *ASR/LP3* and downstream targets should be established since these have not yet been determined.

518 **Conflict of interest**

519 No conflicts of interest during the making of this study.

520

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- 636

637

Species	Sequence name	Accession number
<i>Pinus taeda</i> L.	<i>LP3-0-1; LP3-0-2; LP3-0-3; LP3-1; LP3-2; LP3-3</i>	U67135; PITA_00002958; PITA_00009264; U52865; U59451; U59424
<i>Pinus pinaster</i> Ait.	<i>LP3-0-1; LP3-0-2; LP3-0-3; LP3-03; LP3-0-4; LP3-0-5; LP3-0-6; LP3-0-7; LP3-1; LP3-3</i>	PPI00000827; PPI00033797; PPI00061525; PPI00057047; PPI00018463; PPI00045720; PPI00057443; HM483166; HM483350
<i>Pinus sylvestris</i> L.	<i>LP3-0-1; LP3-0-2; LP3-0-3; LP3-03; LP3-0-4; LP3-0-5; LP3-1; LP3-2; LP3-3;</i>	PSY00000189; PSY00033385; PSY00014816; PSY00003359; PSY00030448; GQ262453; FJ201639; HQ110044
<i>Picea abies</i> L.	<i>LP3-0-1; LP3-0-2; LP3-0-3; LP3-0-4; LP3-1</i>	MA_60383g0010; MA_10429943g0; MA_785227g001; MA_470517g001; MA_45729g0010
<i>Picea glauca</i> (Moench) Voss	<i>LP3-0-1; LP3-0-2; LP3-0-3; LP3-03; LP3-0-4; LP3-0-5</i>	PGL00016950; PGL00010547; PGL00013943; PGL00026768; PGL00017146
<i>Picea sitchensis</i> (Bong.) Carr.	<i>LP3-0-1; LP3-0-2; LP3-0-3; LP3-03; LP3-0-4; LP3-0-5</i>	PSI00017214; PSI00001767; PSI00009226; PSI00001649; PSI00017214
<i>Cupressus sempervirens</i>	<i>LP3-0-1</i>	FJ237438

L.

Pseudostuga menziesii LP3-0-1

PME00010941

(Mirb.) Franco

Pinus halepensis Miller LP3-1; LP3-3

HM482200; HM482279

Pinus hwangshanensis LP3-1

KJ921435

W.Y.Hsia

Pinus massoniana Lamb. LP3-1

KJ921431

Pinus echinata Miller LP3-3

KF158939

Pinus canariensis C.Sm. LP3-3

KF046212

Pinus mugo Turra LP3-3

JQ028052

Solanum lycopersicum L. ASR1, ASR2, ASR3

NM_001247208;

NM_001320991;

NM_001309371

Lycopersicon chilense ASR1, ASR2, ASR3

DQ058748; AY217009;

(Dunal) Reiche

DQ058754

Lycopersicon esculentum ASR1, ASR2, ASR3

DQ058745; AY217012;

Mill.

DQ058750

Solanum tuberosum L. ASR1, ASR2, ASR4, ci21B

DQ252504; XM_006359742;

JX576284; U76611

Oryza sativa L. ASR1

XM_015767744;

Amborella trichopoda ASR1

XM_006851361

Baill.

Vitis vinifera L. ASR2

AF281656

Populus trichocarpa Torr ASR3

XM_024602314

& A.Gray ex.Hook

<i>Zea mays</i> L.	ASR3	XM_008647554
<i>Nicotiana tabacum</i> L.	TIP	HE664126

Supplementary Table 1: Sequence names and accession numbers used in phylogenetic tree reconstruction according to species.

Species	Gene name	Accession numbers
<i>Pinus taeda</i> L.	<i>LP3-0-1; LP3-0-2; LP3-0-3;</i> <i>LP3-1; LP3-2; LP3-3</i>	U67135; PITA_00002958; PITA_00009264; U52865; U59451; U59424
<i>Pinus pinaster</i> Ait.	<i>LP3-0-1; LP3-0-2; LP3-0-3;</i> <i>LP3-03; LP3-0-4; LP3-0-5;</i> <i>LP3-0-6; LP3-0-7;</i> <i>LP3-1; LP3-3</i>	PPI00000827; PPI00033797; PPI00061525; PPI00057047; PPI00018463; PPI00045720; PPI00057443; HM483166; HM483350
<i>Pinus sylvestris</i> L.	<i>LP3-0-1; LP3-0-2; LP3-0-3;</i> <i>LP3-03; LP3-0-4; LP3-0-5;</i> <i>LP3-1; LP3-2; LP3-3;</i>	PSY00000189; PSY00033385; PSY00014816; PSY00003359; PSY00030448; GQ262453; FJ201639; HQ110044
<i>Picea abies</i> L.	<i>LP3-0-1; LP3-0-2; LP3-0-3;</i> <i>LP3-0-4; LP3-1</i>	MA_60383g0010; MA_10429943g0; MA_785227g001; MA_470517g001; MA_45729g0010
<i>Picea glauca</i> (Moench) Voss	<i>LP3-0-1; LP3-0-2; LP3-0-3;</i> <i>LP3-03; LP3-0-4; LP3-0-5</i>	PGL00016950; PGL00010547; PGL00013943; PGL00026768;

		PGL00017146
<i>Picea sitchensis</i> (Bong.) Carr.	LP3-0-1; LP3-0-2; LP3-0-3;	PSI00017214; PSI00001767;
	LP3-03; LP3-0-4; LP3-0-5	PSI00009226; PSI00001649;
		PSI00017214
<i>Solanum lycopersicum</i> L.	ASR1, ASR2, ASR3, ASR4	NM_001247208;
		NM_001320991;
		NM_001309371;
		NM_001282319
<i>Solanum tuberosum</i> L.	ASR1, ASR2, ASR4, ci21A,	DQ252504; XM_006359742;
	ci21B	JX576284; U76610; U76611
<i>Populus trichocarpa</i> Torr &	ASR3, ASR2, ASR4	XM_024602314;
A.Gray ex.Hook		Potri.005G193800;
		Potri.005G193900
<i>Zea mays</i> L.	ASR1, ASR2, ASR3	EU963502; XM_008677645;
		XM_008647554
<i>Oryza sativa</i> L.	ASR1, ASR2, ASR3	XM_015767744;
		XM_015779843;
		XM_015794522

Supplementary Table 2: Sequence names and accession numbers from majorly represented species (i.e. species in which three or more ABA/WDS were found) for determining CAI, GC content, ENC and RSCU according to species.

AA	Codon	RSCU	Codon	RSCU	Codon	RSCU	Codon	RSCU
	ASR1		ASR2		ASR3		ASR4	
Ala	Ala_GCU	1,01	Ala_GCU	1,9	Ala_GCU	1,49	Ala_GCU	2
	Ala_GCA	1,17	Ala_GCA	1,27	Ala_GCA	1,21	Ala_GCA	1,44
	Ala_GCC	1,33	Ala_GCC	0,73	Ala_GCC	0,88	Ala_GCC	0,48

Arg	Ala_GCG	0,48	Ala_GCG	0,1	Ala_GCG	0,42	Ala_GCG	0,08
	Arg_CGU	0	Arg_CGU	0	Arg_CGU	1,5	Arg_CGU	0
	Arg_CGA	0	Arg_CGA	0	Arg_CGA	1	Arg_CGA	2,12
	Arg_AGA	0	Arg_AGA	0	Arg_AGA	1,5	Arg_AGA	1,76
	Arg_CGC	0	Arg_CGC	0	Arg_CGC	1,5	Arg_CGC	0,35
	Arg_CGG	0	Arg_CGG	0	Arg_CGG	0	Arg_CGG	0
	Arg_AGG	0	Arg_AGG	6	Arg_AGG	0,5	Arg_AGG	1,76
Asn	Asn_AAU	0	Asn_AAU	0,57	Asn_AAU	0,89	Asn_AAU	1,22
	Asn_AAC	2	Asn_AAC	1,43	Asn_AAC	1,11	Asn_AAC	0,78
Asp	Asp_GAU	0,83	Asp_GAU	1,07	Asp_GAU	0,82	Asp_GAU	1,33
	Asp_GAC	1,17	Asp_GAC	0,93	Asp_GAC	1,18	Asp_GAC	0,67
Cys	Cys_UGU	0	Cys_UGU	0	Cys_UGU	2	Cys_UGU	1,2
	Cys_UGC	0	Cys_UGC	0	Cys_UGC	0	Cys_UGC	0,8
Gln	Gln_CAA	1,56	Gln_CAA	0,86	Gln_CAA	0,78	Gln_CAA	0,86
	Gln_CAG	0,44	Gln_CAG	1,14	Gln_CAG	1,22	Gln_CAG	1,14
Glu	Glu_GAA	0,5	Glu_GAA	0,91	Glu_GAA	0,61	Glu_GAA	0,87
	Glu_GAG	1,5	Glu_GAG	1,09	Glu_GAG	1,39	Glu_GAG	1,13
Gly	Gly_GGU	1,14	Gly_GGU	2	Gly_GGU	2,12	Gly_GGU	1,85
	Gly_GGA	0,79	Gly_GGA	1,33	Gly_GGA	0,82	Gly_GGA	1,48
	Gly_GGC	1,21	Gly_GGC	0,33	Gly_GGC	0,82	Gly_GGC	0,37
	Gly_GGG	0,86	Gly_GGG	0,33	Gly_GGG	0,24	Gly_GGG	0,31
His	His_CAU	0,66	His_CAU	0,68	His_CAU	0,76	His_CAU	1
	His_CAC	1,34	His_CAC	1,32	His_CAC	1,24	His_CAC	1
Ile	Ile_AUU	0,35	Ile_AUU	1,71	Ile_AUU	1,15	Ile_AUU	1,4
	Ile_AUA	1,24	Ile_AUA	1,07	Ile_AUA	1,62	Ile_AUA	1,6
	Ile_AUC	1,41	Ile_AUC	0,21	Ile_AUC	0,23	Ile_AUC	0
Leu	Leu_UUA	0	Leu_UUA	0,96	Leu_UUA	0	Leu_UUA	1,04
	Leu_CUU	1,31	Leu_CUU	0,96	Leu_CUU	1,5	Leu_CUU	2,09
	Leu_CUA	0	Leu_CUA	0	Leu_CUA	0	Leu_CUA	0,26
	Leu_UUG	0,75	Leu_UUG	1,92	Leu_UUG	1,8	Leu_UUG	1,04
	Leu_CUC	2,63	Leu_CUC	2,16	Leu_CUC	1,8	Leu_CUC	1,3
	Leu_CUG	1,31	Leu_CUG	0	Leu_CUG	0,9	Leu_CUG	0,26
Lys	Lys_AAA	1,02	Lys_AAA	0,75	Lys_AAA	0,85	Lys_AAA	0,91
	Lys_AAG	0,98	Lys_AAG	1,25	Lys_AAG	1,15	Lys_AAG	1,09
Phe	Phe_UUU	0,36	Phe_UUU	0,59	Phe_UUU	0,59	Phe_UUU	1,1
	Phe_UUC	1,64	Phe_UUC	1,41	Phe_UUC	1,41	Phe_UUC	0,9
Pro	Pro_CCU	0	Pro_CCU	0,92	Pro_CCU	0,62	Pro_CCU	1
	Pro_CCA	2,18	Pro_CCA	2,77	Pro_CCA	3,08	Pro_CCA	2
	Pro_CCC	1,45	Pro_CCC	0,31	Pro_CCC	0,31	Pro_CCC	0,5
	Pro_CCG	0,36	Pro_CCG	0	Pro_CCG	0	Pro_CCG	0,5
Ser	Ser_UCU	1,5	Ser_UCU	0,46	Ser_UCU	0,55	Ser_UCU	1,4
	Ser_UCA	0	Ser_UCA	0	Ser_UCA	1,09	Ser_UCA	0,6
	Ser_AGU	0	Ser_AGU	0	Ser_AGU	0	Ser_AGU	2,8

Thr	Ser_UCC	1,5	Ser_UCC	1,85	Ser_UCC	1,09	Ser_UCC	0,2
	Ser_UCG	1,5	Ser_UCG	0,92	Ser_UCG	0	Ser_UCG	0
	Ser_AGC	1,5	Ser_AGC	2,77	Ser_AGC	3,27	Ser_AGC	1
	Thr_ACU	2,57	Thr_ACU	0	Thr_ACU	1,6	Thr_ACU	1,57
	Thr_ACA	0,57	Thr_ACA	0	Thr_ACA	0,8	Thr_ACA	1,41
	Thr_ACC	0,57	Thr_ACC	4	Thr_ACC	1,6	Thr_ACC	1,02
	Thr_ACG	0,29	Thr_ACG	0	Thr_ACG	0	Thr_ACG	0
Tyr	Tyr_UAU	0,33	Tyr_UAU	0,67	Tyr_UAU	0,44	Tyr_UAU	1,7
	Tyr_UAC	1,67	Tyr_UAC	1,33	Tyr_UAC	1,56	Tyr_UAC	0,3
Val	Val_GUU	1,23	Val_GUU	2,76	Val_GUU	1,92	Val_GUU	1,8
	Val_GUA	0,31	Val_GUA	0,14	Val_GUA	0,8	Val_GUA	0,6
	Val_GUC	0,77	Val_GUC	0,28	Val_GUC	0,32	Val_GUC	0,8
	Val_GUG	1,69	Val_GUG	0,83	Val_GUG	0,96	Val_GUG	0,8
AA	Codon	RSCU	Codon	RSCU	Codon	RSCU	Codon	RSCU
Ala	LP3-0		LP3-1		LP3-2		LP3-3	
	Ala_GCU	1,53	Ala_GCU	0,94	Ala_GCU	1,28	Ala_GCU	1,35
	Ala_GCA	1,48	Ala_GCA	2,25	Ala_GCA	2,08	Ala_GCA	1,67
	Ala_GCC	0,47	Ala_GCC	0,58	Ala_GCC	0,64	Ala_GCC	0,7
Arg	Ala_GCG	0,52	Ala_GCG	0,22	Ala_GCG	0	Ala_GCG	0,28
	Arg_CGU	0,18	Arg_CGU	0,75	Arg_CGU	3,6	Arg_CGU	0
	Arg_CGA	0,09	Arg_CGA	0,75	Arg_CGA	0	Arg_CGA	0
	Arg_AGA	0,88	Arg_AGA	1,5	Arg_AGA	0	Arg_AGA	0
	Arg_CGC	0,79	Arg_CGC	0	Arg_CGC	0	Arg_CGC	0
	Arg_CGG	0,35	Arg_CGG	0	Arg_CGG	0	Arg_CGG	0
	Arg_AGG	3,71	Arg_AGG	3	Arg_AGG	2,4	Arg_AGG	6
Asn	Asn_AAU	0,69	Asn_AAU	1,14	Asn_AAU	2	Asn_AAU	1,33
	Asn_AAC	1,31	Asn_AAC	0,86	Asn_AAC	0	Asn_AAC	0,67
Asp	Asp_GAU	1,75	Asp_GAU	1,91	Asp_GAU	1,6	Asp_GAU	1,94
	Asp_GAC	0,25	Asp_GAC	0,09	Asp_GAC	0,4	Asp_GAC	0,06
Cys	Cys_UGU	0,89	Cys_UGU	0	Cys_UGU	0	Cys_UGU	0
	Cys_UGC	1,11	Cys_UGC	0	Cys_UGC	0	Cys_UGC	0
Gln	Gln_CAA	0,8	Gln_CAA	0,25	Gln_CAA	0	Gln_CAA	2
	Gln_CAG	1,2	Gln_CAG	1,75	Gln_CAG	0	Gln_CAG	0

Glu	Glu_GAA	0,74	Glu_GAA	0,64	Glu_GAA	0,7	Glu_GAA	0,51
	Glu_GAG	1,26	Glu_GAG	1,36	Glu_GAG	1,3	Glu_GAG	1,49
Gly	Gly_GGU	1,24	Gly_GGU	1,17	Gly_GGU	1,2	Gly_GGU	0,74
	Gly_GGA	1,41	Gly_GGA	1,25	Gly_GGA	1,2	Gly_GGA	2,05
	Gly_GGC	0,62	Gly_GGC	0,83	Gly_GGC	0,8	Gly_GGC	0,65
	Gly_GGG	0,73	Gly_GGG	0,75	Gly_GGG	0,8	Gly_GGG	0,56
His	His_CAU	0,65	His_CAU	0,55	His_CAU	0,57	His_CAU	0,65
	His_CAC	1,35	His_CAC	1,45	His_CAC	1,43	His_CAC	1,35
Ile	Ile_AUU	1,53	Ile_AUU	2,73	Ile_AUU	0	Ile_AUU	1,88
	Ile_AUA	0,12	Ile_AUA	0	Ile_AUA	0	Ile_AUA	0
	Ile_AUC	1,35	Ile_AUC	0,27	Ile_AUC	3	Ile_AUC	1,13
Leu	Leu_UUA	0,17	Leu_UUA	0,38	Leu_UUA	2,67	Leu_UUA	0
	Leu_CUU	0,21	Leu_CUU	0	Leu_CUU	0	Leu_CUU	0,26
	Leu_CUA	0,21	Leu_CUA	0	Leu_CUA	0,67	Leu_CUA	0
	Leu_UUG	1,56	Leu_UUG	0	Leu_UUG	0	Leu_UUG	1,3
	Leu_CUC	1,42	Leu_CUC	1,88	Leu_CUC	0,67	Leu_CUC	1,83
	Leu_CUG	2,43	Leu_CUG	3,75	Leu_CUG	2	Leu_CUG	2,61
Lys	Lys_AAA	0,4	Lys_AAA	0,48	Lys_AAA	0,67	Lys_AAA	0,03
	Lys_AAG	1,6	Lys_AAG	1,52	Lys_AAG	1,33	Lys_AAG	1,97
Phe	Phe_UUU	0,72	Phe_UUU	0,5	Phe_UUU	1,33	Phe_UUU	2
	Phe_UUC	1,28	Phe_UUC	1,5	Phe_UUC	0,67	Phe_UUC	0
Pro	Pro_CCU	0,68	Pro_CCU	0	Pro_CCU	0	Pro_CCU	1,14
	Pro_CCA	1,66	Pro_CCA	3,5	Pro_CCA	4	Pro_CCA	2
	Pro_CCC	1,56	Pro_CCC	0	Pro_CCC	0	Pro_CCC	0,86
	Pro_CCG	0,1	Pro_CCG	0,5	Pro_CCG	0	Pro_CCG	0
Ser	Ser_UCU	2,39	Ser_UCU	0,43	Ser_UCU	3	Ser_UCU	2,1
	Ser_UCA	0,4	Ser_UCA	0	Ser_UCA	0	Ser_UCA	0
	Ser_AGU	0,34	Ser_AGU	0	Ser_AGU	0	Ser_AGU	0,6

Thr	Ser_UCC	0,25	Ser_UCC	0	Ser_UCC	0	Ser_UCC	0
	Ser_UCG	1,34	Ser_UCG	3,86	Ser_UCG	0	Ser_UCG	1,2
	Ser_AGC	1,27	Ser_AGC	1,71	Ser_AGC	3	Ser_AGC	2,1
	Thr_ACU	0,63	Thr_ACU	1,2	Thr_ACU	0	Thr_ACU	1,29
	Thr_ACA	1,6	Thr_ACA	1,6	Thr_ACA	0	Thr_ACA	0,57
	Thr_ACC	1,47	Thr_ACC	0,4	Thr_ACC	1,33	Thr_ACC	2,14
Tyr	Thr_ACG	0,3	Thr_ACG	0,8	Thr_ACG	2,67	Thr_ACG	0
	Tyr_UAU	0,79	Tyr_UAU	1,07	Tyr_UAU	0	Tyr_UAU	0,78
	Tyr_UAC	1,21	Tyr_UAC	0,93	Tyr_UAC	2	Tyr_UAC	1,22
Val	Val_GUU	1,32	Val_GUU	1,21	Val_GUU	1,82	Val_GUU	1,14
	Val_GUA	0,03	Val_GUA	0,48	Val_GUA	0	Val_GUA	0
	Val_GUC	0,44	Val_GUC	0,24	Val_GUC	0,73	Val_GUC	0
	Val_GUG	2,21	Val_GUG	2,06	Val_GUG	1,45	Val_GUG	2,86

Supplementary Table 3: Average RSCU value of each codon per ABA/WDS gene. The most used codon for a given amino acid is indicated in bold.

(a) LP3-0

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval](** if lower bound > 1)	POSTERIOR PROBABILITIES									
				w =	1.8e-05	0.00052	0.0034	0.012	0.033	0.076	0.16	0.41	
1	M	0.063	[1.8e-05,0.41]		0.16	0.16	0.15	0.15	0.14	0.12	0.081	0.032	0.021
2	S	0.19	[1.8e-05,1]		0.12	0.12	0.12	0.12	0.12	0.11	0.093	0.062	0.13
3	E	0.043	[1.8e-05,0.41]		0.17	0.17	0.17	0.16	0.14	0.1	0.057	0.016	0.012
4	E	0.055	[1.8e-05,0.41]		0.17	0.17	0.16	0.15	0.14	0.11	0.066	0.022	0.02
5	K	0.93	[0.41,1]		4.2e-14	1e-09	2.7e-07	1.3e-05	0.00023	0.0023	0.016	0.095	0.89
6	H	0.87	[0.16,1]		1.2e-09	9.6e-07	4e-05	0.00051	0.0034	0.015	0.05	0.13	0.8
7	H	0.79	[0.076,1]		2.4e-09	2e-06	8.2e-05	0.001	0.0068	0.029	0.089	0.18	0.69
8	H	0.056	[1.8e-05,0.41]		0.16	0.16	0.16	0.15	0.14	0.11	0.074	0.026	0.018
9	H	0.87	[0.16,1]		9.5e-10	7.8e-07	3.3e-05	0.00042	0.0028	0.013	0.046	0.13	0.81
10	L	0.74	[0.033,1]		1.5e-05	0.00044	0.0029	0.001	0.026	0.056	0.1	0.15	0.65
11	L	1	[1,1]*	1.2e-19	8.3e-14	1.5e-10	2.5e-08	1.3e-06	3.3e-05	0.00059	0.014	0.99	
12	H	0.42	[0.012,1]		5.5e-05	0.0016	0.01	0.035	0.086	0.16	0.23	0.19	0.29
13	H	0.052	[1.8e-05,0.41]		0.16	0.16	0.16	0.15	0.14	0.11	0.073	0.025	0.015
14	K	0.04	[1.8e-05,0.16]		0.17	0.17	0.17	0.16	0.14	0.11	0.061	0.016	0.008
15	K	0.04	[1.8e-05,0.16]		0.17	0.17	0.17	0.16	0.14	0.11	0.061	0.016	0.008
16	E	0.055	[1.8e-05,0.41]		0.17	0.17	0.16	0.15	0.14	0.11	0.066	0.022	0.02
17	D	0.038	[1.8e-05,0.16]		0.18	0.18	0.17	0.16	0.14	0.1	0.056	0.014	0.008
18	E	0.94	[0.41,1]		4e-14	9.4e-10	2.6e-07	1.2e-05	0.00021	0.0022	0.015	0.088	0.89
19	S	0.96	[0.41,1]		2.9e-14	7e-10	1.9e-07	8.6e-06	0.00015	0.0015	0.01	0.06	0.93
20	E	0.92	[0.41,1]		5.2e-14	1.2e-09	3.4e-07	1.6e-05	0.00028	0.0028	0.02	0.11	0.87
21	N	0.97	[0.41,1]		1.4e-14	3.3e-10	9.1e-08	4.3e-06	8e-05	0.00088	0.0071	0.057	0.93
22	V	0.97	[0.41,1]		1.8e-14	4.2e-10	1.1e-07	5.2e-06	9.5e-05	0.00098	0.0071	0.05	0.94
23	P	0.99	[0.41,1]		2.7e-15	6.4e-11	1.8e-08	8.4e-07	1.7e-05	0.0002	0.002	0.024	0.97
24	S	0.92	[0.16,1]		4.5e-10	3.7e-07	1.6e-05	0.0002	0.0014	0.0066	0.025	0.089	0.88
25	E	0.93	[0.16,1]		1.8e-10	1.5e-07	6.6e-06	9.1e-05	0.00074	0.0044	0.021	0.091	0.88
26	V	0.08	[1.8e-05,1]		0.15	0.15	0.15	0.14	0.13	0.11	0.084	0.037	0.035
27	V	0.89	[0.16,1]		8.7e-10	7.1e-07	3e-05	0.00038	0.0026	0.012	0.041	0.12	0.82
28	C	0.82	[0.076,1]		9.3e-06	0.00027	0.0017	0.0062	0.016	0.035	0.068	0.12	0.75
29	A	0.97	[0.41,1]		1.4e-10	1.2e-07	4.9e-06	6.4e-05	0.00046	0.0023	0.0099	0.048	0.94
30	E	0.08	[1.8e-05,1]		0.15	0.15	0.15	0.14	0.13	0.12	0.085	0.038	0.035
31	T	0.85	[0.076,1]		7.6e-06	0.00022	0.0014	0.0051	0.013	0.03	0.058	0.11	0.78
32	T	0.25	[1.8e-05,1]		0.11	0.11	0.11	0.11	0.11	0.1	0.091	0.069	0.2
33	T	0.28	[1.8e-05,1]		0.1	0.1	0.1	0.1	0.1	0.097	0.089	0.071	0.23
34	A	0.82	[0.033,1]		9.6e-06	0.00028	0.0018	0.0064	0.017	0.036	0.069	0.12	0.75
35	Y	0.069	[1.8e-05,1]		0.15	0.15	0.15	0.15	0.14	0.12	0.083	0.035	0.026
36	G	0.072	[1.8e-05,1]		0.15	0.15	0.15	0.15	0.14	0.11	0.082	0.034	0.029
37	D	0.26	[0.012,1]		9.6e-05	0.0027	0.017	0.059	0.14	0.23	0.27	0.15	0.13
38	E	0.3	[0.012,1]		8.1e-05	0.0023	0.015	0.051	0.12	0.21	0.26	0.17	0.17
39	V	0.062	[1.8e-05,0.41]		0.16	0.16	0.16	0.15	0.14	0.11	0.079	0.03	0.021
40	I	0.7	[0.033,1]		1.9e-05	0.00054	0.0035	0.012	0.032	0.066	0.12	0.16	0.61
41	Q	0.81	[0.076,1]		2.2e-09	1.8e-06	7.7e-05	0.00096	0.0063	0.026	0.079	0.17	0.72
42	S	0.73	[0.033,1]		1.7e-05	0.00047	0.0031	0.011	0.028	0.058	0.1	0.15	0.65
43	A	0.94	[0.41,1]		3.1e-10	2.6e-07	1.1e-05	0.00014	0.00099	0.0048	0.019	0.074	0.9
44	D	0.34	[0.012,1]		7.1e-05	0.002	0.013	0.045	0.11	0.19	0.25	0.18	0.2
45	V	0.061	[1.8e-05,0.41]		0.16	0.16	0.16	0.15	0.14	0.11	0.079	0.03	0.02
46	Y	0.066	[1.8e-05,0.41]		0.15	0.15	0.15	0.15	0.14	0.12	0.082	0.033	0.024
47	A	0.81	[0.033,1]		1e-05	0.00029	0.0019	0.0068	0.018	0.038	0.073	0.13	0.74
48	A	0.21	[1.8e-05,1]		0.12	0.12	0.12	0.12	0.11	0.11	0.093	0.065	0.15
49	G	0.18	[1.8e-05,1]		0.12	0.12	0.12	0.12	0.12	0.11	0.093	0.062	0.13
50	E	0.89	[0.16,1]		7.2e-10	5.9e-07	2.5e-05	0.00032	0.0022	0.01	0.037	0.12	0.83
51	V	0.17	[1.8e-05,1]		0.13	0.13	0.13	0.12	0.12	0.11	0.094	0.06	0.12
52	N	0.96	[0.41,1]		2e-10	1.6e-07	7e-06	9e-05	0.00064	0.0032	0.013	0.058	0.92
53	D	0.91	[0.16,1]		5.4e-10	4.4e-07	1.9e-05	0.00024	0.0017	0.008	0.03	0.098	0.86
54	D	0.96	[0.41,1]		2.3e-14	5.4e-10	1.5e-07	6.8e-06	0.00012	0.0012	0.0089	0.059	0.93
55	K	0.9	[0.16,1]		6.7e-10	5.5e-07	2.3e-05	0.0003	0.002	0.0096	0.035	0.11	0.84
56	F	1	[1,1]*	1.9e-24	3.7e-17	4.4e-13	2.7e-10	3.7e-08	2.2e-06	8.8e-05	0.0052	0.99	
57	A	0.97	[0.41,1]		1.8e-18	1.2e-12	2.2e-09	3.6e-07	1.7e-05	0.00037	0.0049	0.055	0.94
58	E	0.91	[0.16,1]		7e-14	1.7e-09	4.5e-07	2.1e-05	0.00037	0.0036	0.024	0.12	0.85
59	Y	0.19	[1.8e-05,1]		0.12	0.12	0.12	0.12	0.12	0.11	0.093	0.063	0.13
60	E	0.037	[1.8e-05,0.16]		0.18	0.18	0.17	0.16	0.14	0.1	0.055	0.014	0.0076
61	K	0.036	[1.8e-05,0.16]		0.17	0.17	0.17	0.16	0.14	0.1	0.058	0.014	0.0055
62	A	0.055	[1.8e-05,0.41]		0.16	0.16	0.16	0.15	0.14	0.11	0.073	0.025	0.018
63	R	1	[1,1]*	4.9e-14	4.5e-11	3.2e-09	1.1e-07	2.7e-06	5e-05	0.00077	0.016	0.98	
64	K	0.36	[0.012,1]		7.2e-05	0.0021	0.013	0.045	0.11	0.19	0.24	0.17	0.23
65	E	0.054	[1.8e-05,0.41]		0.17	0.17	0.17	0.16	0.14	0.1	0.062	0.021	0.021
66	E	0.037	[1.8e-05,0.16]		0.18	0.18	0.17	0.16	0.14	0.099	0.053	0.014	0.0075
67	K	0.039	[1.8e-05,0.16]		0.17	0.17	0.17	0.16	0.14	0.11	0.062	0.017	0.0071
68	H	0.051	[1.8e-05,0.41]		0.16	0.16	0.16	0.15	0.14	0.11	0.072	0.024	0.014
69	H	0.047	[1.8e-05,0.41]		0.17	0.16	0.16	0.15	0.14	0.11	0.071	0.022	0.011
70	K	0.04	[1.8e-05,0.16]		0.17	0.17	0.17	0.16	0.14	0.11	0.063	0.017	0.0075
71	H	0.41	[0.012,1]		5.9e-05	0.0017	0.011	0.037	0.09	0.17	0.23	0.19	0.27
72	L	0.98	[0.41,1]		6.6e-19	4.5e-13	8e-10	1.3e-07	6.5e-06	0.00015	0.0024	0.036	0.96
73	E	0.037	[1.8e-05,0.16]		0.18	0.18	0.17	0.16	0.14	0.1	0.055	0.014	0.0076
74	E	0.91	[0.16,1]		7.3e-14	1.7e-09	4.7e-07	2.1e-05	0.00038	0.0037	0.024	0.12	0.85
75	L	0.94	[0.41,1]		3e-10	2.5e-07	1e-05	0.00013	0.00094	0.0046	0.018	0.074	0.9
76	G	0.52	[0.012,1]		4e-05	0.0011	0.0073	0.026	0.064	0.12	0.19	0.19	0.39
77	G	0.81	[0.076,1]		2.4e-09	2e-06	8.3e-05	0.001	0.0067	0.028	0.081	0.16	0.72
78	L	0.16	[1.8e-05,1]		0.13	0.13	0.13	0.13	0.12	0.11	0.091	0.056	0.11
79	G	0.083	[1.8e-05,1]		0.15	0.15	0.15	0.14	0.13	0.11	0.084	0.038	0.038
80	T	0.89	[0.16,1]		8.1e-10	6.6e-07	2.8e-05	0.00036	0.0024	0.011	0.04	0.12	0.83
81	V	0.85	[0.16,1]		1.3e-09	1.1e-06	4.7e-05	0.00059	0.004	0.018	0.059	0.15	0.77
82	A	0.085	[1.8e-05,1]		0.15	0.15	0.15	0.14	0.13	0.11	0.084	0.038	0.04
83	A	0.59	[0.012,1]		3e-05	0.00085	0.0055	0.019	0.049	0.098	0.16	0.19	0.48
84	G	0.084	[1.8e-05,1]		0.15	0.15	0						

89	H	0.056	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.074	0.026	0.018
90	E	0.037	[1.8e-05,0.16]	0.18	0.18	0.17	0.16	0.14	0.099	0.053	0.014	0.0075
91	K	0.036	[1.8e-05,0.16]	0.17	0.17	0.17	0.16	0.14	0.1	0.058	0.014	0.0055
92	H	0.05	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.071	0.023	0.014
93	A	0.92	[0.16,1]	5.5e-10	4.5e-07	1.9e-05	0.00024	0.0016	0.0076	0.027	0.088	0.88
94	S	0.95	[0.41,1]	3.7e-14	8.7e-10	2.4e-07	1.1e-05	0.00019	0.0019	0.013	0.073	0.91
95	K	0.039	[1.8e-05,0.16]	0.17	0.17	0.17	0.16	0.14	0.11	0.062	0.017	0.0071
96	K	0.045	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.11	0.066	0.019	0.011
97	D	0.043	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.1	0.059	0.017	0.012
98	P	0.17	[1.8e-05,1]	0.13	0.13	0.13	0.12	0.12	0.11	0.093	0.059	0.11
99	E	0.042	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.1	0.057	0.016	0.011
100	N	1	[1,1]*	2.1e-19	1.4e-13	2.5e-10	4.2e-08	2.1e-06	5.1e-05	0.00084	0.016	0.98
101	A	0.087	[1.8e-05,1]	0.15	0.15	0.15	0.14	0.13	0.11	0.083	0.037	0.043
102	H	0.052	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.073	0.025	0.015
103	R	0.96	[0.41,1]	2.3e-14	5.3e-10	1.5e-07	6.7e-06	0.00012	0.0013	0.009	0.059	0.93
104	H	0.052	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.073	0.025	0.015
105	K	0.044	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.11	0.066	0.019	0.01
106	I	0.82	[0.076,1]	7.9e-06	0.00023	0.0015	0.0054	0.014	0.033	0.067	0.13	0.75
107	E	0.41	[0.012,1]	5.9e-05	0.0017	0.011	0.037	0.09	0.16	0.23	0.19	0.28
108	E	0.048	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.1	0.061	0.019	0.016
109	E	0.043	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.1	0.059	0.017	0.012
110	I	0.68	[0.033,1]	2.1e-05	0.0006	0.0039	0.014	0.035	0.072	0.12	0.17	0.58
111	A	0.11	[1.8e-05,1]	0.14	0.14	0.14	0.14	0.13	0.11	0.087	0.043	0.059
112	A	0.68	[0.033,1]	2.2e-05	0.00062	0.004	0.014	0.036	0.074	0.13	0.17	0.58
113	A	0.93	[0.16,1]	4e-10	3.3e-07	1.4e-05	0.00018	0.0013	0.006	0.023	0.083	0.89
114	A	0.62	[0.033,1]	2.8e-05	0.00081	0.0052	0.018	0.046	0.092	0.15	0.18	0.51
115	A	0.11	[1.8e-05,1]	0.14	0.14	0.14	0.14	0.13	0.11	0.087	0.044	0.06
116	V	0.057	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.075	0.026	0.018
117	G	0.091	[1.8e-05,1]	0.15	0.15	0.15	0.14	0.13	0.11	0.086	0.04	0.045
118	A	0.92	[0.16,1]	4.1e-10	3.4e-07	1.4e-05	0.00018	0.0013	0.0063	0.025	0.09	0.88
119	G	0.055	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.076	0.027	0.016
120	G	0.62	[0.033,1]	2.6e-05	0.00075	0.0048	0.017	0.043	0.089	0.15	0.19	0.51
121	Y	0.076	[1.8e-05,1]	0.15	0.15	0.15	0.15	0.13	0.12	0.084	0.037	0.031
122	V	0.5	[0.012,1]	4.2e-05	0.0012	0.0078	0.027	0.067	0.13	0.2	0.2	0.37
123	F	0.16	[1.8e-05,1]	0.13	0.13	0.13	0.13	0.12	0.11	0.093	0.059	0.11
124	H	0.055	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.074	0.026	0.017
125	E	0.043	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.1	0.059	0.017	0.012
126	H	0.057	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.074	0.026	0.019
127	H	0.054	[1.8e-05,0.16]	0.16	0.16	0.16	0.15	0.14	0.11	0.073	0.025	0.016
128	E	0.042	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.1	0.057	0.016	0.011
129	K	0.04	[1.8e-05,0.16]	0.17	0.17	0.17	0.16	0.14	0.11	0.061	0.016	0.008
130	K	0.045	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.11	0.064	0.018	0.011
131	E	0.055	[1.8e-05,0.41]	0.17	0.17	0.16	0.15	0.14	0.11	0.066	0.022	0.02
132	S	0.72	[0.033,1]	1.8e-05	0.00051	0.0033	0.012	0.03	0.062	0.11	0.15	0.63
133	K	0.06	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.077	0.028	0.021
134	E	0.052	[1.8e-05,0.41]	0.17	0.17	0.17	0.16	0.14	0.1	0.062	0.02	0.018
135	E	0.44	[0.012,1]	5.3e-05	0.0015	0.0098	0.034	0.082	0.15	0.22	0.19	0.31
136	E	0.98	[0.41,1]	1.1e-14	2.6e-10	7e-08	3.3e-06	6e-05	0.00066	0.0052	0.043	0.95
137	K	0.46	[0.012,1]	4.9e-05	0.0014	0.0091	0.032	0.077	0.15	0.21	0.19	0.34
138	E	0.054	[1.8e-05,0.41]	0.17	0.17	0.16	0.16	0.14	0.1	0.064	0.021	0.02
139	A	0.66	[0.033,1]	2.5e-05	0.00071	0.0046	0.016	0.041	0.082	0.13	0.16	0.56
140	E	0.87	[0.16,1]	1.6e-09	1.3e-06	5.5e-05	0.00068	0.0044	0.018	0.053	0.12	0.8
141	G	0.066	[1.8e-05,0.41]	0.15	0.15	0.15	0.15	0.14	0.12	0.082	0.033	0.024
142	K	0.48	[0.012,1]	4.6e-05	0.0013	0.0085	0.03	0.073	0.14	0.2	0.19	0.36
143	K	0.71	[0.076,1]	3.3e-09	2.7e-06	0.00011	0.0014	0.0094	0.041	0.12	0.24	0.59
144	H	0.054	[1.8e-05,0.41]	0.16	0.16	0.16	0.15	0.14	0.11	0.074	0.025	0.016
145	H	0.69	[0.033,1]	1.4e-05	0.00041	0.0027	0.0098	0.027	0.063	0.12	0.18	0.59
146	H	0.46	[0.012,1]	5.1e-05	0.0015	0.0093	0.032	0.079	0.15	0.21	0.19	0.33
147	L	0.8	[0.033,1]	1.1e-05	0.00031	0.002	0.0072	0.019	0.041	0.077	0.13	0.72
148	F	0.16	[1.8e-05,1]	0.13	0.13	0.13	0.13	0.12	0.11	0.093	0.058	0.1
149	Y	0.47	[1.8e-05,1]	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.41
150	V	0.47	[1.8e-05,1]	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.41
151	R	0.47	[1.8e-05,1]	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.41
152	C	0.47	[1.8e-05,1]	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.41
153	H	0.47	[1.8e-05,1]	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.073	0.41

Supplementary Table 4: Ka/Ks values per LP3-0 amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.

(b) LP3-1

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval]	(* if lower bound > 1)				POSTERIOR PROBABILITIES					
				w =	6.2e-10	4.4e-07	2e-05	0.0003	0.0023	0.013	0.054	0.26	1
1	M	0.13	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.11	0.074	0.1	
2	S	0.25	[6.2e-10,1]		0.1	0.1	0.1	0.1	0.1	0.096	0.082	0.22	
3	E	0.14	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.1	0.059	0.12	
4	E	0.95	[0.26,1]		4.7e-15	4.4e-13	9.3e-10	2e-07	1.2e-05	0.00034	0.0056	0.074	0.92
5	K	0.11	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.066	0.082
6	Q	0.85	[0.054,1]		5.8e-10	4.2e-07	1.9e-05	0.00028	0.0022	0.011	0.045	0.14	0.8
7	H	0.12	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.071	0.097
8	H	0.97	[0.26,1]		2.5e-12	1.8e-09	8.2e-08	1.3e-06	1.6e-05	0.00024	0.0035	0.051	0.94
9	H	0.13	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.072	0.1
10	L	0.96	[0.26,1]		6.8e-11	4.8e-08	2.2e-06	3.2e-05	0.00026	0.0015	0.0074	0.053	0.94
11	F	0.26	[6.2e-10,1]		0.098	0.098	0.098	0.098	0.098	0.097	0.095	0.083	0.23
12	H	0.97	[0.26,1]		2.4e-15	2.3e-13	4.3e-10	9.3e-08	5.7e-06	0.00016	0.0028	0.045	0.95
13	H	0.14	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.072	0.11
14	H	0.85	[0.054,1]		5e-10	3.6e-07	1.6e-05	0.00024	0.0019	0.0099	0.04	0.14	0.81
15	K	0.087	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.057	0.064
16	E	0.15	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.062	0.12
17	D	0.94	[0.26,1]		3.5e-15	5e-13	1.1e-09	2.3e-07	1.4e-05	0.00038	0.0063	0.081	0.91
18	G	0.92	[0.26,1]		1.9e-10	1.4e-07	6.4e-06	9.3e-05	0.00073	0.004	0.018	0.089	0.89
19	G	0.97	[0.26,1]		5.5e-15	2.5e-13	5.2e-10	1.1e-07	6.8e-06	0.00019	0.0032	0.05	0.95
20	E	0.84	[0.054,1]		6.4e-10	4.6e-07	2.1e-05	0.00031	0.0024	0.012	0.049	0.15	0.79
21	Q	0.97	[0.26,1]		1.1e-14	1.9e-13	4e-10	8.6e-08	5.3e-06	0.00015	0.0026	0.045	0.95
22	V	0.37	[6.2e-10,1]		0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.081	0.34
23	I	0.38	[6.2e-10,1]		0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.08	0.35
24	E	0.35	[6.2e-10,1]		0.085	0.085	0.085	0.085	0.085	0.085	0.085	0.081	0.32
25	S	0.38	[6.2e-10,1]		0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.08	0.35
26	T	0.38	[6.2e-10,1]		0.081	0.081	0.081	0.081	0.081	0.081	0.081	0.08	0.35
27	D	0.36	[6.2e-10,1]		0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.081	0.33
28	V	0.37	[6.2e-10,1]		0.082	0.082	0.082	0.082	0.082	0.082	0.082	0.08	0.34
29	Y	0.38	[6.2e-10,1]		0.082	0.082	0.082	0.082	0.082	0.082	0.082	0.08	0.35
30	A	0.89	[0.054,1]		3.4e-10	2.4e-07	1.1e-05	0.00016	0.0013	0.0067	0.027	0.11	0.86
31	A	0.18	[6.2e-10,1]		0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.078	0.16
32	G	0.99	[1,1]*	7.2e-17	7.2e-14	1.6e-10	3.4e-08	2.1e-06	6e-05	0.0011	0.022	0.98	
33	N	0.95	[0.26,1]		5.2e-15	4.2e-13	8.8e-10	1.9e-07	1.2e-05	0.00032	0.0053	0.072	0.92
34	V	0.88	[0.054,1]		4.1e-10	3e-07	1.4e-05	0.0002	0.0015	0.0081	0.033	0.12	0.84
35	D	0.99	[1,1]*	5.8e-16	6.5e-14	6.7e-11	1.4e-08	9e-07	2.8e-05	0.00064	0.022	0.98	
36	E	0.97	[0.26,1]		1.2e-14	1.9e-13	3.9e-10	8.4e-08	5.1e-06	0.00015	0.0025	0.042	0.96
37	Y	0.15	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.11	0.11	0.078	0.12
38	E	0.14	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.059	0.12
39	K	0.087	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.057	0.064
40	A	0.92	[0.26,1]		2e-10	1.5e-07	6.7e-06	9.8e-05	0.00077	0.0041	0.018	0.083	0.89
41	K	0.87	[0.054,1]		4.7e-10	3.4e-07	1.5e-05	0.00023	0.0018	0.0093	0.037	0.12	0.83
42	K	0.087	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.057	0.064
43	D	0.88	[0.054,1]		5.2e-10	3.7e-07	1.7e-05	0.00025	0.0019	0.01	0.038	0.11	0.84
44	E	0.14	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.059	0.12
45	K	0.087	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.057	0.064
46	H	0.13	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.072	0.1
47	H	0.14	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.072	0.11
48	K	0.087	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.057	0.064
49	H	0.96	[0.26,1]		7.1e-11	5e-08	2.3e-06	3.4e-05	0.00027	0.0015	0.0077	0.054	0.94
50	M	0.13	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.074	0.099
51	E	0.14	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.059	0.12
52	H	0.13	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.072	0.1
53	L	0.26	[6.2e-10,1]		0.099	0.099	0.099	0.099	0.098	0.098	0.094	0.081	0.23
54	G	0.13	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.068	0.099
55	E	0.15	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.062	0.12
56	M	0.93	[0.26,1]		1.8e-10	1.3e-07	6e-06	8.8e-05	0.00069	0.0037	0.016	0.072	0.91
57	G	0.12	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.073	0.092
58	T	0.89	[0.054,1]		3.4e-10	2.5e-07	1.1e-05	0.00016	0.0013	0.0068	0.028	0.11	0.86
59	V	0.17	[6.2e-10,1]		0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.076	0.14
60	A	0.19	[6.2e-10,1]		0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.079	0.16
61	A	0.19	[6.2e-10,1]		0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.079	0.16
62	G	0.12	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.073	0.092
63	A	0.87	[0.054,1]		4.3e-10	3.1e-07	1.4e-05	0.00021	0.0016	0.0086	0.035	0.12	0.83
64	F	0.27	[6.2e-10,1]		0.097	0.097	0.097	0.097	0.097	0.097	0.094	0.083	0.24
65	A	0.17	[6.2e-10,1]		0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.076	0.14
66	L	0.19	[6.2e-10,1]		0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.08	0.16
67	H	0.85	[0.054,1]		5e-10	3.6e-07	1.6e-05	0.00024	0.0019	0.0099	0.04	0.14	0.81
68	E	0.14	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.059	0.12
69	K	0.1	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.061	0.079
70	H	0.88	[0.054,1]		4.1e-10	2.9e-07	1.3e-05	0.00019	0.0015	0.008	0.033	0.12	0.84
71	A	0.98	[0.26,1]		4.3e-16	1.6e-13	3.3e-10	7e-08	4.3e-06	0.00012	0.0021	0.037	0.96
72	D	0.84	[0.054,1]		6e-10	4.3e-07	2e-05	0.00029	0.0022	0.012	0.047	0.15	0.79
73	K	0.07	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.13	0.11	0.056	0.047
74	K	0.07	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.13	0.11	0.056	0.047
75	D	0.093	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.059	0.069
76	P	0.22	[6.2e-10,1]		0.1	0.1	0.1	0.1	0.1	0.1	0.099	0.082	0.19
77	E	0.11	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.058	0.082
78	H	0.84	[0.054,1]		5.6e-10	4e-07	1.8e-05	0.00027	0.0021	0.011	0.044	0.15	0.79
79	A	0.15	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.11	0.11	0.074	0.12
80	H	0.13	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.071	0.098
81	R	0.87	[0.054,1]		4.4e-10	3.1e-07	1.4e-05	0.00021	0.0016	0.0086	0.035	0.13	0.83
82	H	0.11	[6.2e-10,1]		0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.071	0.087
83	K	0.07	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.13	0.11	0.056	0.047
84	I	0.21	[6.2e-10,1]		0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.081	0.18
85	E	0.11	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.058	0.082
86	E	0.11	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.058	0.082
87	E	0.11	[6.2e-10,1]		0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.058	0.082
88	V	0.89	[0.054,1]		3.6e-10	2.5e-07	1.2e-05	0.00017	0.0013	0.007	0.029	0.11	0.85

89	A	0.16	[6.2e-10,1]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.077	0.13
90	A	0.15	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.11	0.11	0.076	0.12
91	A	0.88	[0.054,1]	4e-10	2.9e-07	1.3e-05	0.00019	0.0015	0.0079	0.032	0.12	0.84
92	A	0.98	[0.26,1]	1.8e-12	1.2e-09	5.7e-08	8.7e-07	9.5e-06	0.00012	0.0017	0.031	0.97
93	A	0.16	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.11	0.11	0.11	0.077	0.13
94	V	0.1	[6.2e-10,1]	0.13	0.13	0.13	0.13	0.12	0.12	0.11	0.069	0.073
95	G	0.11	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.073	0.084
96	A	0.16	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.11	0.11	0.11	0.077	0.13
97	G	0.064	[6.2e-10,1]	0.13	0.13	0.13	0.13	0.13	0.13	0.11	0.06	0.04
98	G	0.13	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.076	0.1
99	Y	0.87	[0.054,1]	4.5e-10	3.2e-07	1.5e-05	0.00022	0.0017	0.0089	0.036	0.13	0.82
100	V	0.12	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.072	0.09
101	F	0.26	[6.2e-10,1]	0.099	0.099	0.099	0.099	0.099	0.098	0.095	0.083	0.23
102	H	0.11	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.071	0.084
103	E	0.094	[6.2e-10,1]	0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.059	0.07
104	H	0.12	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.072	0.088
105	H	0.11	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.071	0.084
106	E	0.74	[0.013,1]	1.1e-09	7.9e-07	3.6e-05	0.00053	0.0041	0.021	0.082	0.22	0.68
107	K	0.064	[6.2e-10,1]	0.13	0.13	0.13	0.13	0.13	0.13	0.11	0.056	0.041
108	K	0.081	[6.2e-10,1]	0.13	0.13	0.13	0.13	0.13	0.12	0.11	0.06	0.057
109	E	0.26	[6.2e-10,1]	0.099	0.099	0.099	0.099	0.098	0.098	0.095	0.082	0.23
110	S	0.35	[6.2e-10,1]	0.086	0.086	0.086	0.086	0.086	0.086	0.085	0.081	0.32
111	K	0.25	[6.2e-10,1]	0.1	0.1	0.1	0.1	0.1	0.1	0.097	0.082	0.22
112	E	0.26	[6.2e-10,1]	0.099	0.099	0.099	0.099	0.098	0.098	0.095	0.082	0.23
113	E	0.26	[6.2e-10,1]	0.099	0.099	0.099	0.099	0.098	0.098	0.095	0.082	0.23
114	E	0.26	[6.2e-10,1]	0.099	0.099	0.099	0.099	0.098	0.098	0.095	0.082	0.23
115	K	0.26	[6.2e-10,1]	0.099	0.099	0.099	0.099	0.099	0.098	0.095	0.082	0.23
116	E	0.26	[6.2e-10,1]	0.099	0.099	0.099	0.099	0.098	0.098	0.095	0.082	0.23
117	A	0.31	[6.2e-10,1]	0.091	0.091	0.091	0.091	0.091	0.09	0.089	0.082	0.28
118	E	0.24	[6.2e-10,1]	0.1	0.1	0.1	0.1	0.1	0.1	0.097	0.082	0.21
119	G	0.31	[6.2e-10,1]	0.092	0.092	0.092	0.092	0.092	0.091	0.09	0.082	0.28
120	K	0.93	[0.26,1]	2e-10	1.5e-07	6.7e-06	9.8e-05	0.00076	0.0041	0.017	0.076	0.9
121	K	0.24	[6.2e-10,1]	0.1	0.1	0.1	0.1	0.1	0.1	0.097	0.082	0.21
122	H	0.3	[6.2e-10,1]	0.093	0.093	0.093	0.093	0.093	0.092	0.091	0.082	0.27
123	H	0.3	[6.2e-10,1]	0.093	0.093	0.093	0.093	0.093	0.093	0.091	0.082	0.27
124	H	0.3	[6.2e-10,1]	0.093	0.093	0.093	0.093	0.093	0.093	0.091	0.082	0.27
125	L	0.35	[6.2e-10,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.081	0.32
126	F	0.36	[6.2e-10,1]	0.084	0.084	0.084	0.084	0.084	0.084	0.083	0.081	0.33

Supplementary Table 5: Ka/Ks values per LP3-1 amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.

(c) LP3-3

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval](** if lower bound > 1)	POSTERIOR PROBABILITIES								
				w =	6.2e-10	4.4e-07	2e-05	0.0003	0.0023	0.013	0.054	0.26
1	D	0.59	[6.2e-10, 2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
2	E	0.59	[6.2e-10, 2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
3	N	0.59	[6.2e-10, 2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
4	D	0.59	[6.2e-10, 2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
5	N	0.59	[6.2e-10, 2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
6	P	0.45	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.14
7	P	0.42	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.13
8	S	0.4	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.12
9	E	0.2	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.057
10	V	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.095
11	V	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.095
12	Y	0.39	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.12
13	S	0.43	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.14
14	E	0.2	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.057
15	T	0.4	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.13
16	T	0.4	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.13
17	T	0.41	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.13
18	A	0.32	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.099
19	Y	0.33	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1
20	G	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.095
21	D	0.19	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.055
22	E	0.18	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.05
23	V	0.2	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.058
24	I	0.37	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
25	Q	0.36	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
26	S	0.36	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
27	A	0.36	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
28	D	0.17	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.046
29	V	0.2	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.057
30	Y	0.35	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
31	A	0.28	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.11	0.086
32	T	2.6	[0.054, 2.9]	2.5e-10	1.8e-07	8.1e-06	0.00012	0.00092	0.0049	0.021	0.096	0.88
33	G	0.2	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.056
34	N	2.8	[2.9, 2.9]*	3.3e-15	7.1e-14	1.5e-10	3.2e-08	2e-06	5.6e-05	0.001	0.021	0.98
35	V	0.22	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.064
36	N	2.3	[0.054, 2.9]	4.9e-10	3.5e-07	1.6e-05	0.00023	0.0018	0.0097	0.041	0.18	0.77
37	S	2.9	[2.9, 2.9]*	4.3e-20	2.2e-14	4.6e-11	9.8e-09	6e-07	1.7e-05	0.00032	0.0074	0.99
38	D	0.17	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.046
39	E	0.16	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.041
40	Y	0.35	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
41	E	0.16	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.041
42	K	0.15	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.038
43	A	0.25	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.075
44	R	2.5	[0.054, 2.9]	2.9e-10	2.1e-07	9.6e-06	0.00014	0.0011	0.0059	0.025	0.11	0.86
45	K	0.15	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.038
46	E	0.24	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.07
47	E	0.16	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.041
48	K	0.15	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.038
49	H	0.27	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.08
50	H	0.32	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.097
51	K	0.15	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.038
52	H	0.27	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.08
53	M	2.5	[0.054, 2.9]	2.8e-10	2e-07	9.1e-06	0.00013	0.001	0.0055	0.024	0.11	0.86
54	E	0.16	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.041
55	E	0.23	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.067
56	V	2.6	[0.054, 2.9]	1.9e-10	1.3e-07	6.1e-06	8.9e-05	0.0007	0.0038	0.016	0.075	0.9
57	G	0.23	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.066
58	G	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.095
59	L	0.37	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.12
60	G	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.095
61	T	2.9	[2.9, 2.9]*	5.8e-20	3e-14	6.2e-11	1.3e-08	8.1e-07	2.3e-05	0.00043	0.0097	0.99
62	M	2.5	[0.054, 2.9]	3.1e-10	2.2e-07	1e-05	0.00015	0.0012	0.0062	0.026	0.12	0.85
63	A	0.34	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
64	T	0.37	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
65	G	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.095
66	A	0.34	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
67	F	0.42	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.13
68	A	0.36	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
69	L	0.45	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.14
70	H	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.095
71	E	0.16	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.041
72	K	0.15	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.038
73	H	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.096
74	A	0.36	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
75	E	0.23	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.11	0.067
76	K	0.15	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.038
77	K	0.15	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.038
78	D	0.17	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.046
79	P	0.44	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.14
80	E	0.19	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.054
81	H	0.34	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
82	A	0.32	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.097
83	H	0.34	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
84	R	0.31	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.094
85	H	0.37	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
86	K	0.21	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.061
87	I	0.37	[6.2e-10, 2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.12
88	E	0.3	[6.2e-10, 2.9]	0.12	0.12	0.12	0.12	0.12	0.11	0.11	0.11	0.09

89	E	0.23	[6.2e-10,2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.067
90	E	0.23	[6.2e-10,2.9]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.1	0.067
91	I	0.37	[6.2e-10,2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.12
92	A	0.41	[6.2e-10,2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.13
93	A	0.41	[6.2e-10,2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.13
94	A	0.41	[6.2e-10,2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.1	0.13
95	A	0.35	[6.2e-10,2.9]	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
96	A	0.59	[6.2e-10,2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
97	V	0.59	[6.2e-10,2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
98	G	0.59	[6.2e-10,2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
99	E	0.59	[6.2e-10,2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
100	G	0.59	[6.2e-10,2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19
101	G	0.59	[6.2e-10,2.9]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.19

Supplementary Table 6: Ka/Ks values per LP3-3 amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.

(a) ASR1

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval]	(* if lower bound > 1)	POSTERIOR PROBABILITIES									
					W =	0.00074	0.007	0.023	0.053	0.1	0.18	0.3	0.55	1
1	M	0.025	[0.00074,0.1]		0.3	0.27	0.21	0.13	0.064	0.021	0.0035	9.2e-05	1e-07	
2	E	0.17	[0.023,0.55]		6.2e-05	0.0051	0.045	0.15	0.28	0.3	0.18	0.039	0.0016	
3	E	0.014	[0.00074,0.053]		0.39	0.32	0.19	0.08	0.021	0.0034	0.00033	1.9e-05	1.2e-06	
4	E	0.014	[0.00074,0.053]		0.39	0.32	0.19	0.08	0.021	0.0034	0.00033	1.9e-05	1.2e-06	
5	K	0.051	[0.007,0.18]		0.018	0.15	0.31	0.31	0.17	0.045	0.0051	0.00011	1.4e-06	
6	H	0.097	[0.023,0.3]		0.00022	0.017	0.13	0.31	0.34	0.17	0.037	0.0019	4.8e-05	
7	H	0.016	[0.00074,0.1]		0.37	0.31	0.2	0.092	0.028	0.0048	0.0004	7.9e-06	1.2e-07	
8	H	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.087	0.024	0.0039	0.00028	4.8e-06	7.1e-08	
9	H	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.087	0.024	0.0039	0.00028	4.8e-06	7.1e-08	
10	H	0.21	[0.023,0.55]		3.6e-05	0.003	0.028	0.1	0.22	0.3	0.25	0.089	0.0049	
11	L	0.32	[0.1,0.55]		8.4e-08	7e-05	0.0022	0.02	0.09	0.24	0.38	0.25	0.014	
12	F	0.69	[0.3,1]		6.8e-18	8e-12	1.9e-08	3.9e-06	0.00022	0.0055	0.072	0.57	0.35	
13	H	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.087	0.024	0.0039	0.00028	4.8e-06	7.1e-08	
14	H	0.22	[0.053,0.55]		6.5e-09	4.7e-05	0.0038	0.051	0.22	0.38	0.28	0.067	0.0078	
15	K	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.087	0.024	0.0037	0.00024	2.6e-06	2e-08	
16	D	0.22	[0.053,0.55]		1.1e-08	7.8e-05	0.0058	0.067	0.24	0.35	0.25	0.08	0.0093	
17	K	0.27	[0.053,0.55]		2.5e-09	1.9e-05	0.0017	0.026	0.14	0.33	0.35	0.13	0.015	
18	A	0.11	[0.023,0.3]		0.00025	0.019	0.13	0.29	0.31	0.17	0.059	0.012	0.0013	
19	E	0.35	[0.053,1]		3.1e-07	0.00024	0.0064	0.044	0.14	0.24	0.26	0.23	0.081	
20	E	0.9	[0.55,1]		5.1e-21	4.4e-14	2.4e-10	9.1e-08	8.8e-06	0.00038	0.0097	0.22	0.77	
21	G	0.83	[0.3,1]		3.2e-20	2.8e-13	1.6e-09	5.7e-07	4.7e-05	0.0015	0.026	0.34	0.63	
22	P	0.77	[0.3,1]		2.3e-16	1.6e-10	1.8e-07	1.9e-05	0.00056	0.0075	0.06	0.4	0.53	
23	V	0.47	[0.18,1]		1.2e-12	8.6e-08	2.9e-05	0.0012	0.017	0.11	0.33	0.44	0.11	
24	D	0.55	[0.1,1]		5.6e-12	3.8e-07	9.8e-05	0.0028	0.023	0.092	0.23	0.43	0.22	
25	Y	0.096	[0.00074,0.3]		0.00021	0.017	0.12	0.31	0.34	0.18	0.033	0.00079	6.9e-06	
26	E	0.27	[0.053,1]		4.3e-09	3.1e-05	0.0026	0.036	0.17	0.33	0.31	0.13	0.028	
27	K	0.016	[0.00074,0.1]		0.36	0.31	0.2	0.093	0.028	0.0048	0.00037	4.8e-06	2.8e-08	
28	E	0.014	[0.00074,0.1]		0.38	0.32	0.19	0.082	0.022	0.0037	0.00037	2.1e-05	1.3e-06	
29	I	0.41	[0.1,1]		5.8e-12	4.3e-07	0.00014	0.0051	0.052	0.2	0.34	0.29	0.11	
30	K	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.088	0.025	0.0038	0.00026	3e-06	2.3e-08	
31	H	0.056	[0.007,0.18]		0.016	0.13	0.29	0.31	0.18	0.058	0.0088	0.00036	7.1e-06	
32	H	0.016	[0.00074,0.1]		0.36	0.31	0.2	0.095	0.03	0.0057	0.00053	1.2e-05	1.5e-07	
33	K	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.088	0.025	0.0038	0.00026	3e-06	2.3e-08	
34	H	0.016	[0.00074,0.1]		0.37	0.31	0.2	0.092	0.028	0.0048	0.0004	7.8e-06	9.9e-08	
35	L	0.49	[0.18,1]		7.9e-13	5.9e-08	2e-05	0.00088	0.013	0.085	0.3	0.48	0.12	
36	E	0.052	[0.007,0.18]		0.019	0.15	0.31	0.3	0.16	0.048	0.0086	0.001	0.0001	
37	Q	0.099	[0.023,0.3]		0.00022	0.017	0.12	0.3	0.33	0.18	0.042	0.0026	6.5e-05	
38	I	0.11	[0.007,0.3]		0.0062	0.055	0.15	0.24	0.26	0.19	0.086	0.012	0.00018	
39	G	0.018	[0.00074,0.1]		0.34	0.3	0.21	0.11	0.037	0.0078	0.00078	1.3e-05	3e-08	
40	K	0.2	[0.053,0.55]		7.1e-07	0.00056	0.015	0.099	0.26	0.33	0.21	0.07	0.0097	
41	L	0.41	[0.1,1]		2.9e-10	2.2e-06	0.00023	0.0045	0.036	0.15	0.36	0.4	0.054	
42	G	0.017	[0.00074,0.1]		0.35	0.3	0.2	0.099	0.032	0.0058	0.00045	5e-06	1e-08	
43	T	0.087	[0.007,0.3]		0.0091	0.078	0.2	0.28	0.25	0.14	0.048	0.0056	0.00015	
44	V	0.53	[0.18,1]		4.2e-15	2.9e-09	3e-06	0.00027	0.0061	0.057	0.26	0.53	0.14	
45	A	0.025	[0.00074,0.1]		0.3	0.27	0.21	0.13	0.06	0.02	0.0037	0.00019	2e-06	
46	A	0.021	[0.00074,0.1]		0.33	0.29	0.21	0.12	0.046	0.012	0.0016	5e-05	4.2e-07	
47	G	0.028	[0.00074,0.18]		0.29	0.26	0.21	0.14	0.071	0.026	0.0058	0.00033	2.2e-06	
48	A	0.021	[0.00074,0.1]		0.33	0.29	0.21	0.12	0.046	0.012	0.0016	5e-05	4.2e-07	
49	Y	0.14	[0.023,0.3]		8.7e-05	0.0072	0.06	0.19	0.31	0.28	0.14	0.019	0.00044	
50	A	0.026	[0.00074,0.18]		0.3	0.27	0.21	0.13	0.065	0.023	0.0049	0.0003	3.2e-06	
51	L	0.033	[0.00074,0.18]		0.27	0.25	0.21	0.15	0.084	0.036	0.0095	0.00067	4.6e-06	
52	H	0.11	[0.023,0.3]		0.00016	0.013	0.097	0.26	0.34	0.22	0.064	0.0038	3.5e-05	
53	E	0.014	[0.00074,0.053]		0.39	0.32	0.19	0.078	0.02	0.0032	0.00031	1.8e-05	1.2e-06	
54	K	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.088	0.025	0.0038	0.00026	3e-06	2.3e-08	
55	H	0.016	[0.00074,0.1]		0.37	0.31	0.2	0.092	0.028	0.0048	0.0004	7.8e-06	9.9e-08	
56	E	0.098	[0.023,0.3]		0.00027	0.02	0.14	0.31	0.32	0.16	0.044	0.0057	0.00043	
57	A	0.024	[0.00074,0.1]		0.31	0.28	0.21	0.13	0.059	0.019	0.0034	0.00016	1.6e-06	
58	K	0.091	[0.023,0.3]		0.00026	0.02	0.14	0.32	0.33	0.16	0.03	0.0011	2e-05	
59	K	0.016	[0.00074,0.1]		0.36	0.31	0.2	0.093	0.028	0.0048	0.00037	4.8e-06	2.8e-08	
60	D	0.013	[0.00074,0.053]		0.4	0.32	0.19	0.072	0.017	0.0026	0.00026	2.2e-05	2e-06	
61	P	0.32	[0.053,0.55]		1e-07	8.5e-05	0.0026	0.023	0.098	0.25	0.37	0.24	0.018	
62	E	0.053	[0.007,0.18]		0.019	0.15	0.31	0.3	0.16	0.05	0.0092	0.00094	7.9e-05	
63	H	0.056	[0.007,0.18]		0.016	0.13	0.29	0.31	0.19	0.059	0.0085	0.00029	5e-06	
64	A	0.36	[0.1,1]		6.6e-10	5.1e-06	0.0005	0.0089	0.062	0.21	0.39	0.29	0.042	
65	H	0.016	[0.00074,0.1]		0.37	0.31	0.2	0.091	0.027	0.0046	0.00037	6.8e-06	8.1e-08	
66	K	0.33	[0.1,1]		1e-09	7.8e-06	0.00071	0.012	0.082	0.26	0.39	0.21	0.037	
67	H	0.015	[0.00074,0.1]		0.37	0.31	0.2	0.087	0.024	0.0039	0.00028	4.8e-06	7.1e-08	
68	K	0.014	[0.00074,0.1]		0.38	0.32	0.2	0.083	0.022	0.0031	0.00018	1.7e-06	1.6e-08	
69	I	0.15	[0.023,0.3]		7.4e-05	0.0062	0.053	0.17	0.3	0.3	0.15	0.018	0.00018	
70	E	0.093	[0.023,0.3]		0.00029	0.022	0.15	0.32	0.31	0.15	0.037	0.0037	0.00025	
71	E	0.014	[0.00074,0.1]		0.39	0.32	0.19	0.08	0.021	0.0035	0.00034	2e-05	1.3e-06	
72	E	0.014	[0.00074,0.053]		0.39	0.32	0.19	0.08	0.021	0.0034	0.00033	1.9e-05	1.2e-06	
73	I	0.25	[0.053,0.55]		3.3e-07	0.00026	0.0074	0.055	0.18	0.32	0.3	0.12	0.013	
74	A	0.1	[0.007,0.3]		0.0071	0.062	0.16	0.25	0.26	0.18	0.073	0.011	0.0003	
75	A	0.025	[0.00074,0.18]		0.3	0.27	0.21	0.13	0.062	0.021	0.0041	0.00021	2.1e-06	
76	A	0.08	[0.007,0.3]		0.0098	0.084	0.21	0.29	0.24	0.13	0.035	0.0024	3.2e-05	
77	A	0.3	[0.053,0.55]		1.4e-07	0.00011	0.0035	0.03	0.12	0.27	0.35	0.2	0.022	
78	A	0.082	[0.007,0.3]		0.0094	0.081	0.2	0.28	0.25	0.13	0.039	0.0031	4.8e-05	
79	V	0.16	[0.023,0.55]		7.4e-05	0.0061	0.052	0.17	0.29	0.29	0.16	0.028	0.0007	
80	G	0.017	[0.00074,0.1]		0.35	0.3	0.2	0.1	0.033	0.0064	0.00056	9.2e-06	3.3e-08	
81	A	0.26	[0.053,0.55]		3.2e-07	0.00025	0.0071	0.052	0.17	0.31	0.3	0.14	0.017	
82	G	0.16	[0.023,0.55]		6.7e-05	0.0055	0.048	0.16	0.29	0.3	0.17	0.027	0.00044	
83	G	0.019	[0.00074,0.1]		0.34	0.3	0.21	0.11	0.038	0.0084	0.00087	1.6e-05	4.3e-08	
84	F	0.28	[0.053,0.55]		1.5e-05	0.0013	0.013	0.055	0.14	0.26	0.32	0.2	0.017	
85	A	0.24	[0.053,0.55]		3.3e-07	0.00026	0.0074	0.055	0.18	0.32	0.31	0.12	0.0092	
86	F	0.12	[0.007,0.3]		0.0053	0.048	0.13	0.22	0.					

89	H	0.018	[0.00074,0.1]	0.35	0.3	0.2	0.1	0.035	0.0075	0.0008	1.9e-05	1.6e-07
90	H	0.019	[0.00074,0.1]	0.34	0.29	0.21	0.11	0.041	0.0099	0.0012	3.3e-05	2.4e-07
91	E	0.014	[0.00074,0.053]	0.39	0.32	0.19	0.08	0.021	0.0034	0.00033	1.9e-05	1.2e-06
92	K	0.015	[0.00074,0.1]	0.37	0.31	0.2	0.088	0.025	0.0038	0.00026	3e-06	2.3e-08
93	K	0.015	[0.00074,0.1]	0.37	0.31	0.2	0.088	0.025	0.0038	0.00026	3e-06	2.3e-08
94	D	0.33	[0.1,1]	2.8e-11	1.8e-06	0.00047	0.013	0.095	0.27	0.35	0.22	0.044
95	A	0.068	[0.007,0.18]	0.013	0.11	0.25	0.3	0.22	0.092	0.02	0.0014	3.9e-05
96	K	0.097	[0.023,0.3]	0.00023	0.018	0.13	0.31	0.33	0.17	0.04	0.0028	0.00013
97	K	0.1	[0.023,0.3]	0.00019	0.015	0.11	0.28	0.34	0.2	0.053	0.0035	9.1e-05
98	E	0.15	[0.023,0.55]	1.9e-06	0.0014	0.033	0.17	0.34	0.3	0.13	0.025	0.0028
99	E	0.22	[0.053,0.55]	6.4e-07	0.0005	0.013	0.085	0.23	0.33	0.25	0.083	0.01
100	K	0.28	[0.1,0.55]	1e-09	7.9e-06	0.00082	0.016	0.11	0.31	0.4	0.15	0.013
101	K	0.099	[0.023,0.3]	0.00027	0.02	0.14	0.31	0.31	0.16	0.046	0.0065	0.00054
102	A	0.26	[0.053,0.55]	2.1e-07	0.00017	0.0051	0.041	0.15	0.31	0.34	0.14	0.0093
103	E	0.52	[0.18,1]	1.2e-17	8.4e-11	3e-07	6e-05	0.0026	0.04	0.25	0.59	0.12
104	G	0.032	[0.00074,0.18]	0.27	0.25	0.21	0.14	0.082	0.035	0.0095	0.00077	8.5e-06
105	G	0.28	[0.053,1]	3e-07	0.00024	0.0067	0.049	0.16	0.29	0.3	0.16	0.031
106	H	0.13	[0.023,0.3]	0.00012	0.0099	0.079	0.22	0.32	0.25	0.1	0.015	0.00094
107	H	0.019	[0.00074,0.1]	0.34	0.3	0.21	0.11	0.039	0.0087	0.001	3.3e-05	7.4e-07
108	H	0.021	[0.00074,0.1]	0.33	0.29	0.21	0.12	0.047	0.013	0.0018	7e-05	1.1e-06
109	L	0.12	[0.007,0.3]	0.005	0.045	0.13	0.22	0.26	0.21	0.11	0.021	0.00044
110	F	0.051	[0.00074,0.3]	0.22	0.21	0.19	0.16	0.11	0.069	0.031	0.0065	0.00022

Supplementary Table 7: Ka/Ks values per ASRI amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.

(b) ASR2

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval]	(* if lower bound > 1)				POSTERIOR PROBABILITIES					
				w =	0.0012	0.0097	0.03	0.064	0.12	0.2	0.32	0.57	1
1	M	0.041	[0.0012, 0.2]	0.27	0.25	0.2	0.14	0.086	0.041	0.013	0.0013	3.6e-06	
2	A	0.31	[0.064, 0.57]	3.1e-05	0.002	0.016	0.059	0.14	0.23	0.3	0.24	0.0095	
3	E	0.026	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.045	0.015	0.0046	0.0013	4.6e-05	
4	E	0.026	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.044	0.015	0.0044	0.0012	4.2e-05	
5	K	0.096	[0.0097, 0.32]	0.013	0.097	0.21	0.27	0.22	0.13	0.048	0.01	0.0002	
6	H	0.21	[0.03, 0.57]	0.00011	0.0066	0.047	0.14	0.24	0.27	0.2	0.093	0.0033	
7	Q	0.17	[0.0012, 0.57]	0.13	0.13	0.13	0.13	0.12	0.12	0.12	0.12	0.0098	
8	H	0.16	[0.0012, 0.57]	0.13	0.13	0.13	0.13	0.12	0.12	0.12	0.12	0.0093	
9	H	0.03	[0.0012, 0.2]	0.31	0.28	0.2	0.12	0.058	0.021	0.0053	0.00081	1.6e-05	
10	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.056	0.019	0.0048	0.00073	1.4e-05	
11	H	0.03	[0.0012, 0.2]	0.31	0.28	0.2	0.12	0.058	0.021	0.0053	0.00081	1.6e-05	
12	L	0.06	[0.0012, 0.32]	0.23	0.21	0.19	0.15	0.11	0.068	0.034	0.0092	0.00014	
13	F	0.19	[0.0097, 0.57]	0.0043	0.034	0.092	0.16	0.22	0.23	0.18	0.079	0.0011	
14	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.056	0.019	0.0048	0.00073	1.4e-05	
15	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.056	0.019	0.0048	0.00073	1.4e-05	
16	K	0.035	[0.0012, 0.2]	0.3	0.26	0.2	0.13	0.068	0.028	0.0089	0.002	5.9e-05	
17	N	0.25	[0.03, 0.57]	8e-05	0.005	0.036	0.11	0.2	0.25	0.23	0.15	0.0075	
18	K	0.56	[0.2, 1]	3.8e-11	1.8e-07	1.7e-05	0.0004	0.0047	0.034	0.17	0.68	0.11	
19	E	0.3	[0.03, 0.57]	5.3e-05	0.0033	0.025	0.081	0.16	0.22	0.25	0.25	0.017	
20	D	0.23	[0.03, 0.57]	0.00015	0.0087	0.057	0.15	0.23	0.23	0.18	0.14	0.01	
21	E	0.38	[0.12, 0.57]	5.5e-08	4.5e-05	0.0017	0.018	0.08	0.2	0.33	0.35	0.022	
22	G	0.55	[0.2, 1]	1.5e-10	6.8e-07	5.4e-05	0.001	0.0088	0.048	0.19	0.63	0.12	
23	G	0.36	[0.064, 0.57]	2.9e-07	0.00015	0.0036	0.025	0.093	0.21	0.32	0.32	0.02	
24	P	0.3	[0.064, 0.57]	3.2e-05	0.0021	0.017	0.062	0.14	0.24	0.3	0.23	0.0078	
25	V	0.5	[0.2, 1]	4.2e-10	1.9e-06	0.00014	0.0024	0.018	0.079	0.25	0.58	0.073	
26	D	0.39	[0.064, 1]	5.2e-07	0.00026	0.0054	0.032	0.093	0.18	0.27	0.38	0.038	
27	Y	0.031	[0.0012, 0.2]	0.31	0.27	0.21	0.13	0.063	0.022	0.0049	0.00034	1.8e-06	
28	E	0.32	[0.064, 0.57]	8.3e-07	0.00041	0.0084	0.048	0.14	0.24	0.29	0.26	0.015	
29	K	0.026	[0.0012, 0.12]	0.33	0.29	0.2	0.11	0.048	0.015	0.0029	0.00031	5.8e-06	
30	E	0.027	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.046	0.016	0.0047	0.0013	4.6e-05	
31	V	0.25	[0.03, 0.57]	0.00013	0.0076	0.05	0.13	0.21	0.23	0.2	0.16	0.01	
32	K	0.025	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.044	0.013	0.0024	0.00025	4.7e-06	
33	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.057	0.02	0.005	0.00075	1.4e-05	
34	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.056	0.019	0.0048	0.00073	1.4e-05	
35	S	0.22	[0.03, 0.57]	0.00014	0.0086	0.058	0.15	0.23	0.23	0.18	0.13	0.0079	
36	H	0.03	[0.0012, 0.2]	0.31	0.27	0.2	0.12	0.059	0.022	0.0056	0.00085	1.6e-05	
37	L	0.34	[0.064, 0.57]	1.3e-05	0.00091	0.0084	0.037	0.11	0.22	0.33	0.29	0.0093	
38	E	0.026	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.044	0.015	0.0044	0.0012	4.2e-05	
39	K	0.32	[0.064, 0.57]	5.6e-07	0.00029	0.0063	0.04	0.13	0.24	0.31	0.26	0.014	
40	I	0.16	[0.0097, 0.57]	0.0055	0.043	0.11	0.19	0.23	0.22	0.15	0.052	0.00077	
41	G	0.03	[0.0012, 0.2]	0.31	0.27	0.2	0.13	0.06	0.021	0.0044	0.00034	4e-06	
42	E	0.15	[0.0097, 0.57]	0.0076	0.058	0.14	0.22	0.23	0.18	0.11	0.052	0.0022	
43	L	0.19	[0.0097, 0.57]	0.0042	0.033	0.09	0.16	0.21	0.23	0.18	0.085	0.0017	
44	G	0.028	[0.0012, 0.12]	0.32	0.28	0.2	0.12	0.054	0.017	0.0033	0.00021	2e-06	
45	A	0.13	[0.0097, 0.57]	0.0079	0.06	0.15	0.22	0.24	0.19	0.1	0.029	0.00058	
46	V	0.37	[0.12, 0.57]	2.2e-07	0.00012	0.0028	0.021	0.081	0.2	0.33	0.35	0.017	
47	A	0.04	[0.0012, 0.2]	0.27	0.25	0.2	0.14	0.083	0.039	0.013	0.0021	2.7e-05	
48	A	0.04	[0.0012, 0.2]	0.27	0.25	0.2	0.14	0.083	0.039	0.013	0.0021	2.7e-05	
49	G	0.03	[0.0012, 0.2]	0.31	0.27	0.2	0.13	0.06	0.02	0.0043	0.00029	2.2e-06	
50	A	0.04	[0.0012, 0.2]	0.27	0.25	0.2	0.14	0.083	0.039	0.013	0.0021	2.7e-05	
51	L	0.38	[0.12, 0.57]	1.9e-07	0.0001	0.0024	0.018	0.073	0.19	0.33	0.37	0.017	
52	A	0.038	[0.0012, 0.2]	0.28	0.25	0.2	0.14	0.079	0.035	0.011	0.0017	2.1e-05	
53	L	0.085	[0.0012, 0.57]	0.19	0.18	0.17	0.15	0.12	0.093	0.061	0.028	0.00079	
54	H	0.11	[0.0097, 0.32]	0.011	0.083	0.19	0.26	0.23	0.15	0.063	0.014	0.00029	
55	E	0.026	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.044	0.015	0.0044	0.0012	4.2e-05	
56	K	0.025	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.046	0.013	0.0026	0.00028	5.4e-06	
57	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.057	0.02	0.005	0.00075	1.4e-05	
58	K	0.18	[0.03, 0.57]	0.00016	0.0098	0.067	0.18	0.27	0.26	0.15	0.053	0.0017	
59	A	0.16	[0.0097, 0.57]	0.0064	0.049	0.13	0.2	0.23	0.2	0.13	0.05	0.0014	
60	K	0.085	[0.0097, 0.32]	0.016	0.11	0.24	0.28	0.21	0.1	0.033	0.006	0.00015	
61	K	0.025	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.046	0.014	0.0026	0.00027	4.9e-06	
62	D	0.026	[0.0012, 0.12]	0.35	0.29	0.19	0.1	0.042	0.014	0.0048	0.0016	6.5e-05	
63	P	0.2	[0.0097, 0.57]	0.0041	0.033	0.089	0.16	0.21	0.23	0.19	0.091	0.002	
64	E	0.026	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.044	0.015	0.0044	0.0012	4.2e-05	
65	H	0.33	[0.064, 0.57]	6.6e-07	0.00033	0.0071	0.044	0.13	0.24	0.29	0.26	0.019	
66	A	0.041	[0.0012, 0.2]	0.27	0.25	0.2	0.14	0.085	0.041	0.014	0.0023	3.2e-05	
67	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.056	0.019	0.0048	0.00073	1.4e-05	
68	K	0.16	[0.03, 0.57]	0.0002	0.012	0.078	0.2	0.29	0.25	0.13	0.041	0.0011	
69	H	0.029	[0.0012, 0.2]	0.32	0.28	0.2	0.12	0.056	0.019	0.0048	0.00073	1.4e-05	
70	K	0.025	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.044	0.013	0.0024	0.00025	4.7e-06	
71	I	0.18	[0.0097, 0.57]	0.0049	0.038	0.1	0.17	0.22	0.22	0.17	0.067	0.001	
72	E	0.098	[0.0097, 0.32]	0.015	0.11	0.22	0.26	0.21	0.12	0.051	0.016	0.00056	
73	E	0.027	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.046	0.016	0.0047	0.0013	4.7e-05	
74	E	0.026	[0.0012, 0.12]	0.34	0.29	0.2	0.11	0.044	0.015	0.0044	0.0012	4.2e-05	
75	I	0.16	[0.0097, 0.57]	0.0056	0.043	0.11	0.19	0.23	0.22	0.15	0.051	0.00067	
76	A	0.042	[0.0012, 0.2]	0.27	0.24	0.2	0.14	0.087	0.042	0.015	0.0025	3.4e-05	
77	A	0.044	[0.0012, 0.2]	0.26	0.24	0.2	0.14	0.09	0.045	0.017	0.003	3.7e-05	
78	V	0.25	[0.03, 0.57]	5.8e-05	0.0037	0.028	0.096	0.2	0.28	0.26	0.13	0.0035	
79	A	0.14	[0.0097, 0.57]	0.0073	0.056	0.14	0.22	0.24	0.19	0.11	0.033	0.00065	
80	A	0.044	[0.0012, 0.2]	0.26	0.24	0.2	0.14	0.089	0.045	0.017	0.003	3.9e-05	
81	V	0.14	[0.0097, 0.57]	0.0072	0.055	0.14	0.22	0.24	0.2	0.11	0.034	0.00082	
82	G	0.03	[0.0012, 0.2]	0.31	0.27	0.2	0.12	0.059	0.02	0.0043	0.00035	4.2e-06	
83	A	0.28	[0.064, 0.57]	4.1e-05	0.0026	0.021	0.075	0.17	0.26	0.28	0.19	0.0078	
84	G	0.12	[0.0097, 0.32]	0.009	0.068	0.16	0.24	0.24	0.17	0.084	0.02	0.00051	
85	G	0.031	[0.0012, 0.2]	0.3	0.27	0.2	0.13	0.064	0.023	0.0053	0.0004	2.6e-06	
86	F	0.18	[0.0097, 0.57]	0.0045	0.036	0.096	0.17	0.22	0.22	0.18	0.078	0.0014	
87	A	0.041	[0.0012, 0.2]	0.27	0.25	0.2	0.14	0.085	0.041	0.014	0.0024	3.2e-05	
88	F	0.059	[0.0012, 0.32]	0.22	0.21	0.19	0.15	0.11	0.069	0.033	0.0075	5.4e-05	

89	H	0.03	[0.0012,0.2]	0.31	0.27	0.2	0.12	0.059	0.022	0.0055	0.00084	1.6e-05
90	E	0.026	[0.0012,0.12]	0.34	0.29	0.2	0.11	0.045	0.015	0.0046	0.0013	4.6e-05
91	H	0.03	[0.0012,0.2]	0.31	0.27	0.2	0.12	0.059	0.022	0.0056	0.00085	1.6e-05
92	H	0.03	[0.0012,0.2]	0.31	0.28	0.2	0.12	0.058	0.021	0.0053	0.00081	1.6e-05
93	Q	0.13	[0.0097,0.57]	0.012	0.088	0.19	0.23	0.2	0.14	0.089	0.052	0.0026
94	K	0.026	[0.0012,0.12]	0.33	0.29	0.2	0.11	0.048	0.015	0.0029	0.00031	5.8e-06
95	K	0.027	[0.0012,0.12]	0.33	0.28	0.2	0.11	0.05	0.016	0.0032	0.00033	5.8e-06
96	D	0.11	[0.0097,0.57]	0.015	0.11	0.22	0.26	0.2	0.12	0.059	0.026	0.0012
97	A	0.14	[0.0097,0.57]	0.008	0.061	0.15	0.22	0.23	0.18	0.1	0.044	0.0022
98	K	0.025	[0.0012,0.12]	0.34	0.29	0.2	0.11	0.044	0.013	0.0024	0.00025	4.8e-06
99	K	0.092	[0.0097,0.32]	0.014	0.1	0.22	0.27	0.22	0.12	0.042	0.0078	0.00019
100	E	0.04	[0.0012,0.2]	0.29	0.26	0.2	0.13	0.07	0.034	0.015	0.0062	0.00028
101	K	0.43	[0.12,1]	1.1e-07	5.8e-05	0.0015	0.012	0.051	0.14	0.3	0.46	0.038
102	K	0.18	[0.0097,0.57]	0.0053	0.041	0.11	0.18	0.22	0.21	0.15	0.084	0.0038
103	E	0.04	[0.0012,0.2]	0.29	0.26	0.2	0.13	0.07	0.033	0.015	0.0062	0.00028
104	V	0.2	[0.0097,0.57]	0.0045	0.036	0.095	0.16	0.21	0.21	0.17	0.1	0.0052
105	E	0.46	[0.12,1]	8e-10	3.5e-06	0.00025	0.004	0.027	0.11	0.29	0.53	0.045
106	G	0.05	[0.0012,0.32]	0.24	0.23	0.2	0.15	0.1	0.055	0.022	0.0042	4.1e-05
107	G	0.41	[0.12,1]	1.9e-07	0.0001	0.0024	0.017	0.066	0.17	0.3	0.41	0.033
108	H	0.072	[0.0012,0.57]	0.22	0.21	0.18	0.14	0.11	0.07	0.043	0.025	0.0015
109	H	0.22	[0.03,0.57]	0.00011	0.0065	0.046	0.13	0.23	0.26	0.2	0.12	0.0056
110	H	0.23	[0.03,0.57]	0.0001	0.0063	0.045	0.13	0.22	0.25	0.21	0.13	0.0071
111	H	0.23	[0.03,0.57]	0.00011	0.0065	0.046	0.13	0.23	0.25	0.2	0.13	0.0074
112	H	0.11	[0.0097,0.32]	0.012	0.086	0.2	0.26	0.23	0.14	0.063	0.018	0.0054
113	H	0.32	[0.064,0.57]	1.3e-05	0.00096	0.0094	0.042	0.12	0.23	0.32	0.26	0.01
114	Y	0.26	[0.03,0.57]	5.2e-05	0.0033	0.026	0.088	0.18	0.27	0.27	0.15	0.0033

Supplementary Table 8: Ka/Ks values per ASR2 amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.

(c) ASR3

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval](*)	POSTERIOR PROBABILITIES									
				if lower bound > 1)	0.00017	0.0036	0.019	0.059	0.14	0.28	0.49	0.81	1
1	M	0.29	[0.00017,1]	0.13	0.13	0.13	0.12	0.11	0.09	0.066	0.043	0.17	
2	A	0.92	[0.28,1]	1.4e-08	6.1e-06	0.00017	0.0016	0.0079	0.027	0.065	0.12	0.78	
3	E	0.16	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.078	0.044	0.021	0.074	
4	E	0.18	[0.00017,1]	0.17	0.17	0.16	0.14	0.12	0.081	0.048	0.024	0.085	
5	K	0.18	[0.00017,1]	0.17	0.17	0.16	0.14	0.12	0.083	0.049	0.025	0.085	
6	Q	0.23	[0.00017,1]	0.15	0.15	0.15	0.14	0.11	0.087	0.058	0.033	0.12	
7	H	0.22	[0.00017,1]	0.15	0.15	0.15	0.14	0.12	0.087	0.057	0.032	0.12	
8	H	0.73	[0.059,1]	0.00011	0.0023	0.012	0.035	0.071	0.11	0.13	0.12	0.53	
9	R	0.75	[0.059,1]	0.0001	0.0021	0.011	0.032	0.065	0.1	0.12	0.12	0.55	
10	L	0.9	[0.14,1]	2.2e-05	0.00047	0.0025	0.0077	0.018	0.036	0.065	0.11	0.76	
11	F	0.42	[0.00017,1]	0.1	0.1	0.1	0.098	0.093	0.086	0.075	0.062	0.28	
12	H	0.71	[0.059,1]	0.00013	0.0027	0.014	0.039	0.078	0.12	0.13	0.11	0.5	
13	H	0.2	[0.00017,1]	0.16	0.16	0.16	0.14	0.12	0.087	0.054	0.028	0.094	
14	K	0.89	[0.28,1]	3e-08	1.3e-05	0.00036	0.0032	0.015	0.044	0.09	0.13	0.72	
15	N	0.64	[0.059,1]	0.00019	0.0039	0.02	0.055	0.1	0.14	0.14	0.11	0.42	
16	R	0.97	[0.49,1]	1.2e-15	2.2e-10	1.8e-07	1.5e-05	0.00039	0.0045	0.028	0.1	0.87	
17	E	0.14	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.077	0.041	0.017	0.054	
18	E	0.64	[0.059,1]	0.00019	0.0039	0.02	0.056	0.1	0.14	0.14	0.11	0.43	
19	E	0.6	[0.019,1]	0.00022	0.0046	0.024	0.065	0.12	0.16	0.15	0.1	0.38	
20	G	0.89	[0.28,1]	1.3e-05	0.00028	0.0016	0.0057	0.016	0.039	0.076	0.12	0.74	
21	G	0.93	[0.28,1]	1.2e-08	5.2e-06	0.00015	0.0014	0.007	0.024	0.062	0.12	0.79	
22	P	0.91	[0.28,1]	1.7e-08	7.5e-06	0.00021	0.0019	0.0094	0.031	0.071	0.12	0.76	
23	V	0.76	[0.059,1]	9.5e-05	0.002	0.01	0.03	0.062	0.097	0.12	0.12	0.56	
24	D	0.59	[0.019,1]	0.00025	0.0052	0.026	0.071	0.13	0.16	0.14	0.096	0.37	
25	H	0.73	[0.059,1]	0.00011	0.0024	0.012	0.036	0.072	0.11	0.13	0.12	0.52	
26	K	0.94	[0.49,1]	7.1e-12	6.5e-08	9.5e-06	0.00026	0.0028	0.016	0.054	0.12	0.81	
27	K	0.13	[0.00017,1]	0.19	0.19	0.18	0.16	0.12	0.076	0.039	0.015	0.044	
28	K	0.85	[0.14,1]	5.5e-08	2.4e-05	0.00065	0.0055	0.024	0.063	0.11	0.13	0.67	
29	V	0.95	[0.49,1]	4.7e-12	4.3e-08	6.3e-06	0.00018	0.002	0.012	0.045	0.11	0.83	
30	K	0.15	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.081	0.045	0.02	0.06	
31	H	0.19	[0.00017,1]	0.16	0.16	0.16	0.14	0.12	0.086	0.053	0.027	0.093	
32	H	0.18	[0.00017,1]	0.17	0.17	0.16	0.14	0.12	0.085	0.051	0.025	0.084	
33	S	0.89	[0.28,1]	2.9e-08	1.2e-05	0.00034	0.0031	0.014	0.043	0.088	0.13	0.72	
34	H	0.66	[0.059,1]	0.00017	0.0034	0.018	0.05	0.096	0.13	0.14	0.11	0.45	
35	L	0.36	[0.00017,1]	0.12	0.12	0.11	0.11	0.1	0.089	0.072	0.053	0.23	
36	Q	0.88	[0.28,1]	3.4e-08	1.5e-05	0.0004	0.0035	0.016	0.047	0.092	0.13	0.71	
37	K	0.88	[0.28,1]	3.3e-08	1.5e-05	0.0004	0.0035	0.016	0.048	0.095	0.13	0.71	
38	I	0.99	[0.81,1]	2.1e-16	4.1e-11	3.3e-08	3e-06	8.6e-05	0.0012	0.011	0.075	0.91	
39	G	0.67	[0.059,1]	0.00016	0.0033	0.017	0.048	0.093	0.13	0.14	0.11	0.46	
40	E	0.63	[0.019,1]	0.00021	0.0043	0.022	0.06	0.11	0.15	0.14	0.1	0.41	
41	L	0.93	[0.28,1]	1.3e-08	5.5e-06	0.00015	0.0014	0.0073	0.025	0.062	0.12	0.78	
42	G	0.18	[0.00017,1]	0.17	0.17	0.16	0.14	0.12	0.086	0.052	0.025	0.082	
43	A	0.76	[0.059,1]	9.5e-05	0.002	0.01	0.03	0.062	0.097	0.12	0.12	0.56	
44	V	0.95	[0.49,1]	4e-12	3.7e-08	5.4e-06	0.00015	0.0018	0.011	0.043	0.11	0.83	
45	A	0.24	[0.00017,1]	0.15	0.15	0.14	0.13	0.11	0.089	0.061	0.035	0.13	
46	A	0.26	[0.00017,1]	0.14	0.14	0.14	0.13	0.11	0.09	0.064	0.039	0.15	
47	G	0.19	[0.00017,1]	0.16	0.16	0.16	0.14	0.12	0.087	0.053	0.026	0.088	
48	A	0.74	[0.059,1]	0.0001	0.0022	0.011	0.033	0.066	0.1	0.12	0.12	0.54	
49	Y	0.91	[0.28,1]	1.7e-08	7.4e-06	0.00021	0.0019	0.0093	0.03	0.071	0.12	0.76	
50	A	0.79	[0.059,1]	7.3e-05	0.0015	0.008	0.024	0.05	0.083	0.11	0.12	0.6	
51	L	0.94	[0.28,1]	8.8e-09	3.9e-06	0.00011	0.001	0.0054	0.019	0.052	0.11	0.81	
52	H	0.66	[0.059,1]	0.00017	0.0034	0.018	0.05	0.096	0.13	0.14	0.11	0.45	
53	E	0.14	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.078	0.042	0.018	0.054	
54	K	0.15	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.081	0.045	0.02	0.06	
55	H	0.2	[0.00017,1]	0.16	0.16	0.16	0.14	0.12	0.087	0.054	0.028	0.094	
56	K	0.15	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.081	0.045	0.02	0.06	
57	A	0.77	[0.059,1]	8.5e-05	0.0018	0.0093	0.027	0.056	0.09	0.12	0.12	0.58	
58	K	0.15	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.081	0.045	0.02	0.06	
59	K	0.13	[0.00017,1]	0.19	0.19	0.18	0.16	0.12	0.076	0.039	0.015	0.044	
60	D	0.14	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.077	0.041	0.017	0.053	
61	P	0.32	[0.00017,1]	0.13	0.13	0.12	0.12	0.11	0.09	0.069	0.047	0.19	
62	E	0.14	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.078	0.042	0.018	0.054	
63	N	0.65	[0.059,1]	0.00018	0.0037	0.019	0.053	0.1	0.14	0.14	0.11	0.43	
64	A	0.76	[0.059,1]	9.2e-05	0.0019	0.0099	0.029	0.06	0.095	0.12	0.12	0.57	
65	H	0.69	[0.059,1]	0.00014	0.0029	0.015	0.042	0.084	0.12	0.14	0.11	0.48	
66	K	0.86	[0.14,1]	4.5e-08	1.9e-05	0.00053	0.0046	0.021	0.057	0.11	0.13	0.68	
67	H	0.2	[0.00017,1]	0.16	0.16	0.16	0.14	0.12	0.087	0.054	0.028	0.094	
68	K	0.15	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.081	0.045	0.02	0.06	
69	I	0.26	[0.00017,1]	0.14	0.14	0.14	0.13	0.11	0.09	0.063	0.038	0.14	
70	K	0.84	[0.14,1]	5.9e-08	2.6e-05	0.00069	0.0059	0.026	0.068	0.12	0.13	0.65	
71	Q	0.65	[0.059,1]	0.00019	0.004	0.02	0.056	0.1	0.14	0.14	0.1	0.44	
72	E	0.14	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.078	0.042	0.018	0.054	
73	I	0.27	[0.00017,1]	0.14	0.14	0.14	0.13	0.11	0.09	0.064	0.039	0.15	
74	A	0.25	[0.00017,1]	0.15	0.14	0.14	0.13	0.11	0.09	0.062	0.036	0.14	
75	A	0.25	[0.00017,1]	0.15	0.15	0.14	0.13	0.11	0.09	0.062	0.036	0.13	
76	V	0.75	[0.059,1]	9.7e-05	0.002	0.01	0.03	0.063	0.098	0.12	0.12	0.56	
77	A	0.23	[0.00017,1]	0.15	0.15	0.15	0.13	0.12	0.089	0.06	0.034	0.12	
78	A	0.24	[0.00017,1]	0.15	0.15	0.14	0.13	0.11	0.089	0.061	0.035	0.13	
79	V	0.23	[0.00017,1]	0.15	0.15	0.15	0.14	0.12	0.089	0.06	0.033	0.12	
80	G	0.19	[0.00017,1]	0.17	0.16	0.16	0.14	0.12	0.086	0.052	0.026	0.086	
81	A	0.78	[0.059,1]	8.2e-05	0.0017	0.0089	0.026	0.055	0.089	0.11	0.12	0.59	
82	G	0.7	[0.059,1]	0.00013	0.0027	0.014	0.04	0.08	0.12	0.13	0.11	0.5	
83	G	0.19	[0.00017,1]	0.16	0.16	0.16	0.14	0.12	0.087	0.053	0.026	0.087	
84	F	0.84	[0.14,1]	4.9e-05	0.001	0.0054	0.016	0.036	0.064	0.095	0.12	0.66	
85	A	0.76	[0.059,1]	9.1e-05	0.0019	0.0099	0.029	0.06	0.095	0.12	0.12	0.57	
86	F	0.4	[0.00017,1]	0.1	0.1	0.1	0.1	0.095	0.086	0.074	0.06	0.27	
87	H	0.16	[0.00017,1]	0.18	0.17	0.17	0.15	0.12	0.083	0.047	0.021	0.066	
88	E	0.14	[0.00017,1]	0.19	0.18	0.17	0.15	0.12	0.076	0.04	0.017	0.052	

89	H	0.16	[0.00017,1]	0.17	0.17	0.16	0.15	0.12	0.083	0.048	0.022	0.071
90	H	0.16	[0.00017,1]	0.18	0.17	0.17	0.15	0.12	0.083	0.047	0.021	0.066
91	Q	0.95	[0.49,1]	5.3e-12	4.8e-08	7.1e-06	0.0002	0.0022	0.013	0.047	0.11	0.82
92	K	0.15	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.081	0.045	0.02	0.06
93	K	0.13	[0.00017,1]	0.19	0.18	0.18	0.15	0.12	0.077	0.04	0.016	0.047
94	E	0.87	[0.28,1]	4e-08	1.7e-05	0.00047	0.0041	0.019	0.052	0.098	0.13	0.7
95	A	0.8	[0.059,1]	6.8e-05	0.0014	0.0074	0.022	0.047	0.079	0.11	0.12	0.62
96	K	0.15	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.081	0.045	0.02	0.06
97	K	0.13	[0.00017,1]	0.19	0.19	0.18	0.16	0.12	0.076	0.039	0.015	0.044
98	E	0.14	[0.00017,1]	0.18	0.18	0.17	0.15	0.12	0.077	0.041	0.017	0.054
99	K	0.86	[0.14,1]	5.1e-08	2.2e-05	0.0006	0.0052	0.023	0.061	0.11	0.13	0.67
100	K	0.65	[0.059,1]	0.00018	0.0038	0.019	0.054	0.1	0.14	0.14	0.11	0.44
101	A	0.68	[0.059,1]	0.00017	0.0034	0.018	0.049	0.093	0.13	0.13	0.11	0.47
102	A	0.23	[0.00017,1]	0.15	0.15	0.15	0.13	0.12	0.089	0.06	0.034	0.12
103	E	0.93	[0.49,1]	9.4e-12	8.6e-08	1.2e-05	0.00034	0.0036	0.019	0.062	0.13	0.79
104	K	0.94	[0.49,1]	6.4e-12	5.8e-08	8.5e-06	0.00024	0.0026	0.015	0.053	0.12	0.81
105	G	0.88	[0.28,1]	3.5e-08	1.5e-05	0.00042	0.0037	0.017	0.049	0.096	0.13	0.7
106	R	0.83	[0.14,1]	3.7e-05	0.00078	0.0043	0.014	0.035	0.068	0.1	0.12	0.65
107	H	0.7	[0.059,1]	0.00013	0.0028	0.014	0.041	0.081	0.12	0.13	0.11	0.49
108	H	0.2	[0.00017,1]	0.16	0.16	0.16	0.14	0.12	0.087	0.054	0.028	0.094

Supplementary Table 9: Ka/Ks values per ASR3 amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.

(d) ASR4

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval](** if lower bound > 1)	POSTERIOR PROBABILITIES								
				w =	6.9e-05	0.0014	0.007	0.021	0.051	0.11	0.21	0.47
1	M	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
2	A	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
3	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
4	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
5	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
6	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
7	H	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
8	H	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
9	F	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
10	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
11	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
12	L	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
13	F	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
14	N	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
15	H	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
16	H	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
17	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
18	N	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
19	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
20	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
21	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
22	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
23	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
24	P	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
25	I	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
26	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
27	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
28	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
29	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
30	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
31	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
32	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
33	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
34	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
35	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
36	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
37	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
38	S	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
39	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
40	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
41	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
42	S	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
43	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
44	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
45	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
46	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
47	N	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
48	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
49	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
50	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
51	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
52	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
53	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
54	S	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
55	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
56	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
57	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
58	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
59	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
60	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
61	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
62	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
63	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
64	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
65	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
66	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
67	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
68	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
69	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
70	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
71	N	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
72	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
73	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
74	S	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
75	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
76	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
77	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
78	S	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
79	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
80	G	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
81	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
82	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
83	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
84	Y	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
85	D	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
86	E	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
87	K	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34
88	T	0.41	[6.9e-05, 1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34

183	G	0.39	[6.9e-05,1]	0.086	0.086	0.086	0.086	0.086	0.085	0.084	0.082	0.32
184	G	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.084	0.084	0.082	0.33
185	G	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.084	0.084	0.082	0.33
186	V	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32
187	G	0.39	[6.9e-05,1]	0.086	0.086	0.086	0.086	0.086	0.085	0.084	0.082	0.32
188	A	0.41	[6.9e-05,1]	0.084	0.084	0.084	0.084	0.084	0.083	0.083	0.082	0.33
189	Y	0.41	[6.9e-05,1]	0.084	0.084	0.084	0.084	0.084	0.083	0.083	0.082	0.33
190	S	0.41	[6.9e-05,1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.082	0.34
191	S	0.41	[6.9e-05,1]	0.084	0.084	0.084	0.084	0.084	0.084	0.083	0.082	0.33
192	E	0.39	[6.9e-05,1]	0.086	0.086	0.086	0.086	0.086	0.085	0.084	0.082	0.32
193	T	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.084	0.084	0.084	0.082	0.33
194	T	0.9	[0.21,1]	6.4e-09	2.4e-06	6.4e-05	0.00059	0.0031	0.012	0.038	0.11	0.84
195	T	0.9	[0.21,1]	6.4e-09	2.4e-06	6.4e-05	0.00059	0.0031	0.012	0.038	0.11	0.84
196	N	0.99	[0.47,1]	2.5e-17	3.7e-12	2.5e-09	2.2e-07	6.8e-06	0.00012	0.0015	0.024	0.97
197	Y	0.67	[0.021,1]	6.7e-05	0.0013	0.0067	0.02	0.044	0.081	0.13	0.17	0.55
198	E	0.83	[0.11,1]	1.7e-08	6.4e-06	0.00017	0.0015	0.0076	0.027	0.073	0.16	0.73
199	E	0.95	[0.47,1]	1e-12	7.7e-09	1e-06	2.8e-05	0.00035	0.0026	0.015	0.077	0.91
200	N	0.58	[0.021,1]	0.00011	0.0021	0.01	0.031	0.066	0.11	0.16	0.17	0.44
201	D	0.93	[0.21,1]	1.6e-09	6.2e-07	1.7e-05	0.00018	0.0011	0.0056	0.023	0.092	0.88
202	D	0.7	[0.021,1]	7.4e-05	0.0014	0.0073	0.021	0.045	0.078	0.11	0.14	0.59
203	S	0.9	[0.21,1]	1.5e-09	6e-07	1.8e-05	0.00021	0.0016	0.0087	0.037	0.13	0.82
204	G	0.61	[0.021,1]	0.00012	0.0023	0.011	0.033	0.067	0.11	0.14	0.14	0.5
205	T	0.76	[0.051,1]	4e-05	0.00079	0.004	0.012	0.028	0.054	0.093	0.15	0.66
206	K	0.95	[0.47,1]	1.7e-09	6.6e-07	1.8e-05	0.00017	0.00099	0.0045	0.018	0.079	0.9
207	T	0.74	[0.051,1]	4.7e-05	0.00091	0.0047	0.014	0.032	0.061	0.1	0.15	0.63
208	S	0.95	[0.47,1]	1.2e-09	4.6e-07	1.3e-05	0.00013	0.00081	0.004	0.017	0.079	0.9
209	E	0.75	[0.051,1]	2.4e-05	0.00047	0.0025	0.0084	0.022	0.052	0.1	0.17	0.64
210	D	0.091	[6.9e-05,1]	0.17	0.17	0.16	0.15	0.13	0.095	0.06	0.027	0.045
211	Y	0.92	[0.21,1]	4.3e-09	1.7e-06	4.4e-05	0.0004	0.0022	0.0087	0.029	0.095	0.86
212	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.07	0.03	0.038
213	E	0.51	[0.021,1]	0.00015	0.0029	0.014	0.041	0.086	0.14	0.18	0.16	0.37
214	E	0.099	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.099	0.065	0.03	0.049
215	K	0.52	[0.021,1]	0.00014	0.0027	0.014	0.039	0.082	0.13	0.18	0.16	0.39
216	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.069	0.03	0.039
217	H	0.12	[6.9e-05,1]	0.15	0.15	0.15	0.14	0.13	0.11	0.083	0.043	0.055
218	H	0.13	[6.9e-05,1]	0.14	0.14	0.14	0.14	0.13	0.11	0.086	0.048	0.065
219	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.07	0.03	0.038
220	H	0.091	[6.9e-05,1]	0.16	0.16	0.15	0.15	0.13	0.11	0.075	0.033	0.037
221	L	0.96	[0.47,1]	2.3e-10	9.1e-08	2.8e-06	3.5e-05	0.00029	0.0018	0.01	0.062	0.93
222	E	0.095	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.098	0.064	0.029	0.047
223	E	0.83	[0.11,1]	1.7e-08	6.4e-06	0.00017	0.0015	0.0076	0.027	0.073	0.16	0.73
224	L	0.78	[0.051,1]	3.7e-05	0.00073	0.0037	0.011	0.026	0.05	0.087	0.14	0.68
225	G	0.11	[6.9e-05,1]	0.15	0.15	0.15	0.14	0.13	0.11	0.075	0.036	0.054
226	G	0.59	[0.021,1]	0.00011	0.0021	0.01	0.03	0.065	0.11	0.16	0.17	0.46
227	L	0.25	[6.9e-05,1]	0.11	0.11	0.11	0.11	0.11	0.1	0.092	0.071	0.18
228	G	0.1	[6.9e-05,1]	0.16	0.16	0.15	0.14	0.13	0.11	0.073	0.034	0.05
229	A	0.12	[6.9e-05,1]	0.15	0.15	0.14	0.14	0.13	0.11	0.082	0.044	0.063
230	V	0.64	[0.021,1]	7.9e-05	0.0015	0.0078	0.023	0.051	0.092	0.14	0.17	0.51
231	A	0.1	[6.9e-05,1]	0.16	0.15	0.15	0.14	0.13	0.11	0.076	0.036	0.048
232	A	0.12	[6.9e-05,1]	0.15	0.15	0.14	0.14	0.13	0.11	0.082	0.044	0.063
233	G	0.076	[6.9e-05,1]	0.17	0.17	0.16	0.15	0.13	0.1	0.066	0.026	0.028
234	A	0.14	[6.9e-05,1]	0.14	0.14	0.14	0.13	0.12	0.11	0.084	0.048	0.082
235	F	0.67	[0.021,1]	6.8e-05	0.0013	0.0068	0.02	0.045	0.082	0.13	0.16	0.55
236	A	0.12	[6.9e-05,1]	0.15	0.15	0.14	0.14	0.13	0.11	0.082	0.044	0.063
237	L	0.29	[6.9e-05,1]	0.11	0.1	0.1	0.1	0.1	0.097	0.09	0.075	0.22
238	H	0.091	[6.9e-05,1]	0.16	0.16	0.15	0.15	0.13	0.11	0.075	0.033	0.037
239	E	0.099	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.099	0.065	0.03	0.049
240	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.07	0.03	0.038
241	H	0.13	[6.9e-05,1]	0.14	0.14	0.14	0.14	0.13	0.11	0.086	0.048	0.065
242	K	0.6	[0.021,1]	9.1e-05	0.0018	0.009	0.027	0.058	0.1	0.15	0.18	0.47
243	A	0.14	[6.9e-05,1]	0.14	0.14	0.14	0.13	0.12	0.11	0.086	0.049	0.079
244	E	0.51	[0.021,1]	0.00014	0.0028	0.014	0.041	0.085	0.14	0.18	0.16	0.38
245	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.069	0.03	0.039
246	D	0.097	[6.9e-05,1]	0.17	0.17	0.16	0.15	0.13	0.094	0.059	0.028	0.051
247	P	0.21	[6.9e-05,1]	0.12	0.12	0.12	0.12	0.11	0.11	0.092	0.067	0.14
248	E	0.099	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.099	0.065	0.03	0.049
249	H	0.67	[0.021,1]	8.8e-05	0.0017	0.0086	0.025	0.052	0.087	0.12	0.14	0.57
250	A	0.14	[6.9e-05,1]	0.14	0.14	0.14	0.13	0.12	0.11	0.085	0.048	0.075
251	H	0.13	[6.9e-05,1]	0.14	0.14	0.14	0.14	0.13	0.11	0.086	0.048	0.065
252	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.07	0.03	0.038
253	H	0.13	[6.9e-05,1]	0.14	0.14	0.14	0.14	0.13	0.11	0.086	0.048	0.065
254	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.07	0.03	0.038
255	I	0.7	[0.021,1]	6.2e-05	0.0012	0.0062	0.018	0.041	0.075	0.12	0.15	0.59
256	E	0.74	[0.051,1]	4e-05	0.00079	0.0041	0.013	0.03	0.06	0.11	0.16	0.63
257	E	0.68	[0.021,1]	7.3e-05	0.0014	0.0072	0.021	0.046	0.082	0.12	0.15	0.57
258	E	0.71	[0.021,1]	7.2e-05	0.0014	0.0071	0.021	0.044	0.075	0.11	0.14	0.61
259	I	0.18	[6.9e-05,1]	0.13	0.13	0.13	0.13	0.12	0.11	0.09	0.059	0.11
260	A	0.13	[6.9e-05,1]	0.15	0.15	0.14	0.14	0.13	0.11	0.081	0.043	0.068
261	A	0.15	[6.9e-05,1]	0.14	0.14	0.14	0.13	0.12	0.11	0.086	0.051	0.085
262	V	0.9	[0.21,1]	7.1e-09	2.7e-06	7.1e-05	0.00065	0.0034	0.013	0.039	0.11	0.83
263	A	0.56	[0.021,1]	0.00011	0.0021	0.011	0.032	0.069	0.12	0.17	0.18	0.42
264	A	0.14	[6.9e-05,1]	0.14	0.14	0.14	0.13	0.12	0.11	0.086	0.049	0.079
265	V	0.68	[0.021,1]	7.2e-05	0.0014	0.0071	0.021	0.046	0.083	0.13	0.15	0.56
266	G	0.096	[6.9e-05,1]	0.16	0.16	0.15	0.15	0.13	0.11	0.075	0.034	0.042
267	A	0.9	[0.21,1]	5.4e-09	2.1e-06	5.5e-05	0.00051	0.0028	0.011	0.037	0.11	0.83
268	G	0.59	[0.021,1]	9.5e-05	0.0019	0.0094	0.028	0.061	0.11	0.16	0.18	0.46
269	G	0.12	[6.9e-05,1]	0.15	0.15	0.15	0.14	0.13	0.11	0.08	0.041	0.057
270	F	0.18	[6.9e-05,1]	0.13	0.13	0.13	0.12	0.12	0.11	0.092	0.061	0.11
271	A	0.14	[6.9e-05,1]	0.14	0.14	0.14	0.13	0.12	0.11	0.085	0.048	0.075
272	F	0.27	[6.9e-05,1]	0.11	0.11	0.11	0.11	0.1	0.099	0.091	0.075	0.2
273	H	0.091	[6.9e-05,1]	0.16	0.16	0.15	0.15	0.13	0.11	0.075	0.033	0.037
274	E	0.1	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.099	0.065	0.03	0.051
275	H	0.091	[6.9e-05,1]	0.16	0.16	0.15	0.15	0.13	0.11	0.075	0.033	0.037
276	H	0.071	[6.9e-05,0.47]	0.17	0.17	0.16	0.15	0.13	0.1	0.066	0.025	0.023

277	Q	0.93	[0.21,1]	4.5e-09	1.7e-06	4.5e-05	0.00041	0.0022	0.0081	0.025	0.081	0.88
278	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.07	0.03	0.038
279	K	0.089	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.1	0.069	0.03	0.039
280	E	0.095	[6.9e-05,1]	0.16	0.16	0.16	0.15	0.13	0.098	0.064	0.029	0.047
281	A	0.14	[6.9e-05,1]	0.14	0.14	0.14	0.13	0.12	0.11	0.086	0.049	0.079
282	K	0.7	[0.021,1]	7e-05	0.0014	0.0069	0.02	0.044	0.077	0.11	0.14	0.59
283	E	0.52	[0.021,1]	0.00014	0.0028	0.014	0.04	0.083	0.14	0.18	0.16	0.39
284	E	0.95	[0.47,1]	1e-12	7.8e-09	1e-06	2.9e-05	0.00036	0.0027	0.015	0.081	0.9
285	E	0.98	[0.47,1]	1.6e-13	1.2e-09	1.6e-07	4.8e-06	6.4e-05	0.00057	0.0041	0.038	0.96
286	E	0.98	[0.47,1]	5.2e-14	4e-10	5.8e-08	1.9e-06	3.1e-05	0.00035	0.0032	0.036	0.96
287	E	0.7	[0.021,1]	6.6e-05	0.0013	0.0065	0.019	0.042	0.076	0.11	0.15	0.59
288	A	0.3	[6.9e-05,1]	0.1	0.1	0.1	0.1	0.099	0.096	0.09	0.077	0.23
289	E	0.93	[0.21,1]	4.9e-06	9.6e-05	0.00051	0.0017	0.0044	0.011	0.027	0.08	0.88
290	G	0.84	[0.051,1]	2.4e-05	0.00047	0.0024	0.0073	0.017	0.034	0.063	0.12	0.76
291	K	0.83	[0.051,1]	2.5e-05	0.0005	0.0026	0.0078	0.018	0.036	0.066	0.12	0.75
292	K	0.29	[6.9e-05,1]	0.1	0.1	0.1	0.1	0.1	0.097	0.09	0.076	0.22
293	K	0.3	[6.9e-05,1]	0.1	0.1	0.1	0.1	0.1	0.096	0.089	0.075	0.22
294	H	0.28	[6.9e-05,1]	0.11	0.11	0.11	0.11	0.1	0.099	0.091	0.075	0.2
295	H	0.31	[6.9e-05,1]	0.1	0.1	0.1	0.1	0.099	0.095	0.089	0.077	0.23
296	F	0.38	[6.9e-05,1]	0.089	0.089	0.089	0.089	0.088	0.087	0.085	0.081	0.3
297	F	0.39	[6.9e-05,1]	0.087	0.087	0.087	0.087	0.087	0.086	0.085	0.082	0.31

Supplementary Table 10: Ka/Ks values per ASR4 amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.