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 Abscisic 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.

34 **1. Introduction**

35 Land colonisation by plants during the Paleozoic has forced these to adopt several adaptive

36 strategies to survive desiccation (Edwards and Selden, 1992). These strategies led to the

37 development of organs such as roots for taking up water and the implementation of water stress

38 management tactics like the closure of stomata and the modulation of osmotic pressures within

39 the plant cell in an effort to maintain the plants' water potential (Chaves et al., 2003). Today,

40 many plants species have adapted to be able to cope with drought through millennia of

41 evolution, yet anthropogenic climate change is expected to dramatically affect the growth

42 conditions of most plant species, notably through increased drought occurrence and aridity

43 around the world.

44

45 Drought is a major hazard to the survival and development of commercially important plants,

46 from both crops to forest tree species. In recent years, there has been an observed increase in

47 drought occurrences notably in southern Europe, sub-Saharan Africa and many other areas

48 around the world and this trend will only increase with time as climate change continues to

49 progress (Gudmundsson and Seneviratne, 2016; Ruosteenoja et al., 2018). In this context, it is

50 more important than ever to understand more about the mechanisms by which plants adapt and

51 overcome water deficit stress in an effort to potentially produce more drought resistant varieties.

52

53 Water deficiency as a major stress for plant species is detected in many ways, with the

54 signalling component being mediated largely through the phytohormone Abscisic acid (ABA)

55 which is involved in stress response in plants, notably via its' effects on gene expression and

56 osmotic pressure adjustment within the plant cell (Bray, 1993). ABA is also implicated in the

57 plant response to cold stress and the ripening process. The ABA dependent pathway has been

58 the focus of extensive studies in a multitude of species, notably *Arabidopsis thaliana* L. and

59 *Populus tremula* L.

60

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).

70

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 angiomotin 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 aquaporines, cellulose synthases (CESA) and

80 glucanases. *ASR*1, the most studied of the *ASR* genes, is for example involved in sugar

81 metabolism in response to drought (Dominguez and Carrari, 2015).

82

83 An *ASR* homolog called *LP*3 was first discovered in the roots of loblolly pine (*Pinus taeda* L.)

84 whose background constitutive expression was significantly upregulated in drought conditions

85   (González and Iusem, 2014; Padmanabhan et al., 1997; Wang et al., 2002). For the purposes of

86   this study, while both genes are homologous, the terms *LP3* and *ASR* will be used to describe

87   the gymnosperm and angiosperm sequences, respectively. *LP*3 differs from *ASR* in that it

88   contains a consequent insertion of 35 amino acids between its N-terminal and ABA/WDS

89   regions and is present as a gene family (each individual gene isoform is called *LP*3-0, *LP*3-1,

90   *LP*3-2 and *LP*3-3; *LP*3-2 and *LP*3-3 have only been partially sequenced therefore only partial

91   sequences are available) within pines and other gymnosperms (Chang et al., 1996;

92   Padmanabhan et al., 1997). *LP*3 transport into the nucleus is mediated by the putative C-

93   terminal Nuclear Localisation Signal (NLS) of sequence KKESKEEEKEAEGKKHHH

94   (Padmanabhan et al., 1997; Wang et al., 2002). Alternatively, this NLS sequence might not be

95   necessary due to the short size of the *LP*3 protein which should allow it to diffuse through the

96   nuclear envelope. Indeed research into *ASR* has shown that the NLS sequence to the one

97   described above is not necessary for the ASR protein to diffuse into the nucleus (Ricardi et al.,

98   2012). *LP3* has not been as extensively studied as *ASR*, probably due to the difficulty of genetic

99   studies within gymnosperms. This lack of study is the motivation for this study.

100

101   The objective of this research work is to investigate and compare the rate and mode of evolution

102   of two orthologous genes *LP3* and ASR genes. To achieve our objective we have conducted the

103   following actions: We have (i) retraced the phylogeny of *LP3* as a member of the ABA/WDS

104   family and relate it to the *ASR* genes, (ii) estimated the GC content and Codon Usage Bias

105   (CUB), and (iii) determined the mode of evolution of different subsections of the *ASR/LP3*

106   genes.

107

4

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 1^{e-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 if 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

5

134 FullSeq-tree, ABA/WDS-tree, N-tree and C-tree, respectively. The taxonomic phylogenetic

135 tree was constructed using the Timetree software (Kumar et al., 2017).

136

137 For FullSeq-tree, sequences were aligned using the MUSCLE algorithm (Edgar, 2004), checked

138 for errors and the multiple sequence alignment was exported for further analysis. The Maximum

139 Likelihood (ML) Phylogenetic best fit model was determined in MEGA X by log-likelihood

140 analysis of each model and the one with the highest AICc score was used. The resulting best fit

141 model for the sequences used in tree FullSeq-tree was the Kimura 2 parameter model. The

142 phylogenetic tree was created using the Maximum likelihood method combined with the

143 Kimura 2 parameter model with a gamma parameter of 1, 30 with 1000 permutations.

144

145 ABA/WDS-tree was constructed by isolating the highly conserved ABA/WDS nucleotide

146 domains from the MSA of *LP3* and *ASR* and exporting those for phylogenetic analysis. The ML

147 phylogenetic model was determined in the same manner as previously described, with the

148 resulting best model by log-likelihood analysis being the Kimura 2 parameter model. The tree

149 was constructed using the ML method with the Kimura 2 parameter with a Gamma parameter

150 equal to 1,0846 with 1000 permutations.

151

152 Tree N-tree was constructed by extracting the N-terminal nucleotide region of *LP3* and *ASR*.

153 Due to the presence of incomplete sequences that did not cover this section of the gene, the

154 following sequences were excluded from the phylogenetic analysis: *LP3-0 Cupressus*

155 *sempervirens; LP3-1 Pinus sylvestris; LP3-1 Pinus hwangshenensis; LP3-0 Pinus*

156 *masssoniana; LP3-2 Pinus taeda; LP3-2 Pinus sylvestris* and all *LP3-3* sequences. The ML

157 phylogenetic model was determined in the same manner as previously described, with the

158 resulting best model by log-likelihood analysis result being the Kimura 2 parameter model. The

159   tree was therefore constructed using the ML method with the Kimura 2 parameter model with

160   a gamma parameter equal to 1, 27 with 1000 permutations.

161

162   Tree C-tree was constructed by focusing on the C-terminal NLS/DNA binding regions of the

163   sequences. The ML phylogenetic model was determined in the same manner as previously

164   described, with the resulting best model by log-likelihood analysis result being the Kimura 2

165   parameter model. The following partial sequences were excluded from the phylogenetic

166   analysis due to too short C-terminal sequences: *LP3-0 Cupressus sempervirens, LP3-0 Pinus*

167   *masssoniana; LP3-2 Pinus taeda; LP3-2 Pinus sylvestris* and all *LP3-3* sequences. The tree

168   was therefore constructed using the ML method with the Kimura 2 parameter model with a

169   gamma parameter equal to 1, 5588 with 1000 permutations. Analysis of gene duplication events

170   and construction of the corresponding gene duplication tree was also carried out in MEGA X,

171   using FullSeq-tree as a template on which to perform the analysis.

172

173   ***2.3 GC% and RCSU analyses***
174   Sequence names and accession numbers for determining GC and RCSU content according to

175   species are shown in the Supplementary Table 2

176

177   The Relative Synonymous Codon Usage (RSCU) is a measure of the codon usage bias for a

178   particular amino acid. As such codon bias is can be a measure of how efficient and accurate a

179   given gene translation is. The RSCU of the ABA/WDS genes found in majorly represented

180   species (species in which at least three different ABA/WDS genes are present) was extracted

181   using MEGA X. The average RSCU values per amino acid were then calculated and used to

182   determine which codon was on average the most used in a particular gene. Codons with RSCU

183   values above 1 are abundant, whilst codons with RSCU values below 1 are less abundant.

184   Codons for Methionine and Tryptophane were not included since these amino acids are encoded

185   by only one codon. Stop codons were not included either as they are only involved in

186   transcription termination and therefore not in transcription efficiency.

187

188   Individual gene parameters from majorly represented species such as total GC, GC1, GC2, GC3

189   contents, Codon Adaptive Index (CAI), and Effective Number of Nucleotides (ENC) were

190   computed using CAICal (http://genomes.urv.cat/CAIcal/). The CAI is derived from the codon

191   usage of highly expressed genes in organisms and is positively correlated with transcription

192   levels. As such the CAI is often used as a proxy for expression levels (Sharp and Li, 1987). The

193   ENC is a number corresponding to the overall codon bias in a given gene, with 20 symbolising

194   a complete bias of only one codon per amino acid whereas a value of 61 symbolises a

195   completely unbiased codon usage, with each available codon being used equally for a given

196   amino acid (Wright, 1990). Statistical analyses were done in R using p=0,05 as the significance

197   threshold. Gene parameters were first compared using a Levene test to ensure variance equality

198   among the different genes, followed by either ANOVA or a Kruskal-Wallis test. If either of

199   these indicated the presence of a significantlly different group then a Tukey HSD test was

200   performed in the case of ANOVA and a pairwise Wilcoxon test in the case of a Kruskal-Wallis.

201   Pearson correlations between the different gene parameters were also done. For this the

202   different ASR and LP3 genes were grouped together.

203

204   *2.4 Mode of evolution of different subsections of the ASR/LP3 gene*
205   A codon-by-codon selective pressure analysis provides insights into which amino acids in a

206   protein are undergoing selective constraints or not. This in turn allows one to suggest which

207   amino acids are likely to change over time. Visualisation of codon selective pressure as defined

208   by the ratio of synonymous to non-synonymous codons $\omega = {dN}/{dS}$ on the *LP3-0* gene was

209   done using the complete CDS of all *LP3-0* homologous sequences were uploaded to the

210   Selecton server for selective pressure analysis using the M8 model that allows for positive

211   selection (Stern et al., 2007). The sequences were aligned in the server using the MUSCLE

212   algorithm (Edgar, 2004) and the *Pinus taeda LP3-0* CDS was set as the reference query.

213   Statistical analysis of the calculated selective pressure was also performed using Selecton with

214   default settings by calculating the log likelihood ratio between M8 and the null model M8a.

215   The same procedure was repeated for *LP3-1, LP3-3, ASR1, ASR2, ASR3* and *ASR4*. *P.taeda*

216   *LP3* and *S. lycopersicum ASR* sequences were set as references on which to visualise sites of

217   selective pressure. There were not enough *LP3-2* orthologous sequences for this analysis to be

218   performed on it.

219

3.   Results
3.1 Phylogenetic analysis of LP3 and ASR
222   On a broad level, it can be seen that *LP3-1* is the most ancestral form of *LP3*, from which *LP3-*

223   *2* diverged, followed by *LP3-0* and *LP3-3*. The *ASR* gene phylogeny show that *ASR4* is the

224   ancestral sequence in tomato, followed by *ASR3*, being *ASR2* and *ASR1* the result of are more

225   recent diverge event (Figure 1). The clear distinction between the *ASR* and *LP*3 seems to

226 correlate with the divergence of angiosperms and gymnosperms, around 313 MYA

227 (Supplementary Figure 1, www.timetree.org).
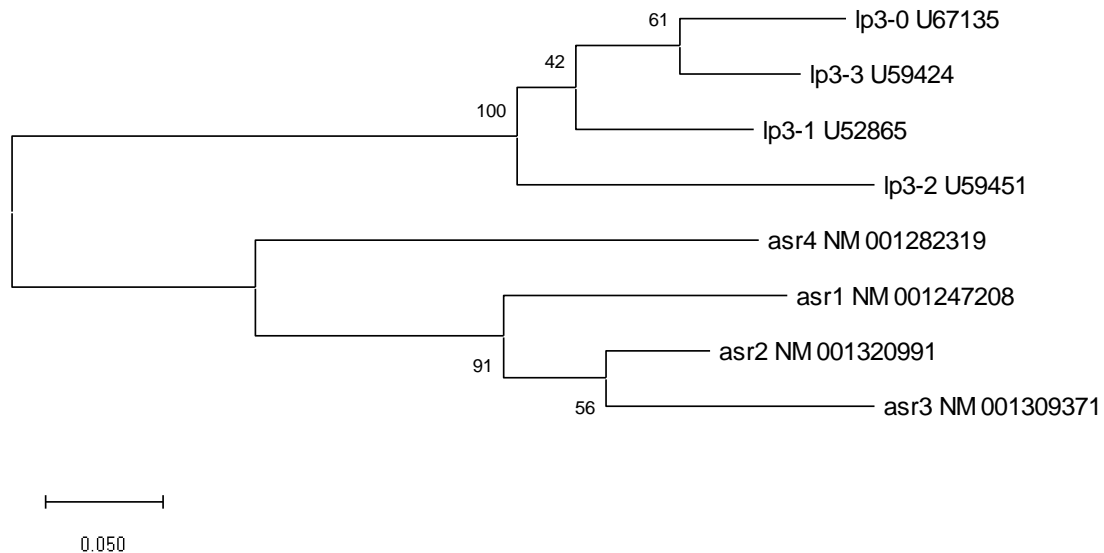
228

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

230 FullSeq-tree (*Figure 2*) shows that there is a clear divergence between the angiosperm ASR and

231 the gymnosperm *LP3* sequences. This could be to certain extent be attributed to the sequence

232 insertion present between the N-terminal zinc binding domain and ABA/WDS regions in

233 gymnosperm. Low bootstrap values within the gymnosperm nodes could be explained by the

234 general high similitude between sequences which would result in them easily swapping

235 positions during different bootstrap analyses. It can be observed that the *LP3* sequences cluster

236 together according to genus and isoform. There is also perfect clustering of *LP3-1* and *LP3-2*

237 sequences within the *Pinus* cluster, however this is not the case when observing the *LP3-3*

238 cluster. In that instance, clustering of *LP3-3* occurs with *LP3-0-2* and *LP3-0-3* of *Pinus*

239 *sylvestris*. This might be indicative of orthology between *LP3-3* and the *Pinus sylvestris*

240 sequences shown. The grouping together of *Pinus taeda LP3-3* and *Pinus taeda LP3-0-2* with

241 a very high bootstrap score could suggest that LP3-0-2 (PITA_00002958) might be actually a

242 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 vin*ifera 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.

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

253

254   Looking at ABA/WDS-tree (Figure 3) which focuses on the central ABA/WDS domain, there

255   is yet again another clear grouping of angiosperm and gymnosperm sequences together. Within

256   the gymnosperm grouping one can observe the sub-grouping of *LP3-1* and *LP3-2* together,

257   while similarly to FullSeq-tree, the *LP3-3* sequences are again broadly grouped together with

258   some *LP3-0* sequences grouped alongside them. The angiosperm sequences also show clear

259   clustering of *ASR1*, *ASR2* and *ASR3* sequences with the *Oriza sativa ASR1* and *Zea mays ASR3*

260   seeming to diverge from the other *ASR* sequences. As in FullSeq-tree, there is also a clear

261   clustering according to genus, with *Picea* and *Pinus* sequences clustering together, respectively.
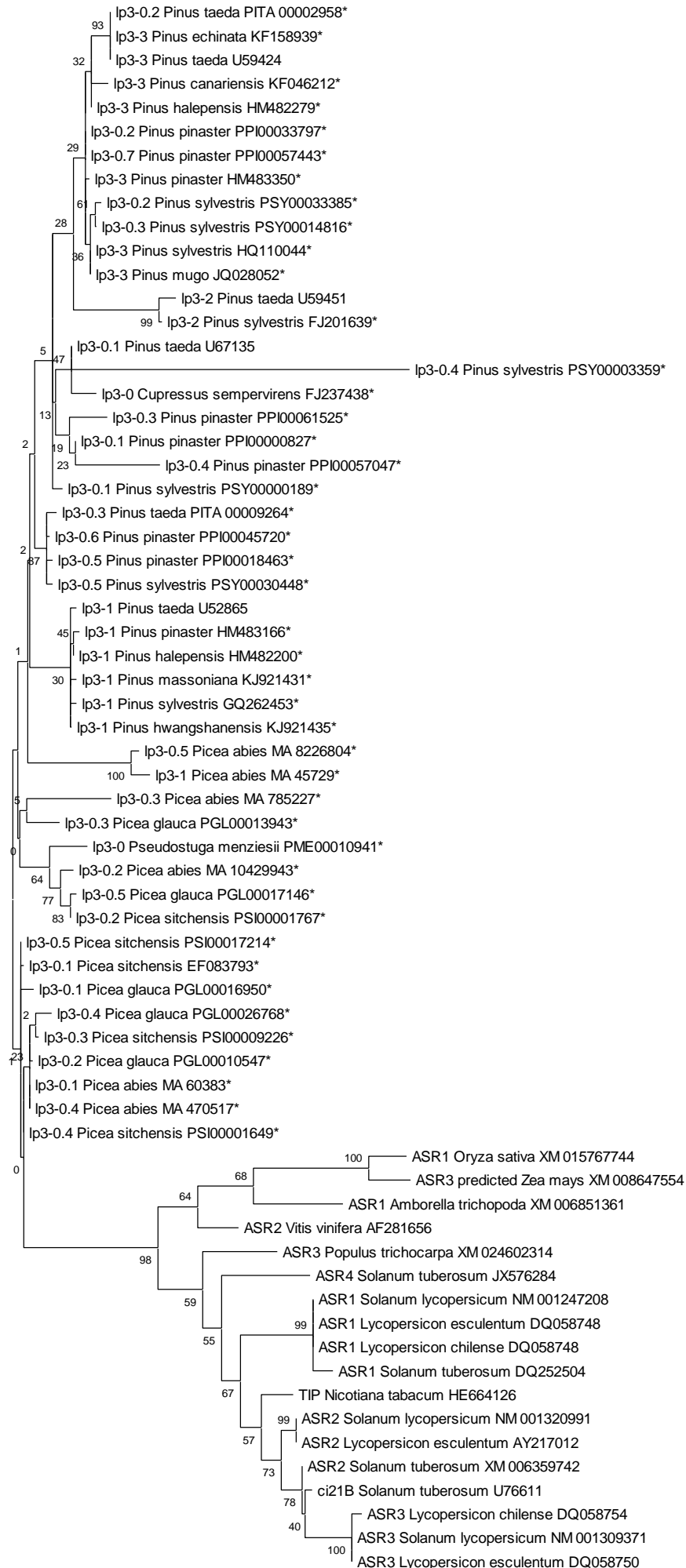
263 *Figure 3: ABA/WDS-tree focusing on the conserved ABA/WDS domain within each gene. Constructed in MEGAX*
264 *using the ML method and the K2 model with gamma=1,0846. Genetic distances are in number of substitutions per*
265 *site. Bootstrap values are shown next to each node*

266

267 N-tree focuses on the N-terminal region of *ASR* and *LP3,* to which zinc ions are theorised to

268 bind (Figure 4), here it can be observed that there is not a definite separation between

269 angiosperm and gymnosperm sequences, with *ASR*2 from *Vitis vinifera* and *ASR*4 from

270 *Solanum tuberosum* being the most divergent sequences when focusing on the N-terminal

271 region. *LP3-1* sequences in *Pinus* formed a different cluster although with low support. After

272 this node, *ASR* and *LP3* sequences mostly segregate according to their order. Like the trees

273 previously analysed, the *ASR* sequences cluster according to *ASR*1, *ASR*2 and *ASR*3, with the

274 *Oriza sativa ASR1* and *Zea mays ASR3* diverging together. In contrast to previous trees, there

275 is a less clear clustering of *LP3* sequences according to genus. There remains however a very

276 short genetic distance between each of the *LP3* sequences, indicative yet again of a high level

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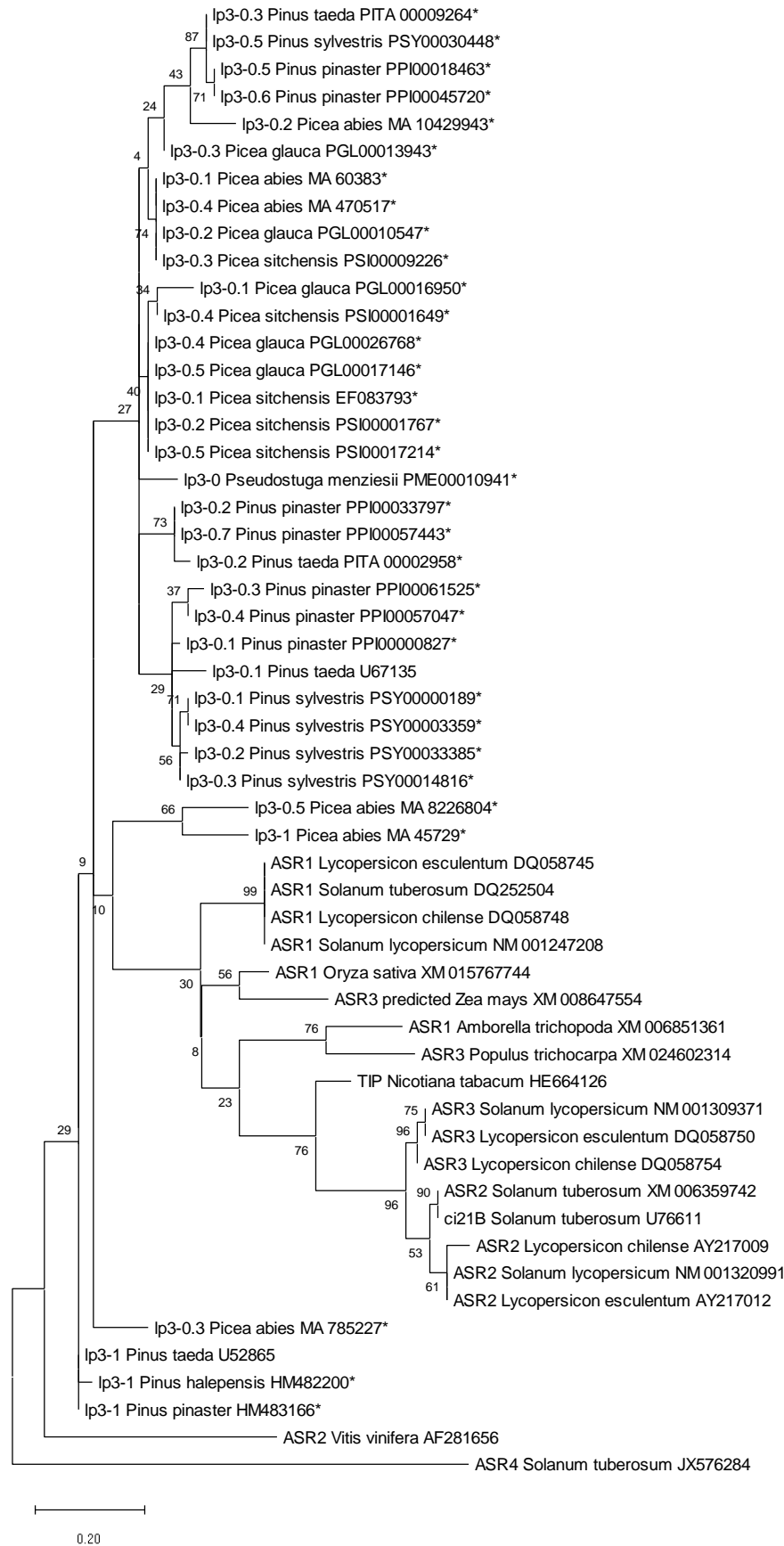
279 *Figure 4: N-tree focusing on N-terminal of ASR and LP3 genes. Constructed with MEGAX and using the ML*
280 *methodand K2 model with gamma =1,3701. Genetic distances are in number of substitutions per site. Bootstrap*
281 *values are shown next to each node.*

282

283 C-tree, which focuses on the variable C-terminal regions of *ASR* and *LP3* which contains the

284 NLS/DNA binding domain (Figure 5), again shows partial segregation of *ASR* and *LP3*

285 sequences. Here the tree is rooted by the *ASR4* of *Solanum tuberosum*, *LP3-0-3 Pinus pinaster*

286 and *Picea abies LP3-0-2* and *LP3-0-3* sequences, indicative that these sequences are the most

287 divergent in the C-terminal NLS region. Subsequently, the *ASR* and *LP3* sequences do segregate

288 according to their order (similar to what can be observed for the other trees). Within the *ASR*

289 cluster the *ASR1, ASR2* and *ASR3* groups show low genetic distances, which suggests that the

290 C-terminal region of those sequences are well conserved. The *LP3* C-terminal sequences also

291 do not show much divergence between them as seen by the small genetic distances between the

292 sequences. The exception are *LP3-0-3, LP3-0-4 and LP3-0-2* sequences of *Picea abies*, which

293 show a high level of divergence from the other *LP3* sequences. The segregation within the *LP3*

294 sequences showed a similar clustering mostly according to the genus.

17

18
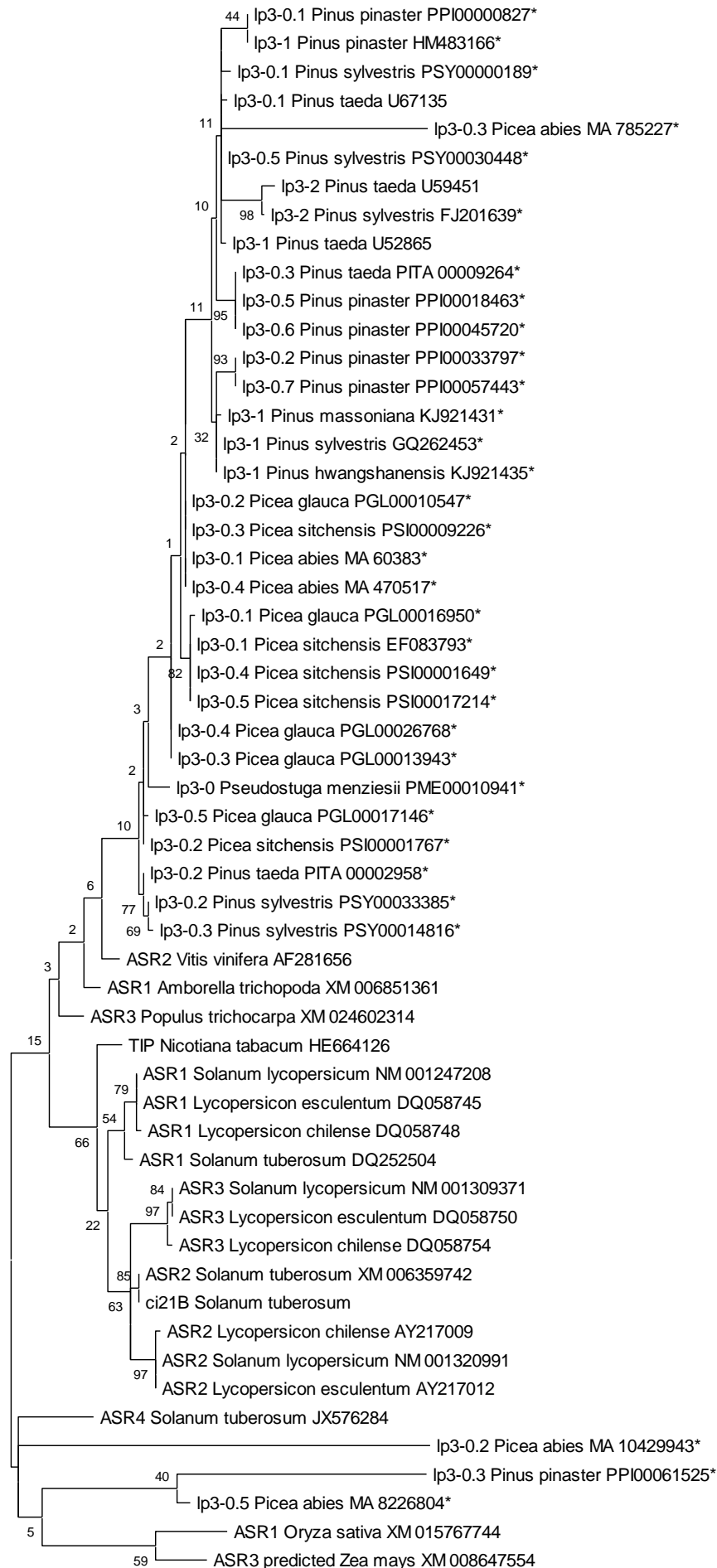
296 *Figure 5: C-tree focusing on the C-terminal region of ASR and LP3 genes. Constructed with MEGA X and using*
297 *the ML method with K2 model and gamma= 1,5588. Genetic distances are in number of substitutions per site.*
298 *Bootstrap values are shown next to each node*

299

3.2 Gene parameters and RSCU analyses

301 There appear to be differences in average preferential codon usage between the different

302 ABA/WDS genes (Table 1, Figure 6). Both LP3_0 and LP3_3 have the same most highly used

303 codon AGG, encoding arginine, at RSCU values 3,71 and 6 respectively. LP3-2 and ASR2 both

304 preferentially use CCA, encoding proline, at RSCU values 4 and 2,77 respectively.

305 Furthermore, ASR2 has a second codon AGC, encoding serine, at RSCU 2,77. LP3_1, ASR3

306 and ASR4 have all got codons encoding for serine as their most used codons with codons UGC,

307 AGC and AGU at RSCU values 3,86 , 3,27 and 2,8 respectively. There were similarities in

308 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	UCG	3,86
LP3_2	Proline	CCA	4
LP3_3	Arginine	AGG	6

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

19

Average RSCU values of ABA/WDS genes
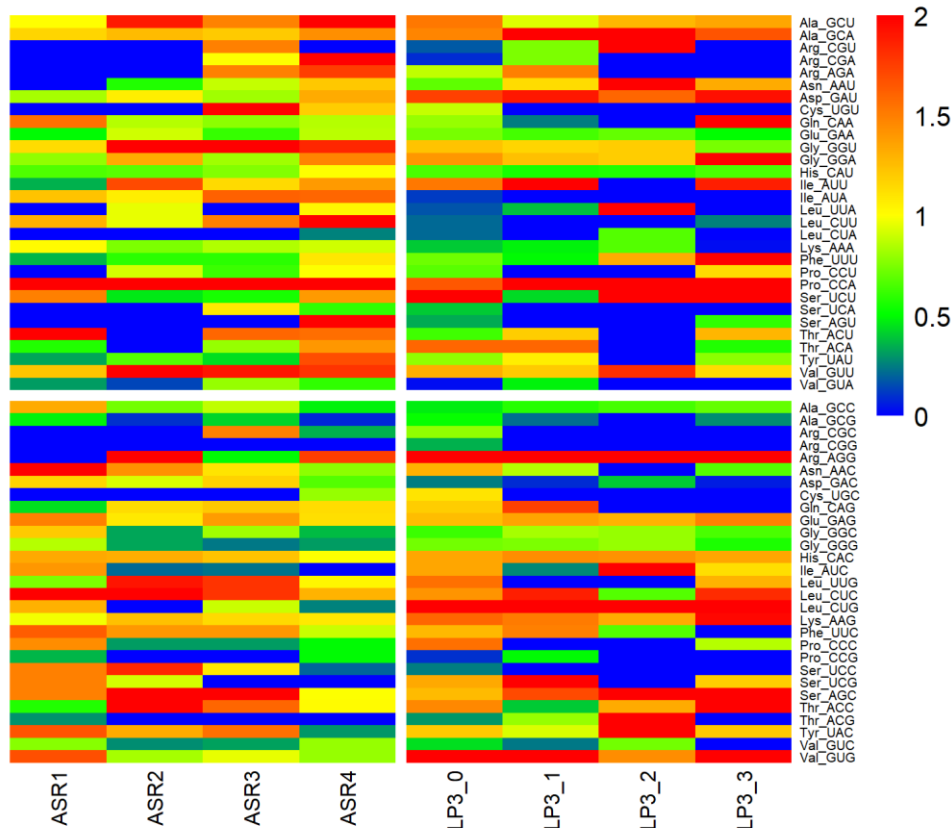
310
311 *Figure 6: Heatmap of average codon usage per ABA/WDS genes. Codons separated according to whether they*
312 *are AU or GC ended. Average codon usage above 1,5 are indicated in red while codon usage lower than 0,5 are*
313 *indicated in blue. Produced in R.*

314   In all cases, the average GC2% of the ABA/WDS genes was lower than both average GC1%

315   and GC3%. With the exception of ASR1, all ABA/WDS genes had on average higher GC1%

316   than GC3% (Table 2). Levene test results showed that only GC1 and GC2 respected the equal

317   variance among groups assumption for ANOVA (p>0,05). Total GC, GC3, ENC and CAI were

318   thus tested using a Kruskal-Wallis test. GC1, GC2 and CAI had significant differences between

319   the ABA/WDS genes (p<0,05) whereas total GC, GC3 and ENC showed no significant

320   difference between the ABA/WDS genes (p>0,05).

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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

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

326   Analysis of GC1 (Figure 7) suggests that on average ASR1 and LP3_2 have a higher GC1%

327   than LP3_0, which itself has a higher GC1% than ASR4. ASR2, ASR3, LP3_1 and LP3_3 do

328   not have significantly different GC1% from ASR1, LP3_2 and LP3_0.
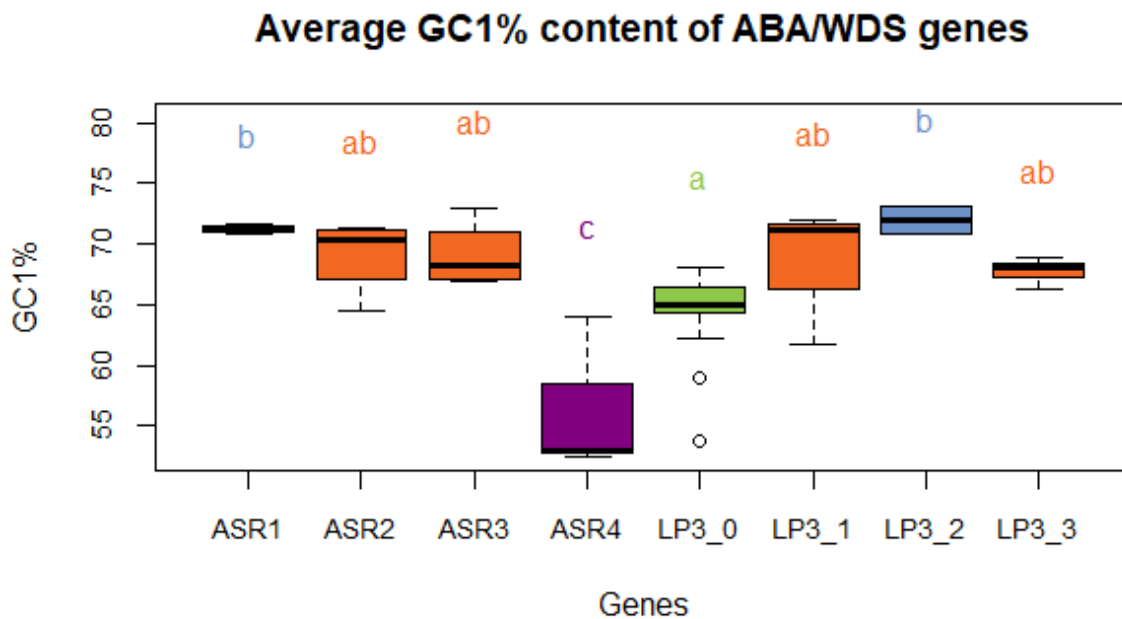
329

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

332   Analysis of GC2% (Figure 8) suggests that ASR4 has on average a significantly higher GC2%

333   than ASR1, LP3_0, LP3_1 and LP3_2. In turn, this analysis suggests that on average LP3_3

334   has a significantly higher GC2% than LP3_0. By contrast, ASR2, ASR3 and LP3_2 do not

335   appear to have significantly different GC2% from each other.
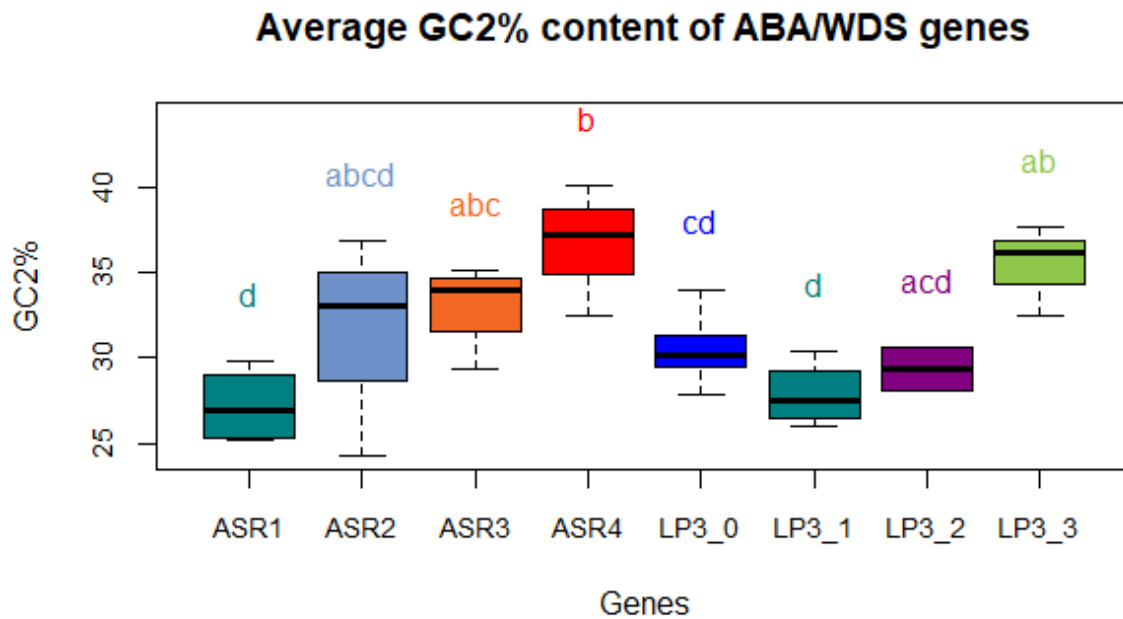
Figure 8: Comparison of the average GC2% per ABA/WDS gene, done in R, using a one-way ANOVA followed by Tukey HSD test.

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

22

349
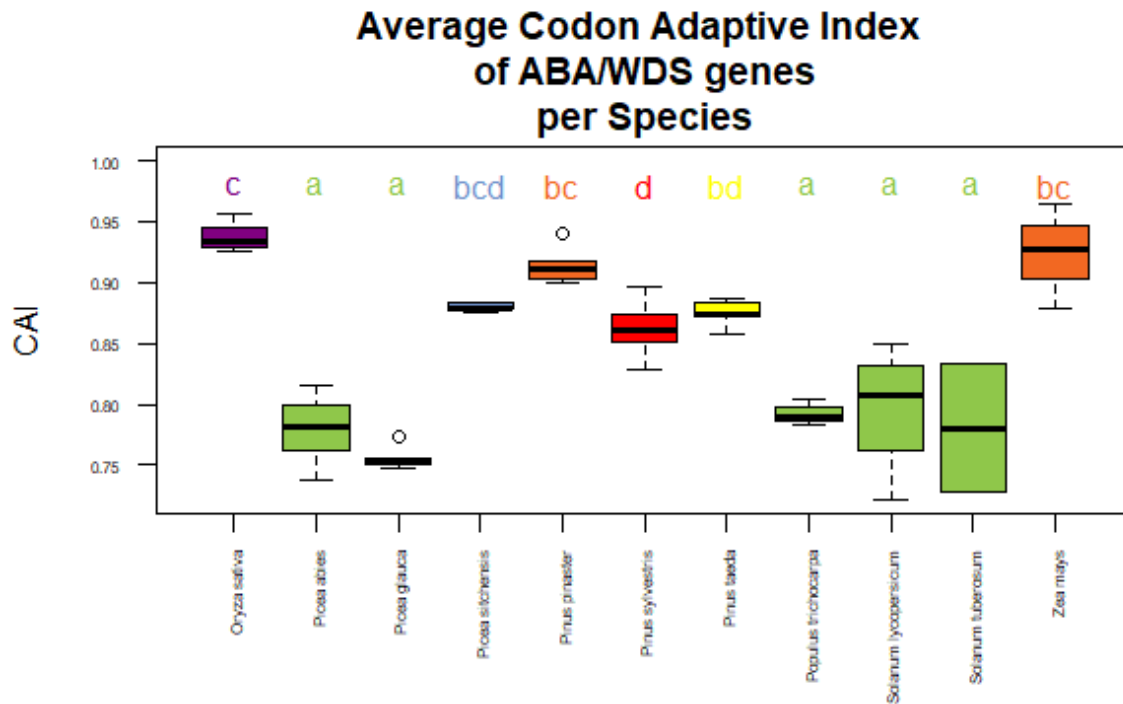
Figure 9: CAI per species of the ABA/WDS genes obtained from the values of majorly represented species, done in R, using a Kruskal-Wallis test followed by a pairwise Wilcoxon test.

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

23

ENC	0.14	**-0.90**	**-0.84**	-0.18	-0.47	**-0.84**

362 *Table 3: Pearson correlation matrix of ASR genes. Correlation values indicated below diagonal and p-values*
363 *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	

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

366

367 ### 3.3 Mode of evolution of different subsections of the ASR/LP3 gene
368 The reference sequences of *LP3-0, LP3-1, ASR1, ASR2, ASR3* and *ASR4* show signs of

369 purifying selection, mainly focused on K, H and E residues, and no sites of positive selection

370 (Figure 10, Figure 11, Figure 13, Figure 14, Figure 15, Figure 16; Supplementary Table

371 3,4,6,7,8,9). In contrast, *LP3-3* presents signs of positive selection on residues N, S and T at

372 positions 34, 37 and 61, respectively (Figure 12,). These residues tend to turn into E, T and A,

373 respectively (w-values = 2,8; 2,9; 2,9; p-values= 2, 1×10^{-14}; 1, 2×10^{-19}; 1, 4×10^{-19},

374 Supplementary Table 5). On average, the ABA/WDS genes investigated here are all undergoing

375 purifying selection, and all tend to similar amino acid sequences and codon usage as shown by

376 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	

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

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.

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.

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.

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.

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.

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.

26

```
  1          11         21         31         41
MAEEKKHHFG GLFNHHKNKE EDTPIEKTTY EETTYEDSEK TSTYGDNTYG
 51         61         71         81         91
EKTSYGDDTY GKKTTTYGDD NKYSEKTSYG DDTYDEKTNT YGDENKYGEK
101        111        121        131        141
TSYSEGDDNK YGEKTSYGGD TYGEKPTSYG GDNTYGEKTS YGGGDENKYG
151        161        171        181        191
EKTSYGEKAS YGGGDDNKYG EKTSYGNEEG GYGGGVGAYS SETTTNYEEN
201        211        221        231        241
DDSGTKTSED YKEEKHHKH LEELGGLGAV AAGAFALHEK HKAEKDEEHA
251        261        271        281        291
HKHKIEEEIA AVAAVGAGGF AFHEHHQKKE AKEEEEEAEG KKKHHFF
```

Legend:

The selection scale:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
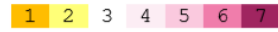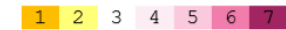
Positive selection   Purifying selection

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

27

415   ABA/WDS domain within *LP3* that is not seen in *ASR*. This can be explained by the action of

416   negative selection acting on the LP3 sequences, or that the rate of substitutions in gymnosperms

417   is lower than in angiosperms (Palmé et al 2009; Buschiazzo et al 2012; De La Torre et al.,

418   2017).

419   This low level of phylogenetic divergence within *LP3* can also generally be observed in the

420   other two domain-based trees (N-terminal tree and C-terminal tree). The N-terminal tree

421   focused on the putative zinc binding domains in the N-terminal region of ASR/LP3 genes,

422   therefore it would make sense that there is a low level of divergence occurring since ASR/LP3

423   requires Zinc ions to adopt their functional conformation (Dominguez and Carrari, 2015;

424   González and Iusem, 2014). A lack of clear segregation between ASR and LP3 can also be

425   indicative of high purifying selective pressures thereby favouring a conserved nucleotide

426   sequence. The lack of a definite separation between angiosperm and gymnosperm sequences is

427   another argument in support of the essential and possibly similar role of the N-terminal domain

428   in both clades.

429   C-tree, which focused on the putative NLS/DNA binding region of ASR/LP3, reveals similar

430   topological properties as the N-tree but with a lower support to the branches discerning the

431   different ASR gene family members. Both *ASR* and *LP3* encode relatively small proteins and

432   in the case ASR1 it has been previously shown that it does not require its putative NLS to enter

433   the nucleus (Ricardi et al., 2012; Rom et al., 2006). This low level of divergence might indicate

434   that the selective pressures focusing on these parts of the genes stem mostly from their role as

435   transcription factors. Following this reasoning, it could be suggested that the sequence

436   corresponding to lp3-0-3 *Picea abies* targets a different gene somewhere along the genome

437   other than the *LP3* gene family.

438   In all cases, it was observed that the LP3 genes had much lower divergence between them than

439   the ASR genes. This is in line with previous research that found that coniferous genes have a

440   low divergence rate among themselves when compared with angiosperm (Buschiazzo et al.,

441   2012). In addition to all the individual reasons listed previously, previous transcriptomic

442   analyses of homologous genes have shown that angiosperm genes tend to diverge much more

443   strongly than coniferous genes (Li et al., 2010). Our phylogenetic analyses are therefore in line

444   with previous known research.

445

446   *4.2 Differences in GC1% and GC2% between genes, differences in CAI between species*

447   While no significant difference was observed in total GC or GC3 content between the

448   ABA/WDS genes, there were differences in the GC1 and GC2 contents between genes. In all

449   cases the GC2 was lower than both GC1 and GC3, a pattern which has been observed in other

450   gene analyses (Song et al., 2017, 2018). In all the major species investigated, CAI was on

451   average highest in *Oryza sativa*, which in turn can be used to predict that ABA/WDS expression

452   levels are highest within *Oryza sativa* (Sharp and Li, 1987). Previous research on ASR

453   expression in rice has shown that it responds strongly to drought stress (Pérez-Díaz et al., 2014),

454   so this high CAI is further indicative of high expression, which in turn lends credence to the

455   other average CAI of ABA/WDS of the other investigated species being indicative of gene

456   expression. It was interesting to see variations in CAI levels between the coniferous species,

457   especially between the *Picea* and *Pinus* genuses, with *Pinus* species exhibiting higher CAI than

458   *Picea* (except for *Picea sitchensis*). This in turn may be indicative that the ABA/WDS

459   expression is higher in *Pinus* than in *Picea*, although a more thorough gene expression analysis

460   within more species of each genus is required to confirm this hypothesis.

461   Previous gene studies have focused on the correlations of CAI with various other factors such

462   as gene length, GC content and ENC (Gun et al., 2018; Song et al., 2017, 2018; Zhou and Li,

463   2009). Our study however showed no significant correlation between sequence length and CAI.

464   CAI is often correlated with GC3% yet this correlation was only significant when concerning

465   ASR genes and not the LP3 genes. Instead CAI was positively correlated with GC1% in LP3,

466   which contrasts with previous gene studies (Gun et al., 2018; Song et al., 2017, 2018). Our

467   study does reflect significant correlations between CAI and ENC within the ABA/WDS genes,

468   indicative of a high translation efficiency found in many highly expressed genes (Sharp and Li,

469   1987; Wright, 1990)

4.3 ASR has a different codon usage than LP3

471   Another factor that contributes to differentiate *ASR* and *LP3* gene families is the RSCU.

472   Differences in codon usage were observed for several amino acids. Yet it was interesting to see

473   that the amino acid with the highest codon bias was serine, although the individual codon with

474   the highest bias was different among different genes. It has already been established that

475   monocots and dicots differ in their codon usage for the homologous genes (Campbell and

476   Gowri, 1990), therefore it is not improbable that gymnosperms would have different codon

477   usages than angiosperms for homologous genes. Highly expressed genes have been shown to

478   have both a more pronounced codon bias and higher overall GC content compared to lowly

479   expressed genes (De La Torre et al., 2015; Song et al., 2017; Kuzniar et al., 2008), however no

480   significant differences in overall average GC content between the ABA/WDS genes were

481   observed in this study.

482   After gene duplication the original and new copies can go down multiple evolutionary paths

483   (Innan, Kondrachov, 2011). While *LP3-3* and *LP3-0* genes have seemingly diverged recently

484   they are affected by different modes of gene-duplication evolution. *LP3-3* presents signs of

485   positive selection on three residues and the rest are evolving either under neutral or purifying

486   selection, whereas *LP3-0* is only affected by purifying selection.

487   In *LP3-3* those three residues (mutation) may have introduced new beneficial functional

488   aspects to the original *LP3* copy resulting in their fixation and maintenance through positive

489   selection. This mode of gene-duplication evolution would suggest the acquisition of a novel

490   function for *LP3-3* gene. Notably purifying selection is acting on Lysine (K), Histidine (H) and

491   Glutamate (E). *LP3* and *ASR*, both belonging to the ABA/WDS gene family, are both highly

492 hydrophilic protein groups therefore the presence of charged, polar amino acids is important in

493 attaining their functional conformations(González and Iusem, 2014; Rom et al., 2006).

494 It has also been suggested that Zinc ions bind to lysine residues in the N-terminal region of both

495 sets of genes, this binding being required for the proteins to finally obtain their functional

496 conformation, thereby further explaining why mutations affecting Lysine are purified. Evidence

497 of purifying selection can also be observed in both the ABA/WDS domain and C-terminal

498 containing a putative NLS/DNA binding amino acid sequence, implying that both are important

499 for the overall functioning of the genes. This is logical when considering that expressions of

500 both *LP3* and *ASR* are upregulated in presence of ABA and that both act as transcription factors

501 in response to water-deficit stress (Padmanabhan et al., 1997; Wang et al., 2002).

502

503 ### *4.4 Conclusion and future perspectives*
504 Overall, this study highly suggests that while *ASR* and *LP3* may have originated from the same

505 common ancestor, they have undergone significant shifts in codon usage, maybe due to

506 different evolutionary constraints. Different *ASR* genes have already been studied in depth, with

507 *ASR1* being the most substantially studied of them. This is not the case for *LP3* for which more

508 research opportunities are available. Further studies into *LP3* mutants could produce similar

509 phenotypes as observed in *ASR* mutants. Precise functions and genomic targets of *LP3* could

510 be hypothesized by homology with genes targeted by *ASR*. Precise mapping of the *LP3* genes

511 onto the *Pinus taeda* genome should also be done. Further research could establish the presence

512 of paralogous genes of *LP3* within *Pinus taeda* and their precise role in drought response. Since

513 the responses of plants to cold stress are similar to their responses to drought stress, research

514 into how *ASR* and *LP3* are affected in terms of expression and cellular function in conditions

515 of cold stress would also be an interesting research objective. Finally, a precise expression

516 network between ASR/LP3 and downstream targets should be established since these have not

517 yet been determined.

Conflict of interest

No conflicts of interest during the making of this study.

Acknowledgments

32

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634   mitochondrial genomes. Mol. Biol. Rep. 36, 2039–2046.
635   https://doi.org/10.1007/s11033-008-9414-1
636
637

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

L.

Pseudostuga menziesii (Mirb.) Franco	*LP*3-0-1	PME00010941
Pinus halepensis Miller	*LP*3-1; *LP*3-3	HM482200; HM482279
Pinus hwangshanensis W.Y.Hsia	*LP*3-1	KJ921435
Pinus massoniana Lamb.	*LP*3-1	KJ921431
Pinus echinata Miller	*LP*3-3	KF158939
Pinus canariensis C.Sm.	*LP*3-3	KF046212
Pinus mugo Turra	*LP*3-3	JQ028052
Solanum lycopersicum L.	*ASR*1, *ASR*2, *ASR*3	NM_001247208; NM_001320991; NM_001309371
Lycopersicon chilense (Dunal) Reiche	*ASR*1, *ASR*2, *ASR*3	DQ058748; AY217009; DQ058754
Lycopersicon esculentum Mill.	*ASR*1, *ASR*2, *ASR*3	DQ058745; AY217012; DQ058750
Solanum tuberosum L.	*ASR*1, *ASR*2, *ASR*4, ci21B	DQ252504; XM_006359742; JX576284; U76611
Oryza sativa L.	*ASR*1	XM_015767744;
Amborella trichopoda Baill.	*ASR*1	XM_006851361
Vitis vinifera L.	*ASR*2	AF281656
Populus trichocarpa Torr & A.Gray ex.Hook	*ASR*3	XM_024602314

Zea mays L.	*ASR*3	XM_008647554
Nicotiana tabacum L.	TIP	HE664126

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

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

						PGL00017146	

Picea sitchensis (Bong.) Carr.   *LP*3-0-1; *LP*3-0-2; *LP*3-0-3;   PSI00017214;   PSI00001767;

*LP*3-03; *LP*3-0-4; *LP*3-0-5   PSI00009226;   PSI00001649;

PSI00017214

Solanum lycopersicum L.   *ASR*1, *ASR*2, *ASR*3, ASR4   NM_001247208;

NM_001320991;

NM_001309371;

NM_001282319

Solanum tuberosum L.   *ASR*1, *ASR*2, *ASR*4, ci21A,   DQ252504;   XM_006359742;

ci21B   JX576284; U76610; U76611

Populus trichocarpa Torr &   *ASR*3, *ASR2, ASR4*   XM_024602314;

A.Gray ex.Hook   Potri.005G193800;

Potri.005G193900

Zea mays L.   *ASR1, ASR2, ASR3*   EU963502;   XM_008677645;

XM_008647554

Oryza sativa L.   *ASR*1, *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

Group								
	Ala_GCG	0,48	Ala_GCG	0,1	Ala_GCG	0,42	Ala_GCG	0,08
Arg	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**

AA	Codon	RSCU	Codon	RSCU	Codon	RSCU	Codon	RSCU
	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	**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**
	LP3-0		LP3-1		LP3-2		LP3-3	
Ala	**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
	Ala_GCG	0,52	Ala_GCG	0,22	Ala_GCG	0	Ala_GCG	0,28
Arg	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

	Codon	Value	Codon	Value	Codon	Value	Codon	Value
	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	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**
	Thr_ACG	0,3	Thr_ACG	0,8	**Thr_ACG**	**2,67**	Thr_ACG	0
Tyr	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  0.01   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   0.14   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    A      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    0.15   0.14   0.13   0.12   0.087  0.04   0.037
85    A      0.59   [0.012,1]             3.2e-05  0.00093 0.006   0.021  0.052  0.1    0.16   0.18   0.47
86    F      0.71   [0.033,1]             1.8e-05  0.00053 0.0034  0.012  0.031  0.064  0.11   0.16   0.62
87    A      0.1    [1.8e-05,1]                    0.14    0.14    0.14   0.14   0.13   0.11   0.088  0.044  0.056
88    L      0.94   [0.41,1]              3.4e-10  2.8e-07 1.2e-05 0.00015 0.001  0.005  0.019  0.068  0.91
```

Pos	AA	w-score	CI									
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-05,0.41]	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.

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS AMINO Ka/Ks [Confidence Interval](* if lower bound > 1)   POSTERIOR PROBABILITIES

POS	AMINO	Ka/Ks	[Confidence Interval]	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	0.12	0.11	0.074	0.1
2	S	0.25	[6.2e-10,1]	0.1	0.1	0.1	0.1	0.1	0.1	0.096	0.082	0.22
3	E	0.14	[6.2e-10,1]	0.12	0.12	0.12	0.12	0.12	0.12	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    2.9
========================================================================================================================
```

POS	AMINO	Ka/Ks	[Confidence Interval](* if lower bound > 1) w =	6.2e-10	4.4e-07	2e-05	0.0003	0.0023	0.013	0.054	0.26	2.9
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	0.11	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	0.11	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	0.11	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	[0.26,2.9]	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.

Selecton Bayesian Ka/Ks Results
Displayed on sequence 1

POS	AMINO	Ka/Ks	[Confidence Interval](* if lower bound > 1)	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	[0.023,0.3]	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	0.26	0.21	0.1	0.015	0.00015
87	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
88	E	0.014	[0.00074,0.053]	0.39	0.32	0.19	0.079	0.021	0.0033	0.00032	1.9e-05	1.3e-06

(a) ASR1

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 ASR1 amino acid. First are represented amino acid position, then amino acid, w-score, confidence interval and Bayesian posterior probabilities.

(b) ASR2

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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
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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	0.00054
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

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Selecton Bayesian Ka/Ks Results
Displayed on sequence 1
========================================================================================================================
POS    AMINO   Ka/Ks   [Confidence Interval](* if lower bound > 1)          POSTERIOR PROBABILITIES
                                               w =   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     0.14    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
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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

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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
===================================================================================================================
```

POS	AMINO	Ka/Ks	[Confidence Interval]	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	0.34
2	A	0.41	[6.9e-05,1]	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	0.34
4	E	0.41	[6.9e-05,1]	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	0.34
6	K	0.41	[6.9e-05,1]	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	0.34
8	H	0.41	[6.9e-05,1]	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	0.34
10	G	0.41	[6.9e-05,1]	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	0.34
12	L	0.41	[6.9e-05,1]	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	0.34
14	N	0.41	[6.9e-05,1]	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	0.34
16	H	0.41	[6.9e-05,1]	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	0.34
18	N	0.41	[6.9e-05,1]	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	0.34
20	E	0.41	[6.9e-05,1]	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	0.34
22	D	0.41	[6.9e-05,1]	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	0.34
24	P	0.41	[6.9e-05,1]	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	0.34
26	E	0.41	[6.9e-05,1]	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	0.34
28	T	0.41	[6.9e-05,1]	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	0.34
30	Y	0.41	[6.9e-05,1]	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	0.34
32	E	0.41	[6.9e-05,1]	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	0.34
34	T	0.41	[6.9e-05,1]	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	0.34
36	E	0.41	[6.9e-05,1]	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	0.34
38	S	0.41	[6.9e-05,1]	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	0.34
40	K	0.41	[6.9e-05,1]	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	0.34
42	S	0.41	[6.9e-05,1]	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	0.34
44	Y	0.41	[6.9e-05,1]	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	0.34
46	D	0.41	[6.9e-05,1]	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	0.34
48	T	0.41	[6.9e-05,1]	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	0.34
50	G	0.41	[6.9e-05,1]	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	0.34
52	K	0.41	[6.9e-05,1]	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	0.34
54	S	0.41	[6.9e-05,1]	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	0.34
56	G	0.41	[6.9e-05,1]	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	0.34
58	D	0.41	[6.9e-05,1]	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	0.34
60	Y	0.41	[6.9e-05,1]	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	0.34
62	K	0.41	[6.9e-05,1]	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	0.34
64	T	0.41	[6.9e-05,1]	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	0.34
66	T	0.41	[6.9e-05,1]	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	0.34
68	G	0.41	[6.9e-05,1]	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	0.34
70	D	0.41	[6.9e-05,1]	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	0.34
72	K	0.41	[6.9e-05,1]	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	0.34
74	S	0.41	[6.9e-05,1]	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	0.34
76	K	0.41	[6.9e-05,1]	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	0.34
78	S	0.41	[6.9e-05,1]	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	0.34
80	G	0.41	[6.9e-05,1]	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	0.34
82	D	0.41	[6.9e-05,1]	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	0.34
84	Y	0.41	[6.9e-05,1]	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	0.34
86	E	0.41	[6.9e-05,1]	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	0.34
88	T	0.41	[6.9e-05,1]	0.083	0.083	0.083	0.083	0.083	0.083	0.083	0.34

89	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
90	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
91	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
92	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
93	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
94	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
95	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
96	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
97	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
98	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
99	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
100	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
101	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
102	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
103	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
104	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
105	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
106	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
107	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
108	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
109	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
110	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
111	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
112	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
113	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
114	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
115	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
116	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
117	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
118	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
119	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
120	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
121	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
122	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
123	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
124	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
125	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
126	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
127	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
128	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
129	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
130	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
131	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
132	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
133	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
134	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
135	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
136	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
137	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
138	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
139	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
140	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
141	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
142	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
143	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
144	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
145	D	0.99	[0.47,1]	6.4e-11	2.6e-08	7.9e-07	1e-05	8.7e-05	0.00061	0.0039	0.033	0.96
146	E	0.85	[0.11,1]	2e-05	0.0004	0.0021	0.0063	0.015	0.03	0.056	0.11	0.78
147	N	0.97	[0.47,1]	3.5e-13	2.6e-09	3.5e-07	1e-05	0.00013	0.0011	0.0069	0.05	0.94
148	K	0.91	[0.21,1]	6.4e-09	2.5e-06	6.4e-05	0.00058	0.0031	0.012	0.036	0.11	0.84
149	Y	0.96	[0.47,1]	9.8e-13	7.3e-09	9.8e-07	2.7e-05	0.00033	0.0025	0.014	0.072	0.91
150	G	0.67	[0.051,1]	4.8e-05	0.00094	0.0049	0.015	0.038	0.078	0.14	0.18	0.55
151	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
152	K	0.7	[0.021,1]	6.2e-05	0.0012	0.0061	0.018	0.041	0.074	0.12	0.15	0.59
153	T	0.82	[0.051,1]	2.1e-05	0.00041	0.0021	0.0068	0.017	0.037	0.071	0.13	0.74
154	S	0.9	[0.21,1]	7e-09	2.7e-06	7e-05	0.00064	0.0034	0.013	0.039	0.11	0.83
155	Y	0.57	[0.021,1]	0.00011	0.0021	0.011	0.032	0.068	0.12	0.17	0.17	0.43
156	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
157	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
158	K	0.39	[6.9e-05,1]	0.086	0.086	0.086	0.086	0.085	0.085	0.084	0.082	0.32
159	A	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32
160	S	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32
161	Y	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32
162	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
163	G	0.89	[0.11,1]	1.4e-05	0.00028	0.0015	0.0045	0.011	0.022	0.043	0.095	0.82
164	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
165	D	0.39	[6.9e-05,1]	0.087	0.087	0.087	0.087	0.087	0.086	0.085	0.082	0.31
166	D	0.4	[6.9e-05,1]	0.086	0.086	0.085	0.085	0.085	0.085	0.084	0.082	0.32
167	N	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.084	0.084	0.082	0.32
168	K	0.39	[6.9e-05,1]	0.086	0.086	0.086	0.086	0.085	0.085	0.084	0.082	0.32
169	Y	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32
170	G	0.88	[0.11,1]	1.5e-05	0.0003	0.0015	0.0047	0.011	0.023	0.045	0.097	0.82
171	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
172	K	0.39	[6.9e-05,1]	0.086	0.086	0.086	0.086	0.085	0.085	0.084	0.082	0.32
173	T	0.4	[6.9e-05,1]	0.084	0.084	0.084	0.084	0.084	0.084	0.083	0.082	0.33
174	S	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32
175	Y	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32
176	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
177	N	0.39	[6.9e-05,1]	0.087	0.087	0.087	0.087	0.087	0.086	0.085	0.082	0.31
178	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
179	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
180	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
181	G	0.4	[6.9e-05,1]	0.084	0.084	0.084	0.084	0.084	0.084	0.083	0.082	0.33
182	Y	0.4	[6.9e-05,1]	0.085	0.085	0.085	0.085	0.085	0.085	0.084	0.082	0.32

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	0.085	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	[0.051,1]	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.