RESEARCH ARTICLE

Coevolution study of tau and α-synuclein suggests a connection between their normal interaction in neurons and the Parkinson's disease-associated mutation A53T

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Abstract

Alpha-synuclein lies at the center of Parkinson's disease etiology, and polymorphisms in the gene for the microtubule-associated protein tau are risk factors for getting the disease. Tau and α synuclein interact in vitro, and α -synuclein can also compete with tau binding to microtubules. To test whether these interactions might be part of their natural biological functions, a correlated mutation analysis was performed between tau and α -synuclein, looking for evidence of coevolution. For comparison, analyses were also performed between tau and β - and γ -synuclein. In addition, analyses were performed between tau and the synuclein proteins and the neuronal tubulin proteins. Potential correlated mutations were detected between tau and α -synuclein, one involving an α -synuclein residue known to interact with tau *in vitro*, Asn122, and others involving the Parkinson's disease-associated mutation A53T. No significant correlated mutations were seen between tau and β - and γ -synuclein. Tau showed potential correlated mutations with the neuronspecific βIII-tubulin protein, encoded by the *TUBB3* gene. No convincing correlated mutations were seen between the synuclein and tubulin proteins, with the possible exception of β -synuclein with βIVa-tubulin, encoded by the *TUBB4A* gene. While the correlated mutations between tau and α -synuclein suggest the two proteins have coevolved, additional study will be needed to confirm that their interaction is part of their normal biological function in cells.

Keywords: Correlated mutations analysis, mutual information, tauopathy, Alzheimer's disease, axon, neurodegenerative, intrinsically disordered protein, protein-protein interaction



Introduction

Pathology involving the protein α -synuclein is a defining feature of Parkinson's disease. A diagnosis of the disease can only be confirmed by observation of this pathology in neurons, in the form of Lewy bodies and neurites, proteinaceous deposits containing α -synuclein in its pathological, fibrillar form. In the brains of roughly 70% of Parkinson's disease patients, autopsy also reveals neurofibrillary tangles, distinct proteinaceous containing microtubuledeposits the associated protein tau in a fibrillar, hyperphosphorylated form. (1)Neurofibrillary tangles are a typical feature of Alzheimer's disease, as well as a group of neurodegenerative diseases known collectively tauopathies.(2) as Polymorphisms of the genes for α -synuclein and tau, SNCA and MAPT, respectively, are known risk factors for developing Parkinson's disease.(3)

In their monomeric, non-pathological forms, tau and α -synuclein can physically interact in vitro, and α -synuclein can also bind to microtubules, the natural interaction target of tau in neurons. (4) (5) Microtubules form part of the cytoskeleton of the cell and perform many vital roles, such as providing a conduit for the transport of proteins and other intracellular cargoes. Interaction with tau helps stabilize microtubule structure in axons and may play a role in modulating transport along microtubules. (6) (7) The microtubule structure is comprised of α -tubulin/ β -tubulin heterodimer subunits, and in humans there are nine genes encoding α -tubulin proteins and nine genes encoding β -tubulin proteins. (8) Four of the β -tubulin genes are specifically expressed in brain tissue. (9) In contrast to tau, α -synuclein appears to have the opposite effect, destabilizing microtubule structure, and the mechanism of interaction. as well as whether it might play some regulatory role, is the subject of ongoing study. (5) Interaction between γ -synuclein and microtubules is also being studied. (10)

Given the high coincidence of tau and α synuclein pathology and their interaction in vitro, this suggests their interaction might somehow promote the development of Parkinson's disease. This implication suggests a second possibility, namely, that the two proteins might interact in neurons as part of their normal biological function. They are both localized to neuronal axons, concentrated in presynaptic termini in the case of α -synuclein. To explore this question, this work presents a correlated mutation study of the two proteins to look for evidence that they have coevolved during the course of vertebrate evolution. The idea behind correlated mutation analysis is that for two interacting proteins, a mutation in one affecting the interaction might be compensated by a mutation in the other protein, such that functional interaction is maintained, leaving survival unaffected in the species. It is also possible that the second mutation modifies the interaction in way that might enhance survival. In either case, the pair of mutations could then be passed on to daughter species.

There are two other synuclein proteins in humans, β - and γ -synuclein, and for comparison, correlated mutation analyses of them with tau are also presented. In addition, because α -synuclein can possibly compete with tau for microtubule binding, analyses with the tubulin proteins that make up microtubules are presented, including four β tubulins that are specific to brain tissue, β IIatubulin, β IIb-tubulin, β III-tubulin, and β IVatubulin, and two non-tissue-specific tubulins, α Ia-tubulin and β I-tubulin.

Methods

Multiple sequence alignments

The protein sequences of tau, α -, β -, and γ synuclein, as well as α Ia-tubulin (TUBA1A), βI-tubulin (TUBB), βIIa-tubulin (TUBB2A), βIIb-tubulin (TUBB2B), βIII-tubulin (TUBB3), and BIVa-tubulin (TUBB4A) were obtained from protein blast searches (blast.ncbi.nlm.nih.gov) using the human sequences as the initial query. For cases where the choice of ortholog was ambiguous, especially for the highly similar βIIa-tubulin and BIIb-tubulin proteins, human cDNA was also used as the query in a DNA blast search to identify the closest ortholog. The multiple sequence alignments from the blast searches were confirmed using Clustal Omega (www.ebi.ac.uk/Tools/msa/clustalo/).

Sequences with missing regions or ambiguous residues were not used for analysis. In addition, protein sequences of interest could be missing from the annotated genomic sequence for particular species. In such cases, cDNA of a closely related species was used to search the full genomic sequence for the protein gene, but this typically resulted in only partial protein sequences being obtained. As a consequence, each pair of multiple sequence alignments (tau with α synuclein, β -synuclein with β IVa-tubulin, etc.) used for the correlated mutation analyses typically included a different number of species. The residue numbering shown in figures corresponds to that of the human protein sequences. In places where the correlated mutation pairs include a position that corresponds to a gap in the human sequence in the multiple sequence alignment, the residue number is that of the residue immediately preceding the insertion, followed by a lowercase letter indicating the position in the insertion: 'a' for the first position in the insertion, 'b' for the second, and so on. In the notation for mutations, the letter for the human amino acid is given first, and when the human residue is not the ancestral residue, this is stated in the text.

Correlated mutation analysis

The correlated mutation analysis combines a mutual information correlation matrix with a global Z-score analysis of the matrix elements. This approach has been shown to be relatively robust when the number of species is limited, such as when analyzing vertebrate-specific proteins. (11) In the first step, the correlation matrix is calculated with the rows corresponding to the first protein sequence positions and the columns corresponding to the second protein sequence positions using the following equation

$$MI_{ij} = \sum_{m,n} f_{ij}(m,n) ln \left[\frac{f_{ij}(m,n)}{f_i(m)f_j(n)} \right]$$

where MI_{ij} is the mutual information value between position i in the first protein and position i in the second protein, $f_i(m)$ and $f_i(n)$ are the frequencies of amino acid types *m* and *n* at positions *i* and *j*, and $f_{ij}(m, n)$ is the frequency that *m* and *n* occur together in a species at positions *i* and *j*. The sum is taken over the 20 standard amino acids plus the gap, that is, each position can have one of 21 possibilities. Mutual information is similar to covariance, but it differs in that higher values are produced when a greater number of correlated mutations are present. The frequencies, $f_i(m)$, $f_i(n)$ and $f_{ii}(m, n)$ include a pseudocount correction of 1.5 to reduce the impact of sequencing errors on the MI values, the details of which are described elsewhere. (12)

In the second step, the Z-scores of each *MI* value were calculated. Z-scores correspond to how many standard deviations the *MI*

value for a particular pair of positions differ from the average *MI* for those positions with all other residue positions in the protein.

$$Z_{ij} = 0.5 \left[(MI_{ij} - MI_{iav}) / \sigma_i + (MI_{ij} - MI_{jav}) / \sigma_j \right]$$

Where MI_{iav} is the average MI value between position *i* and all positions in the second protein sequence, MI_{jav} is the average MI value between position *j* and all positions in the first protein sequence, and σ_i and σ_j are the corresponding standard deviations. Higher Zscores have been shown to be correlated with a higher probability that the two residue positions are in contact, and thus, have coevolved. (13)

Results

1. Tau and the tubulins

The top Z-scores for the correlated mutation analyses of tau with the six tubulin proteins are shown in figure 1. In humans, tau has six isoforms; the longest form, called 2N4R, has 441 residues. The shorter isoform sequences are subsets of the 2N4R sequence, having zero to two N-terminal inserts (N1, N2), and three or four highly conserved repeat domains (R1-R4) (figure 1a). The first 160 residues of 2N4R tau are highly variable, and there is almost no detectable homology in this region between fish and land vertebrates. Including more species in the analysis can improve the chance that the highest Z-score correlated mutation pairs correspond to genuinely interacting residues (12), so the analyses were repeated without the first 160 residues of tau, allowing the inclusion of fish species (except for ßIIa-tubulin, which is amniote specific). The addition of fish species did not result in a net increase in the top Z-scores, however. For this reason, fulllength 2N4R tau was used in all subsequent analyses.

Also shown in figure 1 are the top Z-scores for the analyses with the tubulin proteins using the hemoglobin beta chain as a negative control. In several cases, the Z-scores for hemoglobin exceed those for tau, which would seem to imply that tau and tubulins do This illustrates one of the not interact. weaknesses of correlated mutation analysis; to wit, the analysis cannot detect interacting residues where one or both is invariant. Roughly a third of tau residues are invariant, mostly in the C-terminal region, which is known to interact with microtubules (14), and over half of the tubulin residues are invariant. Thus, another possibility is that tau interactions with microtubules are dominated by interactions involving at least one invariant residue.

In two cases, the Z-scores with tau exceed those with hemoglobin, with β -tubulin and βIII-tubulin. The top five Z-score correlated pairs with β I-tubulin are shown in figure 2, β III-tubulin in figure 3, and the other four tubulins supplemental figure in 1. Examination of figure 2 reveals another weakness of correlated mutation analysis; the residue pairs are only different in two frog species (Xenopus tropicalis and Xenopus laevis). This illustrates what is known as phylogenetic bias, or phylogenetic noise. The situation can arise where an ancestor of a branch in a family tree happens to have mutations in two non-interacting residues just by chance. All the daughter species will have the same pair of mutations (unless the residues mutate again).

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U	Z-scores	αIa- tubulin	βI- tubulin	β∏a- tubulin	βIIb- tubulin	βIII- tubulin	βIVa- tubulin	
	tau	10.6	11.5	9.1	9.0	12.7	6.9	
	$\Delta_{\rm N160} {\rm tau}$	10.8	11.3	9.7	9.1	11.7	5.9	
	hemo b	10.9	8.4	10.3	8.7	11.5	9.1	

Figure 1. A) Diagram of the tau protein with four domains labeled and residue numbers shown at the start of each sub-region. At the N-terminus is the projection domain with N1 and N2 inserts, followed by the proline-rich domain with P1 and P2 sub-regions, followed by the microtubule-binding domain with four microtubule-binding repeats, followed by the C-terminus region. There are six isoforms of tau in humans, with both N1 and N2 inserts, with just N1, or with neither N1 nor N2 present, combined with microtubulebinding repeat R2 either present or absent. The projection domain is negatively charged, with the Nterminal and N1 insert having the most negative charge, indicated by the red color. The proline-rich domain is positively charged, with P2 having the most positive charge, indicated by the blue color. The microtubule-binding repeats R1, R2 and R3 have a modest net positive charge, while R4 and the C-terminus are net neutral. The asterisks mark the positions of mutations L48P, -149cG (see Methods for gap nomenclature), and S240A involved in correlated pairs with α-synuclein and βIII-tubulin. B) The top Zscores from the correlated mutation analyses of tau with tubulin proteins found in neurons. The top line shows the Z-scores using full-length tau and the second line using tau excluding the first 160 residues $(\Delta_{N160}$ tau). For full-length tau, multiple sequence alignments of 123 vertebrate species on average were used in the analyses, while for Δ_{N160} tau the average number of species was 142. The bottom line shows the top Z-scores for hemoglobin beta chain with the tubulin proteins, as a negative control.

One of the advantages of the Z-score analysis is that the highest values correspond to the most unique patterns of mutations among species. If two chance mutations occur in an ancestor at a deep branch point in the tree, the mutation pattern will be shared by many ancestors, and thus will result in lower Zscores. (13) However, if the mutation pair occurs at a shallow branch, or any branch with few daughter species, a higher Z-score can result. To get around this issue, an ideal correlated mutation pair should pass the "phylogenetic bias test," that is, the mutations should occur in two or more unrelated branches of the tree. Clearly, the top correlated mutation pairs of tau with β Itubulin fail the test.

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Abbreviations: NWM, New Wolrd monkeys; Le+, lemurs, lorises and galagos; Ts, treeshrews; RP, rabbits and pikas; Ho+, odd-toed ungulates; Pa, pangolins; M, moles, shrews and hedgehogs; Afro, Afrotheres; Xe, xenarthrans; Marsup, marsupials; Mo, monotremes; Am, amphibians

Figure 2. The top five correlated mutation pairs for tau with β I-tubulin. The correlated pairs are shown in five columns, with the corresponding residue numbers and Z-scores shown above. There is one row for each species in the multiple sequence alignment. The five columns are divided into four sections for more convenient display. The species are grouped roughly by class, order and/or suborder following standard conventions, and coloring indicates evolutionary distance from humans, blue for primates and more distantly related treeshrews, next green for rodents and glires (rabbits and pikas), yellow for Laurasiatheres (hoofed animals, cetaceans, carnivora, bats, etc.), orange for more distantly related placental mammals (moles, shrews, Afrotheres, xenarthrans, etc.), red for marsupials and more distantly related monotremes, purple for birds and reptiles, and dark blue for amphibians.

Page 7 of 32

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Abbreviations: NWM, New Wolrd monkeys; Le+ lemurs, iorises and galagos; RP, rabbits and pikas; ung, ungulates; horses+, odd-toed ungulates; Pa, pangolins; MSH, moles, shrews and hedgehogs; Mo, monotremes; Am, amphibians

Figure 3. The top five correlated mutation pairs for tau with β III-tubulin. See figure 2 for an explanation of the figure layout. Note that for tau with β III-tubulin, there was a subset of ray-finned fish sequences with sufficient homology to land vertebrate sequences to be included in the correlated mutation analysis, and this group of species is shown in light blue.

In contrast to *βI*-tubulin, the top correlated pair between tau and BIII-tubulin easily passes the phylogenetic bias test (figure 3). Whereas the majority of vertebrates have the pair SE (serine glutamate) in positions 240 and 441 of tau and βIII-tubulin, respectively, the pair AD (alanine aspartate) has arisen in three unrelated branches, in murids (mice and their kin), cetaceans, and in Erinaceus europaeus (European hedgehog). The intermediate pairs, SD and AE, are also seen for a few species; such transitional cases are not unexpected. This is because if either mutation were significantly deleterious to survival, it would be eliminated from the gene pool before the second mutation could occur. The remaining top correlated pairs shown in figure 3 do not pass the bias test, all reflecting the branching of mammals from the other vertebrates, with Z-scores similar to the control case with hemoglobin beta chain (figure 1). In summary, for tau and neuronal tubulin proteins found in neurons, the most convincing candidate for a genuine correlated mutation pair is the highest Z-score pair for tau and βIII-tubulin.

2. Tau and the synucleins

The top Z-scores of the correlated mutation analyses of tau with α -, β - and γ -synuclein and shown in figure 4, and with hemoglobin beta chain as a control. Synuclein proteins consist of a 78-89 amino acid N-terminal region consisting of six (for β -synuclein) or seven (for α - and γ -synuclein) imperfect 11residue repeats, followed by a negatively charged C-terminal region 38-56 residues long (figure 4a). The highest Z-score correlated pair is seen with α -synuclein, and the top five correlated pairs of tau with α synuclein are shown in figure 5. The top correlated pairs with β -synuclein and γ synuclein are shown in supplemental figure 2.

The top tau/ α -synuclein pair Z-score, 8.9, exceeds that of the hemoglobin control, 6.8, indicating a higher probability that the top pair could be a genuine correlated mutation. With β -synuclein and γ -synuclein, the top Z-scores are lower than hemoglobin. These results suggest that tau might have coevolved with α -synuclein, but not with β -synuclein and γ -synuclein is warranted, however, as the top correlated pair with α -synuclein fails the phylogenetic bias test, with the mutation pair occurring only in bovines.

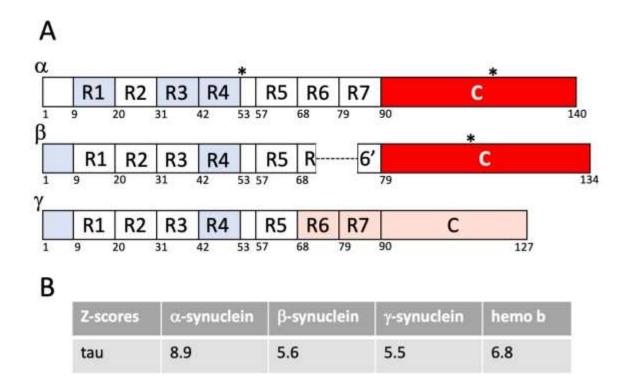


Figure 4. A) Diagram of the synuclein proteins with the 11-residue imperfect repeats (R1-R7) and Cterminal tail (C) indicated with residue numbers shown at the beginning of each region. For β -synuclein the first five residues of the final repeat R6' are homologous to the corresponding residues in R6 of α - and γ -synuclein, and the final six residues are homologous to the corresponding residues in R7 of α - and γ synuclein. The regions with moderate positive charge are shown in light blue, neutral charge in white, moderate negative charge in light red, and the most negative charge in red. The C-terminal tail of β synculein is the most negatively charged (-16 over 56 residues), followed by α -synuclein (-12 over 51 residues), and γ -synuclein (-5 over 38 residues). The asterisks mark the positions of residues involved in correlated mutation pairs, A53T and N122S for α -synuclein with tau, and A102V in β -synuclein with β IVatubulin. B) The top Z-scores from the correlated mutation analyses of tau with the synuclein proteins, and with hemoglobin beta chain as a negative control.

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lemurs+ includes lemurs, lorises and galagos; horses+ includes odd-toed ungulates

Abbreviations: NW, New Wolrd; Ts, treeshrews; RP, rabbits and pikas; MSH, moles, shrews and hedgehogs; Afro, Afrotheres; Xe, xenarthrans; Am, amphibians

Figure 5. The top five correlated mutation pairs for tau with α -synuclein. See figure 2 for an explanation of the figure layout.

The second potential correlated mutation pair in figure 5, with a Z-score of 7.5 and involving residues 48 and 122 of tau and α synuclein, respectively, does pass the phylogenetic bias test. Whereas the majority of vertebrates have the pair LN in these positions, the pair PS has arisen in strepsirrhines (lemurs, lorises and galagos), and in two branches of the rodent tree, in murids and in the common ancestor of Chinchilla lanigera and Octodon degus (common degu). The transitional pair LS is also seen in several species, but PN is not observed; if the correlated pair is genuine, perhaps the tau L48P mutation can only be accommodated after the N122S mutation in α -synuclein has already occurred.

The fourth highest Z-score correlated pair with α -synuclein is noteworthy because it involves a Mendelian mutation. A53T. known to cause an autosomal dominant familial form of Parkinson's disease. In this case, the human disease-causing residue T53 is the ancestral residue. The sixth and eighth highest correlated pairs also involve A53T (the sixth through tenth highest Z-score pairs for tau with α -synuclein are shown in supplemental figure 3). All these pairs seem to fail the phylogenetic bias test, since the A53T mutation pairs appear to have arisen just once in a putative common ancestor of apes, Old World monkeys, and the New World capuchin and squirrel monkeys (Cebus capucinus, Saimiri boliviensis, and Sapajus apella). This is curious, however, because in the standard primate phylogenetic tree (Tree of Life web project. http://tolweb.org/Primates/15963) New World monkeys are more closely related to each other than to Old World apes and monkeys. Assuming the standard tree is correct, there are two possibilities with different phylogenetic bias test outcomes. One possibility is that A53 arose just once in the ancestor of both Old and New World monkeys and reverted to the ancestral T53 in the marmoset *Callithrix jacchus* and night monkey *Aotus nancymaae*, thus failing the phylogenetic bias test. The other possibility is that the mutation to A53 arose twice, in the ancestor of Old World apes and monkeys and in the New World ancestor of capuchin and squirrel monkeys, in which case the test is satisfied.

3. The synucleins and the tubulins

The top Z-scores of the correlated mutation analyses of α -, β - and γ -synuclein with the six tubulin proteins are shown in figure 6, and with hemoglobin beta chain as a control. Unlike tau and the synucleins, which are intrinsically disordered in their monomeric, non-pathological forms, the tubulins fold into a highly conserved, well-defined GTPase protein structure, followed by a more variable, short C-terminal region rich in glutamate residues called the "E-hook" (figure 6a). The highest Z-score correlated mutation pairs are seen for β -synuclein with βIIa-tubulin and βIVa-tubulin; however, the top correlated pairs for BIIa-tubulin all fail the phylogenetic bias test. The top correlated pair for β -synuclein with β IVa-tubulin does pass the test, with mutations in two unrelated branches, for marsupials and for the afrothere Chrysochloris asiatica, and its top five correlated pairs are shown in figure 7. All the other top correlated pairs for α -, β - and γ synuclein with the six tubulin proteins are shown in supplemental figure 4.

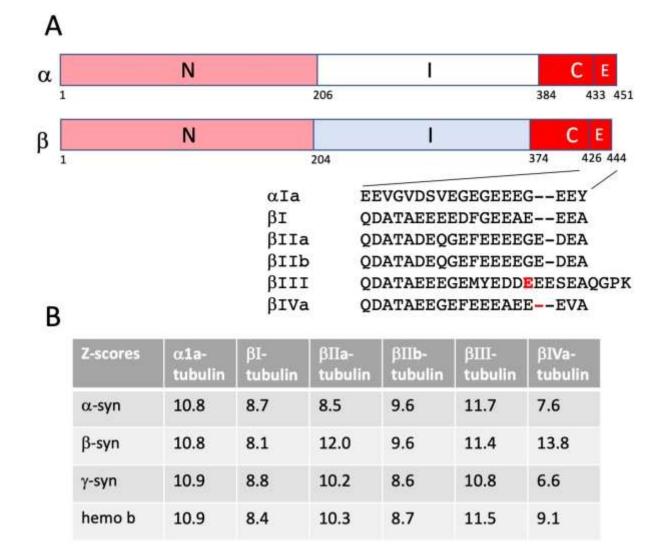


Figure 6. A) Diagram of α Ia- and the β -class tubulins with the three structural subdomains indicated with residue numbers shown at the beginning of each region. The N-terminal subdomain (N) contains the nucleotide binding site and has a moderate negative charge, shown by the light red color. The intermediate subdomain is net neutral for α Ia-tubulin and has a moderate positive charge for the β -class tubulins. The C-terminal domain has the most negative charge, shown in red, and includes the flexible C-terminus "E-hook" region. The E-hook differs for the different β -class tubulins and is shown below, along with α Ia-tubulin for comparison. The E-hook residues involved in correlated mutation pairs are highlighted in red, E441D for β III-tubulin with tau, and -441aE for β IVa-tubulin with β -synuclein. B) The top Z-scores from the correlated mutation analyses with of the synuclein proteins with the tubulin proteins, with hemoglobin beta chain as a negative control.

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P	p	paniscus	A-	٧.	FS.	VV	EE	d a	norvegicus	A -	٧-	FS	VV	EE	-	M nat	alensis	A-	V-	FS	VV	EE	D	reri	o	A-	·¥-	FS.	vv	EE
G	1 8	gorilla	A-	٧-	FS	VV	EE	当ろ	A pahari	Α-	٧-	FS	VV	EE	bats	E fus	cus	A-	٧-	FS	VV	EE	5	rhir	noceros	A-	¥-	F5	vv	EE
음 P	14	abelii	A-	V-	FS	VV	EE	" N	A caroli	A-	٧-	FS	VV	EE		M bra	ndtil	A-	٧-	FS	VV	EE	E	ele	ctricus	A-	¥-	FS	VV	EE
	6 0	moloch	A-	٧-	FS	vv	EE	N N	A musculus	Α.	٧-	FS	VV	EE		M luci	fugus	A-	٧-	FS	vv	EE	1	pur	octatus	A-	V-	F5	MA	EE
Wor	1. 14	eucogenys	A-	٧-	FS	VV	EE	30 0	princeps	A -	٧	FS	VV	EE		R aeg	yptiacus	A-	V-	FS	VV	EE	T	fuly	idraco	A-	V-	F5	VV	EE
d P		anubis	A-	٧-	FS	VV	EE	20	cuniculus	A-	V-	F5	VV	EE	-	C cris	tata	A-	٧-	FS	vv	EE	5	sala	ir i	A-	V-	F5	IA	EE
	A 14	eucophaeus	A-	٧-	FS	VV	EE	m S	scrofa	A-	٧-	FS	VV	EE	HSW	5 ara	neus	A-	٧-	FS	VV	EE	5	trut	tta	A-	V-	FS	IA	EE
D C		atys	A-	٧-	FS	VV	EE	Ne c	hircus	A-	٧-	FS	VV	EE		E eur	opaeus	Α-	V-	FS	VV	EE	0	my	kiss	A-	V -	FS	IA	EE
R.N	1 .	nemestrina	A-	٧-	F5	VV	EE	금 0) aries	A-	٧-	F5	VV	EE	124	O afe	f	A-	M -	FS	vv	EE	0	kist	itch	A-	V-	FS.	IA.	EE
N B	4 n	mulatta	A-	٧-	F.S	VV	EE	ac	virginianus	Α-	٧-	FS	VV	EE	fro	C asia	stica	VE	ME	FS	VV	EE	G	mo	rhua	A-	V-	FS	vv	EE
N N	A 1	ascicularis	A-	٧-	FS	VV	EE	5 8	taurus	A-	٧-	FS	VV	EE		E edu	vardii	A-	M-	FS	VV	EE	P	for	nosa	A-	V-	FS	VV	EE
S c	5	abaeus	A	V-	FS	VV	EE	연日	mutus	A-	٧-	FS	VV	EE	Xe	D nov	emcincti	A-	M-	FS	VV	EE	ρ	reti	culata	A-	V-	FS	VV	EE
T	1	gelada	A-	V-	FS	VV	EE	20 1	bubalis	A-	٧-	FS	VV	EE	3	S har	risii	VE	ME.	FS	VV	EE	p	lati	pinna	A-	V -	FS	VV.	EE
P		tephrosceles	A-	٧-	F.S.	vv	EE	3 ¹⁰ C	ferus	A-	٧-	FS	VV	EE	3	V urs	inus	VE	ME	FS	vv	EE	P.	me	xicana	A-	V-	FS.	VV	EE
R	1	bieti	A-	V-	FS:	VV	EE	8	acutorostrat.	Α-	٧-	FS	VV	EE	등	P cin	ereus	VE	ME	FS	VV	EE	1×	hel	lerii	A-	V-	FS	VV	EE
R		oxellana	A-	٧-	FS	VV	EE	1	obliquidens	A-	٧-	FS	VV	EE	8	O and	tinus	A-	M-	LS	VV	EE	E ×	COL	chianus	A-	V-	FS.	vv	EE
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	b	boliviensis	A-	٧-	FS	VV	EE	20	orca	A -	٧-	F5	VV	EE		A car	olinensis	A-	V-	FS	vv	EE	素り	var	iegatus	A-	V-	F5	vv	DE
a s	24	apella	A-	V-	FS	VV	EE	etace	sinus	A-	٧-	FS	VV	EE	2	P vitt	iceps	A-	V-	FS	VV	EE	T	rub	ripes	A-	V-	FS.	vv	EE
R C	1	acchus	A-	V-	FS	VV	EE	an N	asiaeorienta.	A-	٧-	FS	VV	EE	qa	P biv	ttatus	A-	V -	FS	VV	EE	M	arm	atus	A-	V -	FS	VV	EE
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m P	. 6	coquereli	Α-	٧-	FS	VV	EE	0	1 monoceros	A-	V-	FS	VV	EE		T car	olina	A-	A-	FS	vv	EE	0	lati	pes	A-	V-	FS.	vv	EE
	A n	murinus	A-	٧-	FS	VV	EE		vexillifer	A-	٧-	\$5	VV	EE	18	C pic	ta	A-	A-	FS	VV	EE	A	test	tudineus.	A-	V-	FS	VV	EE
\$ 0	8	garnettii	A-	٧-	FS	vv	EE	금이	simum	A-	٧-	FS	VV	EE	1	G eve	oodei	A-	A -	FS	MV	KD	8	sple	endens	A-	V-	FS.	vv	EE
ज्ञ ¹ T	e	chinensis	A -	V -	FS	VV	EE	horse	asinus	A -	٧-	F5	VV	EE	. A	X tro	picalis	A -	٧-	FS	VV	EE	0	nilo	ticus	A-	V-	FS	VV	EE
D	0	ordii	A-	V-	FS	VV	EE	57 E		Α-	٧-	FS	VV	EE	8	X lae	vis	Α-	V-	FS	MV	EE	H	bur	toni	A-	V-	FS.	vv	EE
3	1	aculus	A-	V-	F.S.	VV	EE	L	canadensis	A-	٧-	FS	VV	EE	물	R biv	ttatum	A-	٧-	F5	VV	EE	M	zeb	ra	A-	V+	FS	VV.	EE
N	4 1	laviventris	A-	٧-	FS	vv	EE	F	catus	Α-	٧-	FS	VV	EE	8	A me	xicanum	V-	٧-	FS	vv	EE	N	brid	hardi	A-	V -	FS	VV	EE
N	A . n	marmota	A-	V-	FS	VV.	EE	A	jubatus	A-	٧-	FS	VV	EE	3	M uni	color	A-	V-	IN	VV	ED	10	ber	gylta	A-	N+	FS	VV.	EE
. t	t	tridecemline	A-	٧-	FS	VV	EE	P	vitulina	Α-	٧-	FS	VV	EE	1.1.1	G ser	aphini	A-	٧-	IN	VV	ED	A	oce	llatus	A-	V-	FS	vv	EE
3 8	d	damarensis	A-	٧-	FS	VV.	EE	S N	schainslandi.	A-	٧-	FS	VV	EE	5	L cha	lumnae	A-	V-	FS	VV	EE	c	gob	io.	A	V-	FS.	VV	EE
rodents	1	anigera	A-	٧-	FS	VV.	EE	1 2 0) rosmarus	A-	٧-	FS	vv	EE		E cala	abaricus	A-	V -	FS	VV	EE	s	luci	operca	A-	V-	FS	vv	EE
R o) d	degus	A-	V-	FS.	vv	EE	8 Z	californianus	A -	V-	FS.	VV	EE	E	L OCL	latus	A-	٧-	FS	VV	EE	L	cro	cea	A-	٧-	FS	VV	EE
N	1 8	galili	A-	٧-	F5	vv	EE	Ű. L	i arctos	Α-	٧-	FS	VV	EE	- T	P kin	gsleyae	A-	V-	FS	VV	EE	s	aur	ata	A-	٧-	FS	vv	EE
н	1	glaber	AE	VE	F5	VV	EE	h	A putorius	A-	٧-	FS	VV	EE		S for	mosus	A-	٧-	F5	VV	EE	OC	mil	l.	A-	٧-	F.S	VV	ED
N	1 0	ochrogaster	A-	٧-	FS	vv	EE	N	A erminea	A-	٧-	F5	vv	EE	df	A me	xicanus	A-	V-	FS	vv	EE	# s	tor	azame	A -	V-	FG	vv	EE
C		griseus	A -	¥-	FS	VV	EE	0	lupus	A -	٧-	FS	VV	EE		C car	pio	A-	٧-	FS	VV	EE								
N	1 1	unguiculatus	A-	V-	FS	VV	EE	TO A	A javanica	A -	V -	FS	VV	EE		P nat	tereri	A-	V-	FS	VV	EE								

Abbreviations: NW, New Wolrd; lemurs+, lemurs, lorises and galagos; Ts, treeshrews; RP, rabbits and pikas; horses+, odd-toed ungulates; Pa, pangolins; MSH, moles, shrews and hedgehogs; Afro, Afrotheres; Xe, xenarthrans; Marsup, marsupials; Mo, monotremes; Lo, lobe-finned fish; Cart, cartilatginous fish

Figure 7. The top five correlated mutation pairs for β -synuclein with β IVa-tubulin. See figure 2 for an explanation of the figure layout. Note that for these two proteins, sequences from numerous fish species are known and included in the analysis, with one lobe-finned fish species in blue, ray-finned fish in light blue, and two cartilaginous fish in green. Also note that birds appear to lack β IVa-tubulin.

Unlike α - and γ -synuclein, there is no experimental evidence linking β -synuclein and microtubules that the author is aware of. Because of this, the potential correlated mutation pair with BIVa-tubulin should be viewed with extra caution. With all the combinations of three synuclein and six tubulin proteins, the odds increase that one combination might happen to have a noninteracting pair of mutations in two unrelated species, that is, the probability of the phylogenetic bias test producing a false positive is higher. Indeed, there are a few instances where top correlated pairs in the control analyses with hemoglobin also appear to pass the phylogenetic bias test (data not shown). Thus, compared to the other two cases of potential coevolution, tau with BIIItubulin and tau with α -synuclein, the evidence for β -synuclein coevolving with βIVa-tubulin is less compelling.

Discussion

The results show potential correlated mutations pairs between tau and BIII-tubulin, between tau and α -synuclein, and perhaps between β -synuclein and β IVa-tubulin. Because microtubules are the natural binding target of tau, coevolution between tau and neuronally expressed tubulin proteins is a given. Indeed, it is surprising that the only convincing candidate for a bona fide correlated mutation pair is with *βIII-tubulin*. As explained in the results, correlated mutation analysis can only detect correlations between non-invariant residues, and it could be that most interactions between tau and tubulins involve at least one invariant residue.

The predicted correlated mutation pair for tau with β III-tubulin does correspond to protein regions expected to interact, however. The tau mutation S240A occurs in the proline-rich region (figure 1a), which, along with the

microtubule-binding repeat region, is necessary for strong binding. (14) The β IIItubulin E441D mutation occurs in the Ehook, the flexible, glutamate-rich C-terminus which extends out from the microtubule where it can easily interact with binding proteins. Glutamate residues in the E-hook are often polyglutamylated, that is, chains of polyglutamate are attached to their side chains. While E441 is not a known polyglutamylation site, its near neighbor is, E438 (15), and another near neighbor, S444, is a phosphorylation site. Perhaps the mutation to aspartate can affect how the Ehook is modified.

The best candidate for a tau/ α -synuclein correlated mutation pair, L48P for tau and N122S for α -synuclein, also corresponds to at least one region expected to interact based on previous experiments. Measured by NMR spectroscopy, N122 is one of the residues most perturbed by interaction with tau. (4) On the other hand, no significant perturbation of tau L48 was seen by interaction with α synuclein; instead, the C-terminal half of the proline-rich region (P2 in figure 1a) was most strongly perturbed. Examining the net charges of the putative correlated pair regions also reveals a seeming discrepancy; both the tau N1 insert, wherein L48 lies (figure 1a), and the C-terminal domain of α -synuclein, containing N122 (figure 4a), are negatively charged. For interactions involving intrinsically disordered proteins, non-specific interactions between oppositely charged regions are more typical.(16) (17) Thus, it appears that L48 and N122 probably do not interact, at least not directly. Perhaps L48 and N122 compete for interaction with a third site, the positively charged proline-rich region of tau, as one possible example. In fact, there is evidence from fluorescence spectroscopy that the tau N1 and proline-rich regions interact.(18). The L48 site is flanked by two phosphorylation sites, S46 and T50,

and the L48P mutation might affect their phosphorylation, which, in turn, could impact electrostatic interactions with the N1 region. Nevertheless, until there is clear structural or functional evidence linking the tau L48 and α -synuclein N122 sites, this potential correlated mutation pair should be considered provisional.

The tau/α -synuclein other correlated mutation pair of interest involves the Parkinson's disease-associated mutation A53T in α -synuclein with -149cG for tau, where 149c- means the third position in the insert after human tau residue 149 in the multiple sequence alignment (see Methods), and G is the ancestral residue. The insert occurs right before the proline-rich domain. Because this mutation pair might have arisen only once, the chance of a false positive is high, that is, it might fail the phylogenetic bias test. On the other hand, it is also possible that it is a genuine correlated pair where the pair of mutations have so far happened only in Old World monkeys and apes, and New World squirrel and capuchin monkeys. In the NMR study cited above, the region around A53 seemed to show weak perturbations in the presence of tau, but below the threshold of significance. In another study of α synuclein coevolution with the enzyme glucocerebrosidase, the top Z-score correlated pair involved α -synuclein A53T. Mutations in the gene for (11) (12)glucocerebrosidase, GBA1, are also risk factors for developing Parkinson's disease. It is intriguing that A53T comes up in both studies, hinting at a connection between disease-causing mutations and correlated mutation pairs, and in fact, such connections are observed for human genetic diseases in general. (19)

There are many proposed mechanisms for how the A53T mutation might cause Parkinson's disease in humans. Most are toxic gain-of-function hypotheses, where the mutation renders α -synuclein neurotoxic or promotes formation of its pathological oligomeric and amyloid forms. Recently, an alternate hypothesis has been proposed, that neurons overexpress the wild type allele to compensate loss-of-function caused by the mutated allele, causing overall α -synuclein levels to rise, thus increasing the likelihood of oligomer and amyloid formation. (20) Mutations linked to higher tau expression levels, in particular, those connected with the H1 haplotype, also appear to be associated with not just Parkinson's disease, but with Alzheimer's disease and many tauopathies as well. (21) (22) The tau -149cG mutation has not been detected in humans, though a nearby mutation A152T appears to be a risk factor for dementia with Lewy bodies, Alzheimer's disease and several tauopathies. (23) (24)

In conclusion, the correlated mutation analysis suggests that tau and α -synuclein might have coevolved, though more experimental evidence is needed to confirm The analysis yields more than just this. evidence of coevolution, however; the correlated mutation pairs can also provide clues regarding the normal biological function of the proteins, and the diseasecausing mechanisms as well. Thus, genome sequencing of non-human species. vertebrates in particular, is a critical tool for understanding the origins of human disease.

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SUPPLEMENTARY MATERIAL

Supplementary figures

- 1. The top five correlated mutation pairs for tau with A) α Ia-tubulin, B) β IIa-tubulin, C) β IIb-tubulin and D) β IVa-tubulin.
- 2. The top five correlated mutation pairs for tau with A) β -synuclein and B) γ -synuclein.
- 3. The sixth through tenth highest correlated mutation pairs for tau with α -synuclein.
- The top five correlated mutation pairs for α-synuclein with A) αIa-tubulin, B) βI-tubulin, C) βIIa-tubulin, D) βIIb-tubulin, E) βIII-tubulin, and F) βIVa-tubulin; for β-synuclein with G) αIa-tubulin, H) βI-tubulin, I) βIIa-tubulin, J) βIIb-tubulin, and K) βIII-tubulin; and for gsynuclein with L) αIa-tubulin, M) βI-tubulin, N) βIIa-tubulin, O) βIIb-tubulin, P) βIIItubulin, and Q) βIVa-tubulin.

Page 19 of 32

Supp. Fig. 1A

an a	1a-tubulin		Corr	elatec	pairs				Con	elated	pairs					Corre	slated	pairs					Corn	elated	pairs	6
	protein	1-14	1.10	1.14	e 11	11.14	prote	in 13	a e X	1.1.3	i la	1.18		protein	1 10	t 1a	1.34	1.10	± 18		protein	÷ 1a	т 1а	1 10	1.10	1.1
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	sapiers	TV.	AV	DV	- V.	RV	C porcellus	11	AV	DV	-V	RV.	۰.	tupus .	TV	AV	DV	N.	RV	p.	mucrosquem	TV.	AV	DV.	-V	1
. #	trogladytes	14	AV	DV	- 4	RV	O cuniculus	TV	C EV	DV	-¥	AV		discolor	TV	AV	DV	÷¥.	RV	6	evgoodei	TV	AV	DV.	-¥	
6	gorila	14	AV	DV	-9	RV	S scrofa	TV	AV	DV	-V	#V		aepptiacus	TV	AV	DV	-W	RV.	×	tropicalis	TV	EV	EV	-V	29
P.	abelii	TV	AV	DV	-W	RV	C hircus	TV	C. AV	DV	-V	RV	E	tuscus	TV	AV	OV	- V	RV	X	laevis	TV	EV	EV	-V	20
	moloch	TV.	AV	DV	-V	RV	O aries	TV	AV	DV	-V.	RV.	M	brandtii	TV	AV.	DV	÷V.	8V	. 5	selar	TL	AI.	10	11	916
	leucogenys	TV	AV	DV	- 98	RV	O virginianu	s TV	AV	OV	- V	RV.	м	lucifugus	TV	AV	DV	÷V.	RV	5	trutta	TI.	AL	01	TL	
M	leucophaeu	TV.	AV	DV	14	RV	8 taurus	11	AV	DV	-V	RV	0	afer	TV	AV.	DV	-V	RV	0	mykiss	TH	AL	01	11	
M	nemestrina	TV	AV	DV	-4	RV	B bison	TV	AV	DV	-¥	RV.	с	asiatica	TV	AV	DV	-9	RV	0	kisutch	TL	AL.	D1	TI	
M	mulatta	TV	AV	DV	-9	RV	8 mutus	TV	AV	DV	V-	RV.	1.	africana	TV	AV	DV	SV.	RV	p.	formosa	51	140	51	TI	
M	fascicularis	TV	AV	DV		RV	C ferus	TV	AV	DV	۰V	RV	0	novemeinct	TV	AV	DV	.4	RV	P	latipinna	51	4	SE	TI	
c	tabseus	TV.	AV	DV	-9	RV	L obliguider	H TV	AV	DV	-V.	RV	5	harrhii	TV	AV.	DV	÷V	8V	P.	mexicana	51	-1	51	TI	
Ρ.	tephroscele	TV	AV	DV	-9	RV	G melas	TV	AV I	OV	·V	RV.	M	domestica	TV	AV	DV.	÷V	RV	×	hellerii	51	4	SE	TL	
	roxeitana	TV.	AV	DV	- 9	RV	O orca	TV	AV	DV	-V	RV		Cinereus.	TV	EV	DV	·V	EV	X	couchianus	51	10	51	TI	
c	capucinus	TV	AV	DV	-4	RV	P sinus	TV	AV	DV	-V	RV	0	anatinus	TV	AV.	DV	-V	#V	x	maculatus	51	-1	51	TI	
5	boliviensis	TV.	AV	DV	199	RV	D leuces	TV	AV	EV.	-V.	RV.	1	peregrinus	TV	GV	DV	÷V.	RV	M	armatus	\$1	146	51	TI	
.5	apella	11	AV	DV.	24	RV	M monocero	5 TV	AV.	EV	V	RV.	5	cameius	TV	AV	DV	.4	RV.		heterociitus	-\$1	1	51	TI	
C	jacchus	TV.	AV	DV	-9	RV	L venitter	TV	AV	DV	-V.	RV	A	fuligula	TV	AV	DV	39	AV.	0	latipes	51	-1	St	TL	
	nancymaae	TV	AV	DV	-9	RV	C simum	TV	AV	OV	۰V	RV	0	altera	TV	GV	DV.	÷¥.	RV	A	testudineus	51	-1	51	TI	
	coquereli	TV.	AV	DV.	- 94	RV	E asimus	TV	AV AV	DV	-4	RV	- 1	filicauda	TV.	GV.	DV	-W	RV	0	spiendens	31	-4	51	TI	
M	murinus	TV	AV	DV	-4	RV	E caballus	TV	AV AV	DV	-V	RV	T	guttata	TV	GV	DV	-٧	RV	0	niloticus	51	-1	51	TI	
0	garnettii	TV	AV	DV	N.	RV	P pardus	TV	AV	DV	-V	RV	G	galles	TV	AV	DV	19	RV	H	burtoni	-51	14	51	TI	
0	ontii	19	AV	DV	-4	RV	L canadensi	 TV 	AV N	DV	-V	RV	c.	japonica	TV	AV	DV	44	RV.	M	zebra	51	-1	51	TL	
M	flaviventris	111	AV	DV	1.9	AV.	F catus	TV	AV	DV	-V.	RV		tumilis	TV	GV.	DV	÷V	AV.	N	brichardi	30	-4-	51	TL	
M	marmota	TV.	AV	0V	-9	87	A jubatus	TV	AV	DV	-V	KV	0	anna	τv	GV.	0V	÷V.	RV.	1	bergyita	SI.	4	51	TL	
0	griseus	TV.	AV	DV		RV	P vitulina	TV	AV.	DV	-V	RV	T.	guttatus	TV	AV	WV.	-14	RV	c	gobio	SV.	·v.	SV	TV	
	norvegicus	TV	AV	DV	-4	RV	N schauinsla	n TV	AV	DV	-V	RV	P	murals	TV	AV	DV	·V	RV	5	lucioperca	51	-1	51	-1	
	musculus	TV	AV	DV		RV	U arctos	TV	AV	DV	-V	RV	A	carolinensis	TV	AV	DV	- 9	RV		crocea	51	14	St	TI	
1	tridecemiin	19	AV	DV	-4	RV	M putertus	T	AV 1	DV	-V	RV		vitticeps	TV	AV	DV	- 11	RV.	5	aurata	51		sv	TV	
	leucopus	TV	AV	DV	1129	BV	M erminea	TV	AV	DV	V.	8V	T	elegans	TV	AV	EV	· V	HV							

Supp. Fig. 1B

u βITa	tubulin		Cor	relat	ed	pairs						Con	relate	d pairs					Cor	related	f pairs					Com	elated	pairs	Ř.
	protein	± 2A	12	A ±	ZA	τ ZA	13	2Å		protein	± 2A	$\pi 2$	A i 2	A τ 2/	1 T.ZA		protei	n : 2	A + 2	A t 2/	1 1 2/	τ 2A		protein	1 24	1 24	1 ZA	τ 2A	1.2.2
Genus	residue Z-score	2 45 10.2		306 9		167 10	184 -	- C	Genus	ip residue	B	105	i i i	i i i	440	Genus	for residu	• ~ 1	109	306	E a	184	Genus	for residue	443	48	306	107	184
H sap	piens	AD-	61	(V	N	NN	1.14	E .	(F)	leucopus	-0	GN	VN	NN	-E.	0	rosmarus.	. A0	GN	(VN	NN	-E	A	platyrhyncho	AD.	6N	VN	NN.	A
P tro	glodytes	AD.	61	· ¥	N	NN	1.1	E.	C	porcellus	AD.	GN	VN	NN	-E	Z	californian	u AD	61	I VN	NN	7.E	N	nippon	AD	6N	VN.	NN	A
P par	niscus	AD.	-61	(V	N	NN.	194	E	18	damarentis	AD.	GN	VN	NN	18	N	schauinsla	+ AD	GN	C VN	NN	-8	- F.	sherrug:	AD	GN	VN	NN	A
G gor	rifia	AD.	G.	i V	N	NN.	100	E	0	depis	AD.	GN	VN	-SN	-E.	U.	arctos	AD	GN	I VN	NN	· E	C.	vociferus	A0	GN	VN	NN	A
P abr	elli	AD.	61	i. V	N	NN:	164	E	C	princeps	AD.	GN	VN	NN	-E	M	puterius	AD	GN	VN	NN	-E	5	samelus:	AD.	GN	V.N.	NN	A
N leu	readents	AD	GI	i v	N	NN	2.4	E I	0	cuniculus	AD	GN	VN	NN	-6	M	ermines	AD.	GN	VN.	NN	-E	- 6	fuligula	AD.	GN	VN	NN.	A
P ani	ubis	AD-	GI	i v	N	NN	114	E	5	scrota	AD	GN	VN	NN	÷ŧ	c	lupus :	AD	Gt	VN	INN	-6	N	perdicaria	AD.	61	VN	NN	A
C aty	ris .	A0	61	1.4	N	NN		E	c	hircus	AD.	GN	VN	NN	-E.	v	vulpes	AD	61	VN.	NN	36	. C	canorus	-0	6N	VN.	NN	A
M net	mestrina	AD.	Gi	i v	N	NN	344	£1.0	0	aries	AD	GN	VN	NN	-6	- p	discolor	AD	GN	VN	INN	-8	P.	filicauda	-0	GN	VN	NN.	194
M mu	slatta	AD	61	i v	N	NN	1	E	8	taurus	AD.	GN	VN	NN	÷E		aegyptiacu	s AD	GN	. VN	NN	- E	N	chrysocepha	10	GN	VN	NN	1.1
M fan	cicularia	AD	.04	. V	N	NN	124	E 1		bison	AD	GN	VN	NN	-1	H	armiger	AD	GA	VN	NN	-1	1.0	major	-0	GN	VN	NN	tia
C sab	baeus	AD	61	i v	N	NN.		E	c	ferus	AD	GN	VN	NN	-6	E	funcus	A.D	GN	I VN	NN	-6	т	guttata	-0	GN	VN	NN.	
T gel	ladia	AD-	61	i v	N	NN.	114	E U	C	dromedariu	AD	GN	VN	NN	÷E	M	brandtii	TE	61	. VN	INN	18	10	striata	-0	61	VN	NN.	119
R 108	entine	40	63	i v	N	NN		E		acutorostrat	AD	GN	VN	NN	-1	M	lucifugua	78	GN	VN	NN	-1	6	gallus	AD.	GN	VN	NN.	
5 bel	liviensis.	AD	61	V	N	NN	1944	C 12	1	obliguidens	AD.	GN	VN	NN	-0		slecto.	AD	GN	VN	INN	-8	c	coturnix	AD	GN	VN	NN	114
C jap	chus	AD	.61	i v	N	NN.	104	E	0	orca	AD	GN	VN	NN	÷E	c	cristata	AD	61	VN	NN	-E		humilis	-0	GN.	VN	NN	
M mu	innus	AD	.6.8	i v	N	NN	1	E III	i e	sinus	AD	GN	VN	NN	-6	E	europaeus	AD	GA	VN	-N	-8	C.	anna	-0	GN	VN	NN	19
N gal	18	AD	61	i v	N	NN.	-	£	D	leotas	AD	GN	VN	NN	-1	0	afer	AD	GN	VN.	NN	-1	т	guttatus	AD.	GN	VN	NN	
D ord	di	AD.	61	i v	N	NN	114	E U	M	monoceros	AD	GN	VN	NN	-E	T	manutus	AD	61	VN	NN	18		murals	AD.	61	VN	NN	19
2	iniculatus	AD	61	i v	N	NN	-	E	ε	vexilifer	AD.	GN	VN	NN	-E	c	asiatica	TO	GN	VN.	NN	-8	A	carolinensis	AD	65	VS.	NS.	14
M od	hrogaster	AD-	61	V	N	NN.	10.4	E	c	simum	AD.	GN	VN	INN	÷E	- E	africana	AD	Gh	VN	INN		P	vitticeps	AD	VN	IN	SN.	19
M ma	armota	AD	61	V V	N	NN	1.4	E	E	caballus	AD	GN	VN	NN	÷E	0	novemcine	t AD	6.1	VN	NN	-E	T	elegans	AD	¥5	15	55	
C grit	amus	AD.	.6.8	V	N	NN	12/14	E	10	pardus	AD	GN	VN	NN	14	5	hamaii	AD	GN	VN	NN	-6	100	mucrosque	AD	VN	IN	SN	19
M aut	ratus	AD.	61	V	N	NN.	1.4	E	1	canademsis	AD.	GN	VN	NN	-1	M	domestica	AD	GA	VN	NN	-6	6	eveoodei	TO	GN	VN	NN	1.1
	rvegicus	AD	-0.5	i v	N	NN	114			catus	AD	GN	VN	NN	-6	V	unsinus	AD		VN	NN	-1		mydas	AD	GN.	VN	NN	1
	isculus	80	61	10.0	N	NN			1.2.5	aubatus.	AD.	GN		NN	-1		onereus	AD		1000		-8		A. 142.014 (C)					
	decemin	AD			N	NN	34	_		vitulina	AD	GN		NN	E.		anatinus	AD				46							
C lan		AD	221		201	NN.				weddellii	AD	GN			-1		chrysaetos	AD				AG							

Page 20 of 32

Supp. Fig. 1C

ι βΠR	b-tubulin		Co	mel	ated	pairs					Corr	elated	f pairs					C	orrela	sted	pairs					Corn	elated	pairs	F
Gas	protein residue	+ 184	12.2		1 2b	τ 20 345	1 20 441		protein 9 residue 3 Z-score					= 25 441		g reside					t 20 440		Ge	Fresidue			1 184"		
1	Z-score	9.0		8.	8.8	8.5	8.4								- 6	1 2-100							5	g Z-score					
1.1.1.1.1.1.1.1	piera	G		G i	-6	RE	G	c	griseus	-6	-6	G	RE	-6	- L	canadensi	6 9	6	6	-6	RE	-6	N	nippon.	QE	8.8	PE	KG	
P tr	ogladytes.	-6	1	6	-6	RE	-6		norvegicus	-6	-6	-6	RE	-6	- L.	pardinus	- 4	8	-6	-6	RE	-6	5	camelus	QE	KE	PE	KG	
P - pi	aniscus	-6	12	6	-6	RE	+6	8	4 caroli	-0	-6	-6	11	-6	- F.	catus	-4	5 0	-6	-6	RE	+6	A	futgula	QE.	RE:	PE	KG	89
G gt	stilla	- G	1	6	-6	RE	G	6	musculus.	÷6	÷6	G	RE	-6	A	jubatus -	-1	6	-G	÷G.	RE	G		colchicus	QE	KE.	PE	KG	d 1
P at	ielli	-6	3.6	G.	-6	RE	G	1	tridecemlin	-6	>6	- G	RE	· G	. P	vitulina	-1	5	-6	6	RE	-6		filicauda	QE	KE.	PE		81)
N le	ucogenys	÷G		G	-6	RE.	-G	c	lanigera	-6	- G	÷G	RE	- G	- 1	weddellii		6	-6-	-6	RE	+G	1	trailli	QE	KE	PE	KG	8.9
P at	lubis	6	1.4	6	-G	RE	G	P	leucopus	-6	-6	.6	RE	-6	0	rosmarus	- 9	6	6	-6	RE	G	. N	chrysocepha	QE	KE.	PE	KG	
M le	ucophaeu	-6	-	6	-6	RE	-6	0	porceilus	-6	-6	-6	RE	-6	N	schauinsla	n -1	6	-6	-6	RE	G	T	guttata	QE	KE	PE		
C at	VS.	-G		G.	·G	RE	+6	F	damarensis	-6	-6	+G	RE	-6	U	arctos	1	6 3 H	-6	-6	RE	-G	1	strieta	10	88	PE	KG	
M né	emestrina.	+G	2.6	6	6	RE	-6	0	princeps	+6	-G	-G	RE	- G	A	melanoleu	e -i	5	-6	÷G.	RE	G	6	gathis	QE	K.E.	PE	KG	
Mm	ulatta	-G	14	G.	-6	RE.	0	0	cuniculus	-0	-6	-6	11	-G	M	erminea	1.5	6 (15)	-G	-G.	RE	-G		humilis	QE	KE	PE		
M fa	scicularis	٠G	1	6	·G	RE	G	5	scrofe	-6	-6	+G	RE	-6	C	hiput	-	6	-G	-G	RE	+G	c	anna	OE.	KE	PE	KG	
C 14	baeus	-6	1	6	-6	RE	-6	0	hircus	-6	+6	. 6	RE	-6	- P.	discolor	1	a () (6	-6	RE	-6	A	sinensis	EE	QE	KE	KG	
T gt	rinda	-6		Ġ	-6	RE	-6	C	aries	-6	-6	-6	RE	-G	M	notalensis	4	G .	-6	-6	RE	-G	P	muralis		Q.E	RE		
Pte	phroscele	-6	124	G.	·6	RE	-6	C	virginianus	-6	-6	-G	RE	-G		segyptiaca	184	6 311	-G	-6	RE	-G	P.	vitticeps	EE.	QE	RE	KG	
R ro	unitaria	-6	1	6	-6	85	-6		taunus	-6	-6	16	RE	-6	H	armiger	-1	5 C	-6	-6	RE	-6	T.	elegans	EE.	QE	RE	KG	
C ca	pucinus	-6	4	6	-G	8.5	-0	0	mutua	-6	-G	-6		-6		fuicus	-1	1	-V	-V	RE	-V		тистондыя	11	10	RE	.60	
5 bi	liviensis	÷G	-	6	-G	88	-G	0	ferus	-G	-6	+G	RE	-G	M	lucifugue.	-1	6	-6	-G	RE	+G	τ	picta	EE.	QE.	KE	KG	
5 40	rella	-6	22	4	-0	RE	-6	c	dromedariu	-6	-6	-6	RE	-0		alecto.	- 6	411	-6	-6	RE	+6	6	evgoodel	11	QE.	KE	KG	
A no	ancymaae	-6		G	-G	RE	-G		acutorostrat	-6	-G	-G	RE	-G	. 6	europeeur	-	5	-G	-G	86	-G		tropicalis	DG	0G	KG	KE	
Mm	urinus	-6		6:	-6	RE	-6	1	obliquidens	-6	PG	TG	RE	KG	0	afer	1	5	-6	-6-	RE	-G	1.8	laevis	DG	QG	KG	KE	
0 #	rnettii	-6		6	-6	A.E	-6	0	metas	-6	PG	ΥG	RE	KG	T	manatus	20	5	-6	-6	RE	-6	:5	salar	-6	-6	-6	κ-	
I ct	inensis	II-G	104	G.	-6	RE.	-6	0	orca	-G	PG	TG		KG	c	ssiatics	- (5	G	-G	RE	-G	5	trutta	G	-6	-6		
N RI	158	-G		ű.	-6	RE	-6-	P	sinus	-6	PG	ŤG	HE	KG	1	africana	-1	6	-6	-6	BE.	-G	0	mykiss	-6	-6	-6	K-	
D of	di	-6	1	6	-G	RE	-6		asiaecrietta	-6	PG	16	RE	KG	1	telfaiti	- 6	5 11	-6	-6	88	+6	0	kisutch	-6	-6	-6	R -	
1 10	culus	-6	÷.,	G	-G	RE	-G	0	leucas	-G	PG	TG	RE	KG	5	harrisi	-	5	G	-G	KE	· 6		reticulata	-6	-G	-6	· K -	
M fu	aviventria	-6	114	6	-6	RE	-6	Ň	monocerus	-0-	PG	16	RE	KG	M	domestica	-	5	-6	6	KE	-4	1	lationna	-6	-6	-6	K-	
	aniculatus	6		6	-6	81	-6	L	vesitifer	-6	PG	ΥG	RE	KG	v	ursinus	-1			-6	KE	-6	× x	heliorii	-6	-6	-6	×-	
Mos	dvogaster	I G		6	G	88	-G	E	simum	-6	-G		RE	· 6		cinereus		5	G	G	KE	-G		couchiamus	G	-G	-6		
	armota	-G		6	-6	HE.	-6	E	asinus	-6	-6	+G	HE	· 6	0	anatims	-1	6	-6	-6	KE	-G	x	maculatus	-6	-6	-6	K-	
	nguiculatu	-6	24	G	· G	RE	-6		cabalus	-6	-6	-6	RE	-G		chrysaetor	0			PE	KG	KE		splendens	-6	-6		K-	
H gi		- G		7.1	-G	RE	-G		pardus	-G	-6	-G	RE	·G		forsteri	0			PE	KG	KE	-			-			

Supp. Fig. 1D

u βIVa-tubulir	n	Corr	elate	d pairs				Cart	related	pairs.					Corre	elated	pairs					Corn	elated	pairs	2
protein	1.4	1.1.4	1.4	s x 4a	3.40	protein	1.4	1.4	6 e 4	τ 40	1.44		protein	1.40	1 40	τ 40	1.44	τ 4a		protein	1.40	1.44	1.40	1 43	
Genesidue Z-score	217 6.5	196 E	8 3 65		260 4.0	Genis Z-score		309	1 2 3	318	54	Genus	residue	55	309	15 .35	318	195	Genus	g residue Z-score	35	309	S 55	31.6	260
H saplers	11	VA	ET	VT	IV	M unguiculatu	s IT	VA	ET	VT.	IV	Ŧ	catus	IT	VA.	ET	VT.	14	P	mucrosquem	VS.	VA.	ES	V5	ΞŪ
P troglodytes	iT	¥4	ET	VT	IV.	H glaber	11	VA	ET	VT.	iv	- 4	jubatus	IT	VA.	ET	VT.	IV.	T	carolina	15	VA.	ET	¥5	
P paniscus	11	VA	ET	VT	IV.	C griseus	11	VA	ET	YT.	IV.		vitulina	17	VA.	ET.	VT	IV .	C .	picta	15	NA.	ET	VS	
G gorilla	IT	VA	ET	VT	IV	M auratus	IT	VA	ET	VT.	EV.	- 6	weddellii	IT	VA.	ET.	VT	19	G	evgoodel	15	WA.	ET	VS.	
P abelli	IT	VA	ET	VT	IV	R norvegicus	17	VA	ET	VT.	IV	0	resmanas	IT.	VA	ET	VT.	IV	×	tiopicalis	15	TS.	ET	15	
H malach	IT	VA.	ET	VT.	IV.	M pahari	IT.	VA	ET	YT.	IV.	2	californianu	IT.	VA.	ET.	VT.	IV.	×	laevis	15	TS	ES	VS	
N leucogenys	IT	VA	ET	VT	IV.	M caroli	IT.	VA	ET	VT.	IV		schaunstan	IT.	VA.	ET	VT.	11	5	salar	15	VS	ET	VS:	
P anubis	iT	VA	ET	VT	IV.	M musculus	IT	VA	ET	YT	TV.	U	arctos	iT.	VA.	ET	VT.	iv.	5	trutta	15	¥5	ET	VS.	
M leucophaeu	IT	VA	ET.	VT	IV	l tridecemin	IT	VA	ET.	VT	IV.	M	putorius	IT	VS	ET.	WT.	IV	0	mykiss.	15	NS.	ET.	VS	
C atys	IT	VA	ET	VT.	IV	C lanigera	17	VA	DT	VT.	FV.	M	erminea	IT	VA.	ET	VT.	11	0	kisutch	15	V5	ET	V5	
M nemestrina	11	VA.	ET	VT	IV	F damarensis	17	VA	ET.	VT	IV	. C	lupus	11	VA.	ET	VT.	IV	p.	formosa	IT	VA.	13	VT	
M mulatta	IT	VA.	ET	VT	IV.	O degus	IT.	VA	ET	VT.	IV.	M	Javanica	IT	VA.	ET	VT	IV.	P.	reticulate	IT	VA.	-1	VT.	
M fascicularia	IT	- VA	ET	VT.	IV	O princeps	IT	VA	ET	VT.	IV	- P.	discolor	1T	VA.	ET	VT.	19	P.	latipinera	15	VA.	ET	VS.	
C sabaeus	IT	VA.	ET	¥.T	iV.	O cuniculus	17	VA	ET.	¥T.	LV.	M	natalensis	11	VA.	ET.	¥T.	iv	P	mexicana	17	¥A.	ET	VT	
T gelada	IT	VA	ET.	VT	IV	5 scrofa	IT.	VA	ET.	VT.	IV		angyptiacus	IT	VA	ET.	VT.	VV	*	bellers	15	NA.	ET.	VS	12
P tephroscele	11	VA	ET	VT.	IV	C hirous	11	VA	ET	VT.	IV.		armigar)T	VA.	ET	VT.	IV	×	couchianus	15	VA.	ET	VS.	
R bieti	IT	VA.	IT	VT	IV	O arties	IT	VA	1 ET	VT	IV	÷	fuscus	IT	VA	-T	VT	IV	×	maculatus	15	VA.	ET	VS.	
R rovellana	1T	V.A	8.7	VT	IV.	O virginianus	IT.	VA	TT.	¥T.	IV.	M	brandtil	11	VA.	-T	VT	14	c	variegatus	IT.	VA.	ET.	VT.	
C capucinus	11	VA	ET	VT	IV	B taurus	IT	VA	ET	VT.	1V	M	lucifugue	IT	VA.	-T.	VT.	11	M	armatus	IT	VA.	ET	VT.	
5 boliviensis	IT	VA	ET	¥T.	11	B mutus	17	VA	ET.	YT.	1¥	C	cristata	11	VA.	ET.	VT.	IV		heteroclitus	IT.	¥A.	ET	VT.	
5 apella	IT	VA	ET	VT	IV	C ferus	IT	VA	ET	VT	IV.	5	araneus	IT	VA.	KT	VT.	IV	0	latipes	IT	VA.	ET	VT.	
C jacchus	IT	VA	1.1	VT	IV	B acutorostra	E IT	VS	ET	VT.	IV	£	europaeus.	IT	VA.	-A	¥T.	11	A	testudineus	IT.	VA.	-1	VT.	
A nancymase	11	VA.	ET	VT	IV	L obliguidens	111	VA	111	VT.	IV	0	afer	IT	VA	ET.	VT.	IV	8	spiendem	15	VA.	÷Ť.	V5	
₽ coquereli	IT	VA	ET	VT	IV.	6 melas	IT.	VA	ET	¥T.	IV	c	asiatica	17	VA	EA	VT.	IV	0	niioticus	IT.	VA.	ET	VT.	
M muninus	17	VA	ET	VT	IV.	O orca	IT	VA	ET	VT.	1V	D	novemainst	11	VA	ET	VT.	11	11	burtoni	11	VA.	ET	VT.	
O garnettii	it	V.A.	ET	VT	IV.	P sinus	11	VA	ET	VT	IV	5	harrisli	17	VA.	ET	VT.	IV.	M	zebra	IT	VA.	ET	VT	
7T chinensis	IT	VA	ET	VT	IV	N asiaeorient	IT IT	VA	ET	VT	IV	× V	ursieus	IT	VA.	ET	VT.	IV	N	brichardi	IT	WA.	ET	VT	
N gallà	IT	VA.	ET	VT	IV.	D. Jeucas	IT	VA	ET	VT.	IV.		cinereus	IT	VA.	ET	VT.	TV	. 6	bergyita	15	VA.	75	VS.	
D ondi	11	VA.	ET	VT	IV	M monoceros	IT	VA	11	VT	IV.	0	anatinus	15	VA	ET.	VS	11	A	ocellatus	15	VA	-6	VS	
J jaculus	IT	VA	ET	VT	IV	L vesilifer	IT	VA	ET	VT.	IV.	A	sinersis	IT	VA	ET	VT	IV	c	gobio	IT.	TS	-5	VT	
M flavioentris	IT	VA		VT	IV.	C simum	11	VA	ET	VT.	IV	A	mississippen	IT	VA	ET.	VT.	11	5	lucioperca	IT.	VA.	-A	VT.	
P maniculatus	IT	V.A	ET	¥T.	IV.	E asinus	IT.	VA	ET	¥T.	iv	P	muralis	¥\$	VA	ET	15	11	1	crocea	IT	¥X.	ET	VT	
M-ochrogaster	IT	VA	ET	VY	IV	E cabalho	IT	VA	ET.	VT	EV.	A	carolinensis	VS	VA.	ET	15	11	5	aurata	11	VA.	ET	VT	
M marmota	17		ET	VT	IV	L canadensis	IT	VA	ET	VT.	IV		vitticeps	VS	VA.	ET	VS	IV							

Page 21 of 32

Supp. Fig. 2A

u β-synuclein		Cor	relat	ied ;	pairs					Corr	elated	pairs						Corre	elated	pairs					Corr	elated	pairs	f
protein	1. (5	÷εβ	5τ	ß۶.	τ β5	τ β5		protein	1 (15	τ β5	τ βS	× (15	i t (65			protein	τ β5	τ β5	τ β5	× (55	+ 85		protein	1 BS	× (15	i τ β5	τ β5	1.11
Geng residue	40	10 H			229 4	4 9	Genus	P residue	40	ž z	208	22 4	267	-	Specie	residue	430	163	208	22.9	4	Genu	ipecies	430	5	208	129	267
H sapiers	DV.	VE	5	F	VF	KF	- ñ	tridecemline	DV	VE	SF	VF.	KF	Ň	1 em	inea	DV	VE	SE	VE	KF	1 P	muralis	DA	MD	SF	VE	1.00
P trogladytes	0Y	VE	5	6	¥#	KF	6	lanigera	DV	YE	SE	VE	KF		hip		DV.	VE	SF	VF	KF		carolinensis	DV	ME	SF	VF.	
P paniscus	09	VE	5	1	VF	KI		leucopus	DV	VE	51	146	KF		vid		DV.	VE	51	VE	KF	P	vitticeps	DV	VE	58	VE	K
G gorila	DV.	VE			VF	KF.		porcellus	DV	VE	SF	VF	KF		l java		DV	VE	SF	VF	KF	T	elegans	DA	10	SF	VF	к
P abelli	DV	VE		F	¥¥.	KF		demanensis.	DY	VE	SF.	VF	KF		656		DV.	VE	SF	VF	RF	T	sirtalia.	DA	10	SF	VE	
H moloch	DV	VE	1.5	F	VE	KF		degui	DV	VE	SF	VF	KF			alensis	DV.	VE	SF	VF	KF		mucrosqua	DV	VE	SF	VF	×
N leucogenys	DV	VE		F	VE	KF		princeps	DV	VE	SF	VE	KF			yptiacus	DV	VE	SE	VE	KF	1	carolina	DA.	IE	SF	VF	1
P anubis	ov	VE			VF	KF		cuniculus	DV	YE	SF	VE	KF		ant		DV	VE	SF	VF	KF		picta	DA	VE	SF	VE	
M leucophaeus		VE		F	VF	KF		scrota	DV	VE	SF	WF.	KF		fun		DV		SF	VF	KF		evgoodei	DA	VE	SF	VE	
C atys	DV	VE		F	VF	KF		hircus	DV	VE	SF	VF.	KF		t bra		DV	VE	SF.	VF	KF		mytias	DA	VE	SF	VF	
M nemestrina	DV	VE		E.	VF.	KF		aties	DV	VE	SF	VE	KI			fugus	DV	VE	51	VF	KF		tropicalla	DV	TE	GL	IL	i i
M mulatta	DV	VE	1.00		VF	KF		virginianus	DV	VE	SF	VF	KF		aler		DV	VE	SF	VF	KF		laevis	DV	VE	GL	11	
M fascicularia	DV	VE		E.	WF.	KF		Eaurus	DV	VE	SE	NF.	KF		eris		DV	VE	SF	VE	KF	ŝ	salar	DV	VE	SF	VE	
			1.00			11111			DV			100.00	KF										A CONTRACTOR OF A CONTRACTOR OFTA CONTRACTOR O		100.70			
C sabaeus	DV				VF	KF		bison	1170 0	VE	SF	VE			ara		DV	VE	SF	VF	KF		trutta	DV	VE	SF	VF	22
T gelada	DV	VE		F.	VF	KF		mutus	DV	VE	SE	WE.	K.F			opaeus	DV	VE	SE	VF	KF		rmyklas.	DV	VE.	SF	VF	20
P tephroscele		VE			VF	KF		ferus	DV	VE	SF	VP.	KF		afe		EM	VE	SF	VF.	KF		kisutch	OV	YE	SF	VF	
II bieli	DV	VE		E.	VF	K.F		dromedarius	DV	VE	: SF.	VF	KF			natus	EM	VE	SF	VF	KF		formosa	DV.	VE.	55	VF	10
R roxellana	DV	VE		F	VF	KF	8	acutocostrata	DV	VE	SF	VF	KF		asia		EM	VE	5F	VF	KF		reticulata	DV	VE	\$P	VF	
C capucinus	DV	VĒ	5	F	VF.	KF	- L.	obliquidens	DV	VE	-58	VF	KF	- £	tell	a¥1	EM	VE	(SF)	VF.	KF		latipinna	OV	VE	58	VF	9
5 boliviensis	DY	VE	5	F.	VF	KF	G	melas	DV	VE	5F.	A.	KF	0	nov	emainct	DM	VE	SE	VF.	KF	P	mexicana	DV	VE.	SF	VF	1
S apella	DV	٧f	5	F.	VF	KF	0	orca	DV	VE	SF	VF.	KF	5	har	rhii	DM	VE	SF	VF	KF	X	heilerii	DV.	VE	SF	VF	3)
C jacchus	DV	VE	5	£	VF	KF	- P.	sinus	DV	VE.	SE		KF	Y	uni	mus	DM	VE.	SF	VE	KF	X	couchismus	0.1	VE.	SF	¥F.	
A nancymase	DV	VE	. 5	F.	VF	KF	N	asiaeoriental	DV	VE	SE	VE	KŦ	- #	chi	reus	DM	VE	SE.	VF	KF	×	maculatus;	DV	VE.	5.5	VF	80
P coquereil	DV	VE	5	F	VF	KF	D	leucas .	DV	VE	SE	VF.	KE	0	úns	tinus	DM	iD	51	VF.	KF	c	variegatus	DV	VE	SF	VE	10
M muninus	DV	VE	13	£	V#	KF.	M	monocerus	DV	VE.	SF	V.	KF	- A	chr	saetos	DV	VE	SF	VF.	KF	M	armatus	DV	VE	58	VF	55
O garnettii	DV	VE	- 5	F	VF	KF	1	vexilifer	DV	VE	SF.	WF.	KF	0	10	aehollan	DV	VE	SF	VF	KF	F	heterocitus	DV	VE	SF	VF.	1
N galili	DV	VE	5		VF	KF	Ċ	simum	DV	VE	SF	VF	RF	-	144	eula	DV	VE	SF	VF	KF	0	latipes	DV.	VD	54	VF	1
D ordi	DV	VE	- 5	8	VF.	KF	1	atimus	DV	VE.	SE	¥F.	KF	N	per	dicaria	DV	VE	SF	VE	KF	A	textudineus	DV	VE	SF	VF	
1 jaculus	DV	VE	5	é.	VE	KF		caballus	DV	VE	SF	VF.	KF		1.000	thicus	DV	VE	SE	VE	KF		splendens	BV	VE	5F	VF	ŝ
M flaviventria	DV	VE	1100		VF	KF		pendus	DV	VE	SF	VF	KF		fase		DV	VE	SF	VF	KF		niloticus	DV	VE	SF	VF	1
P maniculatus	DV	VE		F	VF	KF		canadensis.	DV	VE	SF	VF	KF		atte		DV	VE-	SF	VE	KF		burtoni	DV	TE	SF	VE	-
M ochrogaster	0.77	VE		F	VF	KF		pardinus	DV	YE	SF	VF	KF		ALC: N		DV	VE	SF	VF	KF		zebra	DV	IE	SF	VE	
M marmota	DV				¥F.	KF		catus	DV	VE	51	VF	KF		trai		DV	VE	55	VE	KF		brichardi	DV	VE	SF	VF	1
M unguiculatur	0.01	VE		F	VF	KF		lubatus	DV	VE	SF	VF	KF			vocepha	DV	VE	SF	VF	KF		bergylta	DV	VE	58	VF	23
H glaber	DV	VE	1	£	VE	KE		vitulina	DV	VE	SF	VE	KF		gut		DV	VE	SE	VE	KE		ocellatus	DV	VE	SF	VE	
	DV	VE	100		VE	KF	1.1	rosmanus	DV	VE	SF	VF	KF		stri		DV	VE	SF	VF	KF		gobio	DV	VE	SF	VF	1
C griseus	OV				VF	KF			DV	VE			KF								KF		and the second s					
M auratos		VE						californianu	0.00		SF	VE				leagris	DV	VE	SF	VF			lucioperca	DV	VE	SF	VF	
R norvegicus	DV	VI			V#	K.F		schaumslan	DV	VE	58	WP.	KI		gall		DV	VE	38	VF	KF		стосна	DV	VE	57	VF	
M pahari	OV	VE	1	1.0	VF	KF		arctos	DV	VE	34	VF	KF	-	Jap		DV	VE	SF	VF	KF	5	aurata	DV	VE.	SF	VF	10
M caroli	OV.	VE		F	VF	KF		melanoleus	DV	VE	SF	VE	KF		hur		DV	VE	SF	VF	KF							
M museulus	DV.	. V E	. 5	£11.	VF.	KF	M	putortus	DV.	YE.	31	NF.	KF	. C	ant	18	DV	VE	: 51	VE	K.F							

Page 22 of 32

Supp. Fig. 2B

au y-synucleir	ю. —	Ct	arrei	lated	pairs					Co	rrelate	d pair	8					Corn	elated	pairs					Corr	wlated	pairs	i.
protei	1 1.15		15	: 15	1 15	2 15		protein	1 15		15 1 1	6 t 1	5 ± 15	e.		protein	1.75	1 15	1 15	+ 15	* 15		protein	+ 15	+ 15	1.75	1 15	. 10
Ganus Z-score		277 -	(1997) (1997)	179 34	276 7.5	20 35	-	residue	422	277	179	276			species	residue	E H	115	179	376	8 8	Genu	Testdue	÷.	207	179	83	8
H sapiens	ST	111		PG	QE	-V		porcellus	ST	10	2 11	5 06	e iv			alercis	51	11-3	PG	0E	1.V	Ň	meleagris	ST	14	PG	QE	61.5
P troglodyter	ST	1	1	PG	QE	-¥	F	damarensis	ST.	. 1	- PI	1 01	-9		t and	vptiacus	51	1-	PG	QE	LV	6	gattus.	ST.	14	PG	QE	-1
P paniscus	ST	1		PG	QE	·V.	0	degus	ST	1	. P.	5 QE		1.00	4 am	iger	ST	1.	PG	0E	LV	c	japonica	ST	10	PG	QE	2 -1
G gorilla	ST	1		PG	QE	· V		princeps	ST	1	- P1			1	E fus	CNS.	51	1.	PG	QE	LV		humilis	ST	10	PG	QE	
P abelii	ST	101	1	26	QE	· V	0	cuniculus	ST	11	. Pi	1 01			M Sea	ruttii	51	1.	10	QE	1V.	C	anna	57	1.	PG	QE	114
H malach	ST	1		PG	G.E	-V	5	scrofa	ST		P	1 08	· V	1	ale:	tto	ST	1.	FG	QE	1.V	1	guttatus	ST	1-	PG	QE	
N leucogenys	ST		100	PG	QE	-V	c	hircus	ST	11	. PI	5 QE	-V	1	erls.	tata	51	1.	PG	QE	MV	A	sinensis	ST	1.	PG	QE	614
P anubis	ST	1	-	PG	QE	-V	0	atles	ST	1	- PI	10	-V	3	s ara	neus	ST	1-	PG	0.E	MV	A	mississippe	ST		PG	QE	
M leucophaer	I ST	1	-	PG	GE.	-V		virginianus	ST		. p				E eur	opanus	51	1-	PG	QE	MV	P	muraits	ST	WV.	PG	QE	G
C stys	ST	1		PG	Q.E	V		taunus	ST	- 1	. PI	10 1	-9	1	. ma	natus	57	1-	28	10	LA	A	carolinensi	ST	VV.	PG.	QE	G
M nemestring	ST	121	18	PG	QE	-٧		bison	ST	11	- Pi	F 00	P NV	1	C ask	tica	ST.	10	PG	DE	LV	μ	vitticeps	ST	.99	PG	DE	
M mulatta	ST	1		PG	QE	- V	8	mutus	ST	1	- PI	a a e	- V	1	E telf	airi	57	1-	PG	QE	LV	. 1	elegans	ST	VV.	PG	QE	2
M fascicularis	51		23	PG.	QI	-7	C	ferus	ST	1	- PI	: 01			0 100	emonet	ST.	11-	PG	QE	MV	P.	mucrosque	ST	VV.	PG	QE	133
C sabaeus	ST	1	- 1 C	PG	QE.	-V	C	dromedariu	ST.		- PI	: 01	-٧	1	5 that	risii	51	1-	KG	QE	GV	Ť	carolina	ST.	1-1	PG	QE.	
T gelada	ST	1		PG	QE	·V.		acutorestrat	AT	1	. PI	1 95		1 - 1	W dor	nestica	51	1.	KG.	Q.E	GV	c	picta	ST.	34.1	PG	QE	1
P tephroscell	5T	1	-	PG	QE	¥	L	obliguidens	ST	1	. 01	0	·V	1	1	inus	ST	1.	8.0	1p	GV	6	expondel	ST	1.	PG	QE	2.1
R bieti	ST.	101	4.8	PG	10	-V	6	melas	ST		- 01	1 01	-4	1 - 1 - 1	cn.	erena -	51	1.	KG.	DE	GV.	c	mydas	ST	1+	PG	10	
R rosellana	ST	1		PG	Q.E	·V	0	orca	57	1	- 01	1 08	·V) and	tinus	57	IA.	KG	QE	5V	x	tropicalis	ST	10	PG	QE	
C capucinus	51			PG	QE	-V	P	sinus	ST	1	- 91	Q E	÷ .v	1	i de	viartos.	51	1-	PO	QE	-V	X	lawyis	ST.	1-	PG	QE	
5 boliviensis	ST	1	a 6	PG	QE	·V.	N	asiaeorienta	ST		- 01	1 01	.v		t plat	hybyech	ST	1.	PG	QE	· V	\$	salar	ST	30	-G	QE	5.4
S apella	ST	-		PG	QE	·V.	D	Inucas	ST	1	. 91	1 95	. V	1 - 1	A out	icularia	51	1.	PG	QE	W.	5	trutta	ST	3.	-6	QE	
C jacchus	ST	34	+	PG	QE	-V	N	t monoceros	ST		- QI	0.01	- v	1	A for	teri	ST	1.	PG	1D	-V.	0	mykisa	ST	1-	-6	QE	1
A nancymaa	ST	191		PG	QE	-V	L	vesilifer	ST	18	- Pi	5 QE	·V	100	N nip	poli	51	1.	FG	QE	· V	0	kisutch	ST	THE	+G	QE	3.1
# coquereii	ST	1		PG	QE	-v	c	simum	ST	1	. Pi	5 Q.E	LV	1	E chi	THE	ST	1.	*6	QE	·V	\$	alpinus	ST	10.	-6	QE	
M murinus	51			PG	Q.E	-V.	E	asinus.	AA.	1	- PI	5 QE	LV		E per	egrinus	ST.	1-	₽G	3.0	÷V.	μ	formosa	ST	116	PG	QE	1
O garnetti	ST	1		PG	QE	·V	E	caballus	4.4		- PI	5 Q.E	LV	1	4 018	noides	51	1-	PG	QE	-V	P	reticulata	ST.	10	PG	Q.E.	. 0
N gališ	ST	1	1	PG	QE	-V.	P	pandus	51	1	. P.	3 .Qf	MI		C . w00	ifenus	ST	1.	PG	QE	W.	P	latipinna	ST	3.	PG	QE	0
0 ordă	ST.	1	-	26	30	-V	P	concolor	ST	. 3	- PI	10	T	1	0 max	aehollan	ST	1-	20	10	•V		mexicana	ST.	1-	PG	QE.	
J jaculus	ST	391		PG	3.0	-V	1.	canadensis	ST		- Pi	5 08	2 11	1	i can	velus	57	1-	PG	.QE	-V.	×	hellerii	51	1+	PG	QE.	8
M flavorentris	51	1		PG.	QE	-V	F	catus	ST.	- 3	- 11	3. Q8	11		4 full	gula	57	1-	PG.	QE	-V	x	couchianus	ST.	10	PG.	QE	Ó
P maniculatu	s 5T			PG	QE	-٧	A	jubatus	ST.	1	- 11	5 QI	11		v per	dicaria	ST.	1-	PG	QE	-V	x	maculatus	ST.	16	PG	QE	0
M ochrogaste	r ST	1	6	PG	QE	-V	p p	vitulina	ST	. 8	- PI	5 Q.E	MV	1	P. coli	chicus	57	1-	PG	QE	-V	¢	variegatus	ST	1-	PG	QE	. 4
M marmote	ST	1	+ - 1	PG	QE	· · V	L	weddelin	ST.	13	- P(a qf	MV	(: pel	agica	85	1.	PG.	Q£	+V	M	armatus	ST	1-	RG	QE	0
M unguiculati	5 ST	1	-	PG.	QE.	·V	0	rosmanus	ST	1	- PI	1 Q I	MV	1	C can	onus	ST	1-	PG	3.0	-V		heteroclitu	ST.	1-	PG	QE	0
# glaber	ST	100	481	PG	QE	-V.	Z	californianu	ST.		. PI	i QE	MY	- 0	alte 2	19.	ST	16	PG	QE	·V	0	latipes.	ST	1.	66	QE	0
C griseus	ST	1		PG.	QE	-V	N	schaumslan	ST	- 4	- 11	1 Q I	MV	1	filie	auda	57	10		Qž	-V	A	testudineu	ST.	10	KG	QE	
M auratus	ST		- 1	PG	3.0	-٧	U.	arctos.	ST	1	- PI	a 1	MV		trai		51	10	PG	91	-V	. 11	spiendens	ST	3-	RG	QE.	. 0
R norvegicus	ST	1	w .	PG	Q.E.	٠V	A	melanelleuc	ST.	. 8	- PS	5 Q.E	MV	1	4 chr	socepha	57	16	PG	QE	-V	0	niloticus	ST.	14	86	×Q.	0
M pahari	51	1	+	10	QE	-4-	N	f putarius	ST		- Pt	a qf	-9		i na	or	57	1.	PG	QE	-¥	H	burtoni	ST	+	RG	KQ	1
M careli	5T	1	-	PG	9.D	٠v	N	l emisea	ST	3	- P.	1 Q E	-V	6	cae	ruleus	51	1-	PG	Q.E.	-V	M	aebra	ST.	1-	86	KQ.	. 0
M muscolus	ST	1		PG	3.D	-V	C	hipus	ST.		P:	5 Q8	GV	1	E gyt	tata	51	11	PG	QE.	·V	L	bergyita	ST	11	66	QE	0
i tridecemile	ST.	1	÷.	PG.	QE	V	V	vulpes	ST	8	÷ 10	s. ai	GV	1	stri	ete.	57	1-	PG	QE	·V	5	lucioperca	SA	10	-6	3.0	0
C tanigers	51	1		PG	Q.E.		N	I Javanica	ST	1.1	- PI	5 QI	ML	1	M uni	color	ST.	J.	₽G	QE	SV.	1	070008	51	16	RG	QE	Q
P leucopus		1		PG	QE	·V	p	discolor	ST.	1	. Pi	5 QE	LA	-	6 ma	ntelli	ST.	1.	PG	QE	·V							

Page 23 of 32

Supp. Fig. 3

tau α -synuclein	11	Corr	elated	pairs					Corre	elated	pairs					Corre	elated	pairs					Corre	elated	pairs	
protein	t as	i t as	t al	ταδ	τ α5		protein	τ α5	τ.α5	5 mS	1 115	t aS		protein	τ α5	τ 05	1 05	τ α5	τ. α5		protein	1 05	1 05	t as	.1 45	τ α5
Great residue Z-score	55	31 N	H 53	182 6.0	189 6.0	Genu	fesidue	5 5	31	53	31	68 189	Genus	f residue	5 53	31	113	31	68 189	Genus	residue	53	31	113	149	68
H sapiens	EA	PG	5A	PG	PG		narvegicus	DT	PG	NT	PG	PG	- 6	concolor	DT	PG	NT	PG	GE	5	camelus	DT	PG	NT	PG	PG.
P troglodytes	EA	PG	SA	PG	PG		pahari	DT	PG	NT	PG	PG	1	catus	DT	PG	NT	PG	GE	- 2	garzetta	DT	PG	NT	PG	PG
P paniscus	EA	PG	SA	PG	PG		caroli	DT	PG	NT	PG	PG	-	ubatus	DT	PG	NT	PG	GE	- A	fuligula	DT	PG	NT	PG	PG
G gorilla	EA	PG	SA	PG	PG		musculus	DT	PG	NT	PG	PG	P	vitulina	DT	PG	NT	PG	GE		perdicaria	DT	PG	NT	PG	PG
P abeli	EA	PG	SA	PG	PG		glaber	DT	PG	NT	SG	AG	1	weddelli	DT	PG	NT	PG	GE		colchicus	DT	PG	ST	PG	PG
H moloch	EA	PG	SA	PG	PG		flaviventris	DT	PG	NT	PG	AG	2	californianus	1000	PG	NT	PG	GE		pelagica	DT	PG	NT	PG	PG
N leucogenys	EA	PG	SA	PG	PG		marmota	DT	PG	NT	PG	AG	N	schauinsland	DT	PG	NT	PG	GE		fasciata	DT	PG	TT	PG	FG
P anubis	EA	PG	5A	PG	PG	1	tridecemline	DT	PG	NT	PG	AG	U.	arctos	DT	PG	ST	PG	GE	c	canorus	DT	PG	NT	PG	PG
M leucophaeus	EA	PG	SA	96	PG	c	lanigera	ET	PG	TT	PG	AG	A	melanoleuca	DT	PG	ST	PG	GE	c	altera	DT	PG	NT	PG	PG
C atys	EA	PG	SA	PG	PG		degus	DT	PG	NT	PG	AG	M	putorius	ET	PG	NT	PG	GE	p.	filicauda	DT	PG	NT	PG	PG
M nemestrina	EA	FG	SA	PG	₽G	c	porcellus.	DT	PG	ST	PG	TG	M	erminea	ET.	PG	NT	PG	GE	= e	trailii	DT	PG	NT	PG	PG.
M mulatta	EA	PG	SA	PG.	₽G	0	princeps	DT	26	NT	PG	GG	c	lupus	DT	PG	NT	PG	GE		major	DT	PG	NT	PG	PG
M fascicularis	EA	26	SA	PG	PG	0	cuniculus	DT	PG	NT	PG	GE	V.	vulpes	DT	PG	NT	P.G	GE	T	guttata	DT	PG	NT	PG	PG
C sabaeus	EA	PG	SA	PG	₽G	5	scrofa	DT	₽G	NT	PG	GE		discolor	DT	PG	ST	PG	GE	- K.	striata	DT	PG	NT	PG	PG
T gelada	EA	#G	5A	PG	PG	c	hircus	DT	PG	NT	56	GE	M	natalensis	GT	PG	NT	PG	GE	A	mantelli	DT	PG	NT.	PG	PG
P tephrosceles	EA	PG	5A	PG	PG	0	aries	DT	PG	NT	ŚG	GE		aegyptiacus	DT	PG	NT	PG	GE	- N	meleagris	DT	PG	ST	PG	PG
R bieti	EA	PG	56	PG	PG	0	virginianus	DT	PG	NT	50	GE	1	funcus	GT	PG	NT	PG	GE	G	gallus	DT	PG	ST	PG	PG
R roxellana	EA	PG	5A	26	₽G	. 8	taurus	DT	PG	NT	56	GE	M	brandtii	GT	26	NT	PG	GE	c	coturnix	DT.	PG	ST.	PG	PG
C capucinus	EA	FG	TA	PG	PG	.8	trison	DT	PG	NT	5 G	GE	M	luctfugus	GT	PG	NT	PG	GE	P	humilis	DT	FG	ST	PG	FG
5 boliviensis	EA	PG	TA	PG	PG		mutus	DT	PG	NT	SG	GE	P	alecto	DT	PG	NT	PG	GE	c	anna	DT	PG	NT	PG	KG
S apella	EA	PG	TA	PG	PG	c	ferus	DT	PG	ST	PG	GE	c	cristata	DT	PG	NT.	PG	GE	T	guttatus	DT	PG	NT	PG	PG
C jacchus	ET	PG	TT	₽G	PG	c	dromedarius	DT	PG	ST	PG	GE	Ε	europaeus	-T.	PG	NT	PG	GE	A	sinensis	DT	PG	NT	PG	PG
A nancymaae	ET	₽G	TT	PG	PG	8	acutorostrat	DT	PE	NT	PE	GE	T	manatus	DT	PE	ST	PE	GE	A	mississippen	DT	PG	NT	PG	FG
P coquereli	DT	PG	NT	PG	AG	1	obliquidens	DT	QE	NT	TE	GE	1	africana	DT	PG	NT	PG	GE	P	muralis	DT	PG	ST	PG	VG
M murious	DT	₽G	NT	PG	AG	G	melas	DT	QE	NT	TE	GE	E	telfairi	AT	PG	NT	PG	ME	A	carolinensis	DT	PG	ST	PG	VG
O garnettii	DT	PG	5T	PG	AG		orca	DT	QE	NT	TE	GE	D	novemcinctu	DT	PG	ST	PG	AE	P	vitticeps	DT	PG	NT	PG	VG
T chinensis	ET	PG	5T	PG	PG		sinus	DT	Q.E	NT	TE	GE	- A	chrysaetos	DT	PG	NT	PG	PG		bivittatus	DT	PG	NT	PG	TG
D ordli	DT	PG	NT	PG	AG	N	aslaeoriental	DT	QE	NT	TE	GE	A	platyrhynch	DT	PG	NT	PG	PG	T	sirtalis	DT	PG	NT	PG	TG
J jaculus	ET	PG	NT	PG	AG	D	heucas	DT	QE	NT	TE	GE	A	cunicularia	DT	PG	NT	PG	PG	T	carolina	DT	PG	NT	PG	AG
N galili	DT	PG	NT	PG	PG	M	monoceros	DT	QE	NT	TE	GE	A	forsteri	DT	PG	NT	PG	PG	c	picta	DT	PG	NT	PG	AG
M ochrogaster	DT	PG	NT	PG	PG	- K.	vexilifer	DT	PE	NT	TE.	GE	N	nippon	DT	PG.	NT.	PG	PG	G	evgoodei	DT	PG	NT	PG	AG
M unguiculatus		PG	NT	PG	PG		simum	DT	PG	NT	PG	GE	F.	cherrug	DT	PG	NT	PG	PG	¢	mydas	DT	PG	NT	PG	AG
C griseus	DT	PG	NT	PG	PG		asinus	DT	PG	NT	PG	GE	F.	peregrinus	DT	PG	NT	PG	PG		tropicalis	GT	PG	51	PG	PG
M auratus	DT	PG	NT	PG	₽G		caballus	DT	PG	NT	PG	GE	c	vociferus	DT	PG	NT	PG	PG	×	laevis	GT	PG	NT	PG	TG
P leucopus	DT	PG	NT	PG	PG	P	pardus	DT	PG	NT	PG	GE	0	novaehollan	DT	PG	NT	PG	PG							

Page 24 of 32

Supp. Fig. 4A

α-syn. αla-tub.		Corn	elated	pairs					Corre	elated	pairs					Corre	elated	pairs					Corre	elated	d pairs	
protein	115 la	o51a	o\$1a	u\$ 1a	a51a		protein	o\$1a	uS 1a	a51a	u5 1a	α5 1a		protein	0.5 1a	u51a	uS 1a	u51a	o:5 1a		protein	a51a	u\$1a	o5 1a	α51a	u\$14
0 p residue			5 40 10.6		57 10.6	Genus	Fresidue	440	140	440	440	440	Genus	species residue	440	140	440	56	57	Genus	residue	136	140	440	56	57
H sapiens	YY	AV	VV	AV	EV		hircus	YV.	AV	VV.	AV	EV	- L.	africana	VV.	AV	WV.	AV	EV		clupeoides	-1	-11	141	-1	-1
P troglodytes	TV	AV	VV	AV	EV	0	aries	YV	AV	VV.	AV.	EV	D	novemanct	YV.	TV	VV	AV	EV		electricus	-1	-1	-1	+1	-1
G gorila	Y٧	AV	VV	AV	εv	0	virginianus	YV	AV	VV	AV	EV	T	guttatus	YV	AV	VV	AV	ĒΫ	5	salar	YI	-1	-1	- 41	-1
P abeli	YV	AV	VV	AV	EV	8	taurus	YV	AV	VV	AV	EV	5	camelus	YV	AV	VV.	AV	EV	5	trutta	41	-1	+1	-1	-1
H moloch	YV	AV	VV.	AV	EV	8	mutus	YV.	AV	VV.	AV.	EV	C	coturnix	YV	AV	VV.	AV	EV	0	mykiss	YI.	-1.	1	-1	-1
N leucogenys	11	AV	٧V	AV	EV	8	bubalis	YV	AV	VV.	AV	EV	G	gallus	YV	AV	VV.	AV	EV	0	kisutch	YI.	-1	-1	-1	-1
M leucophaeu	YV	AV.	VV	AV	EV	. 8	bison	YV	AV	VV.	AV	EV		petegrinus	YV	AV	VV.	AV	EV	- P	formosa	-1	-1	41	-1	1
M nemestrina	YV	AV	VV	AV	EV	c	ferus	YV	AV	VV.	AV	EV	c	anna	YV	AV	VV.	AV	EV	- P	latipinna		-1	+1	-1	-1
M mulatta	YY	AV.	VV.	AV	EV	- 6	obliquidens	YV	AV	VV.	AV	EV	c	livia	YV.	AV	WV.	AV	EV	P.	mexicana	-1	-1	141	-1	-1
M fascicularis	YV	AV	VV	AV	EV	G	melas	YV	AV	VV.	AV	EV	- E	garzetta	YV.	AV	VV	AV	EV	х	hellerii	-1	-1	-1	-t	4
C sabaeus	YV	AV	VV	AV.	EV	0	orca	YV.	AV	VV.	AV	EV	· P	filicauda	YV	AV	VV.	AV	EV.	х	couchianus	-1	11	61	4	-1
P tephroscele	YY	AV	VV	AV	EV	P	sinus	YV	AV	VV.	AV	EV	. C	altera	YV	AV	VV	AV	EV	x	maculatus	-1	-1	-1	-1	-1
R rmellana	YV	AV	VV	AV	EV	0	leucas	VV.	AV	VV	AV	EV	1	albicollis	YV	AV	WV.	AV	EV	- T	rubripes	-V	-V	-V	÷V.	-V
C capucinus	11	AV	VV	AV	EV	M	monoceros	YV	AV	VV.	AV	EV	c	moneduloid	YV	AV	VV	AV	EV	M	armatus	-1	-6	-1	-1	- 14
5 boliviensis	YV	AV	VV	AV	EV	1	vexilifer	YV.	AV	VV	AV.	EV	Τ.	guttata	YV	AV	VV	AV	EV	0	latipes	-1	-1	-1	-1-	-1
5 apela	YY	AV	VV.	AV	EV	c	simum	YV	AV	VV.	AV	EV	p	humilis	YV.	AV	VV	AV	EV	٨	testudineus	-1	-1	-1	-1	-1
C jacchus	YY	AV	VV.	AV	EV	E .	asinus	YV.	AV	VV.	AV	EV	- P	muralis	VV.	AV	WV.	AV	EV	- 0	splendens	-1	-1	-1	-1	-1
A nancymaae	٧V	AV	VV	AV	EV	E	caballus	YV	AV	VV.	AV	EV	A	carolinensis.	YV.	AV	VV	۸V	EV	0	niloticus	-1	-1	+1	-1	-1
P coquereli	YV	AV	VV	AV	EV	P	pardus.	YY	AV	VV	AV	EV	P .	vitticeps	YV	AV	VV.	AV	EV	- 11	burtoni	-1	-1	61	-1	-1
M. murinus	YV	AV	VV.	AV	EV	F.	catus	YV	AV	VV	AV	EV	p	bivittatus	YI	AL	VI.	AL	El	M	zebra	1	-1	-1	-1	-1
O garnettii	YV	AV.	VV	AV	EV	- A	jubatus	YV	AV.	VV.	AV	EV	G	evgoodei	VV.	AV	WV.	AV	EV	N	brichardi	-1	-4	161	11	-1
D ordii	YV	AV	VV	AV	EV	P	vitulina	YV	AV	VV.	AV	EV	x	tropicalis	YV	AV	VV	AV	EV	£.	bergyita	-1	-8-	-1	-1	-1
M flaviventris	۴V	AV.	VV	AV	EV	N	schauinslan	YV.	AV	VV.	AV	EV	x	laevis	YV	AV	VV.	AV	EV	с	gobio	-V	-¥	-V	-V	-1
M marmota	WV.	AV	VV	AV	EV	u	arctos	YV	AV	VV.	AV	EV	N	parkeri	YV.	AV	VV.	AV	EV	5	lucioperca	-1	-1	-1	-1	-1
I tridecemlin		AV.	VV.	AV	EV	M	putorius	YV	AV	VV.	AV	EV	- A.	bivittatum	YV	AV	WV.	AV	EV	1	croces	-1	-11	-1	11	-1
C porcellus	YV	AV	VV.	AV	EV	M	erminea	YV	AV.	VV.	AV	EV	A	mexicanum	YV	AV	VV.	AV	ΞV	5	aurata	-V	-V	-V	-V	
C griseus	YV	AV	VV	AV	EV	c	lupus	YV.	AV	VV	AV	EV	1	chalumnae	YV	AV	VV.	AV	EV	С	milli	YV	AV	vv	AV	EV
P leucopus	YV	AV	vv	AV	EV	P	discolor	YV	AV	VV.	AV	EV		calabaricus	YV	AV	-V.	-¥	-1	A	radiata	YI	AL	vi	AL	U
R norvergicus	YY	AV.	VV.	AV	EV	E	fuscus	YV	AV	VV.	AV	EV	P	kingsleyae	YV	-V	-v	+V	+V	8	typus	YI	AL	VI	AL	EI
M musculus	YV	AV	٧V	AV	EV	M	brandtii	YV	AV	VV	AV	EV	5	formosus	YI.	+1	14	+1	-8							
O cuniculus	WV.	AV	VV	AV	EV	M	lucitugus	YV	AV	VV.	AV	EV	A	mexicanus	4	-1	-1	-1	-11-							
S scrota	YV	AV	VV.	AV	EV	R	aegyptiacus	YV	AV	VV.	AV	EV	p	nattereri	-1	-1	11	-1	-1							

Supp. Fig. 4B

x-syn (βI-tub.		Corr	elated	pairs					Corn	elated	pain	1				Corr	elatec	pairs					Corn	elated	pairs	
	protein	u\$83	a583	a581	a\$83	a5 81		protein	a583	a\$ 81	a\$ 81	α\$83	1 05 81		protes	n a58	1 a5 81	u\$ 81	u\$ 91	a581		proteix	0583	0583	a5 81	a\$81	058
Genus	residue Z-score	11 Å	12 72	¥# 7.0	38	104 6.8	Genu	residue Z-score	n ĉ	12 442	2 4	3.8	10 12	Genu	residu Z-score	. 17	5:5	24	3 6	124	Genu	residu 2-scon	Iđ	11 20	2 4	3 4	104
	apiens	GE	KE	V5	T5	EA		caroli	GE	KE	VS.	T5	EA	. P.		GE	KE	VS	TS	EA	- p	kingsleyae	GE	KE	VS	TS	EA
Pti	roglodytes	GE	KE	V5	TS	EA	M	musculus	GE	KE.	VS.	TS	EA	E	fuscus	GE	KE	VS.	TS	EA	5	formosus	GE	KE	¥5	TS	EA
6.8	prila	GE	KE	VS.	15	EA	0	princeps	GE	KE	45	15	EA	- 64	brandtii	GE	KE	WS.	TS:	EA	A	maxicanus	GE	KE	VS	15	DS
P a	belii	GE	KE	¥5	75	EA	0	cuniculus	GE	KE	¥5	15	EA		aegyptiacu	. GE	KE	V5	TS.	EA		nattereri	GE	KE	V5	TS	DS
	holoch	GE	KE	V5	T5	EA	. 5	scrofa	GE	KE	VS	T5	EA	P.	alecto	GE	K.E.	VS	TS.	EA	D	dupeoides	GE	K.E.	VS	TS	EA
NR	eucogenys	GE	KE	V5	75	EA	C	hircus	GE	KE	V5	15	EA	c	cristata	GE	KE	V5	T5	EA	5	salar	GE	KE.	V5	TS.	EA
P a	nubis	GE	KE.	V5	TS	EA	0	aries	GE	KE.	V5	TS	EA	E	telfairi	GE	KE.	VS	TS	EA	5	trutta	GE	KE	VS	TS	EA
Mit	rucophaeu	GE	KE	VS	TS	EA	0	virginianus	GE	KE.	VS	TS	EA	т	manatus	GE	KE.	¥\$	TS	EA	0	mykiss	GE	KE	VS	TS	EA
C a	tys	GE	KE	VS.	TS.	EA	18	CAUTUS	GE	KE		15	EA	D.	novemcinc	t GE	KE	VS.	TS.	EA	0	kisutch	GE	KE	V5	TS.	EA
Min	emestrina	GE	KE.	V5	T.5	EA	. 8	mutus	GE	KE.	V5	15	EA	N	perdicaria	GE	KE.	VS	TS.	EA	5	alpinus	GE	KE.	¥5	TS	EA
Mit	nulatta	GE	KE.	VS.	15	EA		bubalia	GE	KE	VS.	TS	EA	P.	colchicus	GE	KE	VS	TS	EA	6	morhua	GE	KE	VS	TS	EA
M fi	ascicularis	GE	KE	V5	75	EA	C	ferus	GE	KE	¥5	15	EA	G	gallus	GE	KE	VS	TS	EA	् म	formosa	GE	KE	V5	TS.	EA
C s	abaeus	GE	KE	V5	TS	EA	C	dromedariu	GE	KE	VS.	TS	EA	- A	cunicularia	GE	KE	VS.	TS	EA	- #	reticulata	GE	KE	VS	TS	ES
TR	elada	GE	KE	¥5	T5	EA	v	pacos	GE	KE.	¥5	15	EA	A	chrysaetos	GE	KE	. 125		EA	P	latipinna	GE	KE.	- 75	TS	ES
Pt	ephroscele	GE	KE		15	EA	8	acutorostrat	GE	KE	.98	15	-A	c	pelagica	GE	KE	WS.	TS:	EA	p	mexicana	GE	KE	VS.	15	185
R B	ieti	GE	KE	¥5	TS.	EA	1	obliquidens	GE	KE	¥5	15	-A	- P	fasciata	GE	KE	VS	TS.	EA	X	helierii	GE	KE.	V5	TS	EA
Re	oxellana	GE	KE.	VS.	15	EA	6	meias	GE	KE	VS	15	-A	C	canorus	66	KE	VS	TS	EA	x	couchianus	GE	KE	VS.	TS	EA
S b	oliviensis	GE	KE	-V5	75	EA	0	orca	GE	KE.	V5	15	DA	- M	undulatus	68	KE.	VS.	TS:	EA	x	maculatus	GE	KE.	VS.	T5.	1.1
5 4	pella	GE	KE	. 15	TS	EA	. P.	sinua	GE	KE	VS	15	- A	E.	garzetta	GE	KE	VS	TS	EA	c	variegatus	GE	KE	VS	TS	ES
A n	ancymaae	GE	KE	- 15	.15	EA	N	asiaeorienta	GE	KE	¥\$	T5	-A	P	filicauda	GE	KE	- 95	15	EA	Τ.	rubripes	50	KD	VS.	TS	05
PO	oquereli	GE	KE	V5	TS.	EA	D	leucas	GE	KE	V5	TS	-A	C	moneduloi	d GE	KE	V5	TS	EA	M	armatus	GE	KE	¥5	TS.	N5
M.n	hurinus	GE	KE	¥5	T\$	EA	M	monoceros	GE	KE	¥5	T5	-A	T	guttata	GE	K.E	V5	TS	EA	0	latipes	GE	XE	٧5	TS	DS
Td	hinensis	GE	KE	VS	T5.	EA	1	vesilifer	GE	KE	VS	15	DA	1.	striata	GE	KE	V5	TS	EA	A	testudineu	GE	KE	VS.	15	DS
D o	edil .	GE	KE	42	T5	GA	C	simum	GE	KE	٧5	T5	EA	P.	humilis	GE	KE	٧s	TS	ΕA	8	splendens	GE	KE	VS	TS	ES
1.1	eulus	GE	KE	45	15	EA	÷.	asinus	GE	KE	45	15	EA		muraits	GE	KE	V5	TS	EA	0	niloticus	GE	KE	VS	15	05
	laviventris	GE	KE	45	TS	EA		caballus	GE	KE	¥5	15	EA	A	carolinensi	5. L I I D D		¥\$	TS	DA		burtoni	GE	KE.	VS	15	05
	armota	GE	KE	V5	TS.	EA		pardus	GE	KE	V5	TS	EA	· P	vitticeps	GE		VS	T.S.	NA		zebra	GE	K.E.	VS	TS.	D 5
1 1	ridecemlin	GE	KE	¥5	T5	EA	P	concolor	GE	KE	¥5	T.5	EA	- P	bivittatus	GE	KE	VS	TS	EA	N	brichardi	GE	KE.	¥5	TS	DS
	anigera	GE	KE	VS	75	EA	1.1	catus	GE	KE	VS.	15	EA	т	sirtalis	GE		VS.	15	EA		bergytta	50		VS	15	85
Cp	orceilus	GE	KE	VS	TS.	EA	. A.	jubatus	GE	KE	¥5	TS	EA	т	carolina	GE	KE.	-VS	TS	EA	- A	ocellatus	GD	RD.	.42	TS.	DS
	laber	GE	KE	VS	15	EA	P.	vitulina	GE	KE	VS	TS	EA	c	picta	GE		VS	15	EA		eopio .	GE	KE.	VS	15	DA
Mo	chrogaster	GE	KE	42	T5	EA	1	weddellii	GE	KE	¥5	15	EA	G	evgoodel	GE	KE	45	15	EA	- 5	lucioperca	GD		VS	.15	DS
	riseus	GE	KE	V5	TS.	EA	N	schaumslan	GE	KE.	V5	TS	EA	c	mydas	GE	KE.	V5	TS	EA	1	crocea	50	KD	VS	TS	D 5
	naniculatus	GE	KE	-95	TS	EA		arctos	GE	KE	-95	TS	EA	x	tropicalis	GE	KE	95	TS	EA		aurata	GD		45	TS	D5
P. la	eucopus	GE	KE.	VS	75	EA	M	putorius	GE	KE	V\$	15	EA	. ж	laevis	GE	KE	VS.	15	EA	· C	milii	GD		MN	SN	EA
	uratus	GE	KE	45	75	EA		erminea	GE	KE	45	15	EA	R	bivittatum	GE		VS	TS	EA	R	typus	60	KQ	MN	SN	EA
	crvergicus	GE	KE	V5	TS	EA	c	lupus	GE	KE	V5	TS	EA	· 6	chalumnae			VS.	TS.	85							
Mp	ahari	GE	KE.	45	TS.	EA	V	vulpes	GE	KE	85	TS	EA	E	calabaricus	GE	KE	95	TS	EA							

Page 25 of 32

Supp. Fig. 4C

-syn. βΠa-tub.		Corre	elatec	pairs					Corr	elated	pairs						Com	elated	pairs					Corr	elated	pairs	Ê.
protein	u52a	u\$2a	ú52)	4520	u57a		protein	u5 2a	u\$ 21	u52a	a52a	ú528		p	rotein	u\$2a	u52a	u5 2a	u5 2a	a5.2#		protein	u52a	u528	(15-28	a528	1:45
residue	100 -	5 BA	102 84	14 8.4	15 57 11.4	Genus	residue 2-score	100	2 2	440	114	8 5	Genus		esidue -score	443	2 2	102	114	35	Genus	fe residue Z-score	443	1 10	12	11.4	8
H sapiera	10	TE	-E.	18	QA.	N	gall	-D	TE	-1	18	· A	E	caball	au.	LD	TE	E.	÷E	HA	5	camelus	LD	56	0.6	NG	Q
P trogladytes	10	TE	÷E	÷E	Q.A.	H	glaber	10	TE	-E	- E	QT	- P.	pardu	5	LD	TE	÷E	÷E.	A.D.	¢	coturnix	LD	56	0.6	NG	9
P paniscus	10	TE	-E.	3-6	Q.A.	M	ochrogaster	MD	TE.	-6	-1	QA	- F	catus		1.0	TE	-E	-6	QA.	6	galles	10	56	QG	NG	9
G gonila	10	TE.	·E	-E	AD.	c	griseus	LD	TE	-1	· E	Q.A.	A	jubatu	is .	LD	TE	-E	÷E.	QA .	. A	platyrhyrich	LD	56	QG	NG	. 1
P abelli	10	TE	E	SE.	QA.	P	maniculatus	MD.	TE	÷E	÷E	AD	p.	vitulie	a	LD	TE	-E	+E	QA.	A.	fuliguta	1.D	56	0.6	NG	10
N leucogenys	10	TE	14	-6	AD.	P.	leucopus	LD	TE	1	-6	AD	1	wedde	elli	LD	TE.	-1	-E	A.D	. A	chrysaetos	LD	SG	QG.	NG	
F anubis	LD	TE	÷E.	SE.	AD	M	auratys	TD	TE	-1	÷E;	KA	N	schaul	instan	LD	TE	÷E.	÷E	QA	F	cherrug	LD	5G	0.6	NG	13
M leucophaeu	10	TE	-E	-E	QT.		norvergicus	MD	TE	÷E	÷E.	Q.A.	z	califor	unianu	LD	TE	-E	÷E	AD	c	anna	LD	56	QG	NG	1
C atys	10	TE	1.6	-8	A.D	M	munculus	MD	TE	1-6	-1	QA	- U	arctes	CHARGE STATE	LD	TE	-1	-6	AD	c	livia .	LD	50	05	NG	13
M nemestrina	10	TE.	· E	-6	A.D	0	princeps	Q.D.	TE	-E.	-E	Q.A.	M	putori	ius:	LD	TE	-E	÷E.	QA.	c	vociferus	LD	56	QG	NG	3
M mulatta	10	TE	-6	-8	AD	0	curriculus	QD.	TE	3-1	E	DA.	M	ermin		LD	TE	-1	+E	QA.	N	nippon	LD	50	QG	NG	13
M fascicularis	10	TE	-E.	-6	AD.	5	strofa	LD	TE	-6	-6	AD	c	hipus		LD	TE.	-0	-E	A.D	c	canorus	LD	5 G	QG	NG	1
C sabaeus	10	TE	-E	÷£.	DA.	c	hircus	10	TE	3-1	-E	HA	v	vulpes		LD	TE	-E	÷E.	QA .	M	undulatus	FD.	56	QG	NG	11
T gelada	10	TE	-6	-8	QA.	0	aries	LD	TE	-1	-E	HA	p	discole	ter .	LD	TE.	-E	-E	QA.		filicauda	LD.	56	0.0	NG	1
R roxellana	10	TE	-8	-1	DA .		taurus	MD	TE	1-6	-6	HA	1	fuscut	1	1.0	TE	-6	-6	QA.	1.1	albicolits	LD	56	90	NG	89
C capucinus	10	TE.	÷E.	÷E.	HT	8	bubolis	LD	TE	-8	÷E	HA	M	brand	65	VE	TE	- E	÷E.	QA .	c	moneduloid	±0	56	QG	NG	1
5 boliviemia	10	TE	-E	÷E.	HA	8	bison	MD.	TE	-E	÷E	HA	M	lucifug	p25	VE	TE	-E	÷E.	QA.		major	1.0	56	QG	NG	13
5 apella	10	TE	-E	-16	HT	c	ferus.	LD	TE	-6	-8	QA		HEAD	TIACUE	LD	TE	-6	-E	QA.		gattata	1.0	56	QG	NG	ंद
C jatchus	LD	TE	-E	1.6	HT	C	dromedariu	LD	TE	-6	-E	RA	P	alecto	È	LD	TE	·E	÷E.	Q.A.	1	striata	LD	56	QG	NG	1
M murinus	FD	TE.	-E.	÷Ē	QA.	8	acutorostrat	LD	TE	-8	-E	Q.A.	. C	cristat	ia 👘	FD	TE	-E	÷E	Q.A.		humlis	LD	56	QG	NG	1
D ordi	10	TE	-E	-6	0.A	1	obliquidens	10	TE	1.6	-E	A.D	E	europ	arus.	MD	TE	-E	÷E.	QA.	2	albicollis	10	56	0.6	NG	1
J jaculus	MD	TE.	-E	÷Ē.	QT	0	orca.	LD	TE	-6	÷Ē	QA	E.	telfair	£	TE	TE	-E	÷E.	QT.		murais	LD	56	QG	NG.	1
M marmota	:10	TE	÷E.	÷E	QA	P	sinus	LD.	TE	-8	÷E	QA	T.	manat	tus -	MD	TE	+E	÷E.	QA	A.	carolinensis	LD	56	06	NG	13
i tridecemin	10	TE	-E	1.6	AD	D	leucas	LD	TE	-1	÷E	AD	1	africar	18	MD	TE	-E	-E	GA .	- P.	vitticeps	- D	5 G	QG	NG	
C lanigera	LD	TE	-E	-8	QA.	M	monoceros	LD	TE	-8	-E	0.A	D	nover	ncinct.	LD.	TE	E	÷E.	QA .	G	evgoodel	LD	56	QG	NG	1
O degus	LD	TE.	-1	-1	Q.A.	1	vexilifer	LD.	TE	-1	-E	Q.A.	N	perdic	aria	LD	56	0.6	NG	AD		mydas	1.0	56	QG	NG	
C porcellus	1.0	TE	·E.	14	QA .	C	simum	LD	TE	1.6	100	AD	T	guttat	100	LD	54	0.6	NG	QA.							

Supp. Fig 4D

a-syn B	IIb-tub	-	Corr	elate	d pairs					Corre	later	pairs					Corre	elated	pairs					Corr	elated	pairs	
	protein	u.5.2b	a5 28	0.52	b (15 28	0520		protein	a526	uS 26	u5 21	a52b	a52b		protein	a52b	a5 29	a.5 2b	a\$25	u\$2b		protein	a52b	u5 2b	u5 28	a5.2b	052
Genus	residue Z-score	2 Å	54 84	102 -		11	Genus	ijo residue	-	¥ 40	102	11 40	440	Genus	fesidue.	6 Å	54 440	440	101	440	Genus	ipociet residue	-	\$ 40	102	101	121
H sap	iera .	KG	TE	-6	GE	DE	M	ochrogaster	KG	TE	-E	30	SE	A	jubatus	KG	TE	1 E.	GE	30	T	guttata	RE	56	QG	AG	EG
P trop	glodytes	KG	TE	-E	GE	0E	c	griseus	KG.	TE	-E	GE	6E.	p.	vitulina	KG	TE	-E.	GE	DE	1	striata	RE	56	0.6	AG	EG
P par	viscus	XG	TE	-6	GE	DE	10.0	maniculatus	KG.	TE	-6	65	GE	L :	woddellii	KG	TE	-4	GE:	DE	P	humilis	RE	50	0.6	AG	EG
G gor	illa .	KG	TE.	· E	GE	DE		leucopus	KG	TE	-E	GE	GE	N	scheuinslan	KG	TE	-E	GE	DE	A	sinensis	RE.	56	0.5	AG	EG
P abr	dii .	KG	TE	E	6.E	DE	. 8	norvergicus	KG	TE	÷E.	GE	58	U	arctos	KG	TE	E	GE	DE		eurals	8E	56	QG	AG	EG
N les	cogenys	KG	TE	-E	ĠĔ	DE	M	caroli	KG	TE	-6	GE	66		melanoleuc	KG	TE	-6	GE	DE	- P	witticeps.	XE	56	QG	÷G	16
P ani	abis	KG	TE	E	GE	DE	M	musculus	KG	TE	-1	GE	GE	M	erminea	KG	TE		GE	DE	P	bivittatus	KE	56	QG	AG	EG
M leu	cophaeu	KG	TE	-E	GE	DE	0	princeps	KG.	TE	÷E	6 E	DE	c	hipus	KG	TE	-E	GE	DE	- C	picta	RE	56	QG	AG	DG
C sty	a contractor	84	TE	-6	GE	DE	0	cuniculus	KG	TE	-6	3.0	DE	- #	discolor	KG	TE	-1	GE	DE	6	evgoodei	88	56	0.6	AG	DG
M ner	nestrina	KG	TE	÷E	GE	DE.	5	scrola	KG	TE.	-E	GE	DE	M	natalensis	KG	TE	÷E.	SE	DE	. X	tropicalis	KG.	SE	+E	-6	DE
M mu	latta .	KG	TE	-6	68	DE	c	hincus	KG.	TE	-8	GE	DE	E .	funcus	RV	TE	10	GE	DE	×	lievix	×a.	50	-6	-8	NE
M fasi	cicularis.	KG	TE	-6	ĠĔ	30	0	artes	KG	TE	-6	10	DE	M	lucifugus	RG	TE	-6	GE	DE	N	parkeri	8.6	SE.	0.E	GE	DE
C sab	arus	KG	TE	-E	GE	DE	0	virginianus	KG	TE	-£	GE	DE	R.	aegyptiacus	KG	TE	1.6	GE	30	義	bivittatum	KG	TE	QE	68	NE
T gel	ada .	KG	TE	-8	68	10	. 8	taurus		TE	-6	G£	DE		slecto	KG	TE	-6	61	EE	. A	mexicanum	8.6	58	10	AE	DE
P tep	hroscele	KG	TE	-6	50	DE		mutus	KG	TE	-6	GE	DE	1.1	europaeus	KG	TE	-6	GE	DE	1.	chalumnae	KG.	58	11	NE	AE
R rox	ellana	KG	TE	· • E	68	DE	. 8	bubalis	: KG	TE	-6	GE	DE	£	teffairi	KG	TE	-£	GE	DE	A	mexicanus	86	5	V.	3.	D-
C. cap	ucinus	KG	TE	-6	38	DE	c	ferus	KG	TE	÷E	SE	DE	E	edwardii	KG	TE	-6	GE	DE		nattereri	KG.	5-	V-	1.	D-
\$ bol	Mensia	KG	TE	-1	5.0	DE	c	dromedartu	KG	TE	-1	58	DE	+	manatus	KG	TE	-1	GE	DE	5	salar	KG	5-	Q+	A	D-
5 apr	dla	86	TE	-E	GE	DE	. 6	acutorostrat	KG	TE	-E	GE	DE	L.	africana	KG	TE	. E.	6E.	DE	5	trutta	84	5-	Q-	A.	D-
A nar	cymaae	×G	TE	-8	6E	DE	Ł	obliquidens		TE	-6	GE	DE	5	camelus	RE	56	9.0	AG	£G	0	mykias	KG	5-	Q-	A-	D-
M mu	rinus	KG	TE	÷E	GE	0E	G	melas	KG.	TE	÷E	GE.	DE	P.	colchicus	RE	56	90	AG	EG	0	kisutch	KG	5-	Q-	Ai	0-
O gar	nettii	KG	TE	-E	68	DE	0	orca	KG	TE	-6	6E	DE	6	gallus.	RE	56	Q6	AG	£G	6	morhua	16	5-	N-	A-	0-
T chi	nensis	KG	TE	-8	61	DE	11 P	sinue	KG	TE	:-8	GE	DE	A	fuligula	3.8	56	QG	AG	EG	- P	reticulata	KG.	3-	Q-	A-	1.
0 ord	N	KG	TE	÷ E	GE	DE	N	asiaeorienta	KG	TE	-E	GE	DE	A	chrysaetos	RE	56	QG	AG	EG	P	latipinna	KG.	5	Q -	A -	E-
J. jac	ulus	86	TE	-6	68	DE	0	leucas	KG	TE	-6	61	DE	£.	anna	RE	56	06	66	EG	x	heferii	8.6		q.	A.	E-
M fin	riventria	KG	TE	-E	66	DE	M	monoceros	KG	TE	-E	GE	DE	¢	iteis	RE	56	QG	AG	EG	×	couchianus	KG	5-	Q-	A-	-E-
M ma	mota	KG	TE	-£	GE.	DE	1	vesdiktor	KG.	TE	-6	GE	DE	A	forsteri	RE	\$6	0.6	AG	EG	×	maculatus	KG	5	9	A-	E-
I trid	locemin	KG	TE	-E	6.6	DE	C	simum	KG	TE	-6	6 E	DE	N	nippon	RE	56	Q6	AG	EG	8	spiendens	86	5-	φ.	A-	1.
C lan	igera	KG	TE	-6	GE	DE	E	4587648	KG	TE	-1	GE	DE	E	tra/36	88	56	QG	AG	EG	c	mili	KG	SE	3.0	VE.	11
C por	cellus	KG	TE	÷E	GE	DE	E	caballus	KG	TE	- E	GE	DE	P	filicauda	RE	56	0.6	AG	EG							
N gal	18	KG	TE.	-8	-1	DE		pardus	KG	TE	-6	68	DE	- F.	albicollis	RE	3.0	0.0	AG	EG.							
H glai	ber	KG	TE	-1	Gt	10	F	catus	KG	TE	-1	GE	DE	c	manedulaid	RE	56	QG	AG	EG							

Page 26 of 32

Supp. F	Fig. 4E
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ı-syn	βIII-tub.	11	Corre	elated	pairs					Corn	elated	pairs					Corr	elated	pairs					Corre	elated	pairs	
	protein	a583	a583	a5 83	a\$83	a5 B3		protein	u5.83	aS 83	o.5 B3	a\$83	a5 83		protein	u\$83	a5.83	(15 B3	a5 83	a583		protein	a583	α583	a583	a583	uS B
Genus	fa residue Z-score		102 11.5	101 449 11 1		43 43 10.9	Genus	residue Z-score	54 449	449	449	249	449	Genus	spe residue Z-score	449	449	449	23	449	Genus	residue Z-score	54 94	449	449	94	-
H	sapiens	TP	-P	GP	FP	KP	P.	leucopus	TP	· P	GP	FP.	KP	U	arctos	TP.	- P	GP	FP	KP	C	altera	5A	QA	AA	LA	RA
P	troglodytes	T.P.		GP	FP	KP		auratus	TP	- P	GP	Ŧ₽	KP	M	putorius	TP.	- p	GP	FP	KP	c	moneduloid	SA	QA.	AA	LA	RA
Ρ.	paniscus	TP	·P	GP	FP.	KP	Я.	norvergicus	TP	- P	GP	FP	KP	M	erminea	TP	- p-	GP	FP	KP	T	guttata	5A	A.D	AA	LA	84
G	gorilla	TP	- P	GP	FP	KP	M	pahari	TP	÷ P	GP	FP	KP	C	lupus	TP	. p	GP	FF	KP	. 1	striata	5A	QA	AA.	LA	84
P	abelli	TP	-P	GP	FP	KP	M	caroli	TP	- P.	GP	÷P.	KP	v	vulpes	TP	-p	GP	FP	KP	A	mississipple	5A	QA.	AA	LA	8/
N	leucogenys	Τ₽	-P	GP	FP	KP	M	musculus	TP	- P	GP	FP	KP	p.	discolor	TP	· P	GP	£P.	KP	P	muralis	5A	QA	AA	FA	8.1
P.	anubis	TP	-P	GP	FP.	KP	0	princeps	TP	· P	GP	FP	KP	E	fuscus	TP	p	GP	FP.	RP	A	carolinensis	56	QG	GG	FG	
c	atys	TP	-p	GP	FP	KP	0	curriculus	TP	- P	GP	#P	KP	M	brandtii	TP	-p	GP	FP.	RP	. P	vitticeps	SA.	QA	-A	FA	1.1
M	fascicularis	TP	p	GP	FP.	KP	C	hircus	TP	· P	GP	₽₽.	KP	M	lucifugus	TP	- p	GP	FP	RP	T.	sirtalis	5A	QA.	AA.	FA	1.1
c	sabaeus	TP	-p	GP	FP	KP	0	virginianus	TP	- P	GP	FP.	KP	R.	aegyptiacus	TP.	-p	GP	FP.	KP	Ť	carolina	54	QA.	AA	LA	81
T.	gelada	TP	1.0	GP	FP.	KP	8	taurus	TP	÷P.	GP	FP	KP	E	europaeus	TP	p.	GP	FP.	KP	C	picta	5A	QA.	AA	LA	R/
P	tephroscele	TP	.p	GP	FP	KP		bubalis	TP	- P	GP	#P.	KP	E.	telfairi	TP	-p	GP	FP	KP	G	evgoodei	5A	QA	AA	LA	81
. R	bieti	TP	-P	GP	\$0	KP	¢	ferus.	TP.	- P.	SP.	FP.	KP	E	edwardii	TP.	- P	GP	80	KP	c	mydas	SA	QA	AA	LA.	
	roxellana	TP	-p	GP	FP.	KP	C	dromedariu	TP	- P	SP	FP.	KP	T	manatus	TP.	-p	GP.	FP.	KP.	x	tropicalis	5-			1.	×-
c	capucinus	TP.	-0	SP	FP.	KP	v	pacos	TP.	- P	SP.	FP	KP	1	africana	TP	-P	GP	FP.	KP.	x	laevis	5-	14	56	1.5	8
5	boliviensis	TP.	-P	GP	EP.	KP	- L.	obliquidens	TP	- P	GP.	F.P.	KP	N	perdicaria	5A	A.D	AA	LA	RA	N	parkeri	5-	Q-	6-	L-	R -
C	jacchus.	TP	-P	GP	FP	KP	0	orca	TP.	- P	GP	FP	KP	5	camelus	SA.	QA	AA	LA	RA	R	bivittatum.	TG	QG	66	LG	× (
P	coquereli	TP	- P	GP	FP	KP	P	sinus	TP	- P.	GP	FP	KP	N	meleagris	SA	QA	AA	LA	RA	A	mexicanum	5.	Q-	A-	4.4	- 8-
0	garnettii	TP	-0	GP	FP.	KP	N	asiaeorienta	TP.	- P	GP	FP	KP	P	calchicus	SA	QA	AA	LA	RA	1	chalumnae	50	EQ	NQ	LQ	80
T	chinensis	TP	-P	GP	FP	KP	D	leucas	TP	- P	GP	₽₽.	KP	G	gallus	SA.	Q.A.	AA.	LA	RA	E	calabaricus	50	QQ	60	LQ	
D	ordi	TP	-P	GP	FP	KP	M	monoceros	TP	- P	GP	FP	KP	A	platyrhynch	SA.	QA	AA	LA	RA	P	kingsleyae	SP	QP	DP	LP	
1	jaculus :	TP	·P	GP	FP.	KP	1	vexilifer	TP	- P.	GP.	FP	KP	A	fuligula	SA	QA	AA	LA	BA	5	fermosus	5Q	QQ	50	LQ	- 84
M	flaviventris	TP	-9	GP	FP	KP	C	simum	TP	÷ P	GP	FP	KP	A	chrysaetos	SA	QA	AA	LA	RA	A	mexicanus	50	VQ	TQ	LQ	
1	tridecemin	TP	-P	6P	FP	KP	E	asinus	TP.	· P	GP	₽₽	KP	E	cherrug	5A	Q.A.	AA.	LA	RA	p	nattereri	50	VQ	TQ	LQ	
C	lanigera	TP	-P	GP	FP	KP	£.	caballus	TP	- P	GP	FP	KP	c	anna	SA	AD.	GA.	LA	RA	E	electricus	50	70	PQ	LQ	K
0	degus	TP	- P	GP	FP	KP	P	pardus	TP	· P.	GP	FP	KP	p.	fasciata	5A	AD.	AA.	LA	RA	5	salar	5A	QA.	AA	LA.	
c	porcellus	TP	0	GP	FP.	KP	P.	concolor	TP	- P	GP	F.P.	KP	C	vociferus	S.A.	QA	AA	LA	RA	5	trutta	SA	QA	AA	LA	81
N	galiti	TP	-p	- 9	EP.	KP	A	jubatus.	TP	- P	GP	F.P.	KP	N	nippon	5A	QA	AA	LA	RA	0	mykiss .	SA	QA	AA	LA	×1
. 11	glaber	TP	-p	GP.	\$P	KP	p	vitulina	TP	- p	GP	FP	KP	C	canorus	\$A	Q.A.	AA.	LA	RA	0	kisutch	5A	QA.	AA	LA	. 10
M	ochrogaster	TP	-p	GP.	FP	KP	- 6	weddellii	TP	-P	GP	FP.	KP	M	undulatus	57	QT	AT	LT	RT	5	alpinus	50	00	AQ	LQ	
c	griseus	TP	-p	GP	FP.	KP	N	schauinslan	TP:	- P	GP	F.P.	KP	1	trailli	SA	D.A.	AA	LA	RA	c	milli	SP	QP	VP	LP	
	maniculatus	TP	-p	GP.	FP.	KP	z	californianu	TP	- P	GP	F.P.	KP	P	filicauda	SA.	QA	AA	LA	8.A	11	typus	SP	QP	VP	LP	81

Supp. Fig. 4F

yn. βIVa-tub) ,	0	orre	lated	pairs					Corr	elated	pairs					Corr	elated	pairs					Corr	elated	d pairs	E.
protein	a\$4	la of	54a	a54#	u\$4a	o.54a		protein	α\$4a	α\$4a	a\$4a	a\$4a	o54a		protein	u\$4a	a\$4a	a\$4a	u\$4a	a\$4a		protein	a\$4a	u54	u\$4	a\$4	1 05
Constant Period	15 1 8.1	35 7	55	un 55 7.4	56 US 7.4	55 H 7,4	Genus	fesidue	12	10	5	58	55 35	Genus	species residue	12 35	10 55	5 5	58	5 5	Genus	species	13 35	10		1 56 55	1 55
H sapiens	KT	())	(T)	MT	KT.	TT.		galili	KT	KT.	MT	KT.	TT		vitulina	KT.	KT	MT	KT.	TT		formosus	KT	KT.	MT	KT	T
P troglodytes	KT	t 9	(T	MT	KT.	TT	H	glaber.	KT.	KT	MT	KT	TT	£ .	weddelli	KT	KT	MT	KT.	TT	A	mexicanus	KA	KT	KA	KA	1
P paniscus	KT	1	TT)	MT	KT.	TT	M	ochrogaster	KT	KT	MT	KT	TT	N	schauinsian	KT.	KT	MT	KT.	TT	P.	nattereri	KT	KT	KT	KT	
G gorilla	KT		T	MT	KT	TT	c	griseus	KT	KT	MT	KT	TT	2	californianu	KT	KT	MT	KT.	TT	D	dupeoides	KT	KT	MT	KT	
P abelii	KT	.)	T	MT	KT.	TT	- P	maniculatus	KT	KT	MT	KT	TT		arctos	KT	KT	MT	87	TT	E	electricus	KT	KT.	MT	KT	833
H moloch	67		TT.	MT	KT.	TT	M	auratus	KT.	KT	MT	KT	TT	M	putorius	KT	KT	MT	KT.	TT	5	sələr	KT	65	MT	KT	26
N leucogenys	KT		T1	MT	KT.	TT	. 8	norvergious	KT	KT.	MT	KT	TT	M	erminea	KT	KT	MT	KT.	TT	\$	trutta	KT	*5	MT	KT	533
P anubis	KT	r)	CT.	MT	KT	TT	M	pahari	KT.	KT	MT	KT	TT	c	lupus	KT	KT	MT	KT.	TT	0	mykiss	KT	KS	MT	KT	2.3
M leucophaeu	KT	1 0	(T	MT	KT.	TT	M	caroli	KT.	KT.	MT	KT	TT	P	discolor	KT	KT	MT	KT.	TT	0	kisutch	KT.	KS	MT	KT	
C atys	KT	t)	(T	MT	KT.	TT	M	musculus	KT	KT	MT	KT	TT	M	natalensis	KT	RT	MT	KT	TT	G	morhua	KA	R5	LA	KA	
M. nemestrina	KT		(T	MT	KT.	TT	0	princeps	KT	KT	MT	KT	TT	8	fuscus	KT	KT	MT	KT.	TT	P.	formosa	KT	KT	MT	KT	
M mulatta	KT	r 9	(T	MT	KT	TT	0	cuniculus	KT	KT	MT	KT	TT	M	brandtii	KT	KT	MT	KT	TT	P	reticulata	KT	KT	MT	KT	
M fascicularis	KT	1.1	(T	MT	KT.	TT	5	scrofa	KT	KT	MT	KT	TT	M	locifugus	KT	KT	MT	KT.	TT	P	latipinna	KT	85	MT	KT	
C sabaeus	KT		TT.	MT	KT.	TT	c	hircus	KT	KT	MT	KT	TT		aegyptiacus	KT	KT	MT	KT	TT	p.	mexicana	KT	KT	MT	KT	
T gelada	KT		(T	MT	KT.	TT	0	aries	KT	KT	MT	KT	TT	C .	cristata	KT	KT	MT	KT	TT	×	hellerii	KT	KS	MT	KT	
P tephroscele	KT	()	TT.	MT	KT.	TT	0	virginianus	KT	KT	MT	KT	TT	E	europaeus	KA	KT	MA	KA	TA	×	couchianus	KT.	KS	MT	KT	
R bieti	KT	110	(T	MT	ST.	TT	8	taurus	KT	KT.	MT	KT	TT		edwardii	KT.	KT.	MT	KT	TT	X	maculatus	KT	KS	MT	KT	
R roxellana	KT		CT.	MT	KT.	TT	8	mutus	KT	KT	MT	KT	TT	b	novemcinct	KT	KT	MT	KT.	TT	c	variegatus	KT	KT	MT	KT	
C capucinus	KT.	e 0	T	MT	KT.	TT	8	bubals	KT	KT	MT	KT	TT	A	sinensis	KT	KT	MT	KT	TT	T	rubripes	KS	KS	MS	KS	
S boliviensis	KT		T)	MT	81	TT	c	ferus	KT	KT	MT	KT	TT	۸	mississipple	KT.	KT	MT	KT.	TT	M	armatus	KT	KT	MT	KT	
S apella	KT	e la	(T	MT	KT.	TT	8	acutorostrat	KT	KT.	MT	KT	TT	- p	muralis	KT.	RS	MT	KT.	TT	0	latipes	KT	KT	MT	KT	
C jacchus	KT	6	TT.	MT	KT.	TT	L.	obliquidens	KT.	KT.	MT	KT	TT	A	carolinensis	KT	KS	MT	KT.	TT	A	testudineus	KT.	KT.	MT	KT	
A nancymaae	KT	.)	T)	MT	KT.	TT	G	melas	KT	KT	MT	KT	TT	P	vitticeps	KT.	KS	MT	KT	TT	8	splendens	KT	KS	MT	KT	
P coquereli	KT	()	T)	KT	KT.	TT.	0	orca	KT	KT.	MT	KT	TT	P.	bivittatus	KT	KS	MT	87	TT	0	niloticus	KT.	KT.	MT	KT	
M murinus	KT	E 3	T)	KT	KT.	11	P	sinus	KT.	KT.	MT	KT.	TT	T	carolina	KT.	KS	MT	KT.	TT	H	burtoni	KT.	KT.	MT	KT.	
O garnettii	KT		TT.	87	KT.	TT	N	asiseorienta	KT.	KT	MT	KT	TT	c	picta	KT	KS	MT	KT.	TT	M	zebra	KT	KT	MT	KT	
T chinensis	KT		TT:	MT	KT.	TT	D	HUCH	KT	KT.	MT	KT	TT	G	evgoodei	KT	KS	MT	KT.	TT	N	brichard	KT	KT	MT	KT	
D ordii	KT		(T	MT	KT.	TT.	M	monoceros	KT	KT	MT	KT	TT	x	tropicalis	KT	KS	MT	8.7	TT	- E -	bergyita	KS	RS	MS	KS	
) jacutus	KT	1 3	T	MT	KT.	TT	1.6	vexilifer	KT	KT.	MT	KT	TT	X	laevis	KS	KS	MS	85	TS	A	ocellatus	RA	KS	KA	-A	
M flaviventris	KT		T	MT	KT	11	c	simum	KT	KT	KT	KT	TT	8	bivittatum	KT	KS	MT	KT	TT	c	gobio	KS	KT	LS	-5	
M marmota	KT		T	MT	KT.	TT	E	asimus	KT	KT	MT	KT	TT	A	mexicanum	KT	KS	MT	KT.	TT	5	lucioperca	BA	KT	MA	- 6	
I tridecemilin	KT		T	MT	KT.	TT	E	caballus	KT.	KT	MT	KT	TT	L	chalumnae	KS	KS	MS	KS	TS:	. L	crocea	KT	KT	IT.	KT	
C lanigera	KT		T	MT	KT.	TT	F	catus	KT	KT	MT	KT	TT	E	calabaricus	KT	KT	MT	KT.	TT	5	aurata	KT	KT	MT	KT	
O degus	KT		CT.	MT	KT	TT		jubatus	KT	KT	MT	KT	TT		kingsleyae	KT	KT	MT	KT.	TT	c	mili	KT	KS	MT	KT	

Page 27 of 32

Supp. Fig. 4G

0.00		"Pr		-D.	in the second					Core	alater	pairs					Corre	datasi	i pairs					For	dates	pairs	
p-sy	n.αla-tub.		com	00000	Press.2					Lurn	caree	Press.					COM	eaced	Press 2					COM	nated	parts	
	protein	(IS 1a	i fis 14	fl5 1a	ß5 1a	ft5 1.a		protein	ļ15 1.a	BS 1a	§\$ 14	JIS 10	ß5 1a		protein	β5 14	βS 1a	βS 1a	βS 1a	BS 1a		protein	\$5 1a	pS 1a	BS 1a	BS 1 #	ØS 10
Contract of the local data	residue		5.000	100.00	# 48 10.5	6 8 10.5	Cleaner	Peciel residue	38	16	49	15 64	45	Genus	species residue	38	16	49	5.6	45	Genus	pecie residue	38	# 8	58	15	51
	sapiens	14	VV.	VV.	VV.	RV		virginianus	1.4		VV	VV.	RV		harrisi	LV	VV.	VV.	VV	BV	D	rerio	MV	AV		MV.	KV
	traglodytes	LV	VV	vv	NY.	RV	B	taunus	LV	WV.	VV.	VV	RV.		cinereus	LV	VV.	vv	VV.	RV	. 5	anshuensa	MI	AL	-1	MI	K1
6	gorilla	1.4	.VV	VV	VV.	RV.	- 8	mutus	14	WV.	VV	VV	RV	0	amatinua	LV	VV	VV	VV.	RV	5	rhinoceros	MI	AL	341	MI	KI
P	abeli	1V	VV	VV.	VV.	RV	В	bubalis	LV.	VV.	VV	VV.	RV	C	coturnix	LV	VV.	VV	VV	·V	E	electricus	MI	AL	-1	MI	KI
	motoch	LV	VV	vv	WV.	HV.	. 8	tison	1.1	VV.	VV.	VV.	RV	G	gallus	LV	NV.	VV	VV.	+V	1.1	punctatus	MI	AL	16.	MI	KL
N	leucogenys	LV	VV.	VV	VV.	RV	c	ferus	LV	WV.	VV	VV.	RV	C.	anna	LV	VV.	VV	VV	-V	1	fulvidraco	MI	AL	-1	MI	KI
N	f leucophaeu	11	VV.	VV	VV.	RV	- L	abilguidens	LV	WV.	VV	VV	RV.	P .	filcauda	LV	WV.	VV	VV.	-1	5	salar	MI	AL	-1	MI	RI
N	I nemestrina	LV	VV	VV	VV.	RV	G	melas	LV	VV.	VV	VV	RV	C	altera	LV	VV.	VV.	VV	-V	5	trutta	MI	AI.	-1	MI	KI
N	f mulatta	LV	VV.	VV.	VV.	RV.	0	orca	1.4	VV	VV	VV.	RV	C.	moneduloid	LV	VV.	VV	VV.	-V	0	mykiss	MI	AL	-1	MI	KI
N	fascicularis	LV	VV	VV	VV	RV	P	sinus	LV.	WV.	VV	VV	ĦΨ.	- T.	guttata	L.V.	VV.	VV	VV	-V	0	kisutch -	MI	AL.	-1	MI	K1
c	sabaeus	LV	VV.	VV	VV.	#V	D	leucas	LV	VV.	VV	VV	RV.	- P	humilis	LV	VV.	VV	VV	W.	10.00	formosa	MI	AL	-1	MI	KI
	tephroscelle	LV	VV.	VV		RV	M	manoceras	LV	VV.	VV.	VV.	RV	P. 1	mutalis	LV	VV.	AV	YY	RV.	p	latipinna	MI	AL	-1	MI	KI
	roxellaria	LV	VV.	VV	WV.	RV	- L	vesilifer	LV.	VV.	VV	VV	RV	A	carolinemis	LV	AV.	AV	WV.	RV	P.	mexicana	MI	AI.	.94	MI	KI
c	capucinus	1.1	VV	VV	VV.	RV.	c	simum	LV	VV.	VV.	VV.	RV		vitticeps	LV	VV.	AV	VV.	RV		hellerii	MI	AL	1	MI	KI
- 5	boliviensia	1.4	VV	VV	VV	HV.	1	asinus	LV	VV.	VV	VV.	RV		bivittatus	11	VI	VI	VI.	RI	K	couchianus	MV	AV	·V.	MV.	KV
- 5	apella	LV	VV	VV	VV	RV.	ŧ	caballus	LV	VV.	VV	VV	RV	1	elegans	LV	WV.	VV	VV.	RV.	×	maculatus	Mi	AF	-1	MI	KI
c	jacchus	LV	VV	vv	VV.	RV	P	pardus	LV	VV	vv	VV	RV		mucrosqua	LV	VV.	vv	VV	RV	M	armatus	MI	AL	-1	MI	KI
	nancymaae	LV	VV	vv	V¥.	RV	ι	canadensis	LV	VV.	VV.	٧V	RV	G	exgoodei	LV	VV.	VV	VV	-V	Æ	heteroclitus	MI	AL	-41	MI	KI
P	coquereli	LV	VV	VV	VV.	#V	1	catus	LV	WV.	VV	VV.	RV.	X	tropicalis	LV	WV.	VV	VV.	RV	0	latipes	MI	AE.	241	MI	KI
N	f murines	LV	VV	vv	VV.	H.V.	A	jubatus	LV	VV.	VV	VV.	RV	X	laevis	LV	VV.	WW	VV	RV		testudineus	MI	AL	-1	MI	KI
0	garnettil	LV	VV	VV	WV.	#V	P	vitulina	LV	VV.	VV	VV	RV	N	parkert	MV	VV.	VV	VV	RV	8	splendens	Mi	At	-1	MI	KI
Ð	ordii	LV	٧V	VV	٧V	RV	N	schainslandi	LV	VV.	VV	VV.	RV		bivittatum	LV	VV.	VV	VV	RV	0	nilaticus	MI	AL	-1	MI	KI
N	f flaviventris	1.4	VV.	VV	44	HV.	U	arctox	1.V	AA.	VV.	88	RV	A.	mexicanum	LV	VV.	WV.	AA.	RV	H	burtoni	MI	Ai	.+1	MI	K1
N	t marmota	1.1	VV.	VV	WV.	RV.	N	putorius	1.A	WV.	VV	VV.	RV			LV	VV	VV	VV	RV	M	zebra	MI	AI.	-1	ML	KI
1	tridecemiin	LV	VV	VV	VV	RV.	N	ermines	1.1	VV.	VV	VV.	RV.	Ġ,	seraphini	ĻΥ	VV.	vv	VV.	RV	N	brichardi	MI	AL	- 1	MI	KI
¢	porcellus	11	VV	VV	VV.	RV.	c	lupus	4.1	VV.	٧V	VV.	RV	- L	chalumnae	tν	VV.	-V	VV	KV.	٤.	bergyita	MV	AV	$\rightarrow V$	MV.	KV
-0	griterus	LV	VV	vv	VV.	KV.	. P	discolar	1.1	VV.	VV	VV.	BV	- E	calabaricus	LV	AV	VV	MV	KV.	C	gobio	ML	AL	-1	MI	KI
	leucapus	LV	٧V	VV	VV.	KV	E	fuscus	LV	VV.	vv	vv	RV	- L.	oculatus	MI	AI	٧I	MI	KI	5	lucioperca	MI	AI	-1	MI	Kt
	norvegicus	LV	VV	vv	VV.	KV.	N	I brandtii	LV	VV.	VV	VV	RV.	P.	kingsleyae	MI	AL	-1	MI	KI	1	crocea	MV	AV	v	MV.	KY
N	musculus	LV	VV	VV	VV	sv	N	lucifugus	EV.	AA.	VV	VV	πv	5	formosus	MV	AV	۰V	MV	KV	5	aurata	MV	AV	+V	MV	KV
0	cuniculus	1.1	VV	VV	VV	HV	R	aegyptiacus	LV.	VV.	VV	VV	RV.	٨	mexicanus	MI.	AL	-1	MI	KI	C	milii	MI	VI.	94	VI.	KI
5	acrofa	LV	٧V	VV	VV	RV	Ö	ater	LV	VV.	VV	VV	RV.	C	carpio	MI	AL	-4.	MI	KI	A	radiata	11	AL	+1	VI.	KI
	hircus	LV	.vv	vv	VV.	RV	C	asiatica	LV	VV.	vv	VV.	RV	- P	nattereri	MI	Al.	-1	MI	KI.							
0	aries	1.1	VV.	vv	WV.	RV.	D	novemeinct	LV	VV.	VV.	VV.	RV.	D	clupenides	MV	AV	-V.	MV	KV							

Supp. Fig. 4H

β-syn. βl-tub.	·PP·			j pairs	é.				Corn	elated	pairs						Corre	lated	pairs					Corr	elated	pairs	
protein	85 81	35 83	AS 81	, ps en	1 ps #1		niedon	BS 81	(15 B)	\$5 83	ps 81	85 81			protein	\$5 93	BS 81	85 81	(5 81	£5 B1		protein	ps 81	85 81	JIS 81	85 81	85 81
Contraction of the state of the	433	437 0	13 6.9	E 5 6.7	2 2 2	lipecies Genus	rsidue	. 495	437	13	132	z r	Gene	species	residue	437	437	13	132 55	77 F	Genus	species	48	437	13	192	2 %
H sapiens	FG	EG	EY	PT	VI.	O prince		ŦG	EG	EY	PT.	W.	- P	ales		FG	EG	£Υ	PT	V1	5	formosus	LE	E.E.	EY.	PT.	VI.
P troglodytes	FG	66	EY	PT	VI	D cunto		FG	EG	EF	PT	VI.	c		ata	FG	EG	EY	PT	¥1	A	mateicanus	FE	33	£Υ	PT	¥1
G gorila	FG	EG	EY	PT	W1	5 scrofa		10	EG	EY	PT	SME:	0			FG	10	EY.	PT	VI	C.	carpie	FD	00	£Υ	PT	VI.
P abelii	FG	EG	EY	PT	VI	C hireus	6 <u>6</u>	ŦG	EG	EY	PT	VI.		#\$kj		FG	EG	EY	PT	VI		nattereri	FE	EE	EY	PT	VI
H moloch	FG	EG	EY	PT	VI	O aries		ŦG	EG	ET	PT	VI.		tell		FG	86	EY.	PT	VI		clupeoides	LE	EE	EY.	PT	VI
N leucogenys	FG	10	EY	P7	VI	O virgin		FG	EG	EY	PT	VI:		mai		FG	10	EY	PT	VI		hypophthal	FE	EE	EY	PT	VI
P anubis	FG	EG	EY	P7	VI.	8 tauru		FG	EG	EY	PT	VE	D		empinet	FG	EG	EY	PT	VI		rerio	FE	EE	EY.	PT.	VI
M leucophaeu	FG	66	EY	PT	VI	B mutu		FG	EG	EY	PT	VI		han		FG	£6.	EY		VI	s	rhinoceros	LE	DE	EY	PT	VI
C atys	FG	EG	EY	PT	VI	R bubol C ferus		FG	EG	EY	81	VI		ana		FG	EG	EA.	PT	VI	T	punctatus	FE	-E QE	EY	PT	VI
M nemestrina M mulatta	FG	10	EY	PT	VI	C ferus C drom	-	FG	EG	ET	-	VI			ficaria	16	10	EV.	PT	VI	1.1	fulvidraco salar	10	QE.	EY		AV
M fascicularis	FG	EG	EY.	PT	VI	V secos	esarou.	FG	EG	EY	PT	VE		colo		FG	10	EY	PT	VI	5	trutta	FE	EE	DF	Q5 Q5	AV
C sabaeus	FG	EG	EY	PT	VI	B acuto			EG	EY.	PT	W.		and.		76	EG	EV.	PT	WI		mykiss	FE	iE.	OF		AV
T gelada	FG	EG	EY	PT	VI	L ablig		16	EG	EY	PT		Ă		sartes.	FG.	16	EY	PT	VI		kisutch	FE.	22	DF	as	AV
P tephroscele	FG	E.G.	EY	PT	VI	G melas		FG	EG	EY.	PT	W.	- 2	0.101		FG	10	EV	PT	VI		morhus	FD.	-p	EF	25	VE
R bieti	FG	EG	EV	PT	VI	O orca		FG	EG	EY	PT	VI.		1100	ulatus	16	EG		PT	VI		formosa	1E	EE.	EV	PT	VI.
# roseilana	FG	10	EV.	PT	VI	If sinus		FG	EG	1.1	PT	VI.	1.0		nutia	10	10	EV.	97	VI	116	reticulate	110	100	EV.	PT	VI
5 boliviensis	FG	10	EV	PT	VI.	N asiaes	vienta	FG	EG	EY.	PT	VI.	c		eduloid	FG	20	EY.	PT	VI	P	latipinna	FE.	EE.	EY	PT	VI.
5 apella	FG	EG	EV	PT	VI	D leuce	1	16	EG	EY	PT	Vi	T	EUD	ata	16	16	EY	97	VI	100	mexicana	HE.	EE	24	PT.	VI
A nancymase	FG	EG	EY	PT	VI	M mono	ceros	FG	EG	ET	PT	VI	1	atrie		# G	EG	EY	PT	¥1	x	hellerii	FE	11	EY	PT	VI
₽ coquereli	FG	EG	EY	PT	VI	L vexili	fer	FG	EG	EY	PT	VI.		him	ilis .	FG	:EG	EY.	PT	VI	X	couchianus	FE	EE	EY.	PT	VI
M murinus	FG	EG	E.Y.	PT	VI	C simur	π.	FG	EG	EY	PT.	VI.		mu	alis.	16	EG	EY.	PT	WI .	×	maculatus	11	EE	EY	PT.	VI:
T chinensis	16	10	EY.	PT	VI	E atinu	0	FG	EG	11	21	VI.	A	tan	änensis	16	EG	EV.	PT	VI	C	variegatus	DE:	11	EY.	*1	VL
D ordi	FG	EG	EY.	PT	VI.	E cabal	us .	FG	EG	EY	PT.	VI.		vitti	ceps	FG	EG	E.V.	PT	W1	T	rubripes	FE	EE	£Υ	PT.	VI.
J jaculus	14	EG	EY	PT	VI	P. pardu		FG	EG	EY	PT.	VI.	- 2	bivi	tatus	16	10	EY	97	W1	M	armatus	PE.	££.	EY	PT.	VI.
M flaviventris	FG	EG	EV	PT	VI	L canad	ensis	FG	EG	EY	PT.	WI.	T	eleg	2115	FG	EG	EY	PT	VI.	F	heteroclitus	FE	EE.	EY	0.5	VI.
M marmota	FG	EG	EY	PT	VI	L parde	INF	ŦG.	EG	EY	PT	VI.	T	sirt	ñs 👘	FG	EG	EY.	PT	VI	0	lutipes	FE	EE	EY.	PT	VI.
i tridecemii	FG	86	EY	PT	VI	F catus		FG.	EG	EY	PT	¥1		mu	rosqua	£6	16	£¥.	PT	¥1	A .	testudineus	FE	-E	EY	PT.	WI.
# damarensis	FG	EG	EV	PT	VI	A jubati	15	FG	EG	EY.	PT.	VI.		can		FG	-G	£Υ	PT	¥1	6	splendens	FE	-6	EY.	PT	VI.
C lanigera	FG	EG	EV	PT	VI.	P vitulir		FG	EG	EY	PT	VI.	c	pict		FG	-6	E¥.	PT	¥1		niloticus	FE	EE	EY	PT	¥1
C porcellus	16	EG	EY	PT	VI	N schair	islandi	ŦG	EG	17	PT	AL.		eve		FG	-6	EY	PT.	¥1		burtoni	FE	11	EY	PT	VI
H glaber	FG	EG	ΞY	PT	VI	0 resma		FG	EG	EY	PT	¥1		mye		FG	-6	EY	PT	VI		zebra	FE	EE	EY	PT	VI.
M ochrogaster		EG	EY.	PT	VI	U arctar		FG	EG	1.1	PT.	VI		trop		LN.	DN	E.A.	PT	VI	N	brichardi		111	EY.	PT	VI
C griseus	FG	EG	EY	PT	VI.	M putor		ŦG	EG	EY	PT	VI.	×			L.N	DN.	£Υ	PT	VI	1.	bergytta	FE.	E.E.	EY	₽T	VI.
M unguiculatu	FG	EG	EY	PT	VI	M ermin	ea 🛛	FG	EG	EY	PT	NI.		1000	tatum.	FG	06	EV	PT	3/1	A	ocellatus	FE	GE	EY.	PT	N1
P maniculatus		80	E.A.	PT	VI	C lupus		FG	EG	EY	PT	VI.		1 unio		10	10	EY	64	VI	c	gobio	PE.	GE	EY.	PT	VI.
P leucopus	FG	EG	EY	PT	VI	V vulpe		FG	EG	EY	PT	VI	6		phini	16	10	EY	PT	VI.	1.8	lucioperca	FE	EE	EY	PT	VI
M auratus	FG	EG	EY	PT	VI	M javan		FG	EG	EY	PT	VI.		- 111	umnae	LE	GE	EY	PS	VI	1	crocea	FE	EE	EY	91	٧I
R norvegicus	FG	10	EY.	PT	VI	P discri	-	FG	EG	EV.	PT	VI	- 6		baricus	LE	DE	EV	PT	VI		aurota		11	EY	PT	VI
M pahari	FG	EG.	EY	PT	AVI.	E fuscu		+6	EG	EY	PT	WF.		ruti		11	11	EY	PT	VI		milli	FE.	11	01	25	¥1
M caroli	FG	EG	EY	PT	VI.	M brand		+6	EG	EY	PT	WI.		11717	Mark .	FE	EE.	EV	PT	VI	\$	torazame :	15	.EE	£.F	195	WV.
M museulus	Fd	EG	EY	PT	VI	R argys	tiarus	FG	EG	EV.	PT	VI.		hing	sleyae	1.0	EE.	EY	9.4	VI							

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Supp.	Fig.	4I
Supp.	I Ig.	T I

-syn (3IIa-tub.	·PP			l pairs					Com	elated	pairs					Corre	elated	pairs					Corr	elated	f pairs	5
	protein	85 Za	βS 2a	β5 2a	ß5 2a	βS 2a		protein	(IS 2a	ß5 2a	β5 2a	ji5 2a	<u>85 2a</u>		protein	₿S 2a	β5 2a	βS 2a	§5 2a	(15 Za		protein	βS 2a	β5 2a	βS 24	βS 2a	βS
Genus	residue 2-score	40 II 12.0	1 mil 1 0 0		100000	A DEALER	Genus	species residue	40	13	231	231	443	Genus	residue	40	231	71	231	443	Genus	residue	40	231	11	126	15
H S	apiens	VA.	EA	FA	EA	ED	c	porcellus	VA.	EA	FA.	EA	ED	C	simum	VA.	EA	FA.	EA	ED	T	manatus	VA:	EA	FA	EA	E
Pt	roglodytes	٧A	EA	FA	EA	ED	N	galili	VA	EA.	FA	EA	E D		caballus	VA.	EA	FA	EA	ED	0	novemcintt	VA	EA	FA	EA	
P p	anlicus	VA	EA	ŦA	EA	ED	H	glaber	VA	EA	FA	E.A.	ED	- P.	pardus	VA	EA	FA	EA	ED	5	harrisii	VA	EA	FA	EA	
GR	orilla	VA	EA	FA	EA	ED	M	ochrogaster	VA	EA.	FA	EA.	ED	1.	canadensis	VA	EA	FA	EA	ED	V	ursinus	VA.	EA	FA	EA	1
P 4	beli	VA	EA.	FA	EA	ED	c	griseus	VA	EA	FA	EA	ED	- F	catus	VA	EA	FA	EA	ED	P .	cinerous	VA	EA	FA	EA	
NI	eucogenys	VA	EA	FA	EA	ED	p	maniculatus	VA	EA	FA	EA	ED	A	jubatus	VA	EA	FA	EA	ED	0	inatinus	VA	EA	FA	EA	
P. 8	nubis .	VA.	EA	FA	EA	ED	P	leucopus	VA	EA	FA	EA	ED.	P .	vitulina	VA	EA	FA	EA	ED	N	perdicaria	VA	EA	FA	EA	3.1B
MI	eucophaeu	VA.	EA	FA	EA	ED	M	auratus	VA.	EA	FA	EA.	ED	N	schauinslan	VA.	EA	FA	EA	ED	C	simutos	VA.	EA	FA	EA	
C a	tys	VA.	EA	FA	EA	ED	- 8	norvegicus	VA	EA	FA	EA	ED	0	rasmarus	VA.	EA	FA	EA	ED.	6.	gatus	VA	EA	FA	EA	
Min	emestrina	VA	EA	FA	EA	ED	M	musculus	VA	EA	FA	EA	εo	2	californianu	VA.	EA	FA	EA	ED	A	fuligula	VA.	EA	FA	EA	
Mr	nulatta	VA.	EA	FA	EA	ED	0	princeps	VA	EA.	FA.	EA.	ED	U	arctos	VA	EA	FA	EA	ED	A	chrysaetos	VA	EA	FA	LA	
Mf	ascicularis	VA.	EA.	FA	EA	ED	0	cuniculus	VA	EA.	FA	DA	ED.	M	putorius	VA	EA	FA	EA	ED	C i	enna	VA	EA	FA	EA	
C S	abaeus	VA	EA,	FA	EA	ED	- 5	scrofa	VA	EA	FA	E.A.	ED	M	erminea	VA.	EA	FA	EA	ED	M	undulatus	VA	EA	FA	EA	
TB	elada	VA	EA	TA	EA	ED	c	hircus	VA	EA	FA	EA	ED	c	lupus	VA	EA	FA	EA	ED	P	filicauda	VA.	EA	FA	ΞA	
Rn	cxellana	VA	EA	FA	EA	ED	0	aries	VA	EA	FA	EA	ED.	- V	vulpes	VA	EA	FA	EA	ED	N	chrysocepha	VA.	EA	FA	EA	
C c	apucinus	VA.	EA.	FA	EA	ED	в	taurus	VA.	EA.	FA	EA.	ED.	P	discolor	VA	EA	FA	EA	ED	C 1	moneduloid	VA.	EA	FA	EA	
S b	cliviensis	VA	EA.	FA	EA	ED.	8	bubalis	VA	EA	FA	E.A.	ED	H	armiger .	VA	EA	FA	EA	ED	T.	puttata	VA.	EA	FA.	EA	
S a	pella	VA	EA	FA	EA	ED	8	bison	VA	EA	FA	E.A.	ED	E	fuscus	VA	EA	FA.	EA	ED	L	striata	VA	EÁ	FA	EA	
C ja	acchus	VA	EA	FA	EA	ED	c	ferus	VA	EA	FA	EA	ED	M	brandtii	VA	EA	FA	EA	VE	P	humilis	VA	EA	FA	EA	
Min	nurinus	¥A.	EA	FA	ΕA	ED	c	dromedariu	VA.	EA	FA	EA.	ED	M	lucifugus	VA	EA	FA	EA	VE	P	muralis	VA.	EA	FA	ΕA	
D 0	rdi	VA	EA	FA	EA	ED	- 0	acutorostrat	VA	EA	FA	EA	ED		aegyptiacus	VA	EA	FA	EA	ED	A	carolinensis	VA	EA	FA	EA	
1 1	aculus	VA	EA	ŦA	DA	ED	L.	obliquidens	VA	EA	FA	E.A.	ED	P	alecto	VA	EA	FA	EA	ED	P -	vitticeps	VA	EA	MA	EA	
Min	narmota	VA	EA	FA	EA	ED	0	orca	VA	EA	FA	EA	ED	c	cristata	VA	EA	FA	EA	ED	T	olegans	VA	EA	FA	EA	
1 6	ridecemilin	VA.	EA	FA	EA	ED	p	sinus	VA	EA	FA	E.A.	ED	ε	europaeus	VA.	EA	FA;	EA	ED	P	mucrosqua	¥A.	ĒĂ	FA	EA	
Fd	lamarensis	VA	EA.	FA	EA	ED	D	leucas	VA	EA	FA	E.A.	ED	0	afer	VA.	EA	FA	DA	ED	6	evgoodei	MI	24	11	DI	
CI	anigera	VA	EA	FA	EA	ED	M	monoceros	VA	EA	FA	EA	ED	c	asiatica	VA.	EA	FA	EA	ED	C	mydas	MI	-1	11	DI	
0 d	legus	VA	EA	FA	EA	ED	- L	vexilifer	VA	EA	FA	EA	ED	E	telfairi	VA	EA	FA	EA	EE							

Supp. Fig. 4J

β-syn. βIIb-ti			Corr	elated	d pairs					Corre	elated	pairs					Corre	slated	pairs					Corre	elated	f pairs	ê
prot	ein j	β5 2b	βS 26	B5 28	β5 2b	85 2b		protein	β5 2b	βS 2b	B5 25	\$5 26	ß5 2b		protein	β5 2 b	β5 2b	85 2B	β5 2b	βS 2b		protein	β5 2b	85 25	65 2b	BS 26	BS 21
Genus Z-sco		4 5 9.6	2 8.9	115 8.7	N 10 7.5	95 Å	benus	species residue	4 59	2	115	240	41	Genus	residue	4 59	241	115	2 440		Genus	residue	4 59	141	115	~ ~	3 3
H sapiens		FY.	DG	EG	DE	PG		maniculatus	FY	06	EG	DE	PG		arctos	FY.	DG	EG	DE	PG		elegans.	FY	DE	EG	DG	PE
P troglodyt	les .	FY	DG	EG	DE	₽G	P	leucopus	۶V	DG	EG	DE	PG	A	melanoleuc	FY	DG	£G	DE	PG	P.	mucrosqua	FY	DE	DG	DG	PE
P paniscus		FY	DG	EG	DE	PG	R	norvegicus	FY	DG	EG	DE	PG	M	erminea	FY	DG	EG	DE	PG	c	picta	FY	DE	EG	DG	PE
G gorilla		FY	DG	EG	DE	PG	N	caroli	FY.	DG	EG	DE	PG	c	lupus	FY	DG.	EG	DE	PG	6	evgoodei	FY	DE	EG	0.6	PE
P abelii		FY	DG	EG	DE	PG	M	musculus	FY	DG	EG	DE	PG	- P.	discolor	FY	06	EG	DE	PG	x	tropicalis	LE.	DG	EG	DE	PG
N leucogen	ere i	FY	DG	EG	DE	₽G	0	princeps	FΥ	DG	EG	DE	PG		armiger	¢γ	DG	EG	DE	PG	х	laevis	LY	DG	EG	DE	PG
P anubis		FY	DG	EG	DE	PG	0	cuniculus	FY	DG	EG	DE	₽G	M	natalensis	FY	DG	EG	DE	PG	N.	parken	FY	DG	EG	DE	PG
M leucopha	eu	₽¥.	DG	EG	DE	₽G	- 5	scrofa	FY	DG	-6	DE	₽G	. 6	fuscus	FY	DV	EG	DE	₽V	. 11	bivittatum	FF.	DG	EG	DE	PG
C atys		FY	DG	EG	DE	PG	C	hircus	FY	DG	EG	DE	P.G	M	lucifugus	FY	DG	E-	DE	PG	A	mexicanum	FY	DG	EG	DE	PG
M nemestri	na -	FV	DG	EG	DE	PG	0	aries	FY	DG	EG	DE	PG	R	aegyptiacus	FY	DG	EG	DE	PG	M	unicolor	FF	EG	EG	EE	PG
M mulatta		FY	DG	EG	DE	PG	0	virginianus	FY	DG	EG	DE	PG	p	alecto	FY	DG	EG	DE	PG	- G	seraphini	LF	DG	EG	DE	PG
M fascicular	ris 👘	FY.	DG	EG	DE	PG	8	taurus	FY	DG	EG	DE	PG	E	europaeus	FY	DG	EG	0E	PG	- k.	chalumnae	LF	DG	EG	DE	PG
C sabaeus		FY	DG	EG	DE	PG	8	mutus	FY	DG	86	DE	PG	0	ater	FY	DG	EG	DE	PG	L	oculatus	FY	DG	EG	DE	PG
T gelada		FY	DG	EG	DE	PG	8	bubalis	FY	DG	EG	DE	PG	c	asiatica	FY	DG	EG	DE	PG	A	mexicanus	FY	DG	EG	D-	PG
P tephroso	ele	FY	DG	EG	DE	PG	C	ferus	FY	DG	EG	DE	PG	E	telfairi	FY	DG	EG	DE	PG	P	nattereri	FY	DG	EG	0.	PG
R roxellana	6	FY.	DG	EG	DE	PG	c	dromedaniu	FY	DG	EG	DE	PG		edwardii	FY	DG	EG	DE	PG	P	hypophthal	FY	DG	EG	D-	TG
C capucinu	8	FY	DG	EG	DE	PG	. 8	acutorostrat	FY	DG	EG	DE	PG	T.	manatus	FY	DG	EG	DE	PG	D	rerio	FY	06	EG	0-	PG
5 boliviens	15	FY	DG	EG	DE	PG	1	obliquidens	FY	DG	EG	DE	PG	5	harrisii.	FY	DG	EG	DE	PG	- 5	anshuiensis	LY	DG	EG	D-	PG
S apella		FY	DG	EG	DE	PG	G	melas	FY	DG	EG	DE	PG	- V.	unsinus	FY	DG	EG	DE	PG	5	rhinoceros	LY	DG	EG	D -	PG
A nancyma	æ	FY	DG	EG	DE	PG	0	OFER	FY	DG	EG	DE	PG	P	cinereus	FY	DG	EG	DE	PG	E	electricus	FY	DG	QS	D-	PG
M murinus		FY	DG	EG	DE	₽G	P.	sinus	FY	DG	EG	DE	PG	0	anatinus	FV.	DG	EG	DE	PG	1	punctatus	FY	DG	EG	Ð	TG
O garnettii		FY.	DG	EG	DE	PG	N	asiaeorienta	FY	DG	EG	DE	PG	P	colchicus	FY	EE	EG	EG	AE	T.	fulvidraco	FY	DG	EG	0-	PG
T chinensis	1	FY	DG	EG	DE	PG	D	leucas	FY	DG	EG	DE	PG	G	gallus	FY	EE	EG	EG	AE	5	salar	FY	DG	EG	D-	PG
D ordii		FY	DG	86	DE	PG	M	monoceros	FY	DG	EG	DE.	PG	A	fuligula	FY	EE	EG	EG	PE	5	trutta	EY	DG.	EG	0-	P.G
J jaculus		FY.	DG	EG	DE	PG	- K.	vexilifer	FY	DG	EG	DE	PG	. A	chrysaetos	FY	EE	EG	EG	PE	0	mykiss	FY	DG	£G	Ð-	PG
M flavivents	ris	FY	DG	EG	DE	PG	c	simum	FY	DG	EG	DE	₽G	. C	anna	FY	EE.	EG	EG	PE	0	kisutch	FY	DG	EG	0-	PG
M marmota	0.00	FY	DG	EG	DE	PG	1	asimus	FY	06.	EG	DE	PG	1	trailii	FY	11	EG	84	AL	6	morhua	EY	DG	EG	0-	PG
I tridecem	lin	FΥ	DG	EG	DE	PG	E	cabalius	FΥ	DG	EG	DE	PG	- P	filicauda	FY	EE	EG	EG	AE	P	reticulata	FY	DG	EG	0-	PG
F damaren	55	FΥ	DG	EG	DE	PG	P	pardus	FY	DG	EG	DE	PG	N	chrysocepha	FY	EE	EG	EG	AE	P.	latipinna	FY	DG	EG	D-	PG
C lanigera		FY	DG	EG	DE	PG	L	canadensis	FY	DG	EG	DE	₽G	ε	moneduloid	FY	EE.	EG	EG	AE	×	hellerii	FY	DG	EG	0-	PG
C porcellus	k	FY	DG	EG	DE	PG	1	pardieus	FY	DG	EG	DE	PG	T	guttata	FY	EE	EG	EG	AE	X	couchianus	FY	DG	EG	D-	PG
N galli		FY	DG	EG	DE	PG	F	catus	FY	DG	EG	DE	PG	L	striata	FY	EE	EG	EG	AE	х	maculatus	FY	ÐG	EG	D-	PG
H glaber		FY	DG	EG	DE	PG	A	jubatus	FY	DG	EG	DE	PG	p.	humilis	FY	EE	EG	EG	AE	8	splendens	FY	DG	EG	0-	PG
M ochrogas	ter .	FY	DG	EG	DE	PG	P	vitulina	FY	DG	EG	DE	PG	p	muralis	FY	DE	£G	06	PE	C	milii	FY	DG	EG	DE	PG
C griseus		FY	DĢ	EG	DE	PG	N	schainslandi	FY	DG	EG	DE	PG	P.	vitticeps	FY	DE	EG	06	PE							
M unguicula	atu:	FY	DG	EG	DE	AG	0	rosmanus	FY	DG	EG	DE	PG	P.	bivittatus	FY	DE	EG	DG	PE							

Supp. Fig. 4K

β-syn	βIII-tub.		Con	related	pairs					Corre	elated	pairs	1				Corn	elated	pairs					Corre	elated	pairs	
	protein	ps a	3 (15 B) (JS 183	jas na	¢5 83		protein	p5 81	i ps 03	gs 03	ps 0.	1 p5 83		protein	p5 80	() (S (B (ps ea	ps 83	ps 03		protein	ps 83	ps 83	<u>β5 83</u>	\$5 83	ps aa
Genus	per residue Z-score	128 11.7	114	1.1.1.1.1.1.1.1			Genus	species residue	441	10	449	17	E	enuan	species residue	441	10	2 45	449	11 449	Genus	residue	441	10	449	449	E 449
H	sapiens	QE	MP	DP	TP	MP	M	auratus	QD	MP	DP	TP	MP	¢	lupus	Q.E.	MP	DP	TP	MP	1	striata	QE	KA.	EA	AA.	LA
. p	troglodytes	QE	MP	DP	TP	MP	R	norvegicus	QD	MP	0P	TP	MP.	V	vulpes	Q.E.	MP	DP	TP	MP	- 2	muralis	QE	KA	DA	AA.	EA.
P	paniscus	QE	MP	0P	TP	MP	M	i piahiari	QD	MP	DP	TP	MP.	N	I Javanica	3.D	MP	DP	TP	MP	A	carolinensis	QE	KG	DG	AG	1.0
6	gorilla	QE	MP	DP	TP	MP	M	caroli	QD	MP	DP	TP	MP		discolor.	3.0	MP	DP	TP	MP		vitticeps	QE.	KA	DA	TA	LA
. P	abeli	QE	MP	DP	TP	MP	M	musculus	QD	MF	DP	TP	MF	H	armiger	Q.E.	MP	DP	TP	MP	T	elegans:	QE	KA	DA	TA	LA
N	leucogenys	QE	MP	DP	TP	MP	0	princeps	QE	MP	DP	TP	MP	Æ	fuscus	QE	MP.	DP	TP	MP	T	sirtalis	QE	KA	DA	A,T	LA
*	anubis	QE	MP	DP	TP	MP.	0	cuniculus.	10	MP	OP	TP.	MP	M	l brandtii	10	MP	DP	TP	MP		mucrosqua	QE.	KA	DA	AA	LA
c	atys	QE	MP	DP	TP	MP	c	hircus	QE	MP	OP	TP	MP	M	1 lucifugus	QE	MP	DP	TP	MF	Τ.	carolina	QΕ	KA	DA	AA	LA
- 14	fascicularis	QE	MP	DP	TP	MP	0	sirginianus	QE	MP	OP	TP	MP	- R	angyptiacus	QE.	MP	DP	TP	MP	C.	picta	QE	KA.	DA	AA.	LA.
C	sabaeus	QE	MP	DP	TP	MP	8	taurus	QE	MP	OP	TP	MP	5	araneus	QE	MP	DP	TP	MP.	G	evgoodei	QE.	KA	DA	AA	LA
T	gelada	QE	MP	DP	TP	MP		bubalis.	0E	MP	OP	TP	MP	E	europaeus	QD.	MP	DP	TP	MP	c	mydas	QE	KA	DA	AA	-A
P	tephroscele	QE	MP	DP	TP	MP	c	ferus	QE	MP	DP	ŤP	MP	0	afer	3.D	MP	DP	TP	1.0	×	tropicalis	QE	K -	Ð-	A-	L-
8	bieti	QE	MP	DP	TP	MP	C.	dromedariu	Q.E	MP	OP	TP	MP	c	asiatica	QD.	MP	DP	TP.	MP		laevis	QE	81	D-	A-	Li
. H	rowellana	QD	MP	DF	TP	MP	۷	pacos	QE	MP	DP	TP	MF	E	telfairi	QD	MP	DP	TP	MP	N	parkeri	QE	×-	D-	A+	L.
C	capucinus	QD	MP	DP	TP	MP	10.45	obliquidens	RD	MP	DP	TP	MP.	- E	edwardii	QD	MP	DP	TP.	MP	. 8	bivittatum	QE	XG	DG	AG	LG
5	boliviensis	QD	MP	DP	TP	MP	0	orca	RD	MP	DP	ŤP	MP	T	manatus	ar	MP	DP	TP	MP	M	unicolar	0.0	KG	EG	AG	1.6
C	jacchus	QD	MP	DP	TP	MP	P	sinus	RD	MP	OP	TP	MP	5	harrisii	QE	MA	DA	TA	LA	G	seraphini	QD	KG	DG	AG	LG
p	coquereli	QE	MP	DP	TP	MP	N	aslaeorienta	RD	MP	0P	TP	MP	V	ursinus	Q.E	MA	DA	TA	LA	1	chalumnae	3.0	KQ	DQ	AQ	VQ
0	garnettii	QE	MP	DP	TP.	MP	D	leucas	RD	MP	DP	TP	MP	P.	cinereut.	Q.E.	MA	DA	TA	LA	- E	calabaricus	0.0	KQ	DQ	AQ	MQ
T.	chinensis	QE	MP	DP	TP	V.P.	M	monoceros	RD	M.P.	DP	TP	MP	0	anatinus	QE	MA	DA	TA	LA	A	ruthenus	QD	K-	D-	A-	L-
D	ordii	QD	MP	DP	TP	10	1.6	vesilifer	RD	MP	DP	TP	VP	N	perdicaria	3,0	KA	EA	AA	LA:	- 6	oculatus	QD	KQ	DQ	AQ	1Q.
1	jaculus	QE	MP	DP	TP	MP	c	simum	QE	MF	OP	TP	MP	N	meleagris	QE	KA	EA	AA	LA	P	kingsleyae	QE	KP	DP	AP	MP
M	fleviventris	QE	MP	DP	TP.	MP	٤.	asimus	QE	MP	DP	TP	MP	- P	coichicus	QE	KA	EA.	AA	LA	5	formasus	QD	KQ	DQ	AQ.	LQ
	tridecemiin	QE	MP	DP	TP	MP		caballus	QE	MP	DP	T P	MP	G	gallus	Q.E.	KA	EA	AA	LA	A	mexicanus	QD	KQ	DQ	AG	MQ
F	damarensis	QD	MP	DP	TP	MP	P	pardus	QE	MP	9 Q	4T	MP	A	fuligula	QE	KA	EA	AA	LA	- P	nattereri	0.0	KQ	DQ	AQ	MQ.
c	lanigera	QE	MP	0P	TP	MP	. 1	canadensis	QE	MP	OP	TP	MP	A	chrysaetos	QE	KA	EA	AA	LA	P	hypophthal	QΕ	KQ	DQ	AQ	VQ
0	degus .	QE	MP	DP	TP	MP	1	pardinus	3.0	MP.	08	TP	MP	c	anna	3.0	KA	EA	AA	LA	E	electricus	QD	KQ.	DQ	AQ	VQ
c	porcellus	QE	MP	DP	TP	MP	A	jubatus	QE	MP	DP	TP	MP	P	fasciata	QE	KA	EA	AA	LA	1	punctatus	QE	KQ	DQ	AQ	VQ
N	galā	QD	MP	DP	TP	MP	P	vitulina	QE	MP	DP	TP	MP	M	undulatus	3.D	KT	ET	AT	LT .	T	fulvidraco	QE	KQ	DQ	AQ.	VQ
H	glaber	QD	MP	DP	TP	MP	N	schainslandi	QE	MP	DP	TP	MP	٤	trailli	3.0	KA	EĄ	AA	LA	5	salar	QE	KA	DA	۸A	DA
M	ochrugaster	00	MP	DP	TP	MP	0	rasmanus	QE	MP	DP.	TP	MP	P	filicauda	a.	KA	EA	AA	LA	5	trutta	3.0	KA	DA	AA	DA
c	griseus	QD	MP	DP	TP	MP	Z	californianu	QE	MP	DP	TP	MP.	N	chrynocepha	QE	KA	EA	AA	LA	0	mykiss	QE	KA.	DA	AA	DA
M	unguiculatu	QE	MP	DP	TP.	MP	u	arctos	QE	MP	DP	TP	MP	c	altern	QE	KA	EA	AA	LA.	0	kisutch	QE	KA	DA	AA	DA
P	maniculatus	QD	MP	DP	TP	MP	M	putorius	3,D	MP	OF	TP	MP	C	monedulaid	QE	KA	EA	AA	LA.	C	mili	QE	KP.	90	AP	MP
	leucopus	QD	MP	DP	TP	MP	M	erminea	QE	MP	DP	TP	MP	T	guttata	3.0	KA	EA	AA	LA.	- 5	torazame	QE	KP.	DP	AP	MP

Supp. Fig. 4L

syn. αla-tub.		Corr	elated	pairs					Corr	elated	pairs					Corre	elated	pairs					Corri	elated	pairs	Ē.
protein	y5 2a	15.20	y5.3a	γ5 1a	yS 1a		protein	75.34	y5 1a	y5 3a	y5 1a	y5 1a		protein	γS 1a	γ5 3a	γS 10	y5 1a	y5 1x		protein	75.10	y5 24	95 I.a	y5 24	175
Genus Z-score	0.0243	51 AB 10.7				Genus	species	240	57	113	94 Å	53	Genus	residue	440	57	440	¥40	140	Genus	species	24	440	110	* *	s
H sapiens	QV	EV	KV.	VV	TV		virginianus	QV	EV	RV.	VV	TV	M	domestica	QV	EV.	AV.	31	TV		natteren	AI.	10	-4	LI	N
# troglodytes	QV.	EV	KV	٧V	TV		taurus	QV	EV	KV.	VV	TV		cinereus	QV	EV.	AV	IV	TV	0	clupeoides	AL.	Q1	-1	6.1	N
G gorilla	av	EV	KV.	VV.	TV.	8	mutus	QV	EV.	KV.	VV	TV	0	anatinus	QV	εv	AV	VV	SV	D	rerio	AL	01	10	Li	N
P abelii	QV	EV	×۷	٧V	τV		bubalis	QV	EΨ	KV.	VV	TV	τ	guttatus	Q.V.	εv	AV	vv	TV	5	rhinocerous	AV	HV	·¥-	LV	N
H moloch	QV	EV	XV.	VV.	TV		bison	QV	EV	KV	VV	TV	5	cameius	QV	EV	vv	vv	TV	- 6	electricus	AT	QI	-1	11	. 8
N leucogenys	QV	EV	KV	vv	TV	c	fenas	QV	EV	KV	WV.	TV	c	coturnie	QV	EV	PV.	vv	TV	1	punctatus	11	Q1	-1	1.1	1
M leucophaeu	QV	EV	KV.	VV.	TV	1	obliquidens	QV	EV	KV.	VV	TV.	G	gallus.	QV	EV	PV	VV	TV	T	fulvidraco	AL	10	11	11	1.9
M nemestrina	QV	EV	KV	٧V	TV	G	melas	QV	EV	ĸν	VV	TV	F	peregrinus	QV	EV	AV	vv	TV	5	satar	AL	QI	-1	1.1	- 3
M mulatta	QV	EV	KV.	VV.	TV.	0	61538	QV	EV	KV.	VV.	TV	c	anna	QV	EV	AV.	vv	TV.	5	trutta	At	QI	-1	11	. 1
M fascicularis	QV	EV	KV	VV.	TV		sinus.	QV.	EV	KV	VV	TV.	c	livia	QV	ΕV	AV	vv	TV	0	mykiss	Al	QI.	-1	1.1	1
C sabaeus	QV.	EV	KV.	VV.	TV	D	leucas	QV.	EV	KV	VV.	TV	P	filicauda	QV	EV	AV	AV	TV.	0	knutch	At	QI	- 14	11	
P tephroscele	QV	EV	KV	VV.	TV:	M	monoceros	QV	EV.	KV	VV.	TV	c	altera	QV	EV	AV	VV.	TV	P	formosa	AL	QI.	11	1.1	- 3
R rosellana	QV	EV	KV.	.VV	TV	1	vesilifer	QV	EV	KV.	VV	TV.		albicolits	QV	EV	AV.	VV	TV	P.	latipinna :	AL	10	- 41	11	19
C capucinus	QV	EV	KV	WV.	TV	c	simum	QV	EΥ	KV.	VV	TV	c	moneduloid	qv	EV	AV	VV	TV.	p.	mexicana	AI	QI	-1	LI	1
5 bolivensis	QV	EV	KV.	VV.	TV	E .	asinus	QV	EV	KV.	WV.	TV	1	guttata	QV	EV.	AV	VV	TV	×	hellerii	AL	10	-1	11	19
5 apela	QV	EV	KV	VV.	TV		cabalius	QV	EV	KV.	VV	TV	P.	humilis	QV	EV.	AV	vv	TV	×	couchianus	AL	Q1	-1	6.1	- 1
C jatchus	QV	EV	KV.	VV.	TV.		pardus	QV	EV.	KV.	VV	TV	P	muralis	QV	εv	DV.	VV	TV.	X	maculatus	AL	01	-1	11	13
А напсутване	QV	EV	KV.	VV	TV	1.6	canadensis	QV	EV	KV.	VV	TV	A	carolinensis	QV	εv	EV	vv	TV.	T	rubripes	AV	HV	·V	LV	1.3
P coquereli	QV	EV	RV	VV.	TV		catus	QV	EV	KV.	VV	TV	P	vitticeps	QV	EV	DV	VV	TV	M	armatus	AL	01	+1	FI	3
M murinus	QV	EV	RV	vv	TV	A	jubatus	QV	£Ϋ	κv	WV.	TV		bivittatus	QI.	EI	61	11	51	F	heteroclitus	Al	Q1	-1	LI	1
0 garnetti	QV	EV	RV	VV.	TV	1.1	vitulina	QV.	EV	KV.	VV	TV	1	elegans	QV	EV	EV	1.1	TV.	0	latipes.	At	QI	11	FI	19
D ordii	QV	EV	KV	vv	TV	N	schauinslan	QV	EV	KV.	VV	TV	p.	muscrosqua	QV	εv	KV.	LV	TV	A	testudineus	AL	91	-8	FI	3
M flaviventris	QV	EV	EV	VV.	TV	U	arctas.	QV	EV	KV.	VV	TV.	x	tropicalis	QV	EV.	PV	LV	SV	8	splendens	At	QI	-1	FL	13
M marmota	Q¥.	EV	EV	VV	TV	M	putorius	QV	EV	TV	VV.	TV	×	laevis	qv	EV	PV	LV	NV.	0	relaticus	AL	QI	-1	FL	9
I tridecemiin	QV	EV	EV	VV	TV	M	erminea	QV	EV	TV	WV.	TV	N	parkeri	qv	EV.	PV	VV.	SV	H.	burtoni	At	10	-16	FI	19
C porcellus	QV	EV	AV.	vv	ŤV	c	lupus	QV	EV.	#V	VV.	TV		bivittatum	QV	EV	PV.	IV.	SV	M	zebra	AL	Q1	11	FI	14
C griseus	QV	EV	KV.	VV	TV	1.0	discolor	QV	EV	KV.	VV.	TV	M	unicolor	QV	EV	HV	1.1	NV	12	bergylta	AS	QI	45	11	13
P leucopus	QV	EV	KV	VV.	TV	E	fuscus	QV	EV	KV.	VV	TV	G	seraphini	EV	EV.	PV.	LV	NV	5	lucioperca	AL	HL	11	FI	- 9
R norvegicus	QV	EV	QV	VV	TV	M	brandtii	QV	EV	KV.	VV	TV	E	chalumnae	QV	DV	PV	LV	SV	1	crocea.	AF	10	. 1	FI.	13
M musculus	QV	EV	QV	VV	TV		angypticus	QV	έV	KV.	vv	TV	E	calabaricus	HV	EV	PV	LV	NV	c	mili	QV	EV	TV	VV.	3
O cuniculus	qv	EV	KV.	VV	TV		asiatica	QV	EV.	KV	VV	TV	E	oculatus	QV	QV	PV	VV	NV	A	radiata	QI	EL	-1	VI	19
5 scrofa	QV	EV	KV.	VV	TV	L	loxodonta	QV	EΫ	TV	VV	TV	P	kingsleyae	AV	MV	PV	LV	NV	R	typus	10	EI	TE	¥1	à
C hircus	av	EV	KV.	AV	TV	p	novemond	QV	EV	TV	VV	TV	5	formasus	AL	ai	PI	LL	NI		100					
O aries	QV	EV	KV.	AV	TV	5	harrisii	QV	EV	AV	IV	TV	A	mexicanus	AL	Q1	4	LL	NI							

Page 30 of 32

Supp. Fig. 4M

	"PF			1000 M	-					10000						in the second						100		in the second	
γ-syn. βl-tub.		Cor	relates	d pairs					Corn	elated	pairs						f pairs					Corn	elated	pairs	
protein	y5 81	1 75 8	1 y5 8	1 yS 81	γ5 B1		protein	γ 5 81	γ\$ B1	y5 81	y5 81	15 81	protein	y5 81	γ5 81	γ5 B3	175 81	5 81		protein	y5 83	y5 81	y5 81	γS 81	y6 83
Genes Z-score		7.4		58 6.6	8 L 5.6	Genus	species residue	442	442	¥ 7	267	2 8	Species Genus	26	2 4	* *	38	2 \$	Genus	fresidue	442	#40	8 2	267	\$ L
H sapiens	YE	TE	Kt	KM	EL	M	musculas	VE-	TE	81	KM	EI	brandtii	YE		K1	KM	E1	1	oculatus	YE	TE	KI.	KM	EL
P troglodytes		TE	RI	KM	EI.		princeps	VE	TE	K1	KM	Eł	aegypticus	VE	TE	KL		£1	P	kingsleyae	V.E.	TE	KI.	KM	EI
G gorilla	VE	TE	KI	KM	EL		cuniculus	VE	TE	KI	KM	EI.	alecto	VE	TE	Kt		EI	- 5	formosias	VE	TE	KL	KM	EL
P abelii	VE	TE	KI	KM	EI		scrofa	¥.E	TE	KI	KM	£I	cristata	ΥE	TE	K1	× M	£1	A	mexicanus	VE	TE	KI	KM	EI
H maloch	VE	1.1.1.1	KI	XM	- 11		hircus	VE	TE	K1	XM	11	estatica	VE	TE	KI	×м	11	- P :	nattereri	VE	AE	KI.	KM	EL
N leucogenys	VE	1.00	KI	KM	EI		aries	VE	TE	K1	KM	El	telfairi	YE	TE	KI		El		dupecides	YE	TE	KI.	KM	EI
P anubis	VE		KI.	RM	EI.		virginianus	VE	TE	KI.	KM	EI	manatus	VE	TE	KE	KM	£1	P	hypophthal	10	AD	KI	KM	EI
M leucophaeu		TE	KI	KM KM	EI		taurus	VE	TE	K1	KM KM	EI.	novement		TE	Ki		EI	5	rerio	VD	AD	KL	KM	EI
C atys M nemestrins	VE	TE	KI KI	KM	11		mutus bubalis	VE	TE	61	XM	EI EI	harrisii domestica	VE	TE	KI	KM KM	£1	7	rhinocerous	VD	AD	KI KI	KM	EL
	VE	110.5	KI	KM	EL				TE	KI				VE					-	punctatus	LD	AD		KM	
M mulatta M fascicularia	VE	TE	KI	KM.	EI		ferus dromedariu	VE	TE	K1 K1	KM KM	EI	anatinus	VE	TE	KI KI	KM	E1 E1	\$	fulvidraco salar	VE		KI RV	RI	EI. DV
C sabarus	VE		KI	KM	EI		paces	VE	TE	KI	KM	EL	perdicaria	VE		Ki		£1	6	trutta	VE	TE	RV	RI	DV
T gelada	VE	TE	KI	KM	EI		acutorostrat	VE	TE	61	XM	EI	colchicus	VE	TE	KI	×M.	EI	0	myklas	VE	TE	RV	RI	DV
P tephroscele		TE	KI	KM	EL		obliquidens	VE	TE	KI	XM	11	gallus	VE	TE	KI	KM	ti.		kitutch	VE	TE	RV	81	DV
R bieti	VE	TE	KI	KM	EI		melas	VE	TE	61	KM	EL	cunicularia	VE	TE	61	KM	EI	5	alpinus	YE	TE	RV	81	DV
R roxellana	VE	TE	KI	KM	EI .		orca	VE	TE	KL	KM	EI	chrysaetos	VE	TE	KI		11	_	formose	VE	TE	RI	KM	
5 bolivensis	VE	TE	KI	KM	EI		sinus	VE	TE	KI	KM	£I	pelagica	VE	TE	KL	KM.	EI	P	reticulata	YE	TE	KI	KM	EI
S apella	VE		KI	KM	EI		asiaeorienta	VE	TE	K 1	KM	Ei	canorus	VE	TE	KL		EI	- p.	latipinna	VE	TE	KI	KM	EI
A nancymase	VE	TE	KL	KM	£1.		Instan	VE	TE	KI	KM	11	undulatus	VE	TE	KL	KM	£1	p	mexicana	VE	TE	KI	KM	E1.
C syrichta	VE.	TE	KI	KM	EI		monoceros	VE	TE	K1	KM	E	filcauda	VE	TE	KI.		£1	×	helleri	YE	TE	KI	KM	EI
P coquereli	VE	TE	KI.	KM	EL		vexilifer	VE	TE	KI	KM	El	moneduloid	1.1.2	TE	KL	KM	61	×	couchianus	VE	TE	KI	KM	EI
M murinus	VE		K1	KM	EL		simum	VE	TE	KI	KM	EI	caeruleus	VE	TE	KI	KM	EI	×	maculatus	VE	TE	KE	KM	EL
T chinensis	VE	TE	KI	KM	EI		asinus	VE	AE	K 1	KM	EI	guttata	VE	TE	KI.	KM.	EI	c	variegatus	VE	TE	KI	KM	EI
D ordii	VE	TE	KL	XM	E1.	1	caballus	VE	AE	KX	KM	181	striata	VE	TE	KE	KM	£1.	T.	rubripes	VD	AD	KI	KM	11
J jaculus	YE	TE	KL	KM	EI.	- P.	pardus	¥E.	TE	K1	KM	Ei	humilis	¥ E	TE	KI.	KM	EI	M	armatus	¥E.	TE	KI.	KM	EI
M flaviventris	VE	TE	KI	KM	E1	. p	concolor	VE	TE	KI	KM	EI	muralis	VE	TE	KL	KM	E1		heterocitus	VE	TE	KI	KM	11
M marmeta	VE	TE	K1	KM	EI	1	canadensis	VE.	TE	KI	KM	Et:	carolinensis	VE.	TE	Kt	KM	EI	0	latipes	VE	TE	KL	KM	EL
I tridecemlin	VE	TE	Kt	KM	EI	- (#)	catus	VE	TE	K1	KM	EF	vitticeps	VE	TE	K1	KM.	EI	A	testudineus	VE	TE	K1	KM	EI
F damarensis	VE	ŤE	KI	KM	EI	. A	jubistus	VE	TE	KI	ĸм	EF	bivittatus	VE	TE	K1	КM	Ŧ1	8	spiendens	VE	TE	KI	KM	El
C lanigera	VE	TE	KI	KM	EI		vitalina	VE.	TE	K1	KM	EI	elegans	VE.	TE	KI.	KM	EI	0	nilotion	¥E.	TE	KI.	KM	EI
C porcellus	VE	TE	KI	KM	EI.	- A.	weddellii	VE	TE	K1	KM	13	muscrosqua	VE	TE.	KI	KM	11		burtoni	VE.	TE	KI	KM	El
H glaber	VE	TE	KI	KM	13	- N	echauinslan	VE	TE	KI	KM	EI .	cerolina	VE	TE	KE	KM	E1	M	tepus	VE.	TE	KI	KM	E1.
M ochrogaster	VE	TE	K1	KM	EI	0	rosmarus	¥E.	TE	K1	KM	ΕI	picta	VE	TE	K)	K M	EI	4	bergylta	VD	TD	KI	KM	EI
C griseus	VE.	TE	KL	XM	E1.	U.	arctos	VE	TE	KL	KM	11	mydas	VE	TE	K1	KM.	11	- 5	lucioperca	VD.	AD.	KI	KM.	EL.
M unguiculatu	YE	TE	Ki.	KM	EI	M	putorius	¥E.	TE	K1	KM	EI	tropicalis	¥ E	TE	K1.	KM	EI	٤.	C'DCER	¥0	TO	KI.	KM	EI
P maniculatus		TE	61	KM	E1		erminea	VE	TE	KL	KM	EF	laevis	VE	TE	KL	KM	11	c	mili	V.D	TD	KI	RM	11
P leucopus	VE	TE	K.I	KM	E)		lupus	VE	TE	KI	KΜ	£1	bivittatum	VE	TE	KL	ĸм	£1	- 8	typut	VQ	TQ	KI	KM	El
M auratus	VE		KI	KM	EI.		vulpes	VE	TE	K1	XM	El	unicolor	VE	TE	K)		EI	5	torazame	VE.	TE	KV	K1	EV
II. norvegicus	VE		KI	KM	GI		javanica	VE	TE	KI	KM	Ð	seraphini	VE	TE	К1	KM								
M pahari	YE		KI	KM	EI		discolor	VE	TE	K1	KM.	EI	chalumnae	¥ E	TE	KI	KM								
M caroli	VE	TE	KI	KM	E1	. E.	fuscus	VE	TE	K1	KM	E1	calabaricus	VE	TE	KI	KM	11							

Supp. Fig. 4N

-syn. βIla-tub.		Corn	elated	f pairs					Corre	elated	pains					Com	elated	pairs					Corn	elated	pairs	
protein Genuer Z-score	y5 24 13 1	8	15 24 25 35	15 24 41	44.94	68	protein Tesidue	ys 125	<u>.</u>	1	1.4	y5 24 354	Genus	proteir Iproje		15 2a 41	1.000	-	27 364	Genus	protein gresidue	12 A	and it	Territoria de		- 5- 10 March 10
₫ ₫ Z-score	10.2	10.0	9.7	9.6	8.8	-	8						1	ž.						Ē	ă					
H sapiens	GD		EA	-p	DS	- 14	glaber	ED.	- D	11	- D	DS	- A	jubatus	GD	-0	EA	-D	DS	- T	guttatus	GD	- D	EA.	-0	DS
P troglodytes	GD	-0	EA	-D	D5	M	ochrogaster	60	· D	E.A.	÷D	D.S.	P	vitulina	60	÷D.	EA	- D	D.5	5	cametus	60	÷0	EA.	- D	05
P puniscus	60	-0	EA	-D	D.S.	- C	griseus	60	-D	EA	-0	DS	L	weddellii	60	-0	EA.	-0	D\$	C	coturnia	60	-0	EA	-0	DS
G gorilla	GD	-D	EA	-D	0.5		maniculatus	ED	-D	EA	-0	DS	N	schauinslan	GD	-D	EA	-D	DS	6	gallus	60	-0	EA.	-D	DS
P abeili	60	-0	EA	-D	DS	- P	leucopus	ED	-D	EA	Ð	DS	0	rosmarus .	60	Ð	EA	-D	D5	- A	platyrhynch	60	-D	EA.	-0	ES
N leucogenys	RD	-0	EA	÷D.	DS	M	auratus	GD	-D	EA.	-D	DS	2	californianu	60	-D	EA	-0	DS	A	fuligula	GD	-0	EA	-D.	ES
P anubis	60	-0	EA	-D	DS		norvegicus	60	·D.	EA.	-D	DS	U	arctos	GD	-0	EA	-0	DS	A.	chrysaetes	60	-0	EA	-D	20
M lescophaeu	GD	-D	ET	÷D.	05	M	musculus	GD	-D	EA.	-0-	DS	14	putorius	GD	-0-	EA	-D	DS	÷	cherrug	GD	-0	EA	-D	DS
C atys	60	-0	EA	-D	DS	ò	princept	VD	-0	EA	-D	DS	M	erminea.	GD	-D	EA	-0	0.5	с	anna	60	-D	EA	-D	DS
M nemestrina	60	-0	EA	-D	D5	0	cuniculus	60	- D	EA	-0	DS	c	lupus	60	-0	EA	-D	D5	c	Evia .	60	-0	EA	-D	D5
M mulatta	60	·D	EA	-D	DS	5	scrofa	GD	· D	EA	· D	DS.	v	vulpes	GD	-D	EA	-0	DS	C	vociferus	60	-0	ÉA.	·D	DS
M fascicularis	GD	-D	EA	-D	DS	c	hircus	GD	-D	EA	-0	AS	P.	discolor	VD	-0	EA	-D	ES	N	nippon	60	-D	EA	-D	D5
C sabaeus	GD	Ð	EA	-0	DS	0	aries	GD	D	EA	Ð	AS	H.	armiger	GD	Ð	EA	-0	EA	C	canorus	GD	-0	EA		D5
T gelada	GD	-0	EA	-D	DS		taurus	GD	-D	EA	-D	AS		fuscus	WE	-E	EA	-E	15	M	undulatus	GD	-0	EA	-D	DS
Il resellana	60	-0	EA	-0	05		bubalis.	60	-D	EA	-0	AS		brandtii.	WE	-E.	DA	-6	ES		filicauda	PE	TE	EA	GE	05
C capucinus	60	·D	DT	-D	05		bison	GD	-0	DA	- D	AS	8	aegypticus	GD	-0	EA	-D	ES	N	chrysocepha	PE	TE	EA	GE	D5
\$ bolivensis	GD		DA	-D	DS		ferus.	GD	-D	DA	-0	DS		alecto	GD	-0	EA	-0	EA	1	albicollis.	21	SE	EA	AL	D5
S apeila	60		OT	D	DS		dromedariu	GD	·D	DA	0	DS		cristata :	MD	-D	EA	-0	DS	c	moneduloid	PE	SE	EA	TE	DS.
C jacchus	60		DT.	D	DS		acutorestrat	GD	D	DA	Ð	DS		europaeus	RD	D	EA	-D	ES		major	TE	SE	EA	TE	DS
C syrichta	60	-0	EA	-D	DS	- 6	obliquidens	GD	-D	EA	-8	DS		asiatica	GD	-D	£T.	-B	DA	T	guttata	PE	SE	EA	TE	15
M murinus	60	-0	EA	-0	DS	0	orca	60	-D	EA	-0	DS.		telfairi	60	-0	DT	-D	DS	- 43	striata	PE.	SE	EA	TE	ES
D ordii	GD	-D	1000	-D	DS		pious	GD	- D	EA	-D	05	12	manatus	GD	-0	EA	-0	DS		humilis	TE	SE	EA	AE	DS
1 Jacobus	60	-0	ET	-D	ES		leucas	60	-0	EA	-0	DS		africana	60	-D	EA	-0	05	1	aibicoilis	AE	E.	EA	-E	DS
M.marmota	60	-0	EA	-0	DS		monoceros	GD	-D	EA	-0	DS		novemeinet	ED	-0	DA	-D	55		muralis	60	-0	EA.	-0	
i tridecemlin	GD		EA	-D	DS		vexilifer	60	-D	EA	-0	DS		harrisii	50	-D	DA	-0	DS		carolinensis	60	-0	EA	-0	
F damarensis	ED	-D	EA	-D	DS		simum	GD	-D	EA	-0	DS		domestica	50	-D	DA	-D	DS	- 2	vitticeps	GD	-0	EA	-D	DS.
C lanigera	GD	-0	EA	-0	05		caballus	GD	-D	EA	-D	DS		ursinus	50	D	DA	-0	DS		elegans	AH	EH	DA	AH	ES
O degus	GD	-0	EA	-D	DS		pardus	GD	-D	EA	-0	DS		cinereus	SD	-D	DA	-D	05		mucrosqua	-0	-D	DA	-0	
C porcellus	-0		EA	-0	05		canadensis	GD	-D	EA	-0	DS	-	anatimus	60	ED	EA	VD	DS	- 2.	mydas	60	-0	EA		
N galili	-0		EA	-D	05		catus	GD	-D	EA	-D	DS		perdicaria	60	-0	EA	-0	ES				-0	1.14		
in Bunn	- 64	1.04	2.14		9.2		Contrast.	and :		2.16	- 10	14.2	14	Pre-Formania	0.0	1.1	2.14		25							

Page 31 of 32

Y-SVI	n. BIIb-tub.	pp.		elater	1 pairs	1				Com	elsted	pairs					Corn	elated	pairs					Corn	elated	pairs	
0.0100	protein	10.94	100.00	cie se	1.00	b y5 2b		protein	10.96	14.36	18.26	Le se	y5 25		protein	1.6.76	Se 24	10.94	16.25	y5 26		protein	10.76	10.75	14.76	y5 25	16.75
		1010		1.000	1000	1.		1.1.1			1.000	2000	a distant and a second							And some					and the second	and the state of t	· · · · · · · · · · · · · · · · · · ·
-	2 residue	62 =0	¥ 33	1092 7.9	79	Contraction of the second s	Genu	residue Z-score	62	34	9 H	22	2 40	Geou	2 residue 2-score	62	34	996	2.6	22	Genus	fe residue Z-score	23	10	192	22	2 8
H		QC.	KV	-6	AE	SE		unguiculatus	QC.	KV.	-6	AE	TE		rosmanus	QC.	KV.	06	AE	TE	1	striata	0C	×V.	EE	EG.	AG
p	troglodytes	90	KV	-G	AE	SE	P	maniculatus	ac	KV.	-G	AE	TE	U	arctes	QC.	κv	-6	AE	TE	- P	humilis	ac	κv	EE	EG	AG
P	paniacus	QC	KV	-6	AL	56	P.	leucopus.	ac	KV	+G	AE	TE	A	melanoleuc	QC	KV	-6	AE	TE	- A	sinensis	QC	KV	AE	50	AG
- 6	gorilla	QC	KV	-6	AE.	SE		norvegicus	QC	KV.	-6	AE	SE	M	erminea	QC	KV.	-6	AE	TE		muralis	QC	KV	AE	\$6	AG
P	abeli	QC	KV	-6	AE	NE	M	caroli	ac	KV	-6	AE	SE	C	lupus	QC	KV	÷G	AE	TE	- P.	vitticeps	ac	KV	EE.	56	AG
N	feucogenys	QC	KV	+6	AE	SE.	M	musculus	QC	KV	· 6	AE	SE	P	discolor	QC	KV	-6	AE	5 E		bivittatus	QC	KV	GE	-6	AG
P	anubis	00	KV	-G	AE	SE	0	princeps	0.5	KV.	+G	AE	TE	H	armiger	QC	KV	-6	AE	TE	т	elegans	QC	KV	GE	DG	SG
N	A leucophaeu	95	KV	-6	AE	SE.	0	cuniculus	ac	KV.	-6	AE	TE	M	natalensis	QC	KV.	-6	AE	SE		mucrosqua	QC	KV	GE	-6	56
¢	atys	QC.	KV	-6	AE	51	15	scrofa	00	KV.	-6	AE	SE	- E	fuscus	QC	KV.	-V	AE	SE	c	picta	30	KV.	AE	16	AG
. 11	A nemestrina	QC	KV	+G	AE	SE	c	hircus	QC	KV.	G	TE	SE	R.	aegyptiacus	QC	KV	-6	AE	TE	×	tropicalis	QC	KV.	AG	TE	58
N	t mulatta	QC	KV	-6	AE.	SE	0	aries	QC	KV.	-6	TE	SE.	- P	alecto	QC	KV	G	AE	TE	×	laevis	QC	KV	AG	IE.	58
N	A fascicularis	QC	KV	-G	AE	58	0	virginianus	30	KV	-G	TE	58	E	europaeus	QC	κv	-6	VE	NE	N	parkeri	3.0	KV	TG	AE.	TE
c	sabaeus	QC	KV	-6	VE	SE	. 8	taurus	ac	KV.	-6	TE	SE	c	asiatica	QC	KV	-6	AE	TE		bivittatum	QC.	KV	AG	TE.	AE
T	gelada	QC	KV	-6	DE	SE		mutus	ac	KV.	-6	TE	SE	E.	telfairi	Q5	KV	-6	AE	SE.	M	unicolor	9.0	K٧	AG	TE	SE
P	tephroscele	QC	KV	+G	AE	58		bubalis	QC.	KV.	÷G	TE	SE	T	monatus	QC	KV	-G	AE.	TE	G	seraphini	QC.	KV	AG	TE	TE
R	roxellana	QC	KV	÷Ġ	AE	5E	c	ferus	QC	KV.	-G	AE	SE	L	africana	QC	κv	-6	AE	AE	- 4	chalumnae	ac	KV	EG	÷E	SE
C	capucinus	25	KV	-6	AE	58	¢	dromedariu	QC	XV	-G.	AE	SE.	5	harrisii	QC	KV	EG	VE	AE	- E.	oculatus	QC.	KV.	÷G.	7.6	61
5	bolivensis	QS	KV	+ G	AE	SE	8	acutorostrat	HS	ĸ٧	- G	TE	5E	M	domestica	QC	KV	EG	¥ E	AE	A	mexicanus	QC	KV	-6	A-	A-
5	apella	QC	KV	-+G	AE	SE	1	obliquidens	HC	KV.	-6	TE	SE	V.	ursinus.	QC	KV	EG	VE	AE		nattereri	30	KV	-G	A-	A-
A	nancymaae	QC	KV	-6	AE	5E	G	melas	HC	RV	÷G	TE	SE.	P.	cinereus	QC	KV	EG	VE.	AE.		hypophthal	ac	KV.	÷G	٨-	A+
C	syrichta	00	κv	-0	AE	TE	0	orca	HC	KV	-G	TE	SE	0	anatinus.	20	κv	EG	EE	AE	D	rerio	QC.	KV	-6	- 44	A-
N	A imurinus	QC	KV	-6	AE	TE		sinus	HC	κv	-G	TE	SE	5	camelus	QC	ĸv	AE	-6	AG	- 5	rhinocerous	QC	κv	-6	٧-	A-
0	garnetti	QC	KV	G	AE	TE	N.	asiaeorienta	HC	KV	G	TE	SE	P	coichicus	QC.	KV	EE	G	AG	E	electricus	:QC	KQ	I.E.	AG	AG
T	chinensis	QC	KV	+G	AE	TE	D	leucas	HC	KV	- G	TE	SE	G	gailus	QC	KV	EE	-6	AG	1	punctatus	QC.	KV	G	A-	A-
D	ordii	QC	KV	÷Ġ.	VE.	TE	M	monoceros	85	KV	÷G.	71	58	A	futgula	QC	KV.	VE.	-G	AG	T	fulvidraco	qc	MI	÷G	A-	Α-
1	jacutus	Q5	KV	-6	AE	TE	- 6 I	vexilifer	115	KV.	-G	TE	56	A	chrysaetos	QC	KV	AE	66	AG	- 5	salar	QC.	KV	66	5-	3-
N	d flaviventris	00	KV	-6	AE	SE	c	simum	0.5	RV	-6	AE.	AE.	c	anna	QC.	KV	AE	66	56	5	trutta	QC	KV	66	5.	A-
f.	f marmota	QC	KV	-G	AE	SE	E	asinus	ac	KV.	- G	AE	AE	¢	livia	QC	KV	AE	66	AG	0	mykiss	QC.	κV	-G	5-	A-
1	tridecemiin	QC	KV	+6	AE	58	E	caballus	ac	XV	-G	AE	AE.	A.	forsteri	QC	KV	AE	66	AG	0	kisutch	.QC	KV	-G	5-	A-
Ŧ	damarensis	QC	KV	-6	AE	TE	. P.	pardus	Q.C	×ν	-6	AE	TE	N	nippon	QC	κv	AE	50	AG	- P	reticulata	QC	κv	+6	A-	A-
c	lanigera	QS	KV	+6	AE	TE	1	canadensis	QC	ĸv	-6	AE.	TE	E	trailli	QC	KV.	AE	EG	AG.	- (P.	latipinna	QC.	KV	-G	A-	T +
c	porcellus	QC	KV	G	AE	TE	F	catis	ac	κv	÷G	AE	TE	P	filicauda	QC	KV	AE	EG	AG	х	hellerii	QC	κv	÷G	A-	A-
	galli	QC	KV	G	PE	TE		jubiatus	QC	KV.	-G	AE	TE		chrysocepha		KV	AE	EG	AG		couchianus	qc	KV	+G	A-	A-
H	glaber	QC	KV	-6	AE	TE	P.	vitulina	ac	κv	DG	A.E	TE		albicoffis	QC	ĸv	EE	EG	AG	х	maculatus	0.C	κv	-6	A-	Α-
N	A ochrogäster	QC	KV	-6	AE	TE	E.	weddellii	QC	KV	DG	AE	TE	¢	manedulaid	QC	KV	ĘΕ	68	AG	8	spiendens	ac	KV.	+6	Ε÷.	Τ-
c	griseus	90	KV	-6	AE	NE	N	schauinslan	qc	KV	06	AE	TE	T	guttata	QC	KV	EE	EG	AG	c	mili	QS	KV.	66	ME	AE

Supp. Fig. 4P

у-зуп.	βIII-tub.	-	Cor	related	pairs					Corri	elated	pairs					Com	elated	pairs					Corre	elated	pairs	ŝ.
	protein	y5.83	i y5 8	9 1 5 83	1 75 83	y5 83		protein	yS 83	y5 83	y5 83	y5 83	y5 83		protein	y5 83	y5-83	y5 83	-5 83	y5 83		protein	15 83	15 83	15.83	y5 87	1 75 B
Genus	residue Z-score	2 10.8	10,1	1.		算 卷 10.7	Genus	residue	20 441	449	17	19	1.6	Genus	tpeoes	22	10,445	445	140	n 4	Genus	species residue	22 441	107	145	15	21
	sapiens	QE.	QP	GP	VP.	EP		norvegicus	QD	9.0	GP.	VP-	EP		javanica	QE	QP	GP	VF	EP		striata	QE	EA	AA	AA	GA
P	troglodytes	QE	Q.P	6.0	VP.	EP	M	pahari	QD	QP	GP	VP.	EP		discolar	QE	QP	6#	VP.	EP	A	mississipple	QE	EA	AA	AA	GA
P	paniscus	QE	QP	GP	VP	EP	M	caroli	00	QP	OP	VP.	£P.	H	armiger	QE.	QP	GP	VP.	EP		muralis	QE	EA:	AA.	AA	GA
G	gorilla	0.E	QP	G.P.	VP.	EP	M	musculus	0.0	QP	GP	VP.	EP	E	fuscus	3.D	QP	GP	NP.	EP		carolinensia.	QE	EG	AG	AG	66
- p	abelli	QE	QP	GP	VP.	EP	0	princeps	QE	QP	6.	NP.	EP.	M	brandtii	QE	QP.	GP	VP.	EP	E.	vitticeps	QE	EA	AA	AA	GA
N.	leucogenys	QE.	QP	GP	VP.	EP	0	cuniculus	3.0	QP	67	٧₽	EP.		aegypticus	3.0	EP	G#	VP.	£P	T	elegans	QE	Q.A.	AA	AA	GA
	anubis	QE:	QP	GP	VF.	EP	C.	hircus	QE	Q.P	GF.	VP.	EP	5	araneus	QE	QP	GP	VP	EP	P	mucrosqua	QE	EA	AA.	AA	6.A
с	atys	QE	QP	6.6	VP.	EP	0	virginianus	Q.E.	QP	GP	VP.	EP	E	europaeus	00	QP	6#	VP.	ΕP	T	carolina	QE	TA	AA	AA	GA
M	fasciculario	91	QP	GP.	VP.	EP	. 8	taurus	10	Q.P.	GP	VP.	E.P.	C	asiatica	0.0	QP.	6.0	VP.	10	C	picts	3.D	TA	AA	AA	GA
c	sabaeus	QE	QP	GP	VP.	EP	8	bubalis	QE.	QP	GP	VP.	EP	£	telfairi	0.0	Q.P.	GP	VP.	EP	c	mydas	Q E	TA	AA	A.A	G/
T	gelada	3.0	QP	GP	.VP	EP	C	fecus	QE.	pp	GP	V#	EP.	T	menatus	QE.	QP	6#	NP.	EP.	X	tropicalis	3.0	1.	. A -	Ari	G-
. 10	tephroscele	3.0	QP	GP	VP	EP	c	dromedariu	0.E	pp	GF	٧₽	EP	- L	pfricana	QE	QP	G#	VP	EP	×	laevis	QE	4.	Α-	A-	6
	bieti	QE	QP	6P	VF	EP	v	pacos	QE	PP	67	VP.	EP.	5	harrisil	QE:	EA	GA.	VA	EA	N	parkeri	3.D	E-	A+	A:	G
	rosellana	QD	QP	6 P	VP	EP	1	obliquidens	HD	QP	GP	٧P	EP	M	domestica	10	EA	GA	YA	EA		bivittatum	QE	ŧG	AG	AG	60
C .	capucinus	Q.D.	QP	GP	VP.	EP	0	orca	HD	QP	GP	N.	E.P.		ursinus	3.0	EA	GA.	AV.	EA		unicolor	QD	16	AG	AG	G
5	bolivensis	QD	QP	GP	VP	EP	P	sinus	HD	QP	61	V.P	E.P.	•	cinereus	Q£	EA	6A	VA	EA	6	seraphini	QD	-G	AG	AG	60
	jatchus	QD	QP	GP	VP	EP	1000	asiaeorienta	HD	QP	G.P.	VP.	£.P.	0		QE	EA	AA:	AA	GA		chalumnae	QE	10.00	AQ	AQ.	
	syrichta	9.0	QP	0.P	VP.	Eb		feucas	HD	QP	GP	VP.	EP.	N	perdicaria	3.0	A.A.	AA.	44	GA.		calabarious	QP	NQ	DA.	AQ	
	coquereli	QE	QP	GP	VP.	EP		monoceros	HD	QP	6P	VP	EP.	5	camelus	QE	EA	AA	AA	GA.		oculatus	QD	50	DA.		
0	garnetti	Q£	QP	6P	VP	EP		vexilifer	HD	QP	GP	VP	EP	N	a share of the second second	QE	÷A	AA	AA	GA		kingsleyae	QE	LP	AP	AP	GF
	chinensis	QE	QP	GP	VP	EP		simum	QE	QP	GP	VP	EP.	P.	colchicus	QE	-A.	AA.	AA.	GA	1.1.1.1	formosus	Q.D		A.C	10222	
	ordii	QD	QP	61	VP	EP		atinus	QE	QP	6P	VP	EP	6	gallus	3,D	-A	AA	AA	GA		mexicanus	QD	-Q	AQ	AQ	
	(acutus	QE	QP	Q.P.	VP	EP		caballus	QE	Q.P	G.P.	VP.	£P.	•	platyrhysch	QE	0.0	AA.	AA	GA		nattereri	QD.		AQ	AQ	2000
	flaviventris	QE	QP	GP	VP	EP	P	pardus	QE	12P	GP	٧P	EP	A		QE	GA	AA.	AA	GA		hypophthai	QE	PQ.	AQ.	DA	
	tridecemlin	QE	QP	GP	VP.	EP	- P	concolor	QE	QP	64	VP.	EP			Q.E.	EA	AA	AA	GA		electricus	d0		AQ	100.00	
	damarensis	ap	QP	GP	VP	EP		canadensis	3.0	QP	GP	VP	EP		cherrug	91	E.A.	AA	A.A.	GA		punctatus	3.D	PQ	AQ	AQ	
	lanigera	QE.	QP	GP	VP.	EP		jubatus	QE	QP	GP	VP	EP	C	anna	2D	EA	AA.	AA	GA		fulvidraco.	QE	-0	AQ.	AQ	1.00
	degus	QE	QP	GP	VP	EP		vitulina	QE	QP	GP	VP	EP.	c	vociferus	QE	EA	AA	AA	GA		salar	QE	EA	AA	AA	64
	porcellus	10	QP	GF	VP	EP		weddellii	10		GP.	VP	EP.	N		90	EA	AA:	AA	GA		trutta	3.0	EA	44	AA	G/
	galik	QD	LP	GP	VP	EP		schauinslan	QE	9.0	GP	VP	EP		canorus	30	EA	AA	AA	GA		mykiss	3.0	-A	AA	AA	6/
	giaber	QD	0.0000	GP	VP	EP		rosmanus	QE	QP	GP	VP	EP	M		30	ET	AT	AT	GT.		kisutch	30	124	AA	AA	GA
	ochrogaster	QD	QP	GP	VP	EP		californianu	QE.	QP	GP	VP	EP	1	trailii	QE.	EA.	88	AA	GA		alpinus	QE	EA	44	AA	G/
	griseus	QD	0.000	GP	VP	EP	1.00	arctos	QE	QP	GP	NP.	EP		filicauta	QE.	EA	AA.	AA	GA		milli	QE	GP	AP	AP	ar
	snguiculatu	10	9.7	GP	VP	EP		putorius	QE	QP	SP.	VP.	EP.	N			EA	AA	AA	GA		typus	QE	QP	AP	AP	GF
	maniculatus	0.0	QP	GF	VP	EP		erminea	QE	9.0	GP:	VP	EP	C		30	EA	AA	AA	GA	18.	torazame	QE	£ P	AP	AP	GP
	leucopus	QD	QP	GP	VP	EP		lupus	QE	QP	GP	VP.	EP	c	moneduloid	QE	EA	AA	AA	GA							
M	auratus	Q.P	GP	GP	VP	E.F.	V	vulpes.	.91	QP	GP	NP.	E.P.	1.1	guttata	10	EA	AA.	AA	GA.							

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Page 32 of 32

Supp. Fig. 4Q

syn. ßIVa-tub				lated	pairs					Corre	elated	pairs					Corre	lated	pairs					Corre	elated	pairs	
proteir	n y54	ia ÿ	5 4a	y5 4a	₂ 5.4a	75.4a		protein	y5 4a	y5 4a	y5 4a	γ5 4a	y5-4a		protein	y5.4a	γ5 4a	y5.4a	y5.4a	75 4a		protein	y5 4a	₇ 5.4a	₁ 5 4a	y5 4a	-25.4
find Z-score		- C (C	65	5.9	. L 5.9	74 5.9 5.9	Genus	Ipedes	443	4	5 5	5 N	2 %	Genue	fp residue	58	46	H R	- 2	74	Genus	fesidue	58	***		5 L	23
H sapiens	6.1	633	ĒΥ	VV.	KV.	VV.	0	grismus	KV.	EV	vv	KV	VV.	U.S.	arctos	XV	EV	VV.	KV.	vv	5	formosius	KV.	Ξ¥	VI.	K1	AL
P troglodytes	KV	1	EV	vv	KV.	vv	M	unguiculatu	κv	EV.	vv	KV	.vv	- M .	putorius	KV.	EV.	vv	KV.	VV	A	mexicanus	KV.	EV	VI.	KI	AI
P paniscus	KV	们目	£¥.	VV	KV.	VV	- P	maniculatus	KV	EV	VV	KV.	VV.	M	erminea	KV.	EV	VV	KV.	VV	- P	nattereri	KV.	£Υ	VI.	KI	AL
6 gorila	KV	6	٤v	٧V	KV.	VV	M	avratus.	KV	EV	VV.	KV	NV	C	lupus	XV.	EV	VV	XV.	IV	0	clupeoides	KV.	EV	VI.	ĸı	AI
P abeli	XV	61B	ΞV	VV.	KV.	VV	R	norvegicus	KV	GV	VV.	KV.	VV	M	javanica	K.V.	EV	VV	XV.	VV	. р.	hypophthal	KV.	EV	VI.	KI	AI
H moloch	KV	6.15	EV	VV.	XV.	vv	M	pahari	KV	EV	vv	KV	VV.	P .	discolor	KV.	EV	VV.	KV.	vv	D	rerio	KV	EV	VI.	.61	AI
N Inscogenys	KV	88	EV	VV.	KV.	VV	M	caroli	KV	EV.	VV	KV.	VV.	H	armiger	KV.	EV	VV.	KV.	VV.	5	rhinócerous	KV.	EV.	VI	81	AI
P anubis	KV	1	EV	VV	XV.	VV	M	musculus	KV	EV	VV.	KV.	VV	M	natalensis	KV.	EV	VV	KV.	VV	E .	electricus	KV	EV	VI.	KI	AI
M leucophaes	K	1810	EV	VV.	XV.	VV	0	princeps	KV.	EV	VV.	KV.	VV	100	funcus	KV.	EV	VV	KV.	vv	1.5	punctatus	KA	EA.	VI.	KI.	AI
C atys	KV	1	ΕV	VV	XV.	VV	0	cuniculus	κv	EV	VV	KV.	VV.	M	brandtii	KV.	EV	VV	XV	VV	Ť	fulvidraco	×ν	EV	VI	81	AI
M nemestrina	KV	ÈŪ	EV	VV.	XV.	VV	5	scrofa	KV.	EV.	vv	KV	VV.		aegypticus	KV.	EV	VV.	RV.	vv	5	salar	RA	DA	VI	KI	AI
M mulatta	KV	1	EV	vv	KV.	VV	c	Nincus	KV	EV	vv	KV.	VV.	C 1	cristata	KV.	EV	VV	KV.	VV	5	trutta	RA.	DA	VI	KI	AI
M. fasciculians		έü	EV.	VV	KV.	VV	0	arres -	KV	EV.	VV	KV.	VV.	5	arametes	KV	EV	WV.	KV.	VV	0	mykits	RA	DA	VI	KI	- 41
C sabarus	KV.	1	EV	vv	KV.	VV	0	virginianus	KV.	EV	vv	KV.	VV.	Ε.	europaeus	KV.	EV	VV	KV.	VV		kilutch	RA.	DA	VI.	KI	A
T gelada	K.V	6 li	EV	VV	KV.	VV		tauries	KV.	EV.	VV	KV.	VV.		mintica	KV.	EV.	V.V	KV.	VV		formosa	EV.	EV	AL	81	A
P tephroscele			EV	VV	EV.	VV		mutus	KV.	EV	VV	KV.	VV		novemcinut	KV.	EV	AV	RV.	VV		reticulata	KV.	EV	VI	81	AI
R bleti	KV		EV	VV.	RV.	vv		buballe	KV.	EV	VV	KV.	VV		harristi	XV	EV	VV	KV.	VV		latipinna	XV.	EV	A1	RI	AI
A roxellana	KV	0.12	EV	VV.	KV.	VV		ferses	KV.	£V	VV.	KV	VV.		uninus	KV	EV	vv	KV.	VV		mexicana	KV.	EV	AL		AI
C capucinus	K.V		EV	VV.	×V.	VV	- 20	acutorostrat	8.1	EV	vv	KV.	VV		civereus.	KV.	EV	VV	KV.	VV		heleri	KV	EV	VI	RI	A
5 bolivensis	KV		EV.	VV.	XV	vv		obliquidens	KV	EV.	vv	KV.	VV		anatinus	KV	EV	VV.	KV.	VV		couchianus	EV.	EV	VE	81	A
5 aprila	KV		EV	VV.	XV.	vv		melas	KV.	EV	vv	KV.	WW	-	simenaia	KV	EV	VV.	KV.	VV		maculatus	KV.	EV	VI		AI
C jacchus	KV		EV	VV.	KV.	vv		orca	KV.	EV	vv	KV	VV		minussipple	KV	EV	vv	KV.	vv		variegatus	KV.	EV	VI	RI	AI
A nancymaae			EV	vv	80	vv		sinus	KV.	EV	vv	KV.	VV		muralis	KV.	EV	VV.	XV.	VV.		rubripes	KV.	EV	WI:	KI	AI
P coqueres	KV		EV	vv	XV.	vv		asiaeorienta	KV.	EV	vv	KV	VV.		carolinensis	KV	EV	vv	KV.	vv		armatus	KV.	EV	VI	KI	AI
M murinus			IV.	vv	XV.	vv		leucas	KV.	EV	vv	KV	VV		vittioeps.	KV.	EV	VV	KV.	vv		heterocitus	EV.	EV	VE	RI	AI
O garnetti	KV		EV	vv	×V.	vv		monoceros	KV	EV	vv	KV.	AV		bivittatus	KV	EV	vv	KV.	vv		latipes	KV.	EV	VI	K1	AI
T chinensis	KY		EV	VV.	KV.	vv		vexilifer	KV.	14	vv	KV	vv		mucrosque	KV.	EV	WV.	KV.	vv		testudineus		EV.	VI	Ki	AI
D ordii	KV.		EV	vv	×V.	vv		simum	KV.	EV.	vv	KV	vv		carolina	KV.	EV	vv	KV.	vv		splendens	KV.	EV	VI	KI	AI
1 jaculus	×.		EV.	vv	84	vv		asmus	KV.		VV	KV.	VV.	-	picta	KV.	EV	WV.	KV.	vv		niloticus	KV.	EV	VI	ĸ	AI
M flaviventria	KV		EV	vv	XV.	vv		caballus	×v.	EV.	vv	KV	vv		tropicalis	xv.	EV	vv	×v.	vv	100	burtoni	xv.	EV	VI	KI	AI
M marmota	KV		EV	VV	EV.	VV		canadensis	KV	EV.	vv	KV	VV		laevis.	KI.	EI	VV	KV.	vv		Lebra	EV.	EV	VI	KI	A
i tridecemin			EV	vv.	KV.	vv		catus	KV	EV	vv	KV	vv		bivittatum	KV.	EV	vv	KV.	vv		bergyita	KY	EV	VI	KI	AI
F damarense			EV	vv	EV.	VV		Jubatus	KV.	EV	vv	KV	WV		unicolor	KV.	EV	VV	XV.	AV		lucioperca	EV.	EV	VE	KI.	Â
	8.1		EV	VV	XV	VV		vitulina	KV.	EV	vv	KV	vv		seraphini		EV	vv	KV.	VV		10100000000000000000000000000000000000	KV.	EV	VI		AI
C lanigera	- KY		EV	VV	XV.	VV		weddelli	KV	EV	vv	KV.	NV		where the property states are	KV KV	EV	AL	MI	AL		crocea mili	KV.	EV		K1	- 21
O degus			2.2	12.57		100.0	100			12.27					chatumnae		10.07				1.00				vv	KV.	
N galii	KV		EV	VV	XV.	VV		schaunslan	KV	EV	VV	KV	VV	and the second s	calabarrous	KV.	EV	VI.	K1	AL	5	torazame	ΨV.	EV	4.4	KV.	. 41
H glaber	KV.		EV	VV.	KV.	VV		nosmanus	KV.	EV	vv	KV	. IV		oculatus	KV.	EV	VE	K1	AL							
M ochrogaste	r KV	6511	EV	VV	×ν	VV	1	californianu	KV.	E.A.	vv	KV	VV.	. P .	kingsleyan	KV.	EV	VI	KE	AL							