Evolution of the Genotype-to-Phenotype Map and the Cost of Pleiotropy in Mammals

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ABSTRACT Evolutionary studies have long emphasized that the genetic architecture of traits holds important microevolutionary consequences. Yet, studies comparing the genetic architecture of traits across species are rare, and discussions of the evolution of genetic systems are made on theoretical arguments rather than on empirical evidence. Here, we compared the genetic architecture of cranial traits in two different mammalian model organisms: the gray short-tailed opossum, *Monodelphis domestica*, and the laboratory mouse, *Mus musculus*. We show that both organisms share a highly polygenic genetic architecture for craniofacial traits, with many loci of small effect. However, these two model species differ significantly in the overall degree of pleiotropy, N , of the genotype-to-phenotype map, with opossums presenting a higher average N . They also diverge in their degree of genetic modularity, with opossums presenting less modular patterns of genetic association among traits. We argue that such differences highlight the context dependency of gene effects, with developmental systems shaping the variational properties of genetic systems. Finally, we also demonstrate based on the opossum data that current measurements for the relationship between the mutational effect size and N need to be re-evaluated in relation to the importance of the cost of pleiotropy for mammals.

KEYWORDS complexity; genetic architecture; marsupials

A central question in evolutionary studies is whether long-term adaptive changes depend critically on the genetic architecture of traits (Steppan *et al.* 2002; McGuigan 2006). Many different approaches have been taken to study this phenomenon in evolutionary biology, most notably the study of constraints to phenotypic evolution (Arnold 1992; Begin and Roff 2003), genetic lines of least evolutionary resistance (Schluter 1996; Marroig and Cheverud 2005), and nearly null spaces (Blows and McGuigan 2015). The general consensus is that the influence of the genetic architecture over long timescales depends on the degree of its stability (Lande 1979; Steppan *et al.* 2002). Genetic systems are evolvable and can be transformed by evolutionary processes (Pavlicev *et al.* 2008; Melo and Marroig 2015). The extent to which

genetic systems change during evolution is therefore essential to our understanding of the evolutionary consequences of the genetic architecture of traits.

The genetic architecture of traits has recently been studied on the level of the genotype-to-phenotype map [G-P map, *sensu* (Hansen (2006))]. G-P maps summarize the statistical relationship between individual genotypes and the phenotype, and are, therefore, a phenomenological treatment of development (Alberch 1991). A major component of G-P maps is the overall degree of pleiotropy (Falconer and Mackay 1996). Pleiotropy refers to the manifold phenotypic effects of a single locus (Stearns 2010). Interest in the degree of pleiotropy is justified by its effects on the direction and rate of adaptation. According to Fisher's geometric model (Fisher 1930), the proportion of advantageous mutations decreases as the mutational effect size increases. Orr demonstrated that this effect is exacerbated as the number of traits commonly affected by a locus increase, and therefore we should observe a significant slowdown in the rate of adaptation (Orr 2000). This phenomenon is referred to as the "cost of complexity" (Orr 2000). Because these models assume that every trait is affected by every gene, an increase in number of traits (*i.e.*,

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complexity) also means increase in pleiotropy, and hence the cost of complexity is, at the same time, the “cost of pleiotropy” (Wagner and Zhang 2011). The importance of the cost of pleiotropy to evolution depends critically on two main aspects of the genetic architecture of traits, namely the scaling of gene effects with pleiotropy and the degree of modularity of the G-P map (Wagner *et al.* 2008). The pleiotropic scaling of gene effects is a topic of considerable debate. In particular, three main models of pleiotropic scaling have been proposed to date. The invariant total effect model (ITEM) assumes that the total effect of a mutation is independent of the degree of pleiotropy (e.g., Orr 2000). As a consequence, the average *per trait* effect of a mutation is expected to decrease with increased pleiotropy (Wagner *et al.* 2008). The Euclidean superposition model (ESM), on the other hand, assumes that the per trait effect of a mutation is independent of the degree of pleiotropy (Wagner *et al.* 2008). Under ESM, the total effect of a mutation is expected to increase with increased pleiotropy. In both ITEM and ESM models, the rate of adaptation decreases with increased pleiotropy, leading to the cost of pleiotropy. However, empirical data has led Wagner *et al.* (2008) and Wang *et al.* (2010) to suggest that the previous two models might not apply to natural populations. According to these studies, the average per trait effect, and the total effect of a mutation, are both positively correlated with the degree of pleiotropy. In this case, an intermediate level of pleiotropy would yield the highest adaptation rate, suggesting that modular pleiotropy might actually facilitate adaptation (Wang *et al.* 2010).

Discussions around the degree of modularity of the G-P map are far less controversial. Numerous quantitative trait locus (QTL) studies have investigated the pleiotropic effects of individual genomic regions on skeletal morphology. The most common finding in these studies is that most QTL effects are modular, with different genomic regions affecting different sets of functionally and developmentally related traits (Kenney-Hunt *et al.* 2008), with a minority of QTL affecting the entire structure, being associated with overall size variation. In studies of the mandible, for example, most QTL affected either the mandible body or the muscle attachment regions of the ascending ramus (Cheverud *et al.* 1997; Mezey *et al.* 2000; Ehrich *et al.* 2003; Klingenberg *et al.* 2004; Willmore *et al.* 2009). Likewise, studies of cranial morphology indicate sets of QTL affecting either facial or neurocranial morphology (Leamy *et al.* 1999). Finally, studies encompassing the whole skeleton again found evidence for modular genetic effects on functionally and developmentally related trait sets (Kenney-Hunt *et al.* 2008). This modularity in the G-P map is considered a result of selection favoring the evolvability of the complex phenotype, and also an important source of mitigation to the overall cost of pleiotropy (Welch and Waxman 2003; Wagner *et al.* 2008). Disruption of this organization is often seen as maladaptive (Wagner and Altenberg 1996).

While evidence in favor of a modular genetic architecture of skeletal traits in mammals is abundant, studies have focused almost exclusively on rodents and primates (Kenney-Hunt

et al. 2008; Roseman *et al.* 2009), and comparisons across taxa are rarely carried out. As a consequence, discussions of the extent to which genetic systems underlying skeletal traits change throughout evolution remains cast on theoretical grounds (e.g., Pavlicev *et al.* 2008).

With decreased cost of high-throughput genotyping, we can now directly compare G-P maps between species. Marsupials have recently emerged as particularly interesting candidates for genetic mapping studies, due to their high levels of phenotypic integration among cranial traits and their distinct patterns of cranial development (Smith 1997; Porto *et al.* 2009, 2015; Shirai and Marroig 2010). In particular, dissecting the differences in cranial architecture between placentals and marsupials can help us determine whether developmental context has a significant impact on the genetic properties of these systems, and, ultimately, in the adaptive dynamics of the species.

Here, we use the intercross of two partially inbred strains of the gray short-tailed opossum, *Monodelphis domestica* (Vandeberg and Williams-Blangero 2010), to map cranial traits. This species was not only the first marsupial selected for genome sequencing (Mikkelsen *et al.* 2007), but has also served as a model organism for developmental studies (Smith 1994, 1997) and several health conditions, such as skin and eye cancer (Ley *et al.* 1991), hypercholesterolemia (Chan *et al.* 2010), nonalcoholic steatohepatitis (Chan *et al.* 2012), and spinal cord injury (Mladinic *et al.* 2005). Our study is divided in five main parts. We start by using a next-generation sequencing (NGS) approach to generate molecular markers that are then correlated to individual differences in cranial morphology within the F₂ intercross population of a strain cross. We then identify QTL contributing to individual differences in cranial morphology, using statistical methods tailored to complex pedigrees. Once QTL are identified, we characterize the G-P map of cranial traits, and establish the relationship between genetic pleiotropy and mutational effect sizes. We also estimate the QTL-based genetic variance/covariance matrix, and test it against several modularity hypotheses, and the results of our earlier quantitative genetic study of the broader population from which the parental strains were selected. Finally, we compare the genetic architecture of cranial traits between opossums and mice. Via that comparison, we investigate whether these two model species differ significantly in their G-P map, with important consequences for their adaptive dynamics.

Materials and Methods

The ATHH × ATHL opossum intercross

The opossum experimental population results from an F₂ intercross of two partially inbred strains, atherosclerosis high (ATHH) and atherosclerosis low (ATHL) (Chan *et al.* 2010), produced at the Texas Biomedical Research Institute. ATHH and ATHL were selected on the basis of their lipemic responses to increased cholesterol and fat in their diet (HCHF diet). Animals from the ATHH strain have increased likelihood

of developing hypercholesterolemia when fed the HCHF diet, while ATHL animals are unresponsive. These strains have been partially inbred from nine founder animals collected in Exu, Brazil (Vandeberg and Williams-Blangero 2010). The mean inbreeding coefficients are 0.75 for ATHH and 0.91 for ATHL; the kinship coefficient between the two strains is 0.24. Despite the close relatedness of the two strains, skeletal differences between them are large; we previously demonstrated that they are even larger than differences observed among several other marsupial species (Porto *et al.* 2015). It should be noted that these skeletal differences are the result of random fixation of distinct alleles in different strains due to inbreeding, as skeletal traits are not associated with blood cholesterol levels. Details of the laboratory populations and the husbandry protocol are described in Chan *et al.* (2010). We measured skeletal traits on 576 animals from the ATHH $\times$ ATHL cross. A total of 12 P₀, 158 F₁, and 406 F₂ animals are included. All experimental protocols were approved by the Texas Biomedical Research Institute Institutional Animal Care and Use Committee.

Genotype-by-sequencing

We used genotype-by-sequencing (GBS) to discover single nucleotide polymorphisms (SNPs), and to genotype the family members for thousands of markers (Elshire *et al.* 2011). Briefly, genomic DNA was extracted from liver tissue using Qiagen DNeasy kits, and digested using a restriction enzyme (*Pst*I) that produces fragments with sticky end overhangs. Barcoded adaptors were ligated onto these fragments to identify each individual in a population (Supplemental Material, Table S1). After adaptor ligation, samples were combined into pooled libraries (96-plex). Libraries were sequenced on six lanes of the Illumina HiSeq2000 at the Institute for Genomic Diversity (IGD-Cornell University), producing a total of 1.167 billion reads. The unique sequence tags identified among the sequencing reads were then aligned to the most recently published *M. domestica* reference genome (MonDom5, 2006) using BWA 0.7.8-r455 (Li and Durbin 2010). A total of 76.4% of those tags were aligned to unique positions, while 7.6% were aligned to multiple positions, and 16.9% could not be aligned. Using only tags that aligned to unique positions, we called SNPs for sequences well-represented in the sequencing reads using the TASSEL 3.0.166 pipeline (Bradbury *et al.* 2007).

In order to minimize the effects of sequencing error, a series of filters was applied to the SNP calls using TASSEL 4.0 (Bradbury *et al.* 2007). We only retained biallelic SNPs, belonging to sites with <20% missing data, and that were mapped to one of the eight pairs of autosomes. Any individual with >20% missing genotypes was excluded from the analysis, removing a total of four individuals. Sites with minor allele frequency lower than 0.05 or genotype classes with < four individuals were also excluded, and we filtered the resulting SNPs for significant deviations from Hardy-Weinberg equilibrium ($P < 0.001$) using plink v.1.07 (Purcell *et al.* 2007). Finally, 531 individuals with 3696 high-quality SNPs were obtained for downstream data

analysis. Given the opossum genetic map size (890 cM) (Samollow *et al.* 2004), we estimate the average intermarker distance in this dataset to be <0.25 cM, which is sufficient resolution for the genetic mapping conducted here. We present the list of markers and their corresponding locations in the Table S2.

Craniofacial traits

Opossum carcasses were frozen immediately after necropsy and then later skinned and dried. Dermestid beetles were used to deflesh the carcasses. Three-dimensional coordinates were then recorded in each skull for 36 landmarks using a Microscribe digitizer (Figure 1). Details of this procedure for measuring specimens are presented in several articles (Cheverud 1995; Marroig and Cheverud 2001; Porto *et al.* 2009). Thirty-five linear measurements were then calculated from the 3D coordinates (Table S3) in order to maintain consistency with previous studies. This set of measurements is homologous to those collected in several other mammalian groups (*e.g.*, Porto *et al.* 2009). Before data analysis, outliers were removed from the craniometric dataset using SYSTAT 11.0. Similarly, measurement repeatabilities were calculated for each trait (Lessels and Boag 1987), and any trait with a repeatability lower than 0.9 was removed from the dataset. Trait-specific QTL mapping of these traits proceeded as detailed below based on the curated database of skull measurements.

QTL mapping for craniofacial traits

We performed trait-specific QTL-mapping using the MIXED procedure in SAS, following Wolf *et al.* (2011). Marker positions were assigned additive genotypic scores -1 (AA), 0 (Aa), and $+1$ (aa), and dominance genotypic scores 1 (Aa) and 0 (AA, aa). Missing genotypes were imputed using TASSEL 4.0 (Bradbury *et al.* 2007). The genetic mapping full model had sex, logarithm of age (days), population structure, and direct genetic effects (additive and dominance), as fixed effects, and kinship as the random effect. Population structure and kinship matrices (Kang *et al.* 2008) were estimated from marker data using TASSEL 4.0 (Bradbury *et al.* 2007). To prevent excessive loss of degrees-of-freedom, we only retained matrix eigenvectors explaining at least 1% of the total variation when fitting the mixed model. The genetic mapping full model was then compared to a null model with no direct genetic effects. We compared the fit of the two models using a likelihood ratio test. LOD scores were calculated as the $\log_{10}$ of the likelihood ratio, when comparing the full model to the null model. Bonferroni corrected genome-wide significance thresholds were then calculated based on the effective number of markers (M_{eff}) (Gao *et al.* 2008). M_{eff} was calculated as number of principal components that together explain 99.5% of the total marker variation (Gao *et al.* 2008). QTL positions were determined by the site with the highest LOD. QTL confidence intervals (CI) were defined as the regions within one LOD drop-off from the main peak, while taking into account the possibility of residual genetic

Figure 1 Landmarks (34) and linear distances (35) on the ventral and lateral view of a *M. domestica* cranium. Landmarks are placed at widely used anatomical features and suture intersections.

variation segregating within peaks due to the partially inbred status of the two strains.

Degree of pleiotropy, N

Trait-specific QTL that cluster together along the genome were tested to determine whether the null model of pleiotropy can be rejected in favor of separate, distinct QTL. This test uses the multivariate method proposed by Knott and Haley (2000), and is described in detail by Ehrich *et al.* (2003). Briefly, the determinant of the residual sum of squares and cross product matrix is compared between two multivariate models, one in which all trait-specific QTL are assumed to fall at a common site, and another that assumes separate peaks. A χ^2 statistic is then calculated based on the following formula:

$$\chi^2 = - \left\{ \text{d.f.} - \frac{1}{2}(n_{\text{traits}} - 1) \right\} \times \ln \left(\frac{|\text{SSCP}_1|}{|\text{SSCP}_p|} \right)$$

where d.f. is degrees of freedom, $|\text{SSCP}_1|$ represents the determinant of the residual sums of squares and cross products of the model assuming separate peaks, and $|\text{SSCP}_p|$ represents the determinant of the residual sums of squares and cross products of the pleiotropy model. In both cases, SSCP matrices are calculated using all traits, regardless of statistical significance. χ^2 statistics surpassing the critical χ^2 value ($P < 0.05$) were considered as rejecting the null hypothesis of pleiotropy. It should be noted that this pleiotropy test is biased in two relevant ways. First, pleiotropy is the null model, and failure to reject it is quite distinct from the acceptance of pleiotropy. Second, failure to reject the single peak model in favor of separate peaks will create a small bias in the distribution of peak probability values that are used in the downstream analyses, since the probabilities are not necessarily being observed at the marker with strongest relationship with a particular trait. However, both of these biases also occur for the mouse QTL results, and should not impact any comparison made between the two species.

Once the pleiotropic QTL were identified, it became possible to estimate their degree of pleiotropy, N . Most QTL studies define N as the number of traits affected by a locus at the genome-wide significance threshold (Wagner *et al.* 2008; Wang *et al.* 2010). In a QTL scan involving thousands of loci, this measurement of pleiotropy becomes overtly conservative. An overtly conservative approach might be useful when the false positive rate needs to be controlled at all costs (e.g., candidate gene approaches). It is less useful when dealing with the genetic architecture of morphological traits, as it leads to underestimation of the true number of traits affected by each QTL. Our measurement of N treats the identified QTL peaks as protected peaks, and calculates N as the number of traits significantly affected by a QTL at the pointwise 5% significance threshold at the peak marker.

Total effect T_E of a QTL, and relationship with pleiotropy

Evolutionary theory predicts that the N of the G-P map should affect the distribution of QTL effects (Wagner *et al.* 2008). To investigate whether this is the case for opossums, we calculated a standardized additive effect vector for each QTL by dividing the additive genotypic value of each trait ($|a|$) by the phenotypic SD of the trait (Kenney-Hunt *et al.* 2008). We then calculated two measurements of total effect. The restricted effect T_{RE} of a QTL was defined as the Manhattan distance spanned by all traits with significant additive effects at peak marker (Hermisson and McGregor 2008). The global effect T_{GE} of a QTL was defined as the Manhattan distance spanned by all traits at peak marker, regardless of significance (i.e., the entire vector). In both cases, the estimate of total effect can be described by the equation:

$$T_E = \sum_i^n |A_i|$$

where T_E refers to total effect, n refers to the number of traits (restricted or global), and A is the standardized additive

genotypic value of trait i . The preference for Manhattan distances is justified by the undesired effects of multiple mutations on Euclidean distances (Hermisson and McGregor 2008).

Once estimates of total effect T_E and N were calculated, we fitted a power function to our data using nonlinear regression models implemented in SYSTAT 11.0. Our model had the form $T_E = aN^b$, where a and b are constants to be estimated. CI for the constants were calculated using SYSTAT 11.0. We then evaluated the statistical significance of the relationship between these two variables through a permutation test. In this permutation test, observed T_E and N values were randomly assigned to 24 hypothetical loci (1000 times), and a null distribution of power functions was estimated based on those permuted datasets. These null power functions represent the pleiotropic scaling of gene effects that would be expected given no biological relationship between these two variables, based on a certain number of QTL.

It is worth noting that the superposition model of pleiotropic effects predicts a linear regression between these two variables ($b = 1$) (Wagner *et al.* 2008). Significant deviations from 1 imply the need for alternate models of pleiotropic scaling of gene effects.

QTL-based G- matrix

While ignoring epistasis, we estimated the QTL-based genetic variance/covariance matrix (G) as:

$$\sigma_x^2 = \sum_i 2p_i q_i \alpha_{i[X]}^2$$

$$\sigma(X, Y) = \sum_i 2p_i q_i \alpha_{i[X]} \alpha_{i[Y]}$$

where i refers to the genetic locus, σ_x^2 is the additive genetic variance for trait X , $\sigma(X, Y)$ is the additive genetic covariance between traits X and Y , p_i is the major allele frequency of locus i , q_i is the minor allele frequency of locus i , and α_i is the average effect of an allele substitution for locus i (Kelly 2009). Once calculated, we then compared G with previously published estimates of G and P (Porto *et al.* 2015) for opossums using random skewers (Marroig and Cheverud 2001).

This comparison of G with previous estimates is important in the context of sampling error. Since detected QTL likely represent only a fraction of the genetic variants segregating in the opossum population, our estimate of G contains a relevant amount of sampling error based on incomplete identification of true QTL. Given that sampling error reduces the overall similarity between matrices that share a covariance structure (see Figure S2 in Porto *et al.* 2015), observing high similarity between matrices is indicative of a high degree of accuracy in the G estimate.

To more explicitly characterize the dimensionality of the genetic signal in our G estimate, we calculated its eigenvalues and compared them to sampling error distributions of eigenvalues (see Nadakuditi and Edelman 2008 for a discussion on high-dimensional signal detection). We estimated the

inherent sampling error in G, given this intercross design, through the use of a random permutation approach. In particular, we randomly permuted the rows of the phenotypic data (1000 iterations), breaking up the relationship between phenotype and genotype. For each iteration, we calculated noise-based α_i at the same marker locations as in the original G. Based on the noise estimates of α_i , we calculated noise G-matrices, and determined their variances along each principal component rank. These sampling distributions of noise variances along each principal component rank were then compared to the observed eigenvalues of G. Whenever the eigenvalues of G were larger than 95% of the noise variances, we considered that the principal component in question presented significant additive genetic variation.

Modularity in G

We assessed modularity patterns in G by correlating its standardized version (*i.e.*, the genetic correlation matrix, G_{corr}) with theoretical matrices based on functional/developmental relationships among traits. Details of this procedure can be found in Marroig and Cheverud (2001) and Porto *et al.* (2009). Briefly, nine modularity hypotheses at different hierarchical levels were tested against G_{corr} , and significant matrix correlations were considered as evidence for the presence of cranial modules. Results from these modularity tests were then compared to results obtained in multiple studies of cranial modularity among mammals (Marroig and Cheverud 2001; Porto *et al.* 2009, 2013; Shirai and Marroig 2010; Garcia *et al.* 2014).

While it is outside of the scope of this manuscript to review the methods currently being used for the detection of modular patterns in correlation matrices [see Melo *et al.* (2016) for a review], it is worth noting that this method for detection of modularity is, at its core, equivalent to a Student's t -test comparing the within- and between-module correlations. It also has appropriate type I and II error rates, given the sample sizes reported here, as evidenced in a recent assessment of error rates in correlation-based methods (Garcia *et al.* 2015).

Comparing N between opossums and mice

To compare the genetic architecture of craniofacial traits across different model species of mammals, we used an independently assembled mouse dataset as a source of comparison. The mouse dataset used in this study is being submitted independently from this manuscript, and results from the 34th generation of an advanced intercross (AIC) of two inbred strains of laboratory mice, large (LG/J) and small (SM/J) (J. M. Cheverud, K. Weiss, L. Geleski, C. Percival, and J. Richtsmeier, unpublished data). The reason we used QTL detected in the 34th generation of this AIC is twofold. First, LG/J and SM/J were selected for large and small body size at 60 days of age (Kenney-Hunt *et al.* 2008). Selection in body weight leads to indirect responses in craniofacial traits, causing alleles with similar signs to be grouped into linkage blocks in the F_2 , and biasing the underlying distribution of pleiotropic effects. By using the 34th generation, most of the

Table 1 Pleiotropic QTL identified in the opossum F₂ intercross

QTL name	Focal Trait	N (Pointwise 5%)	Chromosome	Peak LOD	Peak Position (bp)	CI (bp)
sk.1	MTPNS	3	1	4.20	111,431,571	104,147,886
sk.2	PTAPET	14	1	4.41	295,047,253	247,887,126
sk.3	ISPNS	17	1	6.38	728,311,971	727,542,580
sk.4	NSLZI	8	2	4.04	404,691,454	400,155,973
sk.5	PMZS	10	2	4.98	483,162,151	481,501,539
sk.6	PMZS	5	3	4.38	286,462,644	281,791,986
sk.7	PMZI	6	3	3.99	445,347,789	429,875,987
sk.8	BAEAM	12	4	5.45	315,539,735	314,846,945
sk.9	MTPNS	6	4	4.21	356,712,488	354,312,579
sk.10	BRAPET	14	4	5.00	385,399,261	385,052,987
sk.11	PMMT	22	4	3.96	412,216,124	411,750,315
sk.12	BAEAM	20	5	4.16	115,810,416	114,931,736
sk.13	ZSZI	10	5	4.04	249,404,229	246,992,939
sk.14	APETTS	8	6	4.21	73,725,067	71,330,777
sk.15	OPILD	18	6	4.17	147,387,595	136,407,337
sk.16	LDAS	3	6	4.04	244,021,141	242,148,570
sk.17	ISPNS	20	6	4.24	290,895,570	288,819,489
sk.18	APETTS	10	7	5.41	55,150,735	53,025,774
sk.19	PTBA	15	7	4.07	78,429,479	77,488,388
sk.20	BRAPET	11	7	4.18	189,931,478	186,020,237
sk.21	PMZI	10	7	4.15	255,363,329	254,783,168
sk.22	NSLNA	9	8	4.72	7,723,894	7,635,127
sk.23	APETBA	24	8	5.77	108,158,525	92,722,464
sk.24	PMZI	10	8	4.36	268,086,089	266,335,545

Focal trait refers to the trait with highest LOD at that location. *N* was measured as the number of traits associated with the QTL at the pointwise 5% level. Positions correspond to genomic coordinates obtained from the most recent *Monodelphis* genome assembly (monDom5).

QTL have been reduced to single variants, and we can simulate how they would behave in a F₂ generation in which variants are grouped randomly in blocks, as is the case for opossums. Second, in this generation, murine skulls were measured in a way that can be reproduced based on the opossum 3D landmarks. The degree of colinearity among the selected cranial traits is relevant when estimating the degree of pleiotropy, since traits that are collinearly related will tend to show higher average pleiotropy. By using homologous measurements, we are able to directly compare the genetic architecture of cranial traits between the two species. Details of the mouse laboratory population and the husbandry protocol are described in Norgard *et al.* (2011). The craniometric dataset used to detect murine QTL corresponds to 10 cranial traits measured in 1139 animals from the LG/J and SM/J intercross (Table S4). These traits were replicated in our opossum mapping population, and QTL mapping for this homologous opossum dataset followed the previously described methods. All analyses were carried out following the protocol described in the previous sections.

One of the challenges of using the mouse F₃₄ as a source of comparison to an opossum F₂ relates to the size of linkage blocks and its effect on pleiotropy estimates. An AIC, in its 34th generation, has accumulated recombination events, and has, therefore, considerably smaller linkage blocks than an F₂. We expect the linkage blocks in the F₃₄ to be (1/17) the size of similar blocks in the F₂ at short mapping distances. The smaller blocks imply that a lower number of variants will be in linkage in each QTL. As such, it would not be surprising to find differences in pleiotropy between these two datasets. Therefore, for our comparison of *N* to be meaningful, we controlled for the amount of

recombination occurring in each cross, and simulated *N* of the F₃₄ when in a F₂ condition (*i.e.*, in which less recombination events have occurred). In order to simulate *N* of mice in the opossum F₂ condition, we created a pleiotropy vector for each F₃₄ QTL, in which traits that are affected by the QTL receive a value of 1, with arbitrary sign, and a value of zero otherwise. Each of these QTL was then randomly placed in a hypothetical genetic map, the exact size of the opossum map (890 cM), using a uniform distribution. Since peaks that are >16 cM apart will typically be detected as separate [average interpeak distance = 16 cM (Kenney-Hunt *et al.* 2008)], we divided this hypothetical genetic map into 16 cM linkage blocks, and, whenever QTL peaks fell within the same block, their pleiotropy vectors were combined into a linked QTL, therefore simulating two or more QTL in linkage. We combined pleiotropy vectors within each block by their element-wise sum. The *N* for each linked QTL was then calculated as the number of traits that have values different from zero in the linked pleiotropy vectors. We repeated this whole procedure 1000 times, and calculated the expected distribution of pleiotropic effects in a F₂ population of mice presenting the same amount of recombination as observed in the opossum F₂ population. If the observed *N* in opossums exceeded 95% of these simulated mouse F₂ values, we considered its *N* to be significantly higher. All simulations were run in the R statistical programming language (R Development Core Team 2010) using programs written by the authors.

Data availability

The authors state that all data necessary for confirming the conclusions presented in the article are represented fully

Figure 2 (A) Regression of T_{RE} on the number of traits, N , affected by a QTL. Note that the power exponent (0.94) is not significantly different from 1, in accordance with the superposition model of pleiotropic scaling. (B) Regression of T_{GE} on the number of traits N affected by a QTL. Note that the power exponent (0.426) is significantly different from 1, rejecting the superposition model of pleiotropic scaling. Null expectations for the relationship between T_{RE}/T_{GE} and N are illustrated as gray lines (1000 iterations).

within the article. Data for this manuscript have been deposited at Figshare: https://figshare.com/articles/Data_-_Genetics_-_Porto_et_al_2016/4055961.

Results

Opossum craniofacial traits

Basic statistics of all opossum craniofacial traits are shown in Table S3. The phenotypic variance/covariance matrix is also reported in Table S5, after correction for the effects of sex and age. This matrix is very similar to those observed in natural populations of marsupials (Table S6), and to the matrix estimated for the Texas Biomedical Research Institute colony as a whole (average vector correlation = 0.88; Porto *et al.* 2015). The results obtained in this study should therefore be applicable to *Monodelphis* species in nature.

Opossum QTL peaks

We detected a total of 42 individual-trait QTL (Table S7). Formal tests for pleiotropy combined these individual-trait QTL into 24 pleiotropic QTL (Table 1). The mean LOD score of these pleiotropic QTL is 4.52, with trait IS-PNS having the highest LOD (6.38). CI were generally large in opossums, varying from 0.4 to 48.4 Mb (mean = 11.8 Mb, median = 11.2 Mb). Identification of candidate genes within those CI is complicated by their large size.

In terms of the magnitude of effects, standardized additive genotypic values ($|a|/SD$) calculated at peak LOD varied from 0.002 to 0.598 SD units, with an average value of 0.238 SD units. This average is not significantly different from previously reported values for mice ($t_{842} = -0.958$, $P = 0.338$, Kenney-Hunt *et al.* 2008). Dominance relationships varied considerably among the QTL, when following the classification provided by Kenney-Hunt *et al.* (2006). In particular, 32.4% of the QTL

were codominant at the focal trait ($-0.5 < d/a < 0.5$), 38.2% had one dominant allele ($0.5 < |d|/|a| < 1.5$), 11.8% showed considerable overdominance ($1.5 < d/a < 2.5$), and 17.6% were highly overdominant ($d/a > 2.5$) for trait size. We did not detect any underdominance or strong underdominance in this cross. Finally, standardized dominance deviations ($|d|/SD$) calculated at peak LOD varied from 0.04 to 0.656 SD units, with an average value of 0.2 SD units.

Relationship of N with total effect T_E

The N value obtained from the opossum QTL dataset is presented in Table 1. This distribution has a mean value of 11.88, and a SD of 5.88. A linear regression of the LOD peak value against N fails to detect a significant association between these two variables ($F_{1,22} = 2.2$, $P = 0.15$), indicating a lack of evidence that statistical power increases with N .

Interestingly, the dependence of the total effect T_E on N varies according to how we measure total mutational effect, restricted T_{RE} , or global T_{GE} (Figure 2). The total effect T_E is linearly increasing with pleiotropy when using the restricted T_{RE} ($b = 0.94 \pm 0.13$, Figure 2A), in accordance with the superposition model of pleiotropic effects. When using the global T_{GE} , our estimates of the exponent b are significantly lower than one ($b = 0.426 \pm 0.08$, Figure 2B), leading to a rejection of the superposition model of pleiotropic effects (95% CI of $b = 0.256 < > 0.596$).

In both cases, the observed relationship between T_E and N is significantly different ($P < 0.01$ for both a and b constants) from the null expectation derived from the permutation test (Figure 2, A and B, gray lines).

Modularity in the QTL-based estimate of the G -matrix

The QTL-based estimate of G indicates that additive genetic variation accounts for 48% of the total cranial variation in this

Figure 3 (A) Genetic correlation matrix heatmap. The order of traits can be seen in Table S3; (B) Frequency distribution of trait-specific narrow-sense heritabilities; (C) Percent genetic variance explained by each principal component of G with additive genetic variance above random expectation (see Figure S1 for details).

intercross (Figure 3A). While trait heritabilities are generally moderate (Figure 3B), most of the genetic variation is concentrated in a few dimensions, with allometric size accounting for 68% of the total genetic variance, and the first nine (out of 35) principal components (PC) of G accounting for 96% of total genetic variance (Figure 3C). These first nine PCs are also PCs that have significantly more variance than would be expected given the amount of measurement and sampling error observed in this cross (Figure S1). This number can be interpreted, therefore, as the minimum dimensionality of genetic variation in skull traits in this cross.

Consistent with the multivariate distribution of genetic variation, the overall magnitude of genetic association among traits is high, and in line with previous studies of cranial morphology among marsupials (mean $r_g^2 = 0.31$) (Porto *et al.* 2009, 2015; Shirai and Marroig 2010).

The genetic correlation matrix (G_{corr}) presented no significant correlation with any of the nine modularity hypotheses (Table 2), indicating that hypothesized within-module correlations are not significantly higher than between-module correlations. Since this is an essential premise of modularity, these tests indicate that the pleiotropic patterns of gene effect show no evident modular organization in opossums. Removing allometric size variation (Porto *et al.* 2013) from G_{corr} does not change this result (results not shown). Finally, we also found that G presents substantial similarity to a G-matrix reported in previous studies (mean vector correlation = 0.88, $P < 0.001$, Table S6), and also to the P of this intercross (mean vector correlation = 0.89, $P < 0.001$, Table S6), suggesting that genetic association among traits can be predicted from phenotypic associations.

Comparing opossums and mice

The average N for the murine F_{34} dataset is of 3.74 traits per QTL. Not surprisingly, the distribution of pleiotropy values obtained for the 1000 simulated mouse F_{2s} is significantly higher than in the F_{34} (Figure 4, $P < 0.001$), with a mean value of 4.725, and a SD of 0.236. This increase in pleiotropy in the simulated F_2 condition is an expected consequence of merging of several F_{34} QTL into a single large F_2 -sized linkage blocks.

When using the homologous cranial dataset, the opossum F_2 presents an even higher degree of pleiotropy than the simulated mouse F_{2s} ($N = 6.286$, $P < 0.001$). This result is robust to assumptions regarding the size of linkage blocks, since doubling the average size of the blocks in the simulated mouse F_{2s} to 32 cM still leads to the rejection of the null hypothesis of equal degrees of pleiotropy N ($P < 0.05$).

Discussion

Our results indicate that G-P maps can change considerably during evolution, even without substantial changes in the underlying genetic makeup, supporting the idea that development may play a significant role in shaping the G-P map (Alberch 1991; Salazar-Ciudad and Marin-Riera 2013). While rodents and marsupials share many of their genes (Mikkelsen *et al.* 2007), and present substantial similarities in their overall cranial structure, they also present substantial differences in the G-P map of cranial traits. They share similarities in the sense that the genetic architecture of cranial traits is highly polygenic, and most variants have fairly small effect (~ 0.23 SD), even though that distribution is far from

Table 2 Matrix correlation between G_{corr} and hypothetical modularity matrices (see Porto *et al.* 2009 for details)

Module	Matrix Correlation	<i>P</i>	Modularity Ratio
Oral	0.08	0.22	1.19
Nasal	0.09	0.15	1.32
Zygomatic	−0.07	0.81	0.74
Vault	−0.03	0.59	0.95
Base	−0.01	0.56	0.95
Face	0.01	0.48	1.01
Neurocranium	−0.05	0.63	0.93
Neuro-face	−0.04	0.79	0.96
Total	0.03	0.30	1.04

P, probability; Modularity ratio, Ratio between the within-module correlations and between-module correlations.

being consistent with the infinitesimal model (Lynch and Walsh 1998). They are substantially different in the overall N , which is higher among opossums, and in the degree of genetic modularity, which is higher among mice. We support that assertion by showing that the N estimated for QTL detected in an F_2 intercross population of opossums is significantly higher than that obtained by simulating F_2 intercross populations of mice having the same genetic map size. This simulation protocol is important for two reasons. First, since mouse QTL were originally identified in the 34th generation of an AIC, these loci will tend to have a lower number of genetic variants in linkage per QTL than would be observed in the F_2 condition. The lower the number of variants in linkage per QTL, the lower the expected degree of pleiotropy of such loci. Therefore, by simulating how these QTL would behave in a F_2 condition, we corrected for any bias that might have been present in our original F_{34} estimate of N . Second, by simulating mouse F_2 s 1000 times, we derived a distribution of N against which the opossum N could be tested. This distribution simulates the N that we would have observed if we had measured 1000 F_2 intercrosses of mice.

While the observed differences in pleiotropy are robust to the underlying assumptions, it is still particularly important to clarify what is meant by this term. The definition of pleiotropy is subject to considerable controversy, and tends to vary significantly across studies (Flint and Mackay 2009; Stearns 2010). Most studies agree with defining pleiotropy as the multiple phenotypic effects of a single locus. Disagreements usually arise from the definition of locus. Should we define it as a single nucleotide, a gene, or a haplotype? Here, we follow Ludwig Plate's original definition (Stearns 2010), and define pleiotropy as the manifold phenotypic effects of a single "unit of inheritance". In QTL studies, the unit of inheritance is the haplotype, since QTL offer no guarantee that single variants are the ones responsible for the observed effect. In fact, the F_{34} intercross population of mice used in this study originally presented several variants in strong linkage in the F_2 generation, emphasizing that QTL peaks are often composed of multiple single nucleotide variants. The same seems to hold true for laboratory strains of *Drosophila melanogaster* (Flint and Mackay 2009). While the definition of pleiotropy has important implications for evolutionary studies themselves, the possibility of multiple

Figure 4 The frequency distribution of N obtained by simulating 1000 mouse F_2 populations. Mouse F_2 values present the exact same genetic map size as the opossum F_2 . Note the higher average N of opossums when compared to the mouse F_2 simulations.

variants in strong linkage disequilibrium does not negate the importance of the difference in N we observed between opossums and mice. Given that we used simulations to force both genetic maps to present the same amount of recombination, there are two possible explanations for the observed pattern. Either opossums show some tendency for variants affecting different skull regions to be preferentially bound together in linkage blocks, a process that cannot reasonably be explained under quantitative genetic theory, or it suggests that development might play a significant role in shaping the pleiotropic range of gene effects, a considerably more reasonable hypothesis. Context-dependency of gene effects has been shown in multiple studies (Pavličev and Cheverud 2015), and our results emphasize the need for a better understanding of how changes in developmental context might substantially alter the shape of the G-P map, and ultimately affect the evolutionary dynamics of the species (Marroig *et al.* 2009).

Changes in N and its relationship to the mutational effect size should have substantial effects on the rate of adaptation, the so called cost of pleiotropy conundrum (Orr 2000; Wagner and Zhang 2011). In particular, the opossum shows conflicting evidence with regards to the cost of pleiotropy. While the restricted effect T_{RE} measurement has the total effect scaling linearly with N , the global effect T_{GE} shows a significant reduction in per trait effect with increased pleiotropy. Under a true ESM model of pleiotropic scaling of gene effects, both measurements of total effect should render the exact same results, as one would expect T_{GE} to be equal to T_{RE} . The fact that they do not show the same result emphasizes the need for measurements of total effect or N that are independent of statistical power. As it stands, current discussions of pleiotropic scaling of gene effects are plagued by the fact that these two measurements have an implicit dependency on statistical power. We can only detect loci that have comparatively large effects (Knott and Haley 2000), and, therefore, we can only correctly establish pleiotropy for loci that show certain patterns of pleiotropic scaling. In cases where we have a reduction in per trait effect with increased

pleiotropy, current measurements will tend to underestimate the true N of individual loci, leading to incorrect models for the pleiotropic scaling of gene effects.

In our case, the pleiotropic scaling of gene effects estimated based on T_{GE} suggests we should expect a significant impact of this highly pleiotropic G-P map over the rate of cranial adaptation in marsupial species (Figure 2). This impact should be further exacerbated by the lack of evident modularity in the pattern of pleiotropic effects, a pattern that largely corroborates observations made in previous studies of marsupial cranial morphology (Shirai and Marroig 2010; Porto *et al.* 2015). While no study has directly compared cranial adaptation rates across clades, it is interesting to speculate that empirical evidence on the rate of evolution in cranial morphology among marsupials reported in a few papers seem to corroborate that assertion. In particular, marsupials seem to have much lower rates of cranial evolution than placentals, or any other vertebrate for that matter (Lemos *et al.* 2001; Porto *et al.* 2015). The favored hypothesis used to explain this pattern is based on the fact that marsupials are extremely altricial, born at an exceptionally early stage of development for a mammal. This mode of development is often interpreted as placing early functional requirements on skull structure, consequently constraining morphological diversification. Further studies are needed before this hypothesis can be properly tested, but, in any case, the results presented here ask for some re-evaluation of current measurements of pleiotropic scaling.

Independent of the cost of pleiotropy conundrum, the high pleiotropy and low modularity in opossums is bound to have other important evolutionary consequences for the species (Marroig *et al.* 2009). Genetic correlations can constrain or facilitate evolutionary change along genetic lines of least resistance, a topic that has attracted considerable attention in recent decades (Schluter 1996; Katrina McGuigan *et al.* 2005; Marroig and Cheverud 2005; Hansen and Houle 2008). Previous studies of craniofacial evolution within the genus *Monodelphis* found that strong genetic covariation among traits has influenced the rate of morphological diversification of the *M. breviceaudata* clade, which includes *M. domestica*, with between-species divergence occurring fastest when occurring along the genetic line of least resistance (Porto *et al.* 2015). The observation of strong genetic integration obtained from our random set of QTL corroborates the results presented in these previous studies, and emphasizes the importance of cranial development for marsupial evolution.

Conclusions

We showed that opossums and mice diverge in their genetic architecture of cranial traits, suggesting that G-P maps can evolve significantly even when species share most of their genes. Context-dependency of gene effects is therefore essential to our understanding of the evolution of genetic systems, and of the impact of cranial development on marsupial adaptive dynamics, and is important to current discussions concerning the cost of pleiotropy conundrum. In particular, results

presented for opossums suggest that we may need to re-evaluate not only the measurements being used to characterize the relationship between pleiotropy and mutational effect size, but also the notion that mammals are not subjected to the cost of pleiotropy due to genetic modularity.

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Figure S1 - Observed variance (log-scale) along the principal components of the genetic variance/covariance matrix (black line). The solid red line corresponds to the mean error variance along each principal component and the shaded area around it corresponds to its 95% confidence interval. Whenever the observed eigenvalue is larger than the upper limit of the error variance, we conclude that the principal component in question has significant additive genetic variation. The black arrow indicates the first PC for which there is overlap between the eigenvalues of G and noise.

Table S1 - Barcodes used in the genotype-by-sequencing approach, together with corresponding opossum ID.

Flowcell	Lane	Barcode	ID
C56TAACXX	1	TGACGCCA	K1396
C56TAACXX	1	GGCTTA	K1397
C56TAACXX	1	CTAAGCA	K1612
C56TAACXX	1	GCCTACCT	K2009
C56TAACXX	1	TGCTT	K2167
C56TAACXX	1	ACCAGGA	K2354
C56TAACXX	1	CTCTCGCAT	K2355
C56TAACXX	1	ATGGCAA	K2356
C56TAACXX	1	TCCGAG	K2357
C56TAACXX	1	GGAGTCAAG	K2358
C56TAACXX	1	CATCTGCCG	K3293
C56TAACXX	1	TTATTACAT	K4830
C56TAACXX	1	CAGATA	L0088
C56TAACXX	1	ATTAT	L0090
C56TAACXX	1	CACCA	L0091
C56TAACXX	1	GCAAGCCAT	L0092
C56TAACXX	1	CCACTCA	L0093
C56TAACXX	1	CAGAGGT	blank
C56TAACXX	1	GAAGCA	L0094
C56TAACXX	1	TAGATGA	L0095
C56TAACXX	1	TGAAT	L0096
C56TAACXX	1	GGACAG	L0167
C56TAACXX	1	GCCAACAAG A	L0168
C56TAACXX	1	GAAGTG	L0169
C56TAACXX	1	GAGCGACAT	L0170
C56TAACXX	1	GCGCTCA	L0434
C56TAACXX	1	AATTAG	L0436
C56TAACXX	1	CGCACCAAT T	K1408
C56TAACXX	1	TCACGGAAG	K4761
C56TAACXX	1	GCGTACAAT	K6385
C56TAACXX	1	AACGTGCCT	K7020
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C56TAACXX	7	CACCA	K8669
C56TAACXX	7	GCAAGCCAT	K8815
C56TAACXX	7	CCACTCA	L0282
C56TAACXX	7	CAGAGGT	L0283
C56TAACXX	7	GAAGCA	L0284
C56TAACXX	7	TAGATGA	L0332
C56TAACXX	7	TGAAT	L0335
C56TAACXX	7	GGACAG	L0336
C56TAACXX	7	GCCAACAAG A	L0438
C56TAACXX	7	GAAGTG	L0783
C56TAACXX	7	GAGCGACAT	L0784
C56TAACXX	7	GCGCTCA	L0785
C56TAACXX	7	AATTAG	L1076
C56TAACXX	7	CGCACCAAT T	L1077
C56TAACXX	7	TCACGGAAG	L1149
C56TAACXX	7	GCGTACAAT	L1153
C56TAACXX	7	AACGTGCCT	L1154
C56TAACXX	7	TGGCCAG	L1155
C56TAACXX	7	CATAT	L1885
C56TAACXX	7	ATCTGT	L1888
C56TAACXX	7	TGCCGCAT	L1971
C56TAACXX	7	TAGCGGAT	L1972
C56TAACXX	7	CCTTGCCATT	L1973
C56TAACXX	7	ACTGCGAT	L1976
C56TAACXX	7	GGAACGA	L1977
C56TAACXX	7	CTCGCGG	L2131
C56TAACXX	7	TATCA	L2179
C56TAACXX	7	ACGCGCG	L2180
C56TAACXX	7	CCTCG	L2181
C56TAACXX	7	GCACGAT	L2183
C56TAACXX	7	GTGACACAT	L2184
C56TAACXX	7	AAGACGCT	L2189
C56TAACXX	7	CGTGTCA	L2190

C56TAACXX	7	TATTCGCAT	L2192
C56TAACXX	7	GGTATA	L2193
C56TAACXX	7	TTCGTT	L2195
C56TAACXX	7	ACAACCT	L2196
C56TAACXX	7	AACTGG	L2235
C56TAACXX	7	TAGCCAA	L2236
C56TAACXX	7	GTCGCCT	L2237
C56TAACXX	7	CTCAT	L2405
C56TAACXX	7	TTGCTG	L2406
C56TAACXX	7	TATGT	L2407
C56TAACXX	7	GAATGCAATA	L2425
C56TAACXX	7	CAACCACAAC	L2426
C56TAACXX	7	ATAGAT	L2454
C56TAACXX	7	TCTTGG	L2455
C56TAACXX	7	ATATAA	L2456
C56TAACXX	7	ACTGCT	L2470
C56TAACXX	7	ATGAGCAA	L2472
C56TAACXX	7	ATATCGCCA	L2474
C56TAACXX	7	AATAACCAA	L2475
C56TAACXX	7	ACGGTACT	L2476
C56TAACXX	7	CGCAACCATG	L2778
C56TAACXX	7	CAGTGCCATT	L2978
C56TAACXX	7	TAGCAG	L3143
C56TAACXX	7	GCTCCGA	L3144
C56TAACXX	7	CCGAACA	L4153
C56TAACXX	7	GGTGT	L4154
C56TAACXX	7	TGGCAACAAG	L4715
C56TAACXX	7	CGTGGACAGGT	L4977
C56TAACXX	7	CTTGA	L5063
C56TAACXX	7	CTCTA	L5293
C56TAACXX	7	AATGAACGA	L5295
C56TAACXX	7	GCGCCG	L5298
C56TAACXX	7	TCACTG	L5527
C56TAACXX	7	ACAACCAATC	L5529
C56TAACXX	7	ATCCG	L5533

Table S2 - All single nucleotide polymorphisms used in this study.

Chromosome	Base pair	Major allele	Minor allele
1	456,395	T	C
1	3,507,519	C	T
1	4,004,716	C	T
1	4,091,794	A	T
1	4,885,344	T	A
1	5,492,302	C	A
1	5,492,388	A	C
1	5,511,587	G	A
1	5,527,806	T	C
1	5,527,836	G	A
1	5,652,899	C	T
1	6,343,613	C	T
1	6,343,654	C	T
1	6,881,827	T	C
1	7,403,729	G	C
1	7,403,779	A	G
1	7,403,863	C	T
1	8,007,546	T	C
1	8,007,585	G	C
1	8,180,259	C	T
1	8,334,605	G	A
1	8,466,294	A	C
1	8,990,894	A	G
1	9,975,480	C	T
1	9,975,516	T	C
1	10,208,263	T	A
1	10,762,222	A	T
1	10,762,226	C	T
1	10,849,531	T	C
1	11,531,917	C	T
1	11,947,466	A	G
1	12,335,506	A	C
1	12,335,571	T	C
1	13,476,560	T	A
1	13,476,562	A	C
1	13,476,570	T	G
1	13,814,201	C	G
1	14,364,105	G	A
1	14,364,187	G	A
1	15,807,310	G	A
1	16,198,769	A	G
1	16,198,772	T	C
1	16,198,781	C	T

1	17,214,197	G	A
1	18,902,569	G	T
1	19,097,067	A	G
1	19,480,913	C	T
1	19,520,960	A	G
1	20,153,065	T	C
1	20,925,837	C	T
1	20,925,838	A	G
1	20,925,876	C	T
1	20,925,881	C	T
1	21,594,902	G	A
1	21,598,632	T	C
1	22,910,327	T	C
1	22,910,328	G	T
1	22,967,114	G	A
1	23,246,715	C	T
1	24,238,336	C	T
1	24,238,339	T	C
1	24,532,973	C	T
1	24,533,040	C	T
1	24,533,072	G	C
1	24,645,961	G	A
1	25,996,995	C	A
1	26,971,338	T	C
1	26,971,342	C	T
1	27,119,659	C	T
1	27,555,106	T	C
1	27,555,146	T	C
1	27,555,148	A	G
1	28,427,599	T	C
1	28,427,664	C	T
1	28,532,792	G	A
1	28,607,910	G	A
1	28,607,978	T	C
1	29,700,097	C	A
1	29,700,173	T	G
1	32,903,302	C	T
1	32,903,376	C	T
1	33,124,189	T	A
1	34,843,415	C	T
1	34,915,505	G	A
1	35,658,440	A	T
1	35,980,382	G	T
1	35,980,388	A	G
1	36,035,613	G	A

1	36,433,256	C	A
1	36,500,497	A	T
1	37,182,310	A	C
1	37,416,947	A	C
1	37,593,046	C	T
1	37,593,059	C	T
1	38,153,919	C	A
1	38,154,958	G	T
1	38,157,492	C	T
1	39,722,498	G	A
1	39,916,431	G	A
1	39,916,520	G	A
1	40,046,885	T	C
1	40,046,895	T	C
1	40,280,588	G	A
1	40,351,675	G	A
1	40,661,454	G	A
1	40,876,029	T	A
1	41,051,292	T	G
1	41,051,304	G	T
1	41,051,340	G	A
1	45,413,284	A	G
1	46,392,912	G	A
1	46,943,111	A	G
1	47,736,763	C	T
1	47,736,786	T	C
1	47,736,791	T	C
1	47,736,800	T	C
1	47,929,587	G	T
1	47,929,623	A	G
1	49,090,589	G	A
1	49,136,382	T	C
1	50,719,024	T	C
1	53,197,230	C	T
1	53,292,262	C	A
1	58,136,486	A	C
1	58,136,582	A	T
1	58,182,160	A	G
1	58,182,172	A	G
1	59,123,855	C	A
1	60,530,813	A	G
1	63,021,113	A	T
1	63,401,489	G	A
1	64,028,653	G	T
1	65,046,505	G	A

1	65,468,597	T	C
1	75,396,218	T	A
1	76,168,857	G	T
1	76,431,934	G	A
1	77,328,423	C	G
1	79,747,385	C	G
1	80,717,779	A	C
1	81,921,774	G	A
1	82,168,429	C	T
1	82,176,087	T	G
1	82,557,359	T	A
1	82,711,491	C	A
1	83,203,962	T	C
1	84,680,515	G	C
1	86,075,287	T	C
1	90,830,473	A	G
1	93,182,729	C	T
1	93,182,757	C	T
1	93,447,959	C	T
1	94,739,543	T	A
1	95,724,410	A	C
1	96,029,450	G	C
1	96,262,932	C	G
1	96,904,315	T	C
1	96,904,415	C	T
1	99,210,790	C	T
1	99,210,806	A	G
1	100,156,043	T	C
1	100,156,078	T	C
1	100,279,191	C	T
1	102,813,667	C	T
1	103,241,439	A	C
1	103,241,491	C	T
1	104,147,885	G	T
1	104,147,886	G	T
1	106,371,081	G	T
1	106,371,082	A	T
1	107,070,278	G	C
1	111,097,160	T	A
1	111,327,068	T	C
1	111,431,571	C	A
1	111,571,029	G	C
1	111,857,159	A	C
1	115,253,042	G	A
1	115,253,070	G	A

1	115,253,093	T	C
1	115,403,339	A	G
1	118,158,107	G	T
1	120,148,703	T	C
1	120,702,531	G	C
1	121,180,441	T	A
1	121,187,126	T	G
1	121,744,941	C	T
1	121,746,486	C	T
1	121,746,490	G	C
1	121,885,770	T	C
1	123,251,271	G	T
1	123,834,794	T	C
1	123,879,322	C	T
1	124,438,385	C	T
1	124,510,579	G	C
1	125,167,904	T	C
1	125,681,827	G	C
1	127,080,165	C	T
1	127,080,208	C	T
1	130,971,445	G	A
1	130,971,472	A	G
1	132,054,015	T	C
1	133,045,224	T	G
1	133,795,101	G	C
1	134,277,435	A	G
1	136,830,086	T	C
1	139,478,328	T	A
1	140,892,346	T	C
1	143,539,972	A	C
1	143,827,094	G	C
1	144,492,380	C	A
1	145,472,872	T	A
1	145,802,986	C	T
1	151,350,568	T	C
1	152,125,381	T	C
1	152,319,402	G	C
1	153,205,289	A	G
1	154,851,570	A	G
1	156,021,552	C	T
1	156,262,308	C	T
1	156,972,048	T	C
1	158,131,006	G	A
1	161,303,380	T	G
1	162,853,816	C	T

1	167,571,997	C	G
1	169,475,889	G	A
1	172,676,852	G	C
1	172,752,922	G	C
1	172,786,136	A	G
1	173,068,477	C	T
1	173,443,376	G	A
1	173,557,217	T	C
1	173,640,328	A	G
1	180,941,450	G	A
1	181,094,371	T	G
1	181,441,611	T	C
1	181,746,248	C	T
1	182,111,748	G	C
1	184,157,586	A	T
1	188,172,281	C	T
1	188,196,836	A	G
1	192,934,187	C	T
1	196,151,236	A	G
1	221,974,874	A	G
1	222,856,215	A	C
1	222,910,550	G	T
1	223,092,366	T	C
1	223,092,459	G	A
1	226,635,428	A	G
1	228,341,874	C	T
1	228,341,897	C	T
1	228,341,901	G	A
1	228,341,905	A	G
1	228,670,649	G	A
1	230,818,317	T	C
1	233,523,187	G	A
1	233,549,030	T	A
1	233,549,047	A	T
1	234,365,664	G	A
1	235,137,148	A	G
1	236,566,389	G	A
1	236,566,424	G	A
1	239,742,520	G	A
1	239,804,999	G	A
1	241,075,051	G	A
1	243,234,597	C	T
1	243,234,627	C	A
1	246,396,405	G	T
1	246,518,795	A	G

1	246,518,807	C	T
1	247,887,126	T	C
1	248,439,536	C	A
1	249,614,133	A	G
1	250,348,851	T	C
1	250,348,860	C	T
1	250,348,895	A	T
1	250,741,713	C	T
1	251,198,659	A	C
1	252,001,563	T	C
1	252,200,510	C	T
1	252,981,542	A	G
1	254,928,833	T	G
1	255,539,560	C	A
1	255,916,857	G	A
1	255,916,871	G	T
1	258,607,752	G	T
1	260,846,486	A	C
1	262,092,573	A	C
1	262,092,620	A	G
1	263,840,629	C	T
1	265,936,439	A	G
1	269,888,821	C	T
1	269,888,873	T	A
1	270,327,452	C	T
1	271,303,233	A	G
1	272,184,752	C	G
1	274,405,052	C	A
1	275,121,576	C	A
1	278,519,821	T	C
1	278,519,831	G	A
1	278,519,851	C	T
1	278,519,853	A	T
1	278,519,931	A	G
1	279,762,596	G	C
1	280,208,962	G	A
1	280,208,990	C	T
1	282,490,482	C	T
1	285,814,164	A	G
1	294,215,999	A	G
1	294,862,252	T	C
1	294,953,983	T	C
1	294,953,984	A	T
1	295,047,253	G	A
1	296,267,859	T	C

1	296,267,887	T	A
1	303,156,015	A	G
1	304,912,466	A	C
1	308,102,974	A	G
1	308,450,994	T	C
1	308,482,091	C	T
1	310,273,001	G	A
1	311,392,724	C	T
1	312,254,144	A	G
1	320,525,149	G	A
1	325,173,736	G	A
1	326,789,778	A	G
1	327,831,214	G	A
1	329,731,634	G	A
1	330,944,496	A	G
1	331,877,010	C	T
1	332,614,034	A	C
1	333,704,121	C	T
1	334,225,298	A	G
1	335,488,934	A	G
1	337,786,758	C	T
1	338,055,623	C	T
1	338,055,751	C	T
1	340,362,898	T	C
1	340,362,911	A	T
1	340,362,926	A	T
1	340,362,931	G	T
1	341,118,104	A	T
1	341,118,105	A	C
1	341,118,189	T	C
1	341,118,190	G	A
1	341,118,230	G	A
1	341,134,102	C	T
1	356,678,360	C	T
1	356,678,373	G	A
1	358,834,051	C	T
1	366,198,762	A	T
1	366,646,820	T	C
1	368,096,147	A	G
1	370,685,416	G	T
1	370,685,417	T	G
1	370,898,642	G	T
1	371,138,876	A	G
1	372,281,110	T	C
1	374,231,720	T	C

1	379,185,009	C	T
1	379,373,806	A	C
1	381,339,810	C	T
1	381,339,843	C	A
1	381,339,844	G	A
1	382,225,654	G	A
1	383,782,073	G	A
1	383,903,581	G	C
1	388,862,024	A	G
1	388,862,027	T	A
1	388,862,028	T	A
1	388,862,032	C	T
1	388,862,033	A	T
1	390,382,688	A	C
1	420,463,092	C	T
1	420,621,869	A	G
1	421,273,992	A	G
1	421,847,794	G	A
1	421,847,823	T	A
1	422,085,375	A	G
1	422,634,285	C	G
1	425,210,297	C	T
1	426,427,403	C	A
1	426,435,884	C	G
1	426,436,100	A	G
1	426,436,106	C	G
1	426,436,219	G	A
1	432,184,602	C	T
1	432,296,350	C	T
1	433,707,740	G	A
1	434,352,009	T	C
1	434,644,629	A	G
1	434,644,650	G	A
1	434,689,843	G	A
1	435,352,588	A	G
1	435,352,605	G	A
1	435,352,631	T	C
1	435,387,812	G	A
1	435,387,815	G	T
1	436,424,280	A	G
1	436,494,744	A	G
1	436,644,634	A	C
1	436,881,034	C	T
1	438,238,975	T	C
1	438,567,754	A	G

1	438,567,771	C	T
1	439,436,625	T	A
1	441,510,406	C	T
1	441,510,416	A	G
1	443,751,433	A	G
1	443,751,435	G	C
1	443,751,436	T	C
1	443,751,437	C	T
1	444,131,249	C	A
1	447,251,584	C	T
1	448,253,221	A	G
1	449,421,328	T	G
1	452,770,671	T	C
1	453,185,961	T	C
1	453,185,962	G	A
1	453,185,963	C	T
1	453,185,964	C	T
1	453,185,965	A	G
1	453,185,966	T	C
1	453,185,967	T	A
1	453,185,969	C	T
1	453,185,971	G	T
1	453,185,974	T	C
1	453,185,975	T	C
1	453,185,976	A	T
1	453,185,977	C	G
1	453,185,979	T	A
1	453,374,782	T	C
1	453,374,783	G	A
1	454,107,036	A	T
1	456,511,541	T	C
1	458,130,290	C	T
1	460,202,648	T	C
1	460,265,160	G	T
1	460,813,834	G	A
1	461,149,681	T	C
1	464,332,354	G	A
1	465,612,144	T	A
1	465,612,145	C	G
1	465,612,147	C	T
1	465,612,185	T	C
1	469,585,713	T	C
1	471,545,743	A	G
1	472,679,774	G	A
1	473,036,292	T	C

1	473,036,375	A	G
1	474,342,148	A	T
1	474,342,160	T	G
1	476,670,636	A	C
1	480,153,007	T	C
1	481,845,356	C	T
1	482,877,001	G	A
1	483,411,889	T	C
1	485,492,212	C	A
1	485,697,571	C	T
1	488,476,987	T	C
1	488,477,003	C	T
1	492,230,178	G	A
1	499,000,789	A	G
1	499,000,847	T	C
1	501,929,268	T	G
1	502,475,717	A	G
1	503,651,971	G	A
1	504,112,693	C	T
1	504,400,713	T	G
1	505,550,336	G	A
1	505,550,382	G	T
1	505,687,468	T	A
1	505,687,504	G	A
1	505,782,234	C	T
1	506,193,368	G	A
1	507,438,964	T	C
1	507,439,059	G	A
1	507,785,173	T	C
1	509,172,610	T	C
1	510,114,680	G	C
1	510,114,683	C	T
1	513,585,795	A	G
1	516,477,798	A	T
1	518,385,067	C	T
1	521,140,720	G	C
1	523,747,440	C	T
1	581,319,340	C	A
1	585,045,789	C	T
1	590,388,787	T	C
1	592,576,589	T	G
1	592,576,593	T	G
1	592,576,608	T	G
1	592,950,842	C	A
1	592,950,851	T	A

1	594,002,658	A	C
1	594,002,694	T	C
1	594,002,715	T	C
1	594,560,882	C	T
1	595,629,570	T	C
1	595,629,584	C	T
1	595,764,563	C	T
1	598,317,240	G	A
1	598,317,252	G	A
1	600,042,054	T	A
1	605,066,696	C	T
1	605,066,699	A	T
1	606,505,505	A	G
1	607,929,261	A	G
1	607,929,263	T	C
1	608,543,561	C	T
1	613,327,253	T	A
1	615,837,327	C	G
1	616,037,073	A	G
1	616,091,077	T	G
1	619,562,658	G	C
1	619,562,678	T	C
1	623,258,183	G	A
1	623,258,190	T	A
1	642,702,545	C	G
1	650,897,649	T	A
1	650,897,669	A	G
1	651,811,431	T	G
1	651,898,833	T	C
1	651,898,882	A	G
1	652,910,686	T	C
1	655,360,986	A	C
1	655,360,999	T	C
1	658,699,415	T	C
1	677,381,118	A	C
1	682,758,243	C	T
1	684,354,205	A	C
1	684,542,643	C	T
1	685,531,425	G	A
1	685,657,519	A	G
1	686,660,906	A	G
1	687,722,139	G	A
1	687,722,140	G	A
1	689,311,750	G	A
1	689,353,266	C	T

1	692,661,468	T	G
1	692,661,482	A	G
1	693,700,193	A	G
1	694,790,790	T	G
1	694,790,880	A	G
1	694,790,915	T	C
1	694,806,972	T	C
1	694,806,993	A	G
1	694,900,047	A	G
1	695,856,919	T	C
1	696,561,261	C	G
1	696,727,555	T	C
1	696,910,296	C	T
1	697,383,225	A	T
1	697,885,799	T	G
1	697,888,305	T	C
1	698,319,105	G	A
1	703,578,973	T	C
1	705,743,398	C	T
1	705,743,418	A	G
1	705,965,608	G	A
1	706,209,378	T	G
1	706,622,563	G	C
1	706,657,328	A	G
1	706,680,760	A	C
1	706,680,762	T	C
1	706,935,140	C	T
1	706,971,629	A	G
1	707,039,350	C	A
1	707,755,447	A	T
1	707,880,154	T	C
1	707,880,186	A	G
1	707,914,745	C	G
1	707,920,978	G	A
1	707,930,919	T	A
1	707,937,224	G	C
1	708,132,429	G	A
1	708,140,196	C	T
1	708,140,228	T	C
1	708,146,391	T	C
1	708,418,687	C	T
1	708,418,697	A	G
1	708,418,718	A	G
1	709,297,209	G	C
1	709,460,229	C	A

1	709,823,462	G	C
1	709,823,484	A	G
1	709,823,504	G	A
1	709,967,227	T	C
1	709,967,243	G	C
1	710,093,971	C	T
1	710,382,062	C	T
1	710,961,615	T	C
1	711,004,045	T	A
1	711,004,047	C	T
1	711,280,329	G	T
1	711,299,438	G	A
1	717,213,871	C	T
1	717,413,102	T	C
1	717,522,464	T	A
1	717,522,533	T	C
1	717,579,511	C	T
1	717,579,576	A	G
1	718,399,744	A	G
1	718,639,145	T	C
1	718,639,146	A	G
1	719,535,165	T	C
1	720,802,155	T	C
1	720,802,180	G	T
1	722,262,014	A	T
1	722,294,143	T	A
1	724,402,091	A	G
1	724,430,023	C	T
1	724,430,036	A	G
1	724,430,050	T	G
1	725,969,040	C	T
1	726,759,876	C	T
1	726,954,745	G	A
1	726,954,795	C	G
1	727,021,055	A	T
1	727,021,065	C	A
1	727,396,000	A	G
1	727,396,047	A	G
1	727,470,504	T	C
1	727,470,531	C	A
1	727,484,290	G	A
1	727,542,580	A	T
1	727,571,962	G	A
1	728,095,319	T	C
1	728,147,379	T	G

1	728,214,712	A	G
1	728,310,126	A	G
1	728,310,139	G	T
1	728,310,141	T	G
1	728,310,147	T	G
1	728,311,971	G	A
1	728,321,368	G	A
1	728,364,154	T	C
1	728,407,670	A	G
1	728,544,607	C	T
1	728,544,642	G	A
1	728,562,402	T	G
1	728,562,453	A	T
1	728,799,324	G	T
1	728,935,612	G	C
1	728,935,641	G	T
1	729,557,349	G	C
1	729,638,082	G	A
1	733,015,187	G	T
1	733,015,188	G	T
1	733,015,221	G	A
1	733,940,630	C	T
1	734,348,938	A	C
1	734,348,951	T	A
1	735,911,818	C	T
1	736,166,835	C	T
1	736,166,837	C	T
1	736,232,235	C	T
1	736,251,124	A	C
1	737,031,963	T	C
1	737,622,034	C	A
1	737,938,570	G	A
1	738,271,343	A	C
1	741,116,928	C	T
1	741,296,356	C	T
1	741,367,317	C	T
1	741,692,122	T	G
1	741,692,135	G	A
1	742,231,436	G	A
1	742,231,449	T	A
1	742,367,561	T	C
1	742,367,582	G	C
1	744,796,278	A	G
1	744,872,690	A	G
1	744,947,939	C	T

1	744,947,959	A	C
1	744,989,427	G	C
1	745,001,216	T	C
1	745,001,235	T	C
1	745,001,247	C	G
1	745,045,225	G	A
1	745,146,277	G	A
1	745,165,626	G	A
1	745,165,669	C	T
1	745,168,011	C	T
1	745,409,840	G	A
1	745,409,856	G	A
1	745,945,951	C	T
1	746,187,355	C	G
1	746,187,360	C	T
1	746,330,549	T	C
1	746,687,273	A	G
1	747,236,398	T	C
1	747,293,208	A	C
1	747,293,230	A	G
1	747,315,032	A	G
1	747,361,474	G	A
1	747,361,480	C	T
1	747,361,511	C	T
1	747,361,517	C	T
1	747,426,224	G	T
1	747,463,045	T	G
1	747,517,818	T	C
1	747,517,836	T	A
1	747,517,909	C	T
1	747,624,268	G	C
1	747,723,709	C	T
1	747,936,573	T	C
1	747,936,593	C	T
2	153,432	C	T
2	153,434	T	C
2	169,465	T	C
2	169,468	A	G
2	169,477	G	C
2	169,478	A	C
2	1,088,419	G	A
2	3,332,520	A	G
2	3,332,524	T	C
2	5,161,830	A	G
2	5,185,688	C	G

2	5,438,339	G	A
2	5,890,225	T	C
2	7,950,183	G	A
2	7,950,187	A	G
2	8,672,781	C	A
2	8,716,735	C	A
2	8,716,736	C	A
2	8,716,737	C	A
2	8,716,738	C	A
2	8,785,928	A	G
2	11,090,264	T	G
2	11,090,266	A	G
2	11,090,272	T	G
2	11,090,290	T	G
2	11,900,579	A	G
2	12,618,540	C	T
2	12,618,543	T	C
2	12,618,550	T	C
2	12,618,555	G	T
2	15,377,819	T	C
2	15,377,825	C	T
2	15,377,839	G	T
2	15,377,854	A	T
2	15,465,890	A	T
2	15,674,002	G	A
2	15,785,781	G	A
2	17,028,557	T	C
2	17,411,799	T	C
2	17,415,231	G	T
2	17,556,947	T	G
2	17,556,953	A	T
2	17,556,957	A	T
2	17,556,960	A	T
2	18,987,500	T	C
2	18,987,522	A	G
2	18,987,623	A	G
2	19,155,042	G	T
2	19,169,380	A	G
2	19,575,271	G	T
2	19,644,538	G	A
2	19,644,540	A	G
2	19,938,938	G	C
2	20,127,020	A	G
2	20,127,037	G	C
2	20,267,025	T	C

2	20,644,693	T	C
2	20,644,723	C	T
2	21,369,875	T	G
2	22,599,998	G	A
2	22,646,453	T	G
2	22,646,493	T	A
2	22,874,631	C	T
2	22,874,655	G	A
2	22,900,705	G	A
2	22,921,564	C	G
2	22,921,607	T	C
2	23,268,036	T	C
2	23,268,090	A	C
2	23,792,016	C	T
2	23,820,757	C	T
2	23,820,791	G	A
2	24,323,319	C	G
2	25,012,221	G	A
2	25,187,302	A	C
2	25,437,260	T	G
2	25,437,267	G	A
2	25,612,260	C	T
2	26,235,665	A	G
2	26,235,713	T	C
2	26,264,860	A	G
2	26,543,000	T	C
2	27,721,999	G	A
2	27,722,050	G	A
2	27,976,056	T	C
2	28,726,548	T	G
2	28,800,522	T	C
2	28,800,558	G	A
2	28,800,559	T	C
2	28,800,582	G	T
2	28,810,144	G	A
2	29,474,698	A	G
2	29,474,699	A	G
2	29,723,921	T	C
2	29,723,922	T	G
2	29,731,955	T	C
2	29,744,257	C	T
2	41,360,045	A	C
2	42,302,180	C	T
2	42,646,362	G	T
2	44,789,529	C	T

2	44,933,090	A	T
2	44,933,125	G	C
2	44,933,137	T	C
2	44,933,140	C	T
2	45,475,231	A	G
2	46,890,559	G	A
2	46,890,589	T	G
2	52,954,119	A	T
2	53,184,908	A	G
2	56,773,270	G	C
2	56,773,285	C	G
2	57,594,457	C	T
2	57,594,470	C	T
2	57,594,471	T	A
2	57,594,523	A	G
2	59,592,964	G	A
2	60,029,817	A	G
2	60,409,644	C	T
2	61,235,646	T	A
2	61,875,402	T	C
2	61,875,432	A	G
2	62,393,228	T	A
2	62,986,294	A	G
2	64,065,212	T	C
2	66,392,786	A	T
2	67,265,114	C	T
2	67,265,128	T	G
2	67,311,141	A	C
2	70,195,443	C	T
2	70,935,478	G	T
2	71,898,223	A	G
2	72,335,342	T	C
2	75,376,396	A	T
2	76,004,394	C	T
2	76,026,570	T	C
2	77,157,401	C	T
2	77,157,405	T	C
2	77,516,647	A	G
2	77,696,591	A	G
2	77,696,594	G	C
2	78,276,581	G	A
2	78,326,854	C	T
2	78,536,003	G	A
2	78,536,004	T	A
2	78,973,776	C	T

2	80,472,071	G	T
2	80,584,730	T	C
2	81,975,123	A	G
2	81,975,144	T	G
2	83,275,721	G	A
2	83,275,756	T	C
2	86,657,498	A	C
2	86,657,504	T	C
2	87,748,708	T	C
2	87,868,194	C	A
2	87,868,209	A	G
2	88,565,899	C	A
2	90,120,773	A	G
2	96,796,702	T	C
2	96,899,390	A	G
2	98,764,248	A	G
2	99,714,558	A	T
2	100,897,817	G	A
2	101,542,029	C	T
2	105,292,971	A	G
2	106,106,500	G	A
2	106,106,531	A	G
2	106,113,691	G	A
2	106,113,697	A	G
2	106,113,758	G	A
2	107,476,615	G	A
2	107,760,586	A	G
2	113,075,292	A	C
2	113,075,304	A	C
2	113,353,904	C	T
2	113,719,726	A	G
2	114,958,356	A	G
2	117,620,819	C	T
2	117,971,966	A	G
2	118,511,758	T	C
2	118,635,419	A	G
2	118,691,785	A	C
2	123,084,149	C	G
2	123,125,838	C	A
2	123,397,750	A	G
2	123,665,514	C	T
2	123,795,469	C	T
2	125,326,489	G	T
2	125,326,491	G	C
2	125,326,537	G	A

2	129,517,858	G	T
2	131,895,411	G	A
2	134,424,322	A	G
2	134,988,386	T	A
2	137,092,689	G	C
2	137,092,695	T	C
2	137,092,700	G	C
2	137,092,705	A	C
2	137,092,713	T	C
2	140,892,444	C	T
2	140,892,494	T	G
2	141,144,204	A	G
2	141,833,110	C	T
2	141,833,174	G	A
2	142,662,874	G	A
2	142,824,069	C	T
2	143,620,497	C	T
2	144,179,260	T	G
2	144,179,273	C	A
2	144,564,418	G	A
2	145,089,690	T	C
2	145,974,091	T	C
2	145,974,114	G	C
2	145,974,129	T	C
2	150,342,624	T	G
2	152,842,316	A	T
2	154,940,633	T	C
2	156,497,183	C	T
2	158,193,100	G	A
2	158,193,150	T	C
2	158,193,275	C	T
2	158,193,287	T	C
2	158,429,088	C	T
2	158,614,246	T	C
2	158,864,656	G	C
2	158,864,675	G	T
2	158,876,477	G	A
2	159,371,343	C	T
2	162,126,550	C	T
2	166,062,408	A	G
2	166,103,055	A	T
2	166,292,265	C	G
2	172,634,932	T	C
2	174,732,726	A	C
2	183,813,803	G	C

2	184,919,042	C	T
2	185,632,027	C	T
2	185,794,725	T	C
2	186,400,214	A	C
2	187,200,809	C	T
2	192,092,323	C	T
2	193,451,007	T	C
2	193,456,850	A	G
2	193,456,861	A	G
2	193,456,866	T	G
2	195,435,639	A	T
2	196,091,804	G	A
2	196,091,837	T	C
2	196,091,839	G	A
2	197,791,735	C	A
2	216,396,260	T	C
2	217,302,385	A	G
2	217,713,442	C	T
2	219,009,711	A	C
2	219,009,736	A	T
2	223,120,923	G	T
2	229,312,995	G	C
2	231,875,755	C	G
2	233,927,824	T	C
2	234,954,913	G	A
2	237,159,297	C	T
2	237,871,674	A	G
2	238,025,269	A	G
2	238,025,272	T	C
2	238,365,949	G	A
2	238,937,740	C	A
2	245,768,370	C	A
2	249,819,000	T	C
2	250,732,716	A	G
2	253,495,483	A	G
2	253,495,499	T	G
2	254,366,633	G	A
2	255,206,464	G	A
2	255,236,902	A	C
2	255,236,915	G	T
2	258,314,123	G	A
2	263,720,541	C	T
2	267,338,169	C	T
2	267,338,173	C	T
2	267,338,184	C	T

2	268,372,514	A	G
2	268,873,176	A	G
2	268,873,217	C	T
2	269,570,184	C	T
2	269,570,229	G	A
2	270,100,863	G	C
2	270,100,895	G	A
2	270,190,078	T	C
2	270,291,488	A	G
2	272,332,765	A	C
2	274,877,952	A	G
2	274,877,987	A	G
2	275,575,790	T	A
2	275,575,792	G	A
2	275,575,833	G	A
2	276,254,412	T	C
2	276,518,788	G	A
2	276,652,532	G	A
2	284,441,311	G	A
2	284,441,314	A	G
2	284,441,344	T	G
2	285,697,100	T	C
2	285,697,115	G	C
2	285,697,124	C	G
2	285,697,285	A	G
2	285,697,296	T	A
2	285,698,698	G	T
2	285,698,777	T	A
2	285,698,800	C	T
2	285,698,825	T	C
2	285,698,827	G	A
2	286,500,892	A	T
2	287,380,355	A	G
2	287,380,400	T	C
2	287,990,043	A	G
2	288,745,567	C	T
2	289,010,495	C	T
2	289,911,756	T	C
2	292,794,333	G	A
2	292,794,373	G	A
2	292,794,388	C	T
2	294,027,642	T	C
2	294,516,115	C	T
2	294,569,827	C	T
2	295,892,651	C	T

2	296,108,898	G	T
2	296,108,929	C	T
2	299,996,250	G	A
2	302,123,486	A	G
2	302,751,559	G	A
2	303,008,187	A	T
2	306,088,260	G	A
2	306,419,821	A	G
2	309,305,324	G	A
2	309,305,330	C	T
2	309,886,754	A	G
2	310,446,966	G	C
2	310,726,209	A	C
2	312,525,676	C	T
2	312,525,723	C	A
2	316,340,198	C	T
2	319,333,635	G	A
2	319,333,648	G	A
2	319,680,970	T	G
2	320,852,553	G	A
2	321,260,078	G	T
2	321,260,079	A	G
2	322,087,115	G	C
2	324,226,059	C	A
2	324,611,192	G	C
2	325,202,242	T	A
2	325,521,681	C	A
2	325,521,682	C	G
2	327,488,698	A	G
2	328,688,004	G	A
2	330,001,179	C	T
2	332,814,389	T	C
2	332,814,395	C	G
2	332,889,857	T	A
2	333,284,624	T	A
2	333,562,388	G	A
2	333,759,359	C	T
2	337,858,791	A	C
2	338,589,259	A	G
2	383,224,483	A	C
2	383,224,489	A	C
2	385,919,526	G	T
2	400,155,973	T	C
2	401,974,166	A	C
2	401,974,180	G	T

2	404,633,490	A	C
2	404,633,499	C	T
2	404,633,501	T	C
2	404,691,454	T	C
2	404,691,515	C	G
2	407,011,570	A	G
2	407,011,627	C	G
2	407,011,640	T	G
2	407,011,645	C	T
2	407,469,044	C	T
2	407,536,042	G	C
2	409,984,000	T	G
2	410,577,386	A	G
2	411,364,729	G	A
2	411,918,066	G	A
2	412,417,092	T	C
2	414,205,921	C	G
2	414,215,426	T	C
2	414,215,476	A	C
2	415,792,788	C	T
2	417,017,623	G	T
2	419,547,700	C	A
2	419,547,705	G	A
2	420,786,202	A	G
2	421,047,667	A	G
2	421,391,743	C	T
2	423,021,500	G	A
2	425,732,362	G	A
2	425,988,137	C	T
2	427,659,023	G	A
2	430,333,843	G	T
2	433,094,772	C	T
2	436,811,993	A	T
2	438,647,363	G	A
2	439,158,967	C	A
2	439,707,344	C	T
2	439,707,351	G	A
2	439,707,440	C	T
2	440,323,609	G	A
2	441,539,612	A	T
2	441,539,614	C	T
2	442,009,864	C	G
2	443,115,487	C	T
2	446,967,759	T	C
2	446,967,864	G	A

2	447,223,547	A	T
2	448,708,016	C	T
2	449,313,528	G	A
2	449,313,535	T	C
2	449,501,207	G	A
2	449,501,227	G	A
2	449,570,571	A	G
2	450,911,790	A	C
2	451,045,781	A	G
2	451,260,541	T	A
2	451,260,553	C	T
2	454,621,995	T	A
2	454,622,000	T	C
2	455,255,716	A	G
2	455,728,503	T	G
2	457,359,234	T	G
2	458,336,526	T	C
2	458,587,720	T	C
2	459,286,007	T	A
2	459,286,014	A	T
2	460,544,947	G	A
2	460,545,054	C	A
2	460,948,216	C	A
2	461,482,795	T	A
2	461,773,109	T	G
2	481,501,487	A	G
2	481,501,539	T	A
2	481,501,541	G	A
2	483,162,151	T	G
2	483,305,799	G	A
2	483,609,870	G	A
2	484,851,885	C	T
2	486,496,420	A	C
2	486,496,428	C	T
2	487,969,018	C	T
2	488,359,984	A	G
2	488,642,647	C	T
2	488,719,338	A	C
2	488,719,351	G	A
2	488,719,454	T	C
2	490,208,017	G	A
2	490,654,113	C	G
2	493,096,865	G	A
2	493,631,608	C	T
2	494,311,992	A	G

2	495,730,021	C	T
2	496,315,646	C	T
2	496,315,745	G	A
2	496,315,753	G	A
2	497,556,342	T	C
2	499,979,955	G	C
2	500,140,437	A	C
2	500,701,916	A	T
2	500,701,922	C	T
2	500,927,833	T	C
2	500,927,850	A	G
2	501,226,955	A	G
2	501,488,395	A	G
2	501,986,042	T	A
2	514,665,688	G	C
2	520,391,708	A	C
2	520,479,993	G	C
2	520,480,038	A	G
2	520,792,105	C	G
2	521,263,675	A	T
2	521,712,056	C	T
2	521,728,504	T	G
2	522,574,865	C	T
2	522,574,930	A	C
2	522,633,533	G	A
2	522,633,534	T	C
2	524,509,633	G	A
2	524,509,657	G	A
2	524,533,907	C	G
2	524,533,908	A	T
2	524,533,958	T	C
2	525,314,657	T	G
2	526,139,386	A	G
2	526,377,543	C	A
2	526,858,093	G	A
2	527,674,858	T	C
2	527,881,225	A	G
2	528,050,356	G	A
2	528,386,529	A	G
2	528,395,397	G	A
2	528,987,968	G	C
2	528,999,612	G	C
2	528,999,613	G	C
2	529,012,319	G	A
2	530,145,479	G	A

2	530,931,771	C	T
2	531,020,783	A	G
2	533,631,366	T	G
2	534,524,500	A	T
2	534,532,634	G	A
2	534,561,410	A	G
2	534,646,897	C	G
2	534,646,941	G	A
2	534,728,960	A	T
2	535,684,473	A	C
2	535,684,474	G	C
2	535,684,475	T	G
2	535,684,476	C	A
2	536,354,892	T	C
2	536,354,904	C	T
2	536,685,791	T	C
2	536,751,660	G	A
2	537,136,888	T	C
2	537,151,531	T	C
2	537,263,976	G	A
2	537,463,704	C	A
2	537,544,401	T	G
2	537,814,256	C	T
2	540,166,647	G	A
2	540,166,648	G	A
2	540,185,876	A	C
2	540,502,868	T	C
2	540,531,800	C	G
2	540,531,850	A	G
2	540,951,542	A	G
2	540,951,615	G	A
2	540,965,756	G	C
2	540,965,774	A	G
2	541,137,485	G	A
2	541,302,099	C	T
2	541,399,172	A	G
2	541,404,136	G	A
2	541,538,542	T	C
2	541,538,551	A	G
3	2,525,732	G	C
3	2,525,741	G	C
3	4,700,207	A	C
3	5,225,870	C	T
3	5,303,502	G	A
3	5,303,519	C	T

3	5,423,867	A	G
3	5,432,945	G	C
3	5,807,057	G	A
3	5,807,094	A	G
3	6,756,528	G	A
3	9,435,490	T	A
3	9,477,201	T	C
3	11,168,799	C	T
3	11,528,047	A	C
3	12,777,180	A	G
3	13,787,559	A	C
3	16,800,541	T	C
3	17,088,587	C	T
3	19,356,491	C	T
3	19,663,891	A	G
3	20,102,596	C	T
3	42,861,476	G	A
3	45,426,568	A	C
3	45,426,599	A	G
3	45,426,631	G	T
3	45,867,335	G	C
3	46,348,246	T	G
3	47,665,345	G	A
3	47,867,563	G	A
3	53,441,035	G	T
3	54,365,387	G	T
3	55,075,003	T	C
3	55,388,193	A	G
3	61,565,852	G	A
3	63,341,558	G	A
3	63,398,656	A	G
3	64,444,400	A	G
3	64,466,315	G	A
3	64,466,335	C	A
3	65,822,729	A	C
3	65,822,747	T	C
3	66,165,008	G	T
3	66,386,144	T	C
3	66,386,167	A	T
3	67,366,014	C	T
3	67,372,959	C	A
3	69,324,529	A	G
3	70,996,453	A	G
3	70,996,542	A	G
3	71,067,436	T	C

3	71,154,370	G	A
3	71,154,404	A	C
3	71,265,507	T	G
3	73,754,925	T	A
3	74,032,882	C	T
3	75,596,215	G	A
3	76,047,814	A	G
3	78,581,850	C	T
3	83,078,709	A	C
3	83,078,717	C	T
3	83,186,505	T	C
3	83,885,412	A	G
3	85,035,113	G	C
3	85,182,789	G	A
3	85,182,842	T	C
3	85,182,863	A	G
3	85,608,336	G	A
3	85,608,337	A	G
3	85,608,344	C	T
3	85,608,345	T	G
3	85,608,372	T	A
3	85,624,746	C	T
3	86,543,205	G	T
3	87,680,132	C	G
3	90,069,125	A	G
3	90,069,144	C	T
3	91,103,516	T	C
3	93,103,304	T	C
3	93,492,768	C	A
3	94,662,708	C	T
3	99,140,648	G	A
3	99,140,656	C	T
3	99,140,670	G	A
3	99,811,697	C	T
3	100,048,365	C	T
3	100,233,779	A	G
3	103,929,840	G	A
3	103,929,881	C	T
3	105,166,187	C	A
3	105,166,204	C	A
3	105,478,990	C	A
3	106,439,569	A	G
3	106,585,476	T	C
3	107,532,046	C	T
3	107,532,047	A	G

3	107,532,090	C	T
3	107,829,709	A	C
3	108,926,545	G	C
3	108,926,562	G	A
3	108,939,442	G	C
3	108,939,443	C	G
3	108,957,916	T	C
3	109,448,574	A	G
3	109,448,583	A	G
3	109,448,599	A	G
3	109,448,605	A	G
3	111,095,506	T	C
3	112,375,179	C	T
3	112,470,145	C	T
3	113,839,017	T	G
3	117,573,064	G	A
3	117,620,853	T	G
3	118,997,562	T	C
3	119,957,702	C	T
3	121,554,765	G	A
3	124,691,557	C	T
3	126,646,286	A	G
3	128,811,721	C	T
3	128,811,730	T	C
3	128,811,801	G	T
3	129,473,000	A	G
3	129,473,037	T	G
3	130,996,243	A	G
3	131,143,273	T	C
3	132,139,258	T	C
3	132,427,013	A	G
3	137,004,245	A	G
3	138,928,291	C	T
3	138,928,292	T	G
3	138,928,308	T	C
3	138,928,362	C	G
3	138,928,365	G	A
3	138,952,108	A	C
3	139,554,425	A	G
3	140,203,863	A	T
3	140,658,410	C	A
3	140,699,924	T	C
3	141,077,916	G	A
3	141,077,918	A	G
3	142,166,671	G	C

3	144,133,806	A	G
3	144,133,856	A	G
3	144,463,049	A	T
3	144,843,348	C	G
3	144,843,368	C	G
3	144,843,458	A	G
3	144,843,464	C	T
3	144,957,367	A	G
3	145,879,730	A	G
3	147,728,079	G	A
3	147,728,108	C	G
3	150,741,808	T	C
3	152,752,164	A	T
3	153,691,423	G	A
3	154,311,759	A	G
3	155,979,781	C	T
3	155,979,793	A	C
3	155,979,794	C	A
3	155,979,795	A	C
3	155,979,796	G	A
3	156,970,687	A	G
3	157,721,076	C	T
3	158,097,083	T	C
3	159,949,391	T	C
3	159,949,392	G	A
3	160,793,665	A	G
3	162,336,644	A	T
3	162,370,140	C	T
3	162,370,206	A	G
3	162,370,379	C	T
3	162,950,320	C	A
3	163,726,908	A	G
3	164,251,976	C	T
3	164,251,990	C	T
3	168,102,210	A	G
3	169,187,364	A	G
3	169,187,390	A	G
3	169,337,702	C	T
3	170,080,884	G	A
3	173,743,928	G	A
3	183,635,212	G	A
3	183,635,215	G	A
3	183,635,272	C	A
3	183,635,273	C	A
3	186,370,844	C	G

3	187,009,109	A	T
3	187,093,689	A	G
3	192,565,055	T	C
3	193,296,603	A	T
3	195,857,939	A	T
3	195,893,959	C	T
3	197,184,734	C	T
3	197,650,333	C	G
3	198,552,608	A	C
3	200,531,536	A	G
3	201,776,627	C	T
3	202,529,882	G	C
3	204,127,576	C	G
3	204,127,590	G	T
3	204,917,729	C	G
3	205,311,658	G	A
3	208,083,030	G	T
3	209,968,571	C	T
3	213,438,315	T	G
3	213,438,329	T	G
3	214,184,228	T	C
3	215,836,777	C	T
3	216,682,440	A	G
3	216,682,445	A	G
3	216,682,471	C	T
3	217,148,996	G	T
3	217,149,011	G	A
3	220,064,251	A	G
3	220,064,280	T	A
3	224,670,680	A	G
3	231,219,100	A	G
3	231,817,381	T	A
3	231,817,405	C	A
3	231,817,416	G	C
3	231,817,423	G	A
3	231,817,462	G	A
3	233,749,697	G	A
3	233,749,712	A	C
3	235,296,911	T	A
3	245,226,743	A	G
3	247,373,943	C	T
3	247,456,699	A	G
3	247,456,732	T	A
3	248,206,454	C	T
3	248,603,111	C	A

3	248,603,154	C	T
3	252,374,078	A	G
3	255,187,537	G	A
3	258,982,578	C	T
3	258,982,724	T	C
3	261,201,241	A	T
3	261,364,695	C	T
3	261,504,187	C	G
3	267,494,344	C	A
3	268,330,871	G	C
3	268,567,845	G	T
3	268,759,675	T	C
3	269,023,794	G	A
3	271,628,986	A	G
3	271,628,988	G	A
3	272,878,127	C	T
3	274,191,003	G	A
3	274,651,231	C	T
3	274,651,232	A	G
3	276,080,131	A	G
3	279,647,141	G	A
3	281,791,986	A	G
3	282,867,240	C	T
3	286,462,644	G	T
3	286,462,667	C	A
3	288,483,748	T	C
3	289,149,804	T	C
3	291,024,697	G	A
3	291,419,822	A	C
3	291,431,973	A	G
3	292,862,824	C	T
3	299,092,658	T	G
3	301,149,993	T	C
3	301,694,201	T	C
3	304,066,606	C	T
3	304,316,342	G	A
3	305,204,496	A	G
3	305,311,921	A	G
3	305,311,998	G	T
3	308,733,752	G	A
3	308,733,753	G	C
3	308,900,883	T	C
3	309,121,475	T	C
3	309,832,212	T	G
3	310,447,406	A	G

3	312,374,153	G	A
3	312,409,900	A	G
3	314,202,282	A	T
3	316,146,218	C	T
3	316,646,819	G	C
3	317,423,214	C	G
3	318,616,753	G	A
3	318,875,135	T	C
3	319,522,915	G	A
3	320,193,927	G	A
3	320,447,318	A	G
3	325,118,308	G	A
3	325,121,228	C	T
3	326,285,922	A	C
3	328,091,484	A	G
3	329,953,245	A	G
3	330,773,512	T	A
3	332,333,772	G	A
3	333,897,959	C	G
3	334,911,063	G	A
3	336,779,185	A	G
3	337,359,636	C	G
3	337,609,154	T	A
3	337,880,543	A	G
3	338,349,718	C	T
3	342,623,597	C	A
3	342,764,835	A	C
3	343,127,285	C	T
3	344,618,267	G	A
3	345,124,987	T	G
3	345,124,988	T	G
3	345,124,989	T	G
3	345,124,990	T	G
3	345,427,533	A	C
3	345,427,534	C	A
3	346,870,025	C	T
3	348,160,102	G	A
3	348,160,140	A	G
3	348,308,941	G	T
3	349,968,951	G	T
3	351,846,558	A	G
3	354,455,247	C	A
3	355,538,383	A	C
3	355,774,810	A	G
3	357,809,715	T	A

3	358,215,235	C	T
3	358,777,686	G	A
3	360,979,463	C	G
3	361,135,239	T	C
3	361,135,240	A	C
3	361,135,242	A	C
3	362,144,866	T	C
3	362,144,868	C	T
3	362,144,872	C	T
3	362,144,873	A	C
3	362,199,879	T	A
3	362,467,266	G	A
3	362,744,609	A	T
3	365,046,847	G	T
3	366,280,812	G	A
3	366,514,944	A	G
3	367,849,177	A	T
3	367,849,206	G	A
3	367,916,856	A	G
3	369,102,129	G	A
3	373,422,567	G	T
3	392,646,503	C	A
3	395,500,837	G	A
3	395,500,864	A	G
3	397,868,047	T	C
3	398,531,532	C	T
3	400,135,545	C	T
3	400,135,555	G	A
3	400,176,288	T	C
3	400,176,364	C	T
3	400,984,656	G	A
3	403,297,191	C	T
3	403,721,900	G	A
3	405,424,907	G	A
3	405,424,971	G	T
3	405,973,886	G	T
3	409,057,852	C	T
3	412,579,747	G	T
3	412,579,791	G	A
3	412,912,014	C	A
3	413,106,463	C	T
3	413,106,486	G	A
3	413,106,488	G	T
3	413,725,286	G	A
3	413,965,546	C	A

3	414,032,595	G	A
3	418,305,835	T	C
3	420,414,390	A	G
3	422,026,024	A	C
3	422,026,047	T	C
3	424,495,094	A	G
3	424,617,106	G	T
3	424,617,107	T	G
3	424,661,652	C	G
3	426,491,847	T	A
3	428,717,171	A	C
3	428,717,172	C	A
3	428,717,175	A	G
3	429,029,140	A	G
3	429,875,987	G	A
3	431,442,161	C	G
3	433,167,994	G	A
3	433,167,998	A	G
3	434,686,263	T	G
3	434,764,974	A	G
3	434,773,404	T	C
3	435,313,869	A	C
3	436,546,234	G	A
3	437,565,454	T	C
3	437,694,456	G	A
3	437,850,353	T	C
3	442,619,322	C	T
3	443,509,941	A	C
3	443,509,952	A	C
3	445,347,789	C	A
3	445,947,850	T	C
3	455,979,385	T	G
3	458,268,309	A	G
3	459,027,508	A	C
3	459,593,780	T	C
3	461,043,905	G	T
3	461,388,456	C	T
3	461,848,935	C	A
3	461,848,956	C	T
3	461,909,023	T	C
3	461,909,024	C	T
3	470,259,581	A	G
3	470,259,587	A	G
3	470,259,593	T	C
3	480,475,049	A	G

3	480,537,407	T	A
3	480,537,431	G	A
3	483,665,556	T	A
3	483,665,558	T	A
3	483,665,569	C	G
3	483,665,578	C	A
3	483,665,582	T	G
3	488,591,060	G	T
3	488,759,879	A	G
3	490,924,183	T	A
3	490,924,184	A	T
3	497,615,604	C	T
3	497,618,116	C	T
3	498,320,508	G	A
3	498,320,560	G	T
3	498,320,570	G	A
3	499,085,848	G	A
3	499,085,853	G	A
3	499,564,563	T	A
3	499,580,691	T	C
3	499,970,145	G	A
3	500,033,962	G	A
3	500,052,799	G	A
3	500,287,034	T	A
3	500,448,924	T	A
3	500,448,934	C	G
3	500,703,109	G	A
3	500,703,138	A	G
3	500,848,303	A	G
3	500,848,324	G	A
3	501,260,172	C	T
3	501,260,236	T	C
3	501,322,583	C	T
3	501,322,628	G	C
3	502,780,794	G	A
3	502,896,457	T	C
3	502,937,307	C	T
3	503,446,161	A	T
3	503,498,966	C	T
3	503,498,967	T	C
3	503,749,383	G	C
3	503,749,385	T	G
3	504,386,115	G	A
3	508,549,728	T	C
3	508,744,702	A	G

3	509,301,852	C	A
3	509,327,121	G	C
3	509,327,137	T	C
3	509,329,810	G	A
3	509,410,796	A	G
3	509,780,454	T	C
3	509,954,192	A	C
3	509,954,194	C	A
3	509,954,202	T	A
3	509,954,206	A	T
3	509,954,207	C	T
3	509,954,208	T	G
3	509,954,229	C	T
3	509,954,248	G	C
3	510,119,100	C	T
3	510,119,122	C	T
3	510,119,133	A	T
3	510,119,145	G	A
3	510,145,426	G	A
3	510,151,604	C	T
3	510,210,795	G	A
3	510,229,174	C	A
3	510,229,322	T	C
3	510,458,521	T	C
3	510,458,533	A	C
3	510,458,534	A	G
3	510,458,539	T	G
3	510,572,739	G	A
3	510,572,777	G	A
3	510,572,841	A	C
3	510,639,911	C	T
3	510,639,919	C	T
3	510,642,161	C	T
3	510,780,528	G	A
3	510,780,575	C	T
3	510,786,036	A	G
3	510,786,209	A	T
3	510,802,937	A	G
3	510,809,162	G	T
3	510,809,226	T	G
3	510,809,237	A	G
3	510,923,106	G	T
3	510,927,570	T	A
3	510,929,489	A	G
3	511,138,711	C	T

3	511,138,715	C	T
3	511,424,800	A	T
3	512,153,610	T	C
3	512,550,152	C	G
3	512,603,778	G	A
3	512,756,700	T	C
3	512,870,206	C	T
3	512,881,472	T	C
3	513,067,406	C	T
3	513,067,442	G	T
3	513,067,494	C	G
3	514,166,271	C	G
3	514,519,338	G	A
3	514,598,234	T	G
3	514,666,884	T	C
3	514,715,807	A	C
3	514,735,842	C	A
3	516,185,883	A	G
3	516,227,425	A	G
3	516,348,035	G	A
3	516,483,774	T	C
3	516,685,450	G	A
3	516,685,452	A	G
3	516,695,775	C	T
3	518,015,067	T	C
3	518,015,071	C	G
3	518,015,080	A	G
3	518,015,083	T	C
3	518,220,952	C	T
3	518,375,425	T	C
3	518,375,426	A	G
3	518,375,441	T	C
3	518,713,411	G	A
3	518,841,335	T	C
3	519,484,454	T	G
3	519,838,263	G	C
3	520,507,833	C	T
3	521,005,403	A	G
3	521,183,356	C	T
3	521,183,358	C	T
3	521,183,359	A	C
3	521,183,360	G	C
3	521,401,188	C	A
3	521,575,590	T	A
3	521,575,611	C	G

3	521,873,650	C	T
3	522,267,114	G	A
3	522,270,183	T	C
3	522,270,195	C	T
3	522,300,923	C	T
3	522,411,718	C	A
3	522,411,728	G	C
3	522,846,607	G	C
3	523,167,235	C	A
3	523,375,188	G	C
3	523,375,193	T	C
3	524,023,834	G	T
3	524,269,403	A	G
3	524,269,426	C	G
3	524,838,769	A	G
3	524,838,773	T	C
3	524,885,744	C	T
3	524,885,827	T	A
3	525,402,586	A	G
3	525,466,181	G	A
3	525,563,713	A	T
3	525,563,724	G	C
3	526,390,100	C	T
3	526,431,520	G	A
3	526,431,521	G	A
3	527,020,577	G	A
3	527,949,245	C	G
3	527,949,254	G	A
4	110,459	C	A
4	335,967	T	C
4	625,693	A	G
4	625,694	A	G
4	625,705	A	T
4	643,869	T	C
4	870,736	T	C
4	870,741	G	A
4	1,050,854	T	G
4	1,050,859	G	A
4	1,141,880	C	T
4	1,141,927	C	G
4	1,141,960	A	G
4	1,217,719	T	A
4	1,217,721	T	C
4	1,277,038	T	C
4	1,306,003	A	G

4	1,381,345	G	T
4	1,381,349	A	G
4	1,476,670	T	C
4	1,484,191	C	G
4	1,646,597	C	T
4	1,646,598	C	G
4	3,187,614	G	C
4	3,187,620	C	T
4	3,187,626	T	A
4	3,187,684	G	A
4	3,187,686	T	C
4	3,661,512	C	T
4	4,024,746	C	G
4	4,024,776	A	G
4	4,307,246	C	A
4	4,307,270	G	A
4	4,343,093	T	C
4	4,870,840	G	A
4	4,905,242	T	C
4	4,958,421	G	A
4	5,421,770	G	A
4	5,421,796	C	T
4	6,300,642	C	T
4	6,300,664	C	T
4	6,584,744	A	C
4	6,626,804	G	C
4	6,626,819	A	C
4	7,188,419	T	C
4	8,420,302	G	A
4	8,986,781	A	C
4	9,208,201	T	A
4	9,726,139	T	C
4	9,767,888	A	G
4	9,939,268	T	C
4	10,746,467	C	T
4	10,766,129	C	T
4	10,766,138	C	T
4	11,835,081	T	C
4	12,889,417	G	A
4	13,009,077	A	G
4	13,009,148	G	T
4	13,009,189	A	C
4	13,142,773	C	A
4	15,785,649	A	G
4	15,786,155	C	T

4	16,193,985	T	G
4	16,819,825	T	C
4	17,287,186	C	T
4	17,287,191	C	T
4	18,999,391	T	C
4	21,289,587	T	G
4	21,289,686	T	C
4	21,707,835	A	G
4	21,820,289	G	A
4	21,820,292	G	A
4	21,820,302	C	T
4	22,858,200	T	G
4	23,574,947	C	A
4	24,933,603	T	C
4	24,933,650	G	A
4	25,951,457	C	T
4	25,951,485	A	G
4	27,071,446	A	G
4	27,071,508	G	A
4	27,071,509	G	T
4	28,499,948	T	C
4	29,974,619	G	A
4	30,418,674	A	C
4	40,422,741	G	A
4	41,465,482	T	C
4	43,160,241	A	T
4	43,160,242	C	T
4	49,733,243	T	G
4	49,733,250	T	A
4	54,370,276	T	C
4	58,292,464	T	C
4	58,348,408	T	G
4	58,348,419	G	T
4	58,798,297	G	A
4	61,726,882	T	C
4	62,161,809	A	G
4	63,306,024	G	C
4	64,277,211	C	T
4	64,756,881	T	C
4	65,656,235	G	T
4	65,656,265	T	C
4	68,563,660	C	T
4	68,563,760	T	C
4	68,855,792	T	A
4	69,945,462	T	C

4	70,048,515	G	T
4	70,048,549	T	C
4	73,763,997	A	G
4	73,894,061	G	T
4	78,024,746	T	A
4	78,745,488	G	A
4	79,266,514	A	G
4	79,776,935	A	G
4	81,743,359	C	T
4	82,221,934	G	A
4	82,221,942	C	A
4	83,039,499	C	T
4	83,169,883	A	T
4	83,264,224	C	T
4	84,223,436	C	G
4	91,409,240	A	G
4	97,580,564	C	T
4	97,580,569	A	G
4	99,229,545	T	C
4	103,976,666	T	A
4	111,484,678	T	C
4	119,278,323	C	T
4	119,829,963	C	A
4	122,775,566	C	T
4	124,039,723	A	C
4	124,039,731	G	A
4	124,370,218	C	T
4	126,428,484	T	G
4	126,428,521	T	G
4	129,765,334	A	T
4	131,601,631	G	A
4	131,953,384	G	A
4	132,816,109	T	C
4	132,816,142	T	C
4	133,046,999	C	T
4	135,450,416	C	A
4	136,443,381	C	T
4	140,199,249	G	A
4	144,148,806	G	T
4	144,148,868	A	G
4	145,755,085	G	T
4	147,180,787	G	A
4	152,765,387	A	G
4	155,711,852	C	T
4	176,301,069	C	T

4	176,301,077	T	C
4	176,301,084	C	G
4	176,301,098	T	G
4	178,245,598	T	A
4	178,245,599	A	T
4	178,245,600	T	C
4	178,463,926	C	A
4	182,284,751	A	G
4	184,467,749	C	T
4	184,867,451	T	G
4	184,867,471	G	A
4	184,867,492	C	T
4	185,895,832	C	T
4	186,040,553	C	T
4	187,391,968	A	G
4	187,528,621	T	G
4	189,559,255	C	T
4	191,232,303	T	C
4	194,338,908	G	C
4	200,483,856	C	A
4	202,990,153	T	C
4	202,990,266	G	A
4	207,833,386	G	C
4	209,199,457	T	C
4	210,209,114	G	A
4	210,209,126	C	A
4	210,276,735	T	C
4	210,511,650	T	C
4	214,014,829	C	T
4	214,140,743	G	A
4	215,466,108	C	G
4	218,718,297	T	G
4	218,970,524	G	C
4	219,687,807	G	A
4	219,726,207	A	G
4	220,415,317	G	A
4	221,380,219	A	G
4	222,641,954	A	G
4	224,818,925	G	A
4	225,821,439	C	T
4	226,484,962	C	A
4	227,011,449	A	C
4	227,559,577	G	T
4	228,239,366	C	T
4	228,239,385	C	G

4	229,060,415	C	G
4	229,060,442	T	C
4	229,065,424	A	G
4	229,118,333	T	G
4	229,395,278	A	C
4	229,395,308	C	G
4	230,541,196	G	A
4	230,541,200	C	T
4	231,380,163	G	C
4	232,136,386	C	A
4	232,892,676	C	A
4	233,369,047	A	G
4	234,230,578	G	A
4	236,015,941	G	A
4	237,955,391	A	C
4	239,840,963	C	G
4	240,330,415	G	A
4	240,332,742	T	G
4	241,530,845	G	C
4	241,530,883	A	G
4	241,793,989	C	T
4	243,663,348	T	C
4	243,663,353	G	A
4	244,879,953	C	T
4	244,879,967	C	T
4	246,665,919	C	T
4	247,792,250	C	T
4	248,299,357	C	T
4	249,786,934	G	T
4	250,177,350	A	G
4	250,177,411	T	C
4	260,387,552	A	C
4	262,928,184	C	T
4	265,819,605	T	C
4	266,526,440	C	T
4	267,751,248	C	T
4	267,751,279	C	T
4	267,801,195	T	C
4	267,801,225	G	A
4	269,759,873	T	C
4	272,736,402	G	A
4	274,670,957	T	C
4	275,480,883	T	C
4	277,315,820	C	T
4	277,503,424	T	C

4	279,234,106	G	A
4	281,262,346	T	G
4	282,296,614	A	G
4	282,357,567	C	A
4	282,421,023	C	T
4	282,424,183	C	T
4	282,424,184	T	G
4	282,424,230	G	A
4	283,563,268	G	A
4	283,563,309	A	C
4	283,584,757	T	C
4	283,584,788	G	T
4	285,320,754	C	T
4	285,457,783	G	T
4	285,457,817	T	C
4	285,457,822	C	T
4	285,536,279	G	A
4	285,536,312	G	A
4	285,642,278	G	A
4	285,642,306	G	T
4	285,642,358	A	C
4	286,402,314	C	T
4	286,402,348	T	C
4	286,608,917	G	T
4	286,626,809	G	A
4	286,868,636	A	C
4	290,118,640	A	T
4	290,118,643	C	T
4	290,887,171	C	T
4	291,449,251	T	A
4	291,449,262	G	A
4	292,767,531	A	G
4	293,425,711	G	A
4	294,547,512	A	T
4	296,594,303	C	T
4	298,848,850	A	G
4	300,185,022	G	A
4	300,762,264	C	T
4	302,635,736	G	T
4	302,635,745	T	C
4	304,201,406	T	C
4	312,733,458	A	C
4	312,733,470	G	A
4	313,709,336	A	G
4	314,846,945	G	T

4	315,539,735	C	T
4	316,173,301	A	T
4	316,906,093	G	T
4	318,881,505	C	T
4	319,105,327	C	T
4	319,910,032	A	G
4	319,910,106	G	A
4	321,545,596	C	A
4	325,365,818	G	A
4	325,494,410	G	A
4	326,026,075	G	T
4	328,936,432	G	A
4	331,502,304	G	A
4	333,151,410	C	A
4	341,248,292	A	C
4	342,853,656	A	G
4	342,853,683	A	G
4	345,280,522	C	T
4	345,280,526	T	G
4	347,236,537	C	G
4	347,236,544	C	G
4	349,192,123	T	C
4	352,719,482	A	G
4	354,312,579	T	G
4	354,312,583	C	T
4	354,319,158	C	T
4	354,319,167	G	A
4	354,319,169	A	G
4	354,497,817	A	C
4	354,497,818	A	T
4	354,582,178	A	G
4	354,618,283	T	A
4	354,820,605	G	A
4	354,820,623	T	C
4	354,932,984	C	T
4	355,106,230	G	T
4	355,828,499	C	T
4	356,712,488	T	C
4	356,712,500	T	C
4	358,246,435	T	C
4	359,976,265	A	G
4	361,552,887	A	C
4	361,553,027	G	C
4	362,146,980	G	T
4	362,146,981	T	G

4	362,185,888	G	A
4	362,383,820	G	T
4	362,383,833	A	C
4	362,990,772	A	G
4	363,503,099	C	T
4	363,594,005	T	C
4	363,644,999	G	A
4	363,740,021	T	G
4	363,957,997	G	A
4	364,665,467	T	A
4	364,820,801	G	T
4	366,770,492	C	T
4	367,017,591	A	G
4	367,137,992	T	G
4	367,760,235	A	G
4	367,760,273	G	A
4	368,498,755	T	C
4	369,419,048	G	A
4	369,749,903	T	C
4	369,749,908	T	G
4	370,352,592	T	C
4	370,352,593	G	A
4	370,555,474	T	G
4	370,570,215	T	C
4	370,879,680	T	A
4	370,888,929	G	C
4	375,572,926	C	G
4	376,738,567	C	T
4	376,803,535	A	G
4	376,803,559	A	G
4	377,494,379	G	A
4	377,668,300	G	A
4	378,228,025	C	A
4	378,398,752	C	T
4	381,314,825	A	G
4	381,314,831	A	G
4	381,314,851	A	G
4	385,052,987	A	G
4	385,073,322	A	G
4	385,399,261	C	T
4	385,570,496	A	C
4	385,585,467	C	T
4	385,585,478	C	T
4	385,607,228	A	G
4	385,607,256	A	C

4	385,787,506	G	A
4	385,795,200	C	A
4	386,484,070	T	G
4	388,020,363	A	G
4	388,315,276	C	T
4	389,641,448	G	A
4	390,085,008	G	T
4	391,781,390	G	T
4	392,237,905	G	T
4	392,851,655	A	C
4	392,935,218	T	C
4	393,939,456	A	C
4	394,426,786	T	C
4	394,494,000	T	A
4	394,882,806	T	A
4	397,036,508	G	A
4	397,036,549	T	C
4	397,036,555	C	T
4	397,036,580	C	T
4	397,036,590	A	G
4	397,542,132	T	C
4	397,551,370	G	T
4	397,782,542	A	C
4	397,782,560	T	C
4	397,782,566	A	G
4	397,782,645	A	C
4	397,782,664	G	T
4	397,782,753	C	T
4	398,142,553	A	T
4	398,357,825	A	G
4	398,425,749	C	T
4	398,425,751	T	C
4	399,451,876	A	G
4	399,520,864	A	G
4	399,520,916	T	A
4	399,788,494	T	C
4	400,285,965	G	A
4	401,053,008	C	T
4	401,053,011	T	A
4	401,385,085	T	C
4	401,411,220	A	G
4	401,411,642	G	A
4	401,531,910	A	C
4	401,967,788	A	G
4	402,487,826	G	A

4	402,672,493	C	T
4	402,672,507	A	C
4	402,672,515	C	T
4	402,727,857	T	A
4	403,072,245	A	G
4	403,943,963	C	T
4	403,943,970	A	G
4	403,944,130	C	T
4	403,944,159	G	T
4	403,944,165	A	G
4	404,069,375	A	G
4	404,429,434	A	C
4	404,757,640	C	T
4	404,757,643	G	A
4	404,757,646	A	C
4	404,859,237	T	C
4	404,953,601	A	T
4	404,987,474	C	T
4	404,988,071	T	C
4	405,186,253	A	G
4	405,323,220	G	A
4	405,323,245	C	T
4	405,323,256	C	G
4	407,785,408	G	A
4	407,785,417	C	T
4	407,785,450	A	C
4	407,785,460	A	C
4	407,785,538	C	T
4	407,785,550	T	G
4	407,785,555	C	T
4	407,785,566	C	G
4	409,456,678	A	C
4	409,456,697	T	C
4	409,895,613	G	C
4	410,233,784	G	A
4	411,170,374	A	G
4	411,281,198	C	G
4	411,281,203	C	G
4	411,657,022	C	T
4	411,750,315	T	C
4	412,216,124	A	G
4	412,216,125	A	G
4	412,216,128	G	T
4	412,581,909	G	A
4	412,581,982	C	A

4	412,972,348	G	A
4	412,982,982	C	T
4	413,116,419	G	A
4	413,116,441	G	A
4	413,186,582	G	A
4	414,627,512	G	A
4	414,761,813	A	C
5	291,344	G	A
5	407,196	T	C
5	407,197	A	G
5	638,801	T	A
5	764,456	G	A
5	764,472	A	G
5	1,030,463	C	T
5	1,044,004	A	C
5	1,625,515	C	T
5	1,926,504	T	C
5	2,549,103	T	C
5	6,700,531	T	C
5	6,708,449	T	C
5	6,801,166	T	G
5	7,320,001	G	A
5	7,320,007	C	T
5	7,320,028	G	A
5	7,735,935	T	C
5	7,735,936	G	T
5	7,735,950	C	G
5	7,960,267	A	C
5	8,236,637	C	T
5	8,329,747	A	G
5	8,329,763	T	C
5	10,990,866	G	C
5	11,256,528	G	A
5	11,965,622	G	A
5	12,099,547	C	T
5	12,141,106	A	G
5	12,392,709	A	G
5	12,392,757	C	G
5	13,638,756	T	G
5	14,015,154	G	A
5	14,015,201	G	A
5	14,100,874	C	A
5	14,248,229	C	T
5	14,677,226	G	A
5	15,070,064	G	C

5	15,175,839	A	G
5	15,520,344	G	A
5	16,019,399	A	T
5	16,285,630	C	T
5	16,500,728	C	T
5	16,500,732	C	T
5	16,500,909	C	T
5	16,500,910	A	T
5	16,500,911	T	A
5	18,268,954	C	G
5	18,280,337	G	A
5	18,280,340	G	C
5	18,280,341	C	G
5	18,280,342	G	C
5	18,489,155	C	G
5	18,489,213	C	A
5	19,051,186	C	G
5	21,676,416	T	C
5	23,384,881	G	C
5	24,074,068	T	A
5	24,074,071	C	T
5	24,309,533	A	C
5	25,399,580	A	G
5	25,399,609	C	T
5	27,446,577	C	T
5	28,416,635	C	T
5	30,245,755	T	A
5	30,532,150	A	C
5	31,174,806	G	A
5	32,688,459	G	A
5	33,346,065	C	G
5	34,827,992	G	C
5	35,269,226	G	A
5	38,329,301	C	G
5	38,447,004	C	T
5	38,447,067	C	A
5	41,614,088	T	G
5	41,905,358	A	T
5	43,017,194	T	G
5	43,119,032	G	A
5	43,599,856	T	C
5	43,599,860	C	A
5	43,996,763	C	A
5	45,324,350	C	T
5	46,537,353	C	T

5	47,316,817	C	T
5	48,168,508	G	A
5	48,168,511	G	C
5	48,811,586	T	C
5	49,564,054	C	G
5	51,283,592	T	C
5	51,641,371	C	G
5	51,641,396	C	A
5	51,641,417	A	G
5	51,939,408	G	C
5	52,488,668	G	C
5	54,498,185	G	C
5	57,375,109	A	G
5	61,648,635	G	A
5	72,825,475	A	G
5	77,500,696	T	A
5	77,500,750	C	T
5	78,146,667	G	T
5	79,037,927	G	C
5	79,440,355	C	A
5	79,440,356	C	A
5	81,172,743	A	G
5	83,174,664	C	T
5	85,504,208	G	C
5	87,055,828	G	A
5	92,994,419	C	T
5	96,902,584	T	G
5	97,693,362	C	G
5	99,843,792	A	T
5	102,052,369	G	C
5	102,052,371	A	G
5	103,913,445	G	A
5	106,405,746	G	A
5	107,960,891	C	T
5	107,960,922	T	A
5	108,717,729	T	C
5	112,135,582	C	T
5	113,227,909	T	C
5	113,568,462	C	T
5	113,876,234	T	A
5	113,876,241	G	T
5	114,912,485	G	T
5	114,912,508	G	A
5	114,912,538	T	C
5	114,912,541	T	A

5	114,931,736	C	T
5	115,161,274	A	G
5	115,810,416	A	G
5	116,240,776	C	T
5	116,301,627	T	G
5	116,301,631	C	T
5	116,378,090	A	C
5	117,380,772	T	G
5	119,254,556	T	C
5	119,804,870	C	T
5	119,804,874	G	A
5	123,590,559	A	G
5	123,590,635	A	G
5	123,716,546	A	G
5	124,094,053	T	A
5	124,201,000	C	T
5	124,201,013	T	C
5	124,628,282	A	C
5	124,628,292	G	A
5	127,806,396	C	T
5	127,806,433	A	C
5	127,806,436	C	T
5	128,451,334	C	T
5	128,451,341	T	C
5	128,451,377	C	A
5	128,451,419	T	G
5	129,383,800	C	T
5	130,431,615	A	T
5	130,431,616	A	C
5	130,530,353	G	A
5	130,695,600	C	T
5	130,695,604	A	C
5	130,695,625	C	T
5	132,412,335	G	T
5	135,032,676	G	A
5	135,034,501	G	A
5	135,432,003	G	T
5	135,432,004	T	G
5	136,532,836	G	A
5	136,990,553	A	C
5	138,694,583	A	G
5	138,701,653	T	C
5	138,701,738	G	T
5	139,752,091	T	C
5	139,752,157	C	T

5	140,050,947	G	A
5	140,051,033	C	T
5	140,972,657	A	G
5	140,972,658	G	A
5	140,985,994	T	A
5	140,986,015	T	C
5	143,244,885	C	T
5	143,244,887	A	C
5	145,400,652	A	T
5	145,400,680	G	A
5	145,972,892	T	C
5	146,254,820	T	C
5	146,714,473	C	T
5	146,996,967	T	A
5	146,997,011	C	T
5	147,278,998	C	T
5	147,502,165	C	G
5	149,729,591	C	T
5	150,707,304	A	G
5	153,223,631	C	A
5	153,548,637	A	C
5	157,286,535	G	T
5	157,768,771	A	G
5	158,395,830	A	G
5	158,814,169	T	C
5	158,814,170	G	A
5	160,144,107	G	T
5	160,902,762	A	C
5	160,902,835	A	G
5	162,442,813	G	C
5	166,314,019	C	G
5	168,534,336	A	G
5	169,538,925	G	A
5	169,538,937	C	T
5	169,631,152	T	G
5	169,984,589	A	G
5	170,068,566	C	T
5	172,846,440	C	G
5	173,088,896	A	G
5	176,608,218	A	G
5	178,676,861	C	T
5	178,676,972	T	C
5	180,620,409	C	T
5	181,494,437	C	T
5	181,510,666	G	A

5	182,065,454	T	C
5	182,065,484	C	T
5	183,022,888	T	C
5	183,022,962	T	C
5	183,818,675	G	A
5	183,818,700	A	C
5	183,818,714	A	C
5	183,818,723	G	A
5	184,800,795	A	G
5	185,749,140	T	C
5	185,967,475	A	G
5	187,095,122	G	A
5	187,177,455	T	C
5	188,597,418	A	T
5	188,677,903	G	A
5	192,427,418	T	C
5	196,808,661	G	C
5	197,511,738	C	A
5	198,039,927	T	C
5	198,039,943	G	A
5	198,061,905	C	T
5	198,602,233	T	C
5	199,205,440	A	G
5	199,205,495	A	C
5	201,462,032	A	C
5	201,619,559	C	T
5	205,860,356	C	G
5	206,025,860	T	C
5	206,312,977	G	A
5	206,312,978	A	G
5	206,312,979	G	A
5	206,312,980	A	G
5	211,938,786	G	A
5	211,938,793	A	T
5	211,938,829	T	G
5	212,765,578	A	C
5	213,428,645	C	A
5	216,846,070	T	C
5	216,846,081	T	A
5	217,813,395	C	T
5	217,813,399	T	C
5	217,912,602	T	G
5	218,019,464	G	A
5	218,422,517	T	A
5	225,053,859	T	A

5	226,565,909	T	G
5	229,546,374	G	A
5	229,615,596	A	G
5	229,616,223	A	G
5	229,616,244	T	C
5	232,166,500	G	A
5	232,166,547	G	A
5	232,166,555	T	C
5	232,617,699	A	G
5	232,864,282	A	G
5	233,309,908	C	T
5	233,314,501	A	G
5	234,784,565	T	C
5	236,902,453	T	G
5	238,100,229	A	G
5	240,758,734	A	G
5	242,943,481	T	A
5	243,277,780	G	T
5	243,878,830	A	G
5	244,617,080	C	T
5	244,664,869	A	T
5	245,562,750	G	A
5	246,497,633	C	T
5	246,497,701	T	C
5	246,599,411	G	A
5	246,927,843	T	A
5	246,927,854	T	C
5	246,992,939	T	C
5	246,992,954	A	G
5	247,242,520	A	G
5	247,461,606	G	T
5	248,414,408	T	C
5	248,675,762	C	T
5	248,804,262	G	C
5	249,404,229	A	G
5	249,404,265	G	T
5	249,406,022	C	T
5	249,437,512	C	T
5	249,437,566	A	G
5	249,501,026	G	A
5	249,748,696	A	G
5	251,001,928	G	A
5	251,803,893	A	G
5	252,157,929	C	T
5	252,354,965	G	C

5	252,606,399	C	T
5	252,606,472	A	G
5	253,156,298	C	T
5	254,219,746	C	A
5	254,219,765	G	C
5	254,768,597	A	G
5	254,768,628	T	G
5	255,352,834	T	C
5	255,691,546	T	C
5	256,336,408	C	T
5	256,348,466	A	G
5	256,348,514	C	A
5	257,421,759	C	T
5	257,984,375	A	G
5	258,410,520	T	C
5	258,410,526	T	G
5	258,410,559	C	A
5	258,424,389	G	A
5	261,549,976	T	A
5	262,117,797	C	A
5	262,962,876	T	A
5	262,962,877	G	T
5	262,962,879	G	T
5	262,962,893	A	C
5	264,237,099	G	A
5	264,237,123	C	G
5	264,237,127	C	T
5	266,571,379	G	A
5	267,401,303	C	G
5	268,755,048	A	G
5	280,752,366	G	A
5	280,818,755	G	T
5	281,257,439	G	A
5	281,565,208	A	G
5	282,154,627	G	T
5	283,360,411	G	T
5	283,500,913	T	C
5	283,500,921	C	T
5	283,501,019	A	G
5	283,764,564	C	T
5	283,848,069	A	T
5	283,848,074	G	C
5	283,950,354	C	T
5	283,950,358	G	A
5	284,255,894	A	T

5	284,375,661	C	T
5	287,495,989	T	C
5	287,495,990	A	T
5	288,946,950	C	A
5	289,388,129	T	C
5	290,102,893	G	A
5	290,727,907	T	G
5	291,887,214	G	A
5	291,920,712	A	C
5	292,128,030	T	C
5	292,583,357	C	T
5	292,583,412	C	A
5	292,583,430	C	T
5	294,097,849	C	A
5	294,147,467	A	G
5	295,550,448	G	A
5	295,928,632	G	A
5	296,153,354	G	T
5	296,577,855	G	C
5	296,727,514	A	G
5	296,727,559	A	T
5	296,727,576	G	C
5	296,727,585	C	T
5	296,727,892	C	T
5	299,006,247	G	A
5	299,121,089	C	T
5	299,121,138	C	T
5	299,276,545	A	G
5	299,314,304	G	A
5	299,314,310	G	T
5	299,325,881	T	C
5	299,819,113	C	G
5	300,422,718	C	T
5	302,253,130	C	T
5	302,527,114	T	C
5	302,527,199	T	C
5	303,178,014	T	C
5	303,297,383	T	C
5	303,460,622	C	T
5	303,503,928	T	G
5	303,535,571	G	C
5	303,560,805	A	T
5	303,938,544	G	A
5	304,046,608	G	A
5	304,046,651	C	T

5	304,060,458	A	G
6	582,913	C	A
6	834,301	A	C
6	834,310	T	C
6	1,070,209	T	C
6	1,524,222	A	C
6	1,524,312	C	T
6	1,921,644	C	G
6	1,921,661	T	C
6	2,239,714	C	T
6	2,239,808	T	C
6	2,345,881	G	A
6	2,436,070	C	T
6	4,280,907	A	G
6	4,281,039	G	A
6	4,977,552	G	A
6	6,554,775	A	C
6	7,464,293	T	C
6	7,610,982	G	T
6	7,618,460	C	T
6	7,618,520	A	T
6	7,618,521	T	C
6	10,446,806	C	T
6	10,753,117	G	A
6	12,317,327	G	A
6	12,456,049	A	G
6	12,456,054	C	T
6	15,526,735	A	C
6	29,559,439	G	A
6	29,637,216	C	T
6	29,637,315	G	A
6	30,173,174	C	T
6	30,394,875	C	T
6	30,538,623	C	T
6	30,769,049	G	A
6	34,058,023	C	A
6	34,417,318	A	G
6	34,417,342	G	A
6	35,618,527	C	A
6	35,844,632	G	A
6	36,184,761	A	T
6	37,196,116	G	A
6	37,718,198	A	T
6	38,857,598	T	C
6	39,023,966	G	A

6	40,512,845	A	G
6	42,239,961	T	C
6	43,188,073	G	A
6	44,387,593	C	T
6	45,726,427	T	C
6	47,119,621	C	T
6	47,347,296	T	C
6	47,347,318	C	A
6	48,818,624	A	G
6	49,387,803	C	T
6	51,228,619	T	C
6	52,050,093	C	T
6	54,218,710	C	T
6	54,784,619	G	T
6	54,800,621	G	A
6	54,800,628	A	G
6	54,800,698	T	C
6	56,597,016	C	G
6	57,677,051	G	A
6	57,677,124	G	C
6	58,145,481	G	A
6	58,951,544	G	A
6	58,960,208	C	T
6	58,962,050	T	C
6	60,520,955	T	C
6	60,520,956	G	A
6	63,815,205	A	G
6	63,815,211	T	C
6	65,128,334	A	T
6	65,128,335	A	T
6	65,362,278	T	G
6	65,362,314	G	C
6	65,960,130	G	T
6	65,960,182	C	T
6	67,158,696	A	T
6	67,158,732	C	T
6	67,893,729	G	A
6	68,483,311	A	G
6	69,436,548	A	C
6	71,330,777	C	T
6	72,805,496	G	C
6	73,297,838	G	A
6	73,509,922	C	G
6	73,557,311	T	C
6	73,658,861	C	G

6	73,725,067	C	G
6	73,729,995	A	T
6	73,730,017	T	C
6	73,735,255	G	T
6	73,808,092	A	G
6	77,686,089	C	G
6	79,209,234	A	G
6	79,448,124	C	T
6	79,448,173	G	A
6	79,971,196	G	A
6	79,989,241	A	C
6	80,226,037	C	T
6	80,586,872	G	A
6	81,543,944	A	C
6	81,628,289	T	A
6	81,783,258	C	T
6	81,934,221	C	T
6	82,022,148	C	T
6	82,287,614	C	T
6	82,415,684	A	G
6	85,363,590	G	C
6	86,017,285	G	A
6	92,785,297	G	C
6	92,870,659	A	C
6	95,429,280	T	C
6	95,453,892	T	A
6	95,453,893	G	T
6	99,597,561	C	T
6	99,900,231	C	T
6	101,722,966	A	T
6	102,419,413	T	G
6	103,149,080	G	A
6	103,149,081	C	A
6	103,149,137	T	G
6	103,149,142	A	G
6	108,634,220	T	G
6	108,776,314	G	T
6	108,776,315	T	G
6	108,776,318	T	G
6	108,776,319	T	C
6	109,903,146	C	T
6	110,558,534	C	G
6	111,934,337	T	A
6	114,792,942	A	C
6	114,793,682	A	C

6	119,067,700	T	C
6	124,123,241	T	C
6	124,154,266	T	G
6	125,860,744	G	A
6	125,860,773	A	C
6	126,456,564	T	C
6	128,307,861	T	C
6	133,714,984	C	T
6	133,715,041	G	T
6	135,586,480	C	T
6	136,407,337	A	G
6	136,787,402	C	A
6	139,485,052	T	C
6	139,655,438	G	A
6	142,490,645	G	C
6	142,922,930	C	G
6	143,010,476	A	T
6	144,069,335	G	A
6	144,195,410	C	T
6	144,820,535	C	G
6	144,989,442	A	G
6	145,613,039	C	G
6	145,631,195	A	G
6	146,558,300	C	T
6	146,558,322	C	T
6	147,019,078	G	T
6	147,387,595	C	G
6	147,845,735	T	C
6	147,941,172	T	C
6	148,552,382	C	T
6	149,913,569	A	G
6	150,806,422	C	T
6	150,806,460	T	C
6	151,516,751	G	A
6	153,956,785	C	T
6	153,986,389	A	G
6	154,619,991	G	A
6	154,619,993	T	A
6	154,653,392	T	A
6	154,916,280	G	C
6	155,429,556	A	G
6	155,429,564	C	T
6	156,748,246	G	A
6	157,245,058	C	T
6	157,245,583	C	G

6	157,288,344	T	C
6	157,288,362	G	C
6	157,288,368	G	A
6	157,506,178	C	T
6	157,962,581	C	T
6	158,894,018	T	G
6	159,193,444	T	C
6	160,628,826	T	C
6	161,073,183	C	A
6	161,101,441	C	T
6	161,939,749	G	A
6	161,939,752	C	T
6	161,944,219	A	G
6	163,223,392	T	C
6	163,684,513	A	G
6	163,684,530	G	C
6	163,685,152	A	G
6	164,460,456	A	T
6	164,500,638	A	G
6	166,332,225	A	G
6	166,747,571	T	C
6	167,828,298	C	T
6	167,828,310	T	C
6	169,303,460	A	G
6	169,303,467	A	T
6	170,766,798	A	G
6	171,163,695	T	C
6	178,601,734	C	A
6	178,840,973	A	G
6	178,840,983	T	C
6	183,172,264	G	A
6	183,172,275	C	T
6	188,635,536	T	C
6	193,459,381	G	A
6	193,459,484	A	G
6	193,766,789	A	C
6	193,766,845	C	G
6	193,766,852	G	A
6	193,992,410	A	G
6	193,992,415	G	A
6	193,992,434	A	G
6	193,992,455	G	A
6	194,271,853	C	A
6	194,271,860	A	G
6	195,390,260	T	C

6	195,390,298	C	A
6	196,184,125	C	T
6	196,184,147	C	T
6	196,374,027	C	T
6	199,258,131	A	G
6	199,258,132	A	G
6	201,294,639	C	A
6	201,294,647	C	T
6	201,403,369	A	G
6	201,546,689	A	G
6	202,415,842	C	T
6	203,326,211	G	A
6	203,706,609	A	G
6	204,019,398	C	A
6	204,272,089	T	G
6	204,272,170	C	G
6	204,397,129	A	G
6	204,476,339	T	C
6	209,584,185	C	T
6	209,731,544	A	C
6	209,762,129	C	T
6	209,762,144	C	A
6	212,259,291	C	T
6	212,259,310	G	A
6	212,709,665	C	A
6	212,709,674	G	A
6	213,234,063	G	A
6	213,706,942	C	T
6	213,706,966	G	C
6	213,739,410	G	A
6	213,962,466	C	T
6	214,690,915	G	A
6	214,690,999	G	A
6	215,608,010	A	G
6	216,096,160	T	C
6	217,081,136	T	G
6	217,081,225	A	T
6	217,671,014	C	T
6	218,586,781	C	T
6	219,181,334	T	C
6	219,560,191	T	A
6	219,716,712	T	G
6	219,720,723	C	A
6	219,720,727	G	A
6	220,048,021	C	G

6	220,048,072	T	A
6	220,674,223	A	G
6	221,833,330	T	C
6	222,727,145	C	T
6	223,410,737	C	A
6	223,410,778	T	C
6	223,821,921	C	T
6	223,821,982	C	T
6	224,387,733	C	G
6	225,541,049	T	C
6	226,479,422	A	T
6	228,274,203	A	G
6	232,361,063	A	G
6	232,519,051	G	A
6	233,732,244	C	T
6	236,613,451	G	A
6	236,613,452	T	C
6	237,497,150	T	G
6	237,497,168	G	T
6	238,422,635	C	G
6	239,696,868	T	C
6	239,805,883	C	A
6	239,805,885	A	T
6	239,805,887	T	A
6	239,805,888	A	T
6	239,810,879	T	C
6	241,312,768	T	G
6	241,560,650	G	A
6	241,560,665	T	C
6	242,148,530	C	G
6	242,148,531	A	G
6	242,148,570	T	C
6	244,021,141	C	T
6	244,360,267	T	C
6	244,648,878	A	C
6	244,648,966	G	T
6	244,688,420	G	A
6	244,688,486	A	T
6	244,928,534	G	A
6	245,581,161	A	G
6	245,581,176	G	A
6	245,593,969	G	T
6	245,623,792	G	C
6	245,623,840	T	A
6	246,576,775	C	G

6	246,633,626	A	C
6	246,709,562	A	C
6	247,393,412	G	A
6	247,393,421	T	C
6	247,785,355	A	G
6	248,472,280	A	C
6	248,472,320	C	T
6	248,566,870	G	A
6	248,566,876	G	A
6	248,878,126	C	T
6	248,878,147	G	A
6	249,241,763	G	T
6	250,077,877	C	T
6	250,077,883	T	C
6	251,069,415	C	A
6	251,069,424	C	A
6	251,069,436	T	A
6	251,069,441	T	A
6	251,069,461	A	G
6	251,141,633	A	G
6	251,141,646	G	A
6	251,197,450	C	T
6	251,222,412	C	A
6	251,222,413	T	C
6	251,301,464	T	C
6	251,301,469	G	A
6	251,390,473	T	C
6	251,473,407	G	T
6	251,585,251	A	T
6	252,088,531	A	C
6	252,088,647	A	G
6	252,111,795	C	T
6	252,961,616	C	G
6	254,235,018	A	G
6	255,230,868	C	A
6	255,364,129	T	A
6	256,012,173	G	A
6	256,966,651	A	G
6	259,051,680	G	T
6	259,147,126	T	C
6	259,959,536	G	A
6	259,959,565	C	T
6	260,101,199	C	T
6	262,912,844	A	G
6	262,912,847	A	T

6	262,912,861	G	A
6	263,300,719	C	T
6	264,517,984	A	G
6	264,519,913	T	C
6	267,630,873	G	C
6	271,574,822	A	T
6	271,574,824	C	A
6	271,574,825	T	C
6	272,364,871	A	G
6	272,629,519	G	A
6	273,395,217	G	C
6	275,609,215	C	G
6	276,581,278	C	T
6	276,581,294	G	A
6	276,641,997	T	G
6	276,642,074	G	A
6	277,655,926	A	G
6	278,701,702	T	C
6	283,928,423	G	T
6	283,928,451	G	C
6	288,819,489	C	A
6	290,602,554	T	C
6	290,888,734	T	C
6	290,895,570	T	C
6	291,128,346	T	C
6	291,128,363	A	G
7	556,882	G	A
7	720,301	T	C
7	720,318	G	A
7	859,928	G	A
7	1,100,592	A	G
7	1,100,593	G	A
7	1,201,716	T	C
7	1,201,724	A	G
7	1,201,781	A	G
7	1,643,093	T	A
7	1,656,609	G	T
7	1,656,726	T	C
7	2,320,172	C	A
7	2,588,712	T	G
7	2,621,852	A	C
7	3,793,934	A	G
7	3,793,939	T	A
7	3,793,953	G	A
7	4,139,627	C	T

7	4,229,519	C	A
7	5,802,030	C	A
7	6,640,122	C	T
7	6,891,512	T	C
7	6,891,551	G	T
7	7,951,440	A	T
7	8,002,927	G	A
7	8,002,988	G	A
7	8,397,981	A	G
7	8,913,667	G	C
7	8,969,415	G	T
7	8,969,416	A	T
7	9,278,915	A	G
7	9,586,465	C	T
7	10,565,954	G	A
7	10,565,963	T	C
7	10,565,973	C	T
7	11,532,564	G	T
7	11,532,590	G	C
7	11,635,024	C	T
7	12,239,992	C	G
7	12,240,055	C	A
7	12,290,640	G	A
7	12,290,646	G	A
7	12,801,537	G	A
7	12,801,637	G	A
7	12,980,744	G	A
7	13,649,798	C	A
7	13,649,805	C	A
7	13,649,837	G	A
7	13,649,841	G	A
7	13,742,407	T	G
7	18,438,158	A	G
7	18,438,219	T	A
7	18,760,081	G	A
7	18,760,107	T	C
7	18,766,445	T	C
7	19,805,363	T	C
7	19,805,409	A	G
7	20,109,151	T	G
7	22,114,375	T	G
7	22,696,330	C	T
7	27,547,207	T	G
7	27,547,233	T	G
7	27,547,273	C	T

7	27,618,729	C	T
7	30,284,481	C	T
7	30,360,737	G	T
7	30,889,407	A	C
7	31,815,163	C	T
7	31,815,241	C	A
7	32,779,791	G	C
7	35,379,373	G	A
7	36,397,616	G	T
7	38,171,292	A	G
7	47,181,427	T	C
7	47,365,372	T	G
7	47,365,390	C	T
7	49,688,650	G	C
7	52,858,564	C	T
7	52,858,566	C	T
7	53,025,774	C	T
7	55,150,735	A	G
7	64,592,210	G	A
7	64,592,292	A	C
7	64,651,827	C	T
7	64,651,828	G	A
7	65,272,858	G	A
7	65,272,866	A	C
7	66,568,980	C	A
7	68,373,701	C	T
7	68,373,719	G	T
7	68,373,734	T	G
7	70,721,887	C	A
7	72,797,403	A	T
7	74,192,607	C	G
7	74,675,022	C	G
7	74,713,360	C	A
7	74,713,511	T	C
7	74,936,963	C	T
7	76,034,757	C	A
7	77,488,388	A	G
7	78,426,582	A	G
7	78,429,479	T	C
7	79,432,750	T	C
7	79,516,753	A	C
7	81,529,823	G	T
7	82,076,985	T	G
7	83,238,543	T	C
7	83,391,985	C	G

7	83,391,999	T	C
7	86,757,432	A	G
7	86,757,543	C	G
7	87,254,201	A	G
7	87,254,214	C	T
7	87,254,258	T	A
7	89,480,582	G	A
7	93,021,915	A	G
7	94,228,735	G	A
7	95,403,966	G	A
7	95,706,221	A	G
7	102,536,912	T	C
7	102,614,300	G	A
7	103,055,583	T	C
7	104,089,240	T	C
7	104,089,254	G	A
7	104,089,261	G	T
7	104,546,152	A	G
7	105,742,119	T	C
7	107,303,933	C	A
7	107,655,077	A	T
7	108,569,481	A	C
7	110,015,896	C	G
7	111,227,894	C	T
7	112,708,781	C	T
7	112,708,830	C	T
7	112,795,683	A	T
7	118,647,630	T	A
7	121,936,414	A	T
7	134,126,522	T	C
7	137,939,330	G	A
7	142,007,862	G	C
7	142,007,909	C	A
7	143,413,477	G	T
7	143,413,478	G	T
7	145,459,913	C	G
7	149,370,245	T	G
7	167,937,122	T	C
7	167,937,134	C	T
7	168,861,445	G	T
7	174,122,019	G	A
7	174,442,397	G	C
7	174,697,184	C	T
7	175,740,245	T	G
7	175,740,249	T	G

7	176,396,531	C	A
7	177,000,527	T	C
7	177,553,472	G	C
7	179,113,684	G	A
7	180,813,920	T	C
7	182,997,944	G	A
7	182,998,028	G	A
7	183,010,898	A	C
7	183,413,540	T	C
7	185,165,717	G	A
7	185,165,737	C	T
7	186,020,237	C	T
7	187,728,750	C	T
7	189,880,539	C	T
7	189,931,478	G	T
7	189,989,908	A	G
7	194,499,424	G	A
7	200,608,928	C	G
7	200,608,952	T	C
7	200,644,888	A	G
7	200,807,007	G	A
7	200,807,103	G	A
7	201,485,448	G	A
7	201,799,333	G	A
7	202,425,614	A	G
7	203,009,946	C	T
7	203,378,793	G	A
7	204,180,725	T	C
7	205,102,807	C	T
7	205,102,840	T	C
7	205,732,443	T	C
7	206,665,330	C	T
7	208,810,657	C	G
7	208,810,752	G	A
7	209,012,360	T	C
7	209,610,127	T	A
7	209,620,900	A	C
7	209,804,767	A	C
7	210,423,536	A	G
7	210,423,588	T	A
7	211,772,608	C	A
7	213,593,490	T	A
7	214,782,425	G	A
7	216,174,900	C	T
7	220,182,952	C	T

7	224,847,092	C	T
7	226,696,906	G	T
7	233,859,159	G	A
7	234,416,071	T	C
7	234,476,646	A	C
7	234,492,087	T	C
7	234,644,593	A	G
7	234,644,611	T	G
7	235,119,311	C	T
7	238,571,457	G	T
7	239,184,798	A	G
7	239,500,953	A	C
7	239,783,088	A	G
7	242,024,626	G	T
7	242,052,559	T	C
7	242,303,690	C	A
7	243,547,077	G	A
7	244,713,631	A	C
7	246,820,802	A	T
7	247,365,117	C	G
7	247,932,197	A	T
7	247,932,221	G	A
7	247,985,777	G	A
7	247,985,807	T	G
7	249,802,789	A	G
7	249,974,168	A	G
7	250,568,661	T	C
7	250,642,207	A	G
7	250,642,229	G	C
7	250,753,337	C	A
7	250,887,904	T	C
7	251,663,024	C	T
7	251,800,278	C	T
7	251,800,281	C	A
7	252,382,645	C	T
7	252,382,694	A	G
7	252,493,845	T	C
7	252,493,854	A	T
7	252,493,864	A	G
7	253,207,189	T	C
7	253,207,261	T	C
7	253,281,433	A	T
7	253,553,051	G	T
7	253,651,112	C	T
7	253,745,166	T	C

7	253,801,343	C	A
7	253,801,431	C	T
7	253,903,160	G	A
7	254,014,698	T	C
7	254,175,933	C	T
7	254,187,303	A	G
7	254,464,677	T	G
7	254,783,168	T	C
7	254,918,562	A	G
7	254,918,648	C	G
7	254,918,690	T	G
7	254,918,787	T	G
7	255,363,329	C	T
7	255,363,331	C	T
7	255,369,698	T	G
7	256,802,670	G	T
7	256,802,692	C	T
7	256,993,580	A	G
7	256,993,581	G	A
7	256,993,611	A	G
7	257,247,277	G	A
7	257,499,331	G	A
7	257,707,361	A	C
7	258,187,648	A	G
7	258,357,599	G	A
7	258,630,065	T	A
7	259,059,726	A	G
7	259,557,397	C	A
7	259,604,532	G	A
7	260,448,031	A	G
7	260,472,724	G	C
7	260,597,422	G	A
7	260,597,434	T	G
7	260,642,427	C	T
8	6,996,913	A	G
8	7,635,127	G	C
8	7,723,894	T	G
8	8,027,709	C	T
8	9,176,136	C	T
8	9,763,237	C	T
8	10,008,156	G	A
8	11,969,517	T	C
8	12,354,802	G	A
8	12,354,807	T	C
8	12,372,080	C	G

8	13,708,231	A	T
8	13,991,242	T	C
8	13,991,260	A	G
8	13,991,261	T	C
8	14,232,887	C	T
8	16,096,310	A	G
8	18,214,358	G	A
8	23,144,416	A	G
8	23,245,610	C	T
8	23,245,616	G	T
8	27,900,238	C	A
8	28,535,808	C	T
8	29,193,541	T	C
8	32,007,900	C	T
8	32,233,416	A	G
8	32,233,420	G	A
8	33,827,553	T	C
8	34,419,935	T	A
8	36,007,634	C	G
8	36,007,714	A	T
8	36,007,715	C	T
8	36,343,916	T	C
8	41,173,457	A	T
8	41,384,504	T	C
8	42,293,941	T	G
8	42,597,339	T	G
8	47,199,981	C	T
8	51,324,754	T	C
8	51,324,762	T	G
8	51,324,769	A	G
8	63,777,272	T	C
8	63,982,586	A	G
8	65,153,018	T	C
8	65,153,028	C	T
8	71,586,055	G	C
8	72,280,424	A	G
8	73,128,413	G	C
8	73,278,182	A	G
8	76,214,620	T	G
8	82,829,345	T	G
8	83,678,503	T	A
8	84,015,480	A	T
8	84,513,020	A	G
8	84,513,026	G	A
8	84,513,086	C	G

8	86,307,260	C	T
8	87,615,109	A	C
8	87,819,734	G	T
8	87,828,966	G	A
8	88,403,298	C	T
8	88,403,301	C	A
8	89,711,665	G	A
8	90,075,416	C	T
8	90,373,291	C	T
8	90,491,640	A	C
8	91,998,094	C	T
8	91,998,122	A	C
8	92,115,089	A	G
8	92,115,091	G	C
8	92,722,464	G	C
8	97,823,788	A	G
8	97,823,842	C	A
8	99,760,176	G	T
8	103,907,729	G	A
8	108,158,525	T	C
8	110,588,175	T	G
8	110,997,904	C	T
8	111,359,815	G	T
8	112,889,348	C	A
8	112,908,408	T	C
8	113,144,198	G	A
8	115,085,423	G	A
8	115,750,397	C	G
8	115,750,398	G	A
8	118,788,424	T	C
8	119,172,972	C	T
8	119,172,991	T	C
8	119,370,267	C	T
8	119,370,285	C	T
8	119,370,310	C	T
8	119,400,213	G	C
8	119,410,921	C	T
8	119,410,966	T	C
8	119,411,005	A	G
8	120,078,772	C	T
8	121,053,380	A	G
8	121,857,673	G	C
8	123,362,284	A	G
8	123,362,320	C	T
8	124,775,379	C	T

8	124,775,386	C	T
8	151,316,199	C	A
8	152,590,942	G	A
8	152,590,949	A	C
8	153,792,046	T	C
8	157,989,941	C	T
8	158,656,006	T	A
8	159,609,112	G	A
8	164,287,189	C	A
8	165,417,744	G	A
8	167,732,924	G	A
8	171,478,596	C	T
8	172,428,482	G	A
8	174,391,111	A	G
8	183,878,412	G	A
8	183,878,486	T	C
8	183,878,527	T	C
8	185,803,416	T	C
8	187,195,608	C	T
8	187,273,774	C	T
8	188,361,230	G	A
8	188,656,106	G	C
8	188,662,875	A	G
8	188,665,050	C	T
8	189,670,030	C	T
8	189,793,135	A	T
8	190,341,609	A	T
8	190,341,629	C	T
8	190,382,338	T	A
8	191,932,352	G	A
8	192,925,353	T	C
8	192,925,365	A	T
8	193,152,523	G	A
8	194,665,587	C	T
8	194,976,043	C	A
8	195,160,582	G	A
8	195,535,175	G	A
8	195,882,126	C	G
8	195,882,128	A	G
8	195,882,165	G	A
8	196,161,582	C	T
8	196,161,589	T	C
8	196,161,592	G	T
8	196,851,004	C	T
8	199,469,402	C	T

8	200,159,013	G	A
8	200,159,016	T	C
8	201,200,501	T	C
8	201,919,673	G	A
8	201,919,684	G	C
8	204,928,117	G	A
8	206,273,221	G	A
8	208,130,112	T	G
8	208,130,129	A	C
8	208,130,141	C	T
8	208,130,146	C	A
8	212,068,882	C	T
8	212,068,888	C	A
8	214,221,216	G	C
8	214,221,232	T	G
8	214,221,255	A	C
8	215,526,018	G	C
8	215,721,395	T	C
8	218,522,548	C	T
8	219,794,276	T	A
8	220,740,085	G	A
8	220,931,487	A	G
8	221,017,667	G	C
8	221,289,646	A	C
8	221,511,672	A	G
8	221,541,241	A	C
8	223,060,727	A	C
8	223,134,221	G	A
8	229,063,932	T	A
8	229,063,934	C	A
8	229,063,964	C	T
8	232,971,886	A	G
8	234,440,748	G	A
8	234,440,751	T	G
8	237,415,926	C	T
8	243,262,253	C	G
8	243,721,487	G	A
8	244,136,827	A	C
8	244,136,925	G	A
8	245,274,822	A	T
8	245,274,852	C	T
8	245,277,318	A	G
8	245,277,366	A	G
8	245,277,375	A	G
8	245,687,853	C	T

8	245,687,883	C	T
8	245,945,706	G	A
8	246,103,751	C	T
8	246,103,752	T	C
8	248,085,910	T	A
8	248,085,938	A	C
8	248,085,939	C	A
8	248,085,961	A	T
8	248,548,773	C	T
8	248,548,873	A	C
8	248,650,738	G	A
8	248,650,847	G	A
8	250,082,855	C	G
8	250,082,860	G	C
8	250,082,863	G	C
8	250,371,114	C	T
8	250,515,191	T	C
8	250,517,839	A	G
8	250,517,871	T	C
8	250,517,873	A	G
8	251,145,159	A	T
8	251,145,160	T	A
8	251,182,294	C	T
8	251,671,466	A	G
8	251,671,471	A	G
8	251,729,155	C	T
8	252,114,142	C	T
8	252,149,997	T	C
8	252,951,996	G	A
8	252,952,010	C	A
8	252,952,032	G	T
8	252,952,047	T	A
8	253,496,099	G	C
8	253,867,042	G	A
8	254,146,344	G	C
8	254,736,504	C	T
8	256,828,330	C	G
8	257,128,853	G	A
8	257,128,854	T	A
8	258,916,020	C	A
8	259,286,116	T	C
8	259,286,131	T	C
8	260,080,037	G	A
8	260,080,038	C	T
8	260,080,045	T	C

8	261,711,534	C	T
8	261,991,294	C	G
8	262,192,489	C	A
8	262,759,626	A	T
8	262,917,937	C	T
8	264,133,833	A	G
8	264,191,831	G	A
8	264,397,000	G	T
8	264,495,104	G	A
8	264,495,110	T	C
8	265,666,246	T	C
8	266,335,545	T	C
8	266,967,112	G	A
8	266,967,144	T	C
8	266,967,155	A	G
8	268,064,787	C	T
8	268,086,089	T	G
8	268,325,250	A	T
8	268,325,251	G	T
8	268,325,252	G	T
8	268,346,452	G	T
8	268,964,833	T	C
8	269,145,618	C	T
8	269,145,630	G	A
8	269,870,305	G	T
8	270,917,766	A	C
8	270,917,804	A	G
8	270,944,218	C	G
8	271,079,424	T	C
8	271,220,606	A	G
8	273,110,744	G	C
8	275,409,114	C	A
8	275,409,115	A	C
8	277,400,509	G	A
8	287,606,317	A	G
8	287,606,337	G	A
8	290,424,330	A	G
8	291,154,391	A	G
8	291,154,393	A	G
8	291,918,848	C	G
8	293,504,827	A	G
8	294,260,818	A	G
8	294,260,847	C	A
8	296,581,505	C	T
8	297,858,023	T	C

8	297,858,029	C	T
8	298,381,113	T	C
8	298,434,131	C	T
8	298,434,132	T	G
8	298,434,141	C	T
8	298,477,921	T	C
8	298,685,994	G	C
8	299,204,812	G	C
8	299,205,449	C	T
8	299,417,896	C	G
8	299,670,400	C	T
8	300,473,922	C	T
8	300,900,617	C	T
8	301,262,009	A	T
8	301,351,746	C	T
8	301,452,133	T	C
8	301,452,134	G	C
8	301,452,138	T	C
8	301,922,123	C	T
8	302,736,483	C	G
8	302,736,487	A	G
8	302,736,491	T	G
8	302,736,495	T	G
8	303,684,726	T	A
8	303,934,789	C	T
8	304,539,345	G	A
8	305,571,936	G	A
8	305,783,092	A	G
8	306,487,885	T	C
8	306,667,403	T	C
8	306,791,593	G	A
8	307,075,077	A	G
8	307,075,108	T	C
8	307,158,054	C	T
8	307,380,436	G	C
8	308,173,994	A	G
8	308,525,569	G	A
8	308,525,570	C	G
8	308,525,571	T	A
8	308,525,614	T	G
8	308,857,233	A	C
8	309,286,010	A	T
8	309,286,044	G	A
8	310,094,554	G	A
8	310,094,784	T	C

8	310,094,807	C	T
8	310,459,238	G	A
8	310,467,579	T	C
8	311,482,482	C	T
8	311,482,515	G	A
8	311,482,525	G	A
8	311,758,331	A	C
8	311,758,365	G	A

Table S3- Basic statistics for all 35 cranial traits.

Measurement	Mean	SD	N
IS-PM	4.74	0.44	531
IS-NSL	3.41	0.37	531
IS-PNS	21.17	1.37	531
PM-ZS	9.84	0.70	531
PM-ZI	16.89	0.99	531
PM-MT	17.23	1.05	531
NSL-NA	16.82	1.43	531
NSL-ZS	13.80	0.95	531
NSL-ZI	21.16	1.24	531
NA-BR	10.08	1.01	531
NA-PNS	8.96	0.59	531
BR-PT	4.88	0.36	531
BR-APET	10.90	0.92	531
PT-APET	9.67	0.75	531
PT-BA	13.98	0.94	531
PT-EAM	8.96	0.90	531
PT-ZYGO	8.98	1.06	531
PT-TSP	4.94	0.58	531
ZS-ZI	7.84	0.60	531
ZI-MT	4.67	0.38	531
ZI-ZYGO	10.35	1.24	531
ZI-TSP	11.44	1.29	531
MT-PNS	3.70	0.34	531
PNS-APET	10.93	0.99	531
APET-BA	5.21	0.43	531
APET-TS	4.92	0.32	531
BA-EAM	7.89	0.47	531
EAM-ZYGO	4.39	0.51	531
ZYGO-TSP	5.49	0.84	531
LD-AS	6.70	0.61	531
BR-LD	10.54	1.12	531
OPI-LD	4.26	0.63	531
PT-AS	11.65	0.82	531
JP-AS	4.00	0.41	531
BA-OPI	4.63	0.28	531

Table S4- Correspondence between mouse traits and and their homologous opossum traits. A brief description of each distance is presented. Subscripts R and L refer to right and left sides, respectively.

Trait #	Mouse distance	Description	Opossum homologous
1	CrBaLn	Basicranial length	PNS-BA
2	FcHt	Facial height	NA-PNS
3	FcLn	Facial length	NSL-NA
4	FcLnInf	Palatal length	IS-PNS
5	FcWd	Facial width	ZS _R -ZS _L
6	NeurHt	Cranial vault height	BR-APET
7	NeurLn	Cranial vault length	BR-LD
8	NeurWdInf	Cranial vault width	AS _R -AS _L
9	ZyLn	Zygomatic length	ZI-ZYGO
10	ZyWd	Zygomatic width	ZYGO _R -ZYGO _L

Table S5 - Phenotypic variance/covariance matrix (**P**). We controlled for the effects of sex and age when calculating **P**.

	IS-PM	IS-NSL	IS-PNS	PM-ZS	PM-ZI	PM-MT	NSL-NA	NSL-ZS	NSL-ZI	NA-BR	NA-PNS	BR-PT
1	0.07	0.03	0.11	0.03	0.04	0.06	0.08	0.08	0.08	0.06	0.05	0.01
2	0.03	0.07	0.07	0.04	0.04	0.04	0.05	0.04	0.05	0.02	0.02	0.01
3	0.11	0.07	0.47	0.23	0.32	0.33	0.37	0.30	0.40	0.13	0.15	0.03
4	0.03	0.04	0.23	0.21	0.20	0.19	0.19	0.24	0.22	0.07	0.07	0.02
5	0.04	0.04	0.32	0.20	0.38	0.27	0.28	0.22	0.41	0.06	0.08	0.02
6	0.06	0.04	0.33	0.19	0.27	0.32	0.30	0.22	0.31	0.10	0.10	0.03
7	0.08	0.05	0.37	0.19	0.28	0.30	0.76	0.28	0.38	-0.20	-0.01	0.03
8	0.08	0.04	0.30	0.24	0.22	0.22	0.28	0.34	0.32	0.12	0.11	0.03
9	0.08	0.05	0.40	0.22	0.41	0.31	0.38	0.32	0.50	0.10	0.11	0.03
10	0.06	0.02	0.13	0.07	0.06	0.10	-0.20	0.12	0.10	0.78	0.17	0.13
11	0.05	0.02	0.15	0.07	0.08	0.10	-0.01	0.11	0.11	0.17	0.15	0.02
12	0.01	0.01	0.03	0.02	0.02	0.03	0.03	0.03	0.03	0.13	0.02	0.12
13	0.06	0.05	0.23	0.14	0.15	0.17	0.19	0.18	0.20	-0.11	0.11	-0.02
14	0.05	0.03	0.17	0.09	0.08	0.14	0.15	0.12	0.12	0.06	0.09	0.00
15	0.07	0.04	0.25	0.13	0.15	0.21	0.23	0.17	0.20	0.05	0.11	0.01
16	0.06	0.04	0.19	0.10	0.10	0.17	0.18	0.13	0.14	0.04	0.10	-0.01
17	0.05	0.04	0.19	0.11	0.11	0.15	0.20	0.14	0.15	0.04	0.10	-0.02
18	0.03	0.02	0.10	0.07	0.06	0.07	0.07	0.09	0.08	0.00	0.05	-0.03
19	0.02	0.00	0.11	-0.01	0.16	0.10	0.14	-0.02	0.17	0.00	0.02	0.01
20	0.02	0.01	0.05	0.01	0.06	0.07	0.05	0.02	0.07	0.04	0.01	0.01
21	0.07	0.06	0.24	0.13	0.07	0.19	0.27	0.17	0.13	0.11	0.09	0.02
22	0.09	0.07	0.26	0.15	0.08	0.18	0.28	0.21	0.15	0.11	0.10	-0.01
23	0.01	0.02	0.06	0.05	0.04	0.02	0.05	0.06	0.06	-0.02	0.03	-0.01
24	0.06	0.05	0.22	0.14	0.19	0.18	0.26	0.19	0.24	0.08	0.06	0.01
25	0.03	0.02	0.11	0.06	0.08	0.09	0.10	0.08	0.10	0.03	0.03	0.01
26	0.03	0.02	0.09	0.05	0.05	0.06	0.06	0.07	0.07	0.06	0.04	0.01
27	0.04	0.03	0.14	0.08	0.09	0.10	0.12	0.11	0.12	0.06	0.06	0.02
28	0.01	0.02	0.07	0.05	0.07	0.03	0.09	0.06	0.08	-0.03	0.01	-0.01
29	0.05	0.04	0.14	0.07	0.07	0.10	0.16	0.09	0.11	0.04	0.06	0.00
30	0.04	0.03	0.12	0.07	0.08	0.09	0.09	0.09	0.10	0.08	0.06	0.02
31	0.04	0.06	0.22	0.15	0.19	0.15	0.20	0.17	0.21	-0.36	0.06	-0.14
32	0.05	0.03	0.12	0.06	0.06	0.10	0.13	0.09	0.10	0.05	0.07	0.02
33	0.04	0.04	0.17	0.11	0.11	0.14	0.15	0.13	0.14	0.02	0.07	-0.02
34	0.03	0.01	0.06	0.03	0.02	0.05	0.07	0.04	0.05	0.02	0.04	0.02
35	-0.01	-0.01	0.00	0.00	0.02	0.01	0.01	-0.01	0.01	-0.01	-0.01	0.00

BR-APET	PT-APET	PT-BA	PT-EAM	PT-ZYGO	PT-TSP	ZS-ZI	ZI-MT	ZI-ZYGO	ZI-TSP	MT-PNS	PNS-APET
0.06	0.05	0.07	0.06	0.05	0.03	0.02	0.02	0.07	0.09	0.01	0.06
0.05	0.03	0.04	0.04	0.04	0.02	0.00	0.01	0.06	0.07	0.02	0.05
0.23	0.17	0.25	0.19	0.19	0.10	0.11	0.05	0.24	0.26	0.06	0.22
0.14	0.09	0.13	0.10	0.11	0.07	-0.01	0.01	0.13	0.15	0.05	0.14
0.15	0.08	0.15	0.10	0.11	0.06	0.16	0.06	0.07	0.08	0.04	0.19
0.17	0.14	0.21	0.17	0.15	0.07	0.10	0.07	0.19	0.18	0.02	0.18
0.19	0.15	0.23	0.18	0.20	0.07	0.14	0.05	0.27	0.28	0.05	0.26
0.18	0.12	0.17	0.13	0.14	0.09	-0.02	0.02	0.17	0.21	0.06	0.19
0.20	0.12	0.20	0.14	0.15	0.08	0.17	0.07	0.13	0.15	0.06	0.24
-0.11	0.06	0.05	0.04	0.04	0.00	0.00	0.04	0.11	0.11	-0.02	0.08
0.11	0.09	0.11	0.10	0.10	0.05	0.02	0.01	0.09	0.10	0.03	0.06
-0.02	0.00	0.01	-0.01	-0.02	-0.03	0.01	0.01	0.02	-0.01	-0.01	0.01
0.36	0.20	0.23	0.21	0.21	0.13	0.03	0.01	0.18	0.22	0.07	0.19
0.20	0.27	0.27	0.28	0.26	0.17	0.03	0.01	0.17	0.17	0.03	0.15
0.23	0.27	0.35	0.32	0.28	0.19	0.06	0.03	0.21	0.21	0.04	0.18
0.21	0.28	0.32	0.36	0.32	0.21	0.05	0.02	0.21	0.20	0.04	0.16
0.21	0.26	0.28	0.32	0.34	0.19	0.05	0.01	0.23	0.23	0.05	0.17
0.13	0.17	0.19	0.21	0.19	0.26	0.00	0.00	0.08	0.15	0.04	0.09
0.03	0.03	0.06	0.05	0.05	0.00	0.21	0.05	0.01	-0.01	0.00	0.07
0.01	0.01	0.03	0.02	0.01	0.00	0.05	0.09	0.03	0.03	-0.02	0.04
0.18	0.17	0.21	0.21	0.23	0.08	0.01	0.03	0.39	0.35	0.03	0.23
0.22	0.17	0.21	0.20	0.23	0.15	-0.01	0.03	0.35	0.48	0.06	0.23
0.07	0.03	0.04	0.04	0.05	0.04	0.00	-0.02	0.03	0.06	0.08	0.04
0.19	0.15	0.18	0.16	0.17	0.09	0.07	0.04	0.23	0.23	0.04	0.28
0.06	0.03	0.09	0.06	0.05	0.03	0.02	0.02	0.07	0.08	0.03	0.05
0.07	0.06	0.07	0.06	0.06	0.03	0.01	0.01	0.06	0.08	0.01	0.05
0.10	0.08	0.12	0.07	0.08	0.04	0.03	0.02	0.09	0.12	0.02	0.09
0.07	0.02	0.04	0.04	0.05	0.03	0.01	0.00	0.03	0.07	0.05	0.07
0.12	0.12	0.13	0.15	0.18	0.04	0.04	0.02	0.16	0.21	0.03	0.11
0.10	0.08	0.11	0.09	0.10	0.05	0.02	0.01	0.10	0.13	0.03	0.10
0.40	0.11	0.18	0.17	0.18	0.14	0.04	0.00	0.17	0.24	0.09	0.19
0.10	0.10	0.13	0.11	0.11	0.04	0.04	0.02	0.12	0.14	0.01	0.08
0.18	0.22	0.27	0.29	0.27	0.20	0.03	0.01	0.18	0.18	0.05	0.16
0.05	0.05	0.06	0.06	0.05	0.02	0.02	0.01	0.06	0.07	0.00	0.04
-0.01	0.00	0.00	-0.01	-0.01	-0.01	0.02	0.00	-0.01	-0.03	0.00	0.01

APET-BA	APET-TS	BA-EAM	EAM-ZYGO	ZYGO-TSP	LD-AS	BR-LD	OPI-LD	PT-AS	JP-AS	BA-OPI
0.03	0.03	0.04	0.01	0.05	0.04	0.04	0.05	0.04	0.03	-0.01
0.02	0.02	0.03	0.02	0.04	0.03	0.06	0.03	0.04	0.01	-0.01
0.11	0.09	0.14	0.07	0.14	0.12	0.22	0.12	0.17	0.06	0.00
0.06	0.05	0.08	0.05	0.07	0.07	0.15	0.06	0.11	0.03	0.00
0.08	0.05	0.09	0.07	0.07	0.08	0.19	0.06	0.11	0.02	0.02
0.09	0.06	0.10	0.03	0.10	0.09	0.15	0.10	0.14	0.05	0.01
0.10	0.06	0.12	0.09	0.16	0.09	0.20	0.13	0.15	0.07	0.01
0.08	0.07	0.11	0.06	0.09	0.09	0.17	0.09	0.13	0.04	-0.01
0.10	0.07	0.12	0.08	0.11	0.10	0.21	0.10	0.14	0.05	0.01
0.03	0.06	0.06	-0.03	0.04	0.08	-0.36	0.05	0.02	0.02	-0.01
0.03	0.04	0.06	0.01	0.06	0.06	0.06	0.07	0.07	0.04	-0.01
0.01	0.01	0.02	-0.01	0.00	0.02	-0.14	0.02	-0.02	0.02	0.00
0.06	0.07	0.10	0.07	0.12	0.10	0.40	0.10	0.18	0.05	-0.01
0.03	0.06	0.08	0.02	0.12	0.08	0.11	0.10	0.22	0.05	0.00
0.09	0.07	0.12	0.04	0.13	0.11	0.18	0.13	0.27	0.06	0.00
0.06	0.06	0.07	0.04	0.15	0.09	0.17	0.11	0.29	0.06	-0.01
0.05	0.06	0.08	0.05	0.18	0.10	0.18	0.11	0.27	0.05	-0.01
0.03	0.03	0.04	0.03	0.04	0.05	0.14	0.04	0.20	0.02	-0.01
0.02	0.01	0.03	0.01	0.04	0.02	0.04	0.04	0.03	0.02	0.02
0.02	0.01	0.02	0.00	0.02	0.01	0.00	0.02	0.01	0.01	0.00
0.07	0.06	0.09	0.03	0.16	0.10	0.17	0.12	0.18	0.06	-0.01
0.08	0.08	0.12	0.07	0.21	0.13	0.24	0.14	0.18	0.07	-0.03
0.03	0.01	0.02	0.05	0.03	0.03	0.09	0.01	0.05	0.00	0.00
0.05	0.05	0.09	0.07	0.11	0.10	0.19	0.08	0.16	0.04	0.01
0.08	0.02	0.06	0.02	0.04	0.04	0.08	0.04	0.04	0.02	-0.01
0.02	0.06	0.05	0.01	0.04	0.03	0.04	0.05	0.04	0.03	-0.01
0.06	0.05	0.10	-0.01	0.06	0.05	0.06	0.07	0.06	0.04	-0.01
0.02	0.01	-0.01	0.12	0.05	0.04	0.12	0.00	0.05	-0.02	0.00
0.04	0.04	0.06	0.05	0.20	0.08	0.12	0.10	0.12	0.05	-0.01
0.04	0.03	0.05	0.04	0.08	0.17	0.08	0.07	0.07	-0.03	0.00
0.08	0.04	0.06	0.12	0.12	0.08	0.84	0.02	0.24	0.03	-0.02
0.04	0.05	0.07	0.00	0.10	0.07	0.02	0.22	0.06	0.08	-0.05
0.04	0.04	0.06	0.05	0.12	0.07	0.24	0.06	0.33	0.03	0.00
0.02	0.03	0.04	-0.02	0.05	-0.03	0.03	0.08	0.03	0.13	0.00
-0.01	-0.01	-0.01	0.00	-0.01	0.00	-0.02	-0.05	0.00	0.00	0.08

Table S6 - Pairwise comparison among V/CV matrices. Matrices for all *Monodelphis* species are from Porto *et al.* 2015. Vector correlations close to one indicate that the matrices in question present very similar patterns of association among traits.

P=phenotypic variance/covariance matrix from this study; **G**= genetic variance/covariance matrix from this study; **G**_{Porto et al 2015}= genetic variance/covariance matrix from Porto *et al.* 2015.

Species	M. breviceaudata	M. domestica	M. glirina	M. palliolatta	P	G	G _{Porto et al 2015}
M. breviceaudata	1.00						
M. domestica	0.95	1.00					
M. glirina	0.86	0.89	1.00				
M. palliolatta	0.96	0.96	0.88	1.00			
P	0.88	0.92	0.89	0.89	1.00		
G	0.86	0.87	0.80	0.87	0.89	1.00	
G _{Porto et al 2015}	0.89	0.92	0.85	0.87	0.88	0.88	1.00

Table S7- Individual quantitative trait loci (QTL) identified in the opossum F₂ intercross. Focal trait refers to the trait with LOD above the genomewide significance threshold. Peak position corresponds to genomic coordinates obtained from the most recent *Monodelphis* genome assembly (momDom5).

Focal Trait	Chromosome	Peak position (bp)
MTPNS	1	111,431,571
OPILD	1	250,741,713
ISPM	1	255,916,857
PTEAM	1	282,490,482
PTAPET	1	295,047,253
ISPNS	1	728,311,971
PMMT	1	728,311,971
NSLZS	1	728,321,368
NSLZI	1	728,311,971
LDAS	2	404,691,454
NSLZI	2	419,547,705
ISPNS	2	483,162,151
PMZS	2	483,162,151
PMMT	2	483,162,151
PMZS	3	286,462,644
PMZI	3	445,347,789
BAEAM	4	315,539,735
LDAS	4	354,312,583
MTPNS	4	356,712,488
BRAPET	4	385,399,261
PMMT	4	412,216,124
NAPNS	5	115,810,416
BAEAM	5	115,810,416
ZSZI	5	249,404,229
APETTS	6	73,725,067
NSLZI	6	147,387,595
OPILD	6	147,941,172
PMZI	6	153,986,389
LDAS	6	244,021,141
ISNSL	6	290,895,570
ISPNS	6	290,888,734
PMZS	6	290,895,570
APETTS	7	55,150,735
PTBA	7	78,429,479
BRAPET	7	189,931,478
PMZI	7	255,363,329
NSLNA	8	7,723,894
ISPNS	8	108,158,525
PMZS	8	99,760,176
APETBA	8	108,158,525
APETTS	8	99,760,176
PMZI	8	268,086,089