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# Equivocal evidence for a link between megalencephaly-related genes and primate brain size evolution

DeCasien, A, Trujillo, A, Janiak, MC, Harshaw, E, Caes, Z, Galindo, G, Petersen, R and Higham, J

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| <b>Authors</b>           | DeCasien, A, Trujillo, A, Janiak, MC, Harshaw, E, Caes, Z, Galindo, G, Petersen, R and Higham, J                                  |
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## **Supplementary Materials for ‘Equivocal evidence for a link between megalencephaly-related genes and primate brain size evolution’**

Alex R. DeCasien<sup>1,2,3\*</sup>, Amber E. Trujillo<sup>1,2</sup>, Mareike C. Janiak<sup>4,5</sup>, Etta P. Harshaw<sup>6,7</sup>, Zosia N. Caes<sup>8,9</sup>, Gabriela A. Galindo<sup>1</sup>, Rachel M. Petersen<sup>1,2,10</sup>, James P. Higham<sup>1,2</sup>

1. Department of Anthropology, New York University, New York, USA
2. New York Consortium in Evolutionary Primatology (NYCEP), New York, USA
3. Section on Developmental Neurogenomics, National Institute of Mental Health (NIMH), Bethesda, USA
4. School of Science, Engineering & Environment, University of Salford, Salford, UK
5. Department of Anthropology, Rutgers University, New Brunswick, USA
6. Department of Art History, University of Southern California, Los Angeles, USA
7. Eleanor Roosevelt High School, New York, USA
8. Department of Chemistry, Yale University, New Haven, USA
9. Columbia Secondary School for Math, Science, and Engineering, New York, USA
10. Department of Biological Sciences, Vanderbilt University, Nashville, USA

\*Correspondence: alex.decasien@gmail.com (A.R. DeCasien)

## Supplementary Data Guide

### Supplementary Table S1. Additional results for Aim 2: Testing whether selection pressure on megalencephaly-associated genes is lined to measures of primate brain size when *Callithrix* and *Microcebus* are excluded

Lambda values, coefficient estimates (for the predictors in the third row of table), and associated p-values are provided for 4 models for each gene, including:

#### *Absolute brain size models*

- 1)  $\log(\text{brain size}) \sim \log(dN/dS)$
- 2)  $\log(\text{brain size}) \sim \log(dN) + \log(dS)$

#### *Relative brain size models*

- 3)  $\log(\text{brain size}) \sim \log(\text{body size}) + \log(dN/dS)$
- 4)  $\log(\text{brain size}) \sim \log(\text{body size}) + \log(dN) + \log(dS)$

There is of a significant association between dN/dS and absolute for *GPC3* and *TBC1D7*. Significant p-values ( $p < 0.05$ ) are in bold. Est = coefficient estimate; N spp = number of species included in models. \*Models were run with lambda = 1 since log-likelihood plots of lambda were very flat.

### Supplementary Table S2. Root-to-tip dN/dS, dN, and dS values for candidate genes 1-8

This table contains root-to-tip dN/dS, dN, and dS values for 8 of the 16 candidate genes: *AKT1*, *AKT3*, *BRWD3*, *CCND2*, *EXT2*, *GPC3*, *HEPACAME*, *KIF7*. These values were obtained from PAML branch models, provided in the methods section. Gray boxes containing 'NA' values indicate instances in which exon sequences could not be aligned for the respective species (due to extensive gaps in that area of the genome).

### Supplementary Table S3. Root-to-tip dN/dS, dN, and dS values for candidate genes 9-16

This table contains root-to-tip dN/dS, dN, and dS values for 8 of the 16 candidate genes: *MTOR*, *OFD1*, *PIK3CA*, *PTEN*, *RIN2*, *SPRED1*, *STRADA*, *TBC1D7*. These values were obtained from PAML branch models, provided in the methods section. Gray boxes containing 'NA' values indicate instances in which exon sequences could not be aligned for the respective species (due to extensive gaps in that area of the genome).

### Supplementary Table S4. Accession numbers for candidate genes 1-8

This table contains accession numbers for sequences used in analyses for 8 of the 16 candidate genes: *AKT1*, *AKT3*, *BRWD3*, *CCND2*, *EXT2*, *GPC3*, *HEPACAME*, *KIF7*. Gray boxes containing 'NA' values indicate instances in which exon sequences could not be aligned for the respective species (due to extensive gaps in that area of the genome).

### **Supplementary Table S5. Accession numbers for candidate genes 9-16**

This table contains accession numbers for sequences used in analyses for 8 of the 16 candidate genes: *MTOR*, *OFD1*, *PIK3CA*, *PTEN*, *RIN2*, *SPRED1*, *STRADA*, *TBC1D7*. Gray boxes containing 'NA' values indicate instances in which exon sequences could not be aligned for the respective species (due to extensive gaps in that area of the genome).

### **Supplementary Table S6. Brain and body mass for 23 primate species**

This table contains brain and body masses are provided in grams, and sources for these data (in addition to any relevant notes) are also listed.

### **Supplementary Files**

Each '*gene\_name\_seq.phy*' file contains the alignment compiled for that candidate gene using Geneious (see Methods).

**Supplementary Table S1. Additional results for Aim 2: Testing whether selection pressure on megalencephaly-associated genes is linked to measures of primate brain size when *Callithrix* and *Microcebus* are excluded**

| Gene           | N spp | Absolute brain size |        |              |       |        |        |              |       |         |              |              | Relative brain size |        |         |       |        |        |         |       |        |              |       |
|----------------|-------|---------------------|--------|--------------|-------|--------|--------|--------------|-------|---------|--------------|--------------|---------------------|--------|---------|-------|--------|--------|---------|-------|--------|--------------|-------|
|                |       | dN/dS               |        |              |       | dN     |        |              |       | dS      |              |              | dN/dS               |        |         |       | dN     |        |         |       | dS     |              |       |
|                |       | Lambda              | Est    | P-value      | P-adj | Lambda | Est    | P-value      | P-adj | Est     | P-value      | P-adj        | Lambda              | Est    | P-value | P-adj | Lambda | Est    | P-value | P-adj | Est    | P-value      | P-adj |
| <i>AKT1</i>    | 19    | 1.000               | -0.012 | 0.911        | 0.991 | 1.000  | 0.691  | 0.714        | 0.891 | 0.285   | 0.700        | 0.912        | 1.000*              | 0.001  | 0.986   | 0.986 | 1.000* | -0.659 | 0.563   | 0.800 | -0.259 | 0.565        | 0.879 |
| <i>BRWD3</i>   | 20    | 1.000               | 1.801  | 0.438        | 0.991 | 1.000  | 1.862  | 0.431        | 0.891 | 0.497   | 0.912        | 0.912        | 1.000*              | 0.901  | 0.494   | 0.916 | 1.000* | 0.899  | 0.509   | 0.800 | -0.935 | 0.718        | 0.905 |
| <i>CCND2</i>   | 21    | 1.000               | 0.032  | 0.921        | 0.991 | 1.000  | 0.070  | 0.823        | 0.891 | -2.055  | 0.185        | 0.518        | 1.000*              | 0.051  | 0.779   | 0.916 | 1.000* | 0.057  | 0.759   | 0.800 | -0.408 | 0.666        | 0.905 |
| <i>EXT2</i>    | 21    | 1.000               | 0.014  | 0.990        | 0.991 | 1.000  | 0.093  | 0.932        | 0.932 | -1.885  | 0.457        | 0.861        | 1.000*              | 0.172  | 0.777   | 0.916 | 1.000* | 0.158  | 0.800   | 0.800 | 0.152  | 0.919        | 0.919 |
| <i>GPC3</i>    | 16    | 0.799               | 1.637  | <b>0.017</b> | 0.119 | 0.906  | 1.883  | <b>0.012</b> | 0.168 | -0.714  | 0.455        | 0.861        | 1.000*              | 0.316  | 0.473   | 0.916 | 0.443  | 0.571  | 0.131   | 0.761 | 0.124  | 0.776        | 0.905 |
| <i>HEPACAM</i> | 20    | 1.000               | -0.098 | 0.686        | 0.991 | 1.000  | 0.082  | 0.827        | 0.891 | -1.438  | 0.556        | 0.865        | 1.000*              | 0.039  | 0.776   | 0.916 | 1.000* | 0.067  | 0.755   | 0.800 | -0.281 | 0.841        | 0.906 |
| <i>KIF7</i>    | 21    | 1.000               | -2.206 | 0.149        | 0.522 | 1.000  | -2.135 | 0.170        | 0.793 | 0.678   | 0.818        | 0.912        | 1.000*              | -1.427 | 0.099   | 0.812 | 1.000* | -1.424 | 0.110   | 0.761 | 1.690  | 0.316        | 0.879 |
| <i>MTOR</i>    | 21    | 1.000               | -0.007 | 0.991        | 0.991 | 0.833  | 0.342  | 0.544        | 0.891 | -12.577 | <b>0.007</b> | <b>0.049</b> | 1.000*              | 0.274  | 0.399   | 0.916 | 1.000* | 0.316  | 0.349   | 0.800 | -2.709 | 0.425        | 0.879 |
| <i>OFD1</i>    | 17    | 0.981               | 1.558  | 0.704        | 0.991 | 0.958  | 1.614  | 0.700        | 0.891 | -3.545  | 0.492        | 0.861        | 1.000*              | -0.335 | 0.851   | 0.916 | 1.000* | -0.505 | 0.781   | 0.800 | 1.580  | 0.504        | 0.879 |
| <i>PIK3CA</i>  | 19    | 1.000               | -0.039 | 0.829        | 0.991 | 0.863  | 0.217  | 0.278        | 0.891 | -3.664  | <b>0.003</b> | 0.042        | 1.000*              | 0.024  | 0.817   | 0.916 | 1.000* | 0.050  | 0.669   | 0.800 | -0.617 | 0.561        | 0.879 |
| <i>RIN2</i>    | 21    | 1.000               | 0.611  | 0.706        | 0.991 | 1.000  | 0.528  | 0.723        | 0.891 | -3.899  | 0.089        | 0.312        | 1.000*              | 0.245  | 0.790   | 0.916 | 1.000* | 0.240  | 0.796   | 0.800 | -1.087 | 0.462        | 0.879 |
| <i>SPRED1</i>  | 21    | 1.000               | 0.529  | 0.664        | 0.991 | 1.000  | 0.495  | 0.726        | 0.891 | -0.649  | 0.783        | 0.912        | 1.000*              | -0.469 | 0.506   | 0.916 | 1.000* | -0.311 | 0.699   | 0.800 | 0.959  | 0.479        | 0.879 |
| <i>STRADA</i>  | 21    | 1.000               | -1.283 | 0.138        | 0.522 | 1.000  | -0.900 | 0.377        | 0.891 | -0.298  | 0.899        | 0.912        | 1.000*              | -0.575 | 0.259   | 0.916 | 1.000* | -0.835 | 0.163   | 0.761 | 1.744  | 0.223        | 0.879 |
| <i>TBC1D7</i>  | 21    | 1.000               | 3.462  | <b>0.011</b> | 0.119 | 1.000  | 3.041  | 0.064        | 0.448 | -4.310  | 0.065        | 0.303        | 1.000*              | 1.414  | 0.116   | 0.812 | 1.000* | 0.627  | 0.546   | 0.800 | -2.839 | <b>0.049</b> | 0.686 |

Supplementary Table S2. Root-to-tip dN/dS, dN, and dS values for candidate genes 1-8

| Taxa                               | AKT1  |      |      | AKT3  |      |      | BRWD3 |      |      | CCND2 |      |      | EXT2  |      |      | GPC3  |      |      | HEPACAM |      |      | KIF7  |      |      |
|------------------------------------|-------|------|------|-------|------|------|-------|------|------|-------|------|------|-------|------|------|-------|------|------|---------|------|------|-------|------|------|
|                                    | dN/dS | dN   | dS   | dN/dS | dN   | dS   | dN/dS | dN   | dS   | dN/dS | dN   | dS   | dN/dS | dN   | dS   | dN/dS | dN   | dS   | dN/dS   | dN   | dS   | dN/dS | dN   | dS   |
| <i>Aotus nancymaae</i>             | NA    | NA   | NA   | 0.00  | 0.00 | 0.08 | 0.07  | 0.01 | 0.11 | 0.02  | 0.00 | 0.12 | 0.03  | 0.01 | 0.42 | 0.07  | 0.00 | 0.04 | 0.03    | 0.01 | 0.49 | 0.11  | 0.08 | 0.75 |
| <i>Callithrix jacchus</i>          | NA    | NA   | NA   | 0.00  | 0.00 | 0.09 | NA    | NA   | NA   | 0.02  | 0.00 | 0.18 | 0.03  | 0.02 | 0.45 | 0.12  | 0.01 | 0.06 | 0.02    | 0.01 | 0.51 | 0.12  | 0.10 | 0.82 |
| <i>Cebus capucinus</i>             | 0.01  | 0.00 | 0.35 | 0.00  | 0.00 | 0.08 | 0.09  | 0.01 | 0.11 | 0.02  | 0.00 | 0.14 | 0.04  | 0.02 | 0.46 | 0.19  | 0.01 | 0.06 | 0.01    | 0.01 | 0.45 | 0.13  | 0.09 | 0.75 |
| <i>Cercocebus torquatus atys</i>   | 6.67  | 0.02 | 0.00 | 0.00  | 0.00 | 0.05 | 0.07  | 0.01 | 0.10 | 0.01  | 0.00 | 0.14 | 0.05  | 0.02 | 0.39 | 0.11  | 0.01 | 0.05 | 0.05    | 0.03 | 0.49 | 0.12  | 0.07 | 0.60 |
| <i>Chlorocebus sabaeus</i>         | 0.01  | 0.00 | 0.41 | 0.00  | 0.00 | 0.05 | 0.08  | 0.01 | 0.10 | 0.01  | 0.00 | 0.14 | 0.08  | 0.03 | 0.39 | 0.10  | 0.01 | 0.05 | 0.04    | 0.02 | 0.52 | 0.12  | 0.07 | 0.58 |
| <i>Colobus angolensis</i>          | 0.01  | 0.00 | 0.44 | 0.02  | 0.00 | 0.05 | 0.07  | 0.01 | 0.11 | 0.01  | 0.00 | 0.14 | 0.05  | 0.02 | 0.39 | 0.13  | 0.01 | 0.04 | 0.07    | 0.04 | 0.52 | 0.13  | 0.08 | 0.64 |
| <i>Gorilla gorilla gorilla</i>     | 0.01  | 0.00 | 0.42 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.10 | 0.03  | 0.01 | 0.18 | 0.05  | 0.02 | 0.41 | NA    | NA   | NA   | 0.03    | 0.01 | 0.40 | 0.13  | 0.07 | 0.54 |
| <i>Homo sapiens</i>                | 0.01  | 0.00 | 0.42 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.11 | 0.04  | 0.01 | 0.16 | 0.06  | 0.02 | 0.40 | 0.20  | 0.01 | 0.04 | 0.06    | 0.02 | 0.39 | 0.10  | 0.05 | 0.55 |
| <i>Macaca fascicularis</i>         | 0.01  | 0.00 | 0.39 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.11 | 0.03  | 0.00 | 0.15 | 0.06  | 0.02 | 0.39 | 0.13  | 0.01 | 0.05 | 0.04    | 0.02 | 0.53 | 0.11  | 0.07 | 0.61 |
| <i>Macaca mulatta</i>              | 0.01  | 0.00 | 0.39 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.10 | 0.03  | 0.00 | 0.15 | 0.06  | 0.02 | 0.40 | 0.14  | 0.01 | 0.04 | 0.04    | 0.02 | 0.50 | 0.11  | 0.07 | 0.63 |
| <i>Macaca nemestrina</i>           | 0.01  | 0.00 | 0.40 | 0.00  | 0.00 | 0.05 | 0.07  | 0.01 | 0.10 | 0.01  | 0.00 | 0.15 | 0.05  | 0.02 | 0.39 | 0.16  | 0.01 | 0.04 | 0.04    | 0.02 | 0.52 | 0.12  | 0.07 | 0.63 |
| <i>Mandrillus leucophaeus</i>      | NA    | NA   | NA   | 0.00  | 0.00 | 0.05 | 0.07  | 0.01 | 0.11 | 0.01  | 0.00 | 0.13 | 0.05  | 0.02 | 0.42 | 0.11  | 0.01 | 0.06 | 0.05    | 0.02 | 0.49 | 0.11  | 0.07 | 0.60 |
| <i>Microcebus murinus</i>          | 0.00  | 0.00 | 0.53 | 0.00  | 0.00 | 0.06 | 0.06  | 0.01 | 0.10 | 0.02  | 0.00 | 0.19 | 0.04  | 0.02 | 0.48 | 0.11  | 0.01 | 0.13 | 0.09    | 0.04 | 0.38 | 0.09  | 0.06 | 0.69 |
| <i>Nomascus leucogenys</i>         | 0.01  | 0.00 | 0.37 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.10 | 0.06  | 0.01 | 0.21 | 0.06  | 0.02 | 0.38 | 0.16  | 0.01 | 0.03 | 0.04    | 0.02 | 0.39 | 0.12  | 0.07 | 0.56 |
| <i>Otolemur gamettii</i>           | 0.01  | 0.01 | 0.56 | 0.01  | 0.00 | 0.12 | 0.08  | 0.01 | 0.13 | 0.01  | 0.00 | 0.29 | 0.03  | 0.02 | 0.60 | NA    | NA   | NA   | NA      | NA   | NA   | 0.12  | 0.12 | 1.00 |
| <i>Pan paniscus</i>                | 0.01  | 0.00 | 0.41 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.10 | 0.04  | 0.01 | 0.16 | 0.06  | 0.02 | 0.38 | 0.16  | 0.01 | 0.04 | 0.18    | 0.08 | 0.44 | 0.11  | 0.06 | 0.54 |
| <i>Pan troglodytes troglodytes</i> | 0.01  | 0.00 | 0.42 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.11 | 0.04  | 0.01 | 0.16 | 0.06  | 0.02 | 0.37 | NA    | NA   | NA   | 0.05    | 0.02 | 0.35 | 0.10  | 0.05 | 0.53 |
| <i>Papio anubis</i>                | 0.01  | 0.00 | 0.38 | 0.00  | 0.00 | 0.06 | 0.07  | 0.01 | 0.10 | 0.01  | 0.00 | 0.13 | 0.06  | 0.02 | 0.39 | 0.12  | 0.01 | 0.05 | 0.06    | 0.03 | 0.51 | 0.11  | 0.07 | 0.61 |
| <i>Pongo abelii</i>                | 0.01  | 0.00 | 0.43 | 0.00  | 0.00 | 0.06 | 0.10  | 0.01 | 0.11 | 0.01  | 0.00 | 0.16 | 0.07  | 0.03 | 0.38 | 0.27  | 0.01 | 0.02 | 0.12    | 0.05 | 0.46 | 0.11  | 0.06 | 0.55 |
| <i>Rhinopithecus bieti</i>         | 0.01  | 0.00 | 0.42 | 0.00  | 0.00 | 0.06 | NA    | NA   | NA   | 0.02  | 0.00 | 0.15 | 0.06  | 0.02 | 0.39 | NA    | NA   | NA   | 0.05    | 0.03 | 0.56 | 0.14  | 0.09 | 0.62 |
| <i>Rhinopithecus roxellana</i>     | 0.01  | 0.00 | 0.42 | 0.00  | 0.00 | 0.06 | 0.08  | 0.01 | 0.11 | 0.02  | 0.00 | 0.16 | 0.06  | 0.02 | 0.38 | 0.11  | 0.01 | 0.05 | 0.06    | 0.03 | 0.55 | 0.13  | 0.08 | 0.62 |
| <i>Saimiri boliviensis</i>         | 0.01  | 0.00 | 0.43 | 0.00  | 0.00 | 0.08 | 0.08  | 0.01 | 0.12 | 0.02  | 0.00 | 0.15 | 0.04  | 0.02 | 0.45 | 0.08  | 0.00 | 0.06 | 0.04    | 0.02 | 0.56 | 0.11  | 0.09 | 0.80 |
| <i>Tarsius syrichta</i>            | 0.01  | 0.00 | 0.39 | 0.12  | 0.01 | 0.08 | 0.08  | 0.01 | 0.08 | 0.00  | 0.00 | 0.33 | 0.08  | 0.07 | 0.84 | NA    | NA   | NA   | 0.06    | 0.02 | 0.39 | 0.13  | 0.07 | 0.54 |

Supplementary Table S3. Root-to-tip dN/dS, dN, and dS values for candidate genes 9-16

| Taxa                               | MTOR  |      |      | OFD1  |      |      | PIK3CA |      |      | PTEN  |      |      | RIN2  |      |      | SPRED1 |      |      | STRADA |      |      | TBC1D7 |      |      |
|------------------------------------|-------|------|------|-------|------|------|--------|------|------|-------|------|------|-------|------|------|--------|------|------|--------|------|------|--------|------|------|
|                                    | dN/dS | dN   | dS   | dN/dS | dN   | dS   | dN/dS  | dN   | dS   | dN/dS | dN   | dS   | dN/dS | dN   | dS   | dN/dS  | dN   | dS   | dN/dS  | dN   | dS   | dN/dS  | dN   | dS   |
| <i>Aotus nancymae</i>              | 0.01  | 0.00 | 0.39 | 0.72  | 0.07 | 0.10 | 0.01   | 0.00 | 0.30 | 0.23  | 0.04 | 0.17 | 0.10  | 0.03 | 0.30 | 0.13   | 0.02 | 0.16 | 0.05   | 0.02 | 0.45 | 0.13   | 0.04 | 0.30 |
| <i>Callithrix jacchus</i>          | 0.01  | 0.00 | 0.41 | 0.64  | 0.07 | 0.11 | 0.00   | 0.00 | 0.25 | 0.00  | 0.00 | 0.17 | 0.09  | 0.03 | 0.33 | 0.11   | 0.02 | 0.22 | 0.06   | 0.03 | 0.54 | 0.21   | 0.07 | 0.32 |
| <i>Cebus capucinus</i>             | 0.02  | 0.01 | 0.39 | 0.63  | 0.07 | 0.11 | 0.01   | 0.00 | 0.24 | 0.00  | 0.00 | 0.16 | 0.12  | 0.04 | 0.31 | 0.13   | 0.02 | 0.18 | 0.05   | 0.02 | 0.47 | 0.16   | 0.05 | 0.31 |
| <i>Cercocebus torquatus atys</i>   | 0.01  | 0.00 | 0.38 | 0.60  | 0.06 | 0.10 | 0.11   | 0.02 | 0.19 | 0.00  | 0.00 | 0.12 | 0.09  | 0.02 | 0.26 | 0.11   | 0.02 | 0.18 | 0.06   | 0.03 | 0.57 | 0.19   | 0.06 | 0.33 |
| <i>Chlorocebus sabaeus</i>         | 0.01  | 0.00 | 0.39 | 0.57  | 0.06 | 0.11 | 0.02   | 0.00 | 0.15 | 0.00  | 0.00 | 0.11 | 0.09  | 0.02 | 0.27 | 0.12   | 0.02 | 0.17 | 0.06   | 0.03 | 0.58 | 0.20   | 0.06 | 0.32 |
| <i>Colobus angolensis</i>          | 0.01  | 0.00 | 0.39 | 0.66  | 0.06 | 0.10 | 0.01   | 0.00 | 0.16 | 0.00  | 0.00 | 0.15 | 0.10  | 0.03 | 0.26 | 0.14   | 0.02 | 0.16 | 0.06   | 0.03 | 0.56 | 0.23   | 0.07 | 0.31 |
| <i>Gorilla gorilla gorilla</i>     | 0.00  | 0.00 | 0.37 | NA    | NA   | NA   | 0.02   | 0.00 | 0.14 | 0.00  | 0.00 | 0.10 | 0.10  | 0.03 | 0.27 | 0.14   | 0.02 | 0.14 | 0.06   | 0.03 | 0.48 | 0.24   | 0.07 | 0.28 |
| <i>Homo sapiens</i>                | 0.01  | 0.00 | 0.36 | 0.67  | 0.06 | 0.09 | 0.02   | 0.00 | 0.13 | 0.00  | 0.00 | 0.10 | 0.10  | 0.03 | 0.26 | 0.14   | 0.02 | 0.14 | 0.05   | 0.02 | 0.48 | 0.25   | 0.07 | 0.27 |
| <i>Macaca fascicularis</i>         | 0.01  | 0.00 | 0.39 | 0.61  | 0.06 | 0.10 | 0.02   | 0.00 | 0.15 | 0.00  | 0.00 | 0.12 | 0.11  | 0.03 | 0.26 | 0.13   | 0.02 | 0.16 | 0.06   | 0.03 | 0.58 | 0.22   | 0.07 | 0.31 |
| <i>Macaca mulatta</i>              | 0.01  | 0.00 | 0.40 | 0.60  | 0.06 | 0.10 | NA     | NA   | NA   | 0.00  | 0.00 | 0.11 | 0.11  | 0.03 | 0.26 | 0.15   | 0.02 | 0.15 | 0.06   | 0.03 | 0.58 | 0.21   | 0.07 | 0.32 |
| <i>Macaca nemestrina</i>           | 0.01  | 0.00 | 0.39 | 0.66  | 0.08 | 0.12 | 0.02   | 0.00 | 0.15 | 0.00  | 0.00 | 0.11 | 0.10  | 0.03 | 0.26 | 0.12   | 0.02 | 0.17 | 0.06   | 0.03 | 0.58 | 0.22   | 0.07 | 0.31 |
| <i>Mandrillus leucophaeus</i>      | 0.01  | 0.00 | 0.39 | 0.60  | 0.06 | 0.10 | 0.02   | 0.00 | 0.14 | 0.00  | 0.00 | 0.12 | 0.09  | 0.02 | 0.26 | 0.12   | 0.02 | 0.17 | 0.07   | 0.04 | 0.57 | 0.21   | 0.06 | 0.31 |
| <i>Microcebus murinus</i>          | 0.01  | 0.01 | 0.42 | 0.66  | 0.07 | 0.11 | NA     | NA   | NA   | 0.04  | 0.00 | 0.10 | 0.16  | 0.07 | 0.45 | 0.15   | 0.03 | 0.18 | 0.14   | 0.05 | 0.36 | 0.07   | 0.02 | 0.37 |
| <i>Nomascus leucogenys</i>         | 0.01  | 0.00 | 0.39 | 0.67  | 0.06 | 0.08 | 0.02   | 0.00 | 0.15 | 0.00  | 0.00 | 0.09 | 0.09  | 0.03 | 0.28 | 0.13   | 0.02 | 0.18 | 0.08   | 0.03 | 0.45 | 0.24   | 0.07 | 0.28 |
| <i>Otolemur gamettii</i>           | 0.01  | 0.01 | 0.49 | NA    | NA   | NA   | 0.01   | 0.00 | 0.29 | 0.05  | 0.01 | 0.16 | 0.13  | 0.08 | 0.61 | 0.16   | 0.03 | 0.17 | 0.05   | 0.03 | 0.52 | 0.13   | 0.04 | 0.31 |
| <i>Pan paniscus</i>                | 0.01  | 0.00 | 0.36 | 0.66  | 0.06 | 0.09 | 0.05   | 0.01 | 0.13 | 0.00  | 0.00 | 0.11 | 0.09  | 0.02 | 0.27 | 0.16   | 0.02 | 0.14 | 0.06   | 0.03 | 0.46 | 0.22   | 0.07 | 0.31 |
| <i>Pan troglodytes troglodytes</i> | 0.01  | 0.00 | 0.36 | NA    | NA   | NA   | 0.02   | 0.00 | 0.13 | 0.00  | 0.00 | 0.10 | 0.09  | 0.02 | 0.26 | 0.14   | 0.02 | 0.14 | 0.06   | 0.03 | 0.46 | 0.22   | 0.07 | 0.32 |
| <i>Papio anubis</i>                | 0.01  | 0.00 | 0.39 | 0.60  | 0.06 | 0.10 | NA     | NA   | NA   | 0.00  | 0.00 | 0.11 | 0.10  | 0.03 | 0.26 | 0.13   | 0.02 | 0.16 | 0.07   | 0.04 | 0.57 | 0.18   | 0.06 | 0.36 |
| <i>Pongo abelii</i>                | 0.01  | 0.00 | 0.39 | 0.66  | 0.05 | 0.08 | 0.03   | 0.00 | 0.14 | 0.13  | 0.01 | 0.11 | 0.10  | 0.03 | 0.28 | 0.18   | 0.03 | 0.16 | 0.09   | 0.04 | 0.44 | 0.21   | 0.06 | 0.28 |
| <i>Rhinopithecus bieti</i>         | 0.01  | 0.00 | 0.39 | NA    | NA   | NA   | 0.12   | 0.02 | 0.16 | 0.00  | 0.00 | 0.14 | 0.08  | 0.02 | 0.27 | 0.13   | 0.02 | 0.15 | 0.08   | 0.04 | 0.55 | 0.20   | 0.06 | 0.30 |
| <i>Rhinopithecus roxellana</i>     | 0.01  | 0.00 | 0.39 | 0.67  | 0.06 | 0.09 | 0.03   | 0.00 | 0.14 | 0.00  | 0.00 | 0.14 | 0.09  | 0.02 | 0.27 | 0.13   | 0.02 | 0.15 | 0.06   | 0.03 | 0.52 | 0.20   | 0.06 | 0.30 |
| <i>Saimiri boliviensis</i>         | 0.01  | 0.00 | 0.40 | 0.69  | 0.07 | 0.10 | 0.01   | 0.00 | 0.29 | 0.00  | 0.00 | 0.14 | 0.14  | 0.04 | 0.30 | 0.09   | 0.02 | 0.20 | 0.06   | 0.03 | 0.50 | 0.14   | 0.04 | 0.31 |
| <i>Tarsius syrichta</i>            | 0.01  | 0.00 | 0.47 | 0.56  | 0.06 | 0.10 | 0.00   | 0.00 | 0.25 | 0.00  | 0.00 | 0.16 | 0.09  | 0.06 | 0.67 | 0.12   | 0.01 | 0.12 | 0.19   | 0.28 | 1.45 | 0.10   | 0.03 | 0.33 |

Supplementary Table S4. Accession numbers for candidate genes 1-8

| Taxa                               | AKT1           |                | AKT3           |                | BRWD3        |                | CCND2        |                | EXT2           |                | GPC3           |                | HEPACAM      |                | KIF7           |                |
|------------------------------------|----------------|----------------|----------------|----------------|--------------|----------------|--------------|----------------|----------------|----------------|----------------|----------------|--------------|----------------|----------------|----------------|
|                                    | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq | Model RefSeq   | Known RefSeq | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq | Model RefSeq   | Known RefSeq   | Model RefSeq   |
| <i>Aotus nancymaae</i>             | NA             | NA             | NW_012189090.1 |                |              | XM_012455736.1 |              | XM_012455904.2 |                | XM_012452407.1 |                | XM_012474320.1 |              | XM_012470205.1 | NW_018503064.1 | XM_021674356.1 |
| <i>Callithrix jacchus</i>          | NA             | NA             | NC_013914.1    |                | NA           | NA             |              | XM_009003440.2 |                | XM_002755201.4 |                | XM_008989909.2 |              | XM_009007046.2 | NC_013901.1    | XM_017973300.1 |
| <i>Cebus capucinus</i>             |                | XM_017505398.1 |                | XM_017531947.1 |              | XM_017519568.1 |              | XM_017546077.1 |                | XM_017529398.1 |                | XM_017511970.1 |              | XM_017523932.1 | NW_016107334.1 | XM_017517518.1 |
| <i>Cerocebus torquatus atys</i>    |                | XM_012084168.1 |                | XM_012036296.1 |              | XM_012077287.1 |              | XM_012054215.1 |                | XM_012062330.1 |                | XM_012061024.1 |              | XM_012053250.1 |                | XM_012074364.1 |
| <i>Chlorocebus sabaues</i>         |                | XM_007987997.1 |                | XM_007989955.1 |              | XM_007992160.1 |              | XM_007997271.1 |                | XM_008000918.1 |                | XM_007992737.1 |              | XM_008021374.1 |                | XM_007990356.1 |
| <i>Colobus angolensis</i>          |                | XM_011951392.1 |                | XM_011955702.1 |              | XM_011944125.1 |              | XM_011931071.1 | NW_012119710.1 | XM_011963272.1 |                | XM_011930705.1 |              | XM_011934728.1 |                | XM_011948350.1 |
| <i>Gonilla gonilla gonilla</i>     |                | XM_019009506.1 |                | XM_004028679.2 |              | XM_019019638.1 |              | XM_004052524.2 |                | XM_004050977.2 |                | NA             | NA           | XM_004052354.2 |                | XM_019010423.1 |
| <i>Homo sapiens</i>                | NM_001014432.1 |                | NM_005465.4    |                | NM_153252.4  |                | NM_001759.3  |                | NM_207122.1    |                | NM_001164619.2 |                | NM_152722.4  |                | NM_198525.2    |                |
| <i>Macaca fascicularis</i>         |                | XM_005562350.2 |                | XM_005539655.2 |              | XM_015443968.1 |              | XM_005569850.1 |                | XM_015434882.1 |                | XM_005594608.2 |              | XM_005580044.2 |                | XM_005560478.2 |
| <i>Macaca mulatta</i>              | NM_001261625.1 |                | NM_001266640.1 |                |              | XM_015127729.2 |              | XM_015150849.2 |                | XM_015114422.1 |                | XM_015128213.2 |              | XM_015116033.1 |                | XM_001094468.3 |
| <i>Macaca nemestrina</i>           |                | XM_011755020.1 |                | XM_011729486.1 |              | XM_024787598.1 |              | XM_011745486.2 |                | XM_011724183.1 |                | XM_011741015.2 |              | XM_011732050.1 |                | XM_011752271.1 |
| <i>Mandrillus leucophaeus</i>      | NA             | NA             |                | XM_011981158.1 |              | XM_011970792.1 |              | XM_011996293.1 |                | XM_012001352.1 |                | XM_012001312.1 |              | XM_012001705.1 |                | XM_011986344.1 |
| <i>Microcebus murinus</i>          |                | XM_012746390.2 |                | XM_012751177.2 |              | XM_012790329.2 |              | XM_012783145.2 |                | XM_012790441.1 |                | XM_012764774.1 |              | XM_012752551.2 |                | XM_012763339.2 |
| <i>Nomascus leucogenys</i>         | NM_001165894.1 |                |                | XM_012506588.1 |              | XM_003269007.3 |              | XM_012502279.1 |                | XM_003254461.2 |                | XM_003272634.4 |              | XM_003253336.2 |                | XM_012507116.1 |
| <i>Otolemur gamettii</i>           |                | XM_012498084.1 |                | XM_003798812.2 |              | XM_003803556.3 |              | XM_003796426.3 |                | XM_003781248.1 |                | NA             | NA           | NA             | NW_003852424.1 | XM_003788669.2 |
| <i>Pan paniscus</i>                | NW_003852678.1 |                |                | XM_003808002.3 |              | XM_008978138.1 |              | XM_003820341.3 |                | XM_003808219.2 |                | XM_003814501.2 |              | XM_008973532.1 |                | XM_008973901.2 |
| <i>Pan troglodytes troglodytes</i> |                | XM_003806999.1 |                | XM_016934876.1 |              | XM_016943269.2 |              | XM_001156857.5 |                | XM_508383.5    |                | NA             | NA           | XM_009424434.2 |                | XM_016927405.1 |
| <i>Papio anubis</i>                |                | XM_024348956.1 |                | XM_017958446.1 |              | XM_017954111.2 |              | XM_003905821.2 |                | XM_009186257.2 |                | XM_017954390.2 |              | XM_003910894.3 |                | XM_009210913.2 |
| <i>Pongo abelii</i>                |                | XM_009212375.2 |                | XM_024234045.1 |              | NC_012614.1    |              | XM_002822783.3 |                | XM_002821850.2 |                | XM_024240565.1 |              | XM_002822651.3 |                | XM_009250144.1 |
| <i>Rhinopithecus bieti</i>         | NC_012605.1    |                |                | XM_017870381.1 |              | NA             | NA           | XM_017883284.1 |                | XM_017858114.1 |                | NA             | NA           | XM_017853859.1 |                | XM_017861233.1 |
| <i>Rhinopithecus roxellana</i>     |                | XM_010376937.1 |                | XM_010353265.1 |              | NW_010800240.1 |              | XM_010359145.1 |                | XM_010378049.1 |                | XM_030933937.1 |              | XM_010384619.1 |                | XM_010378635.1 |
| <i>Saimiri boliviensis</i>         |                | XM_003933348.2 |                | XM_003935330.2 |              | XM_003936828.2 |              | XM_003942188.1 |                | XM_003920016.2 |                | XM_003931143.2 |              | XM_010334671.1 |                | XM_003921756.2 |
| <i>Tarsius syrichta</i>            | NW_007245946.1 |                | NW_007245650.1 | XM_008052375.2 |              | XM_008069344.2 |              | XM_008048699.1 |                | NW_007257306.1 | XM_008058453.2 |                | NA           | NA             | XM_008057832.1 | XM_021718842.1 |



Supplementary Table S5. Accession numbers for candidate genes 9-16

| Taxa                               | MTOR           |                | OFD1           |                | PIK3CA         |                | PTEN           |                | RIN2           |                | SPRED1         |                | STRADA         |                | TBC1D7         |                |
|------------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                                    | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   | Known RefSeq   | Model RefSeq   |
| <i>Aotus nancymaae</i>             |                | XM_012473670.1 |                | XM_012434967.2 | NW_012184291.1 | XM_012472256.2 |                | XM_012467566.1 |                | XM_021673566.1 |                | XM_012465033.1 |                | XM_012443842.2 |                | XM_012476566.1 |
| <i>Callithrix jacchus</i>          |                | XM_009000401.2 |                | XM_017968373.1 | NC_013910.1    | XM_002758097.3 |                | XM_017979117.1 |                | XM_008995820.2 |                | XM_002753561.4 |                | XM_002748137.4 |                | XM_008993951.2 |
| <i>Cebus capucinus</i>             | NW_016107330.1 | XM_017503042.1 |                | XM_017508823.1 |                | XM_017506295.1 |                | XM_017536375.1 |                | XM_017512654.1 |                | XM_017530903.1 |                | XM_017549200.1 |                | XM_017521503.1 |
| <i>Cercocebus torquatus atys</i>   |                | XM_012049371.1 |                | XM_012035865.1 | NW_010022159.1 | XM_012086241.1 |                | XM_012063164.1 | NW_012007257.1 |                |                | XM_012034725.1 |                | XM_012070595.1 |                | XM_012031317.1 |
| <i>Chlorocebus sabaues</i>         |                | XM_007980575.1 |                | XM_007991057.1 | NC_023656.1    | XM_007972038.1 |                | XM_007963471.1 |                | XM_007961294.1 |                | XM_008017098.1 |                | XM_008012140.1 |                | XM_007973671.1 |
| <i>Colobus angolensis</i>          |                | XM_011935809.1 |                | XM_011957843.1 | NW_012118155.1 | XM_011958660.1 |                | XM_011938741.1 |                | XM_011963061.1 |                | XM_011932653.1 |                | XM_011947949.1 |                | XM_011962705.1 |
| <i>Gorilla gorilla gorilla</i>     | NC_018424.2    | XM_019011017.1 | NA             | NA             |                | XM_004038036.2 |                | XM_019035119.1 | NC_018444.2    |                |                | XM_019011240.1 |                | XM_004041159.2 |                | XM_004043285.2 |
| <i>Homo sapiens</i>                | NM_004958.3    |                | NM_001330210.1 |                | NM_006218.3    |                | NM_000314.6    |                | NM_001242581.1 |                | NM_152594.2    |                | NM_001003786.2 |                | NM_001143965.3 |                |
| <i>Macaca fascicularis</i>         |                | XM_015442686.1 |                | XM_005592994.2 | NC_022273.1    | XM_005546432.2 |                | XM_005565882.2 |                | XM_005568234.2 |                | XM_005559135.2 |                | XM_005584655.2 |                | XM_005554023.2 |
| <i>Macaca mulatta</i>              |                | XM_015111100.1 |                | XM_001098347.4 |                | NA             | NM_001260965.1 |                | XM_015149571.1 |                | NM_001204360.1 |                | XM_001116286.3 |                | XM_015135572.1 |                |
| <i>Macaca nemestrina</i>           | NW_012015133.1 |                |                | XM_024791672.1 | NW_012011233.1 | XM_011755149.1 |                | XM_011740112.1 |                | XM_011749872.1 |                | XM_011759809.1 |                | XM_011743578.1 |                | XM_011742539.1 |
| <i>Mandrillus leucophaeus</i>      |                | XM_011996603.1 |                | XM_011994830.1 | NW_012102155.1 | XM_011980373.1 |                | XM_011990298.1 |                | XM_011979525.1 |                | XM_011989328.1 |                | XM_011997060.1 |                | XM_011989672.1 |
| <i>Microcebus murinus</i>          |                | XM_012791400.2 |                | XM_012784803.2 |                | NA             |                | XM_012762897.1 | NC_033677.1    |                |                | XM_012766374.2 |                | XM_012747285.2 |                | XM_012753510.2 |
| <i>Nomascus leucogenys</i>         | NC_019839.1    |                |                | XM_030806885.1 | NC_019826.1    | XM_012510799.1 |                | XM_003255173.3 |                | XM_012512259.1 |                | XM_003272817.2 |                | XM_012497582.1 |                | XM_003263521.3 |
| <i>Otolemur gamettii</i>           |                | XM_003793268.2 | NA             | NA             | NW_003852473.1 | XM_003794281.2 |                | XM_003783677.2 |                | XM_003798462.2 |                | XM_003791698.2 |                | XM_003786204.1 |                | XM_003788311.2 |
| <i>Pan paniscus</i>                |                | XM_003822083.3 |                | XM_003805694.3 | NC_027871.1    | XM_014344454.1 | NM_001301760.1 |                | XM_008962962.2 |                | XM_008969805.1 |                | XM_003811345.2 |                | XM_003823152.2 |                |
| <i>Pan troglodytes troglodytes</i> |                | XM_016953950.1 | NA             | NA             | NC_006490.4    | XM_016942318.1 |                | XM_016918822.1 |                | XM_009436892.2 |                | XM_001138171.4 |                | XM_016930624.1 |                | XM_001169035.5 |
| <i>Papio anubis</i>                |                | XM_017960413.1 |                | XM_003917416.4 |                | NA             |                | XM_009214930.1 |                | XM_017945051.1 |                | XM_003900749.3 |                | XM_009190986.2 |                | XM_003897068.2 |
| <i>Pongo abelii</i>                | NC_012591.1    |                |                | XM_024240796.1 | NC_012594.1    | XM_009239559.1 | NM_001131483.1 |                | XM_002830003.3 |                | XM_003780630.1 |                | XM_003780630.1 | NM_001132022.1 |                | XM_009241431.1 |
| <i>Rhinopithecus bieti</i>         | NW_016843223.1 | XM_017887986.1 | NA             | NA             | NW_016803343.1 | XM_017877282.1 |                | XM_017868858.1 |                | XM_017883330.1 |                | XM_017868162.1 |                | XM_017882900.1 |                | XM_017891130.1 |
| <i>Rhinopithecus roxellana</i>     |                | XM_010353522.1 |                | XM_010354059.2 | NW_010789103.1 | XM_010373943.1 |                | XM_010379624.1 | NW_010829246.1 |                | XM_010358441.1 |                | XM_010380047.1 |                | XM_010357133.1 |                |
| <i>Saimiri boliviensis</i>         | NW_003943684.1 |                |                | XM_003920320.2 | NW_003943624.1 | XM_003926921.2 |                | XM_003922436.2 |                | XM_010343724.1 |                | XM_003935735.2 |                | XM_003942437.2 |                | XM_010338117.1 |
| <i>Tarsius syrichta</i>            | NW_007256301.1 | XM_008069778.1 |                | XM_008052678.1 | NW_007251201.1 | XM_008063853.1 |                | XM_008071752.1 | NW_007231443.1 |                | XM_008064441.1 |                | NW_007070541.1 | XM_021707820.1 |                | XM_008056827.1 |

## Supplementary Table S6. Brain and body mass for 23 primate species

| Taxa                               | Brain Mass (g) | Body Mass (g) | Source                     | Notes  |
|------------------------------------|----------------|---------------|----------------------------|--|
| <i>Aotus nancymaae</i>             | 16.78          | 869.98        | DeCasien et al. 2017 [70]  | Brain/body size data for <i>A. lemurinus</i> |
| <i>Callithrix jacchus</i>          | 7.64           | 272.71        | DeCasien et al. 2017 [70]  |  |
| <i>Cebus capucinus</i>             | 73.79          | 2,798.11      | DeCasien et al. 2017 [70]  |  |
| <i>Cercocebus torquatus atys</i>   | 99.81          | 7,770.62      | DeCasien et al. 2017 [70]  |  |
| <i>Chlorocebus sabaesus</i>        | 67.25          | 4,312.00      | Isler et al. 2008 [71]     | Endocranial volumes multiplied by 1.036      |
| <i>Colobus angolensis</i>          | 71.56          | 8,807.66      | DeCasien et al. 2017 [70]  |  |
| <i>Gorilla gorilla gorilla</i>     | 507.25         | 121,327.00    | DeCasien et al. 2017 [70]  |  |
| <i>Homo sapiens</i>                | 1,330.00       | 65,000.00     | Montgomery et al. 2010 [3] |  |
| <i>Macaca fascicularis</i>         | 66.53          | 4,644.11      | DeCasien et al. 2017 [70]  |  |
| <i>Macaca mulatta</i>              | 88.94          | 6,471.73      | DeCasien et al. 2017 [70]  |  |
| <i>Macaca nemestrina</i>           | 109.87         | 7,244.59      | DeCasien et al. 2017 [70]  |  |
| <i>Mandrillus leucophaeus</i>      | 185.96         | 16,251.65     | DeCasien et al. 2017 [70]  |  |
| <i>Microcebus murinus</i>          | 1.72           | 63.93         | DeCasien et al. 2017 [70]  |  |
| <i>Nomascus leucogenys</i>         | 116.08         | 7,320.00      | Montgomery 2011 [72]       |  |
| <i>Otolemur garnettii</i>          | 11.24          | 1,055.59      | DeCasien et al. 2017 [70]  |  |
| <i>Pan paniscus</i>                | 346.24         | 37,522.48     | DeCasien et al. 2017 [70]  |  |
| <i>Pan troglodytes troglodytes</i> | 376.13         | 48,328.00     | DeCasien et al. 2017 [70]  |  |
| <i>Papio anubis</i>                | 171.80         | 17,209.52     | DeCasien et al. 2017 [70]  |  |
| <i>Pongo abelii</i>                | 409.52         | 48,223.06     | DeCasien et al. 2017 [70]  |  |
| <i>Rhinopithecus bieti</i>         | 114.53         | 11,000.54     | Montgomery 2011 [72]       |  |
| <i>Rhinopithecus roxellana</i>     | 122.00         | 14,750.00     | Isler et al. 2008 [71]     | Endocranial volumes multiplied by 1.036      |
| <i>Saimiri boliviensis</i>         | 25.74          | 707.23        | DeCasien et al. 2017 [70]  |  |
| <i>Tarsius syrichta</i>            | 3.48           | 107.54        | DeCasien et al. 2017 [70]  |  |