

80 million years – the divergence time of human and mouse

| <i>Year</i> | <i>Authors</i>  | <i>Paper/Book</i>  | <i>Journal</i>   | <i>Content</i>   | <i>Relation</i> | <i>Country</i> |
|-------------|---|--|--|--|-----------------|----------------|
| 1985        | Wen-Hsiung Li,<br>Chung-I Wu,<br>Chi-Cheng Luo                                  | A New Method for<br>Estimating Synonymous<br>and Nonsynonymous<br>Rates of Nucleotide<br>Substitution Considering<br>the Relative Likelihood<br>of Nucleotide and Codon<br>Changes | Molecular Biology and<br>Revolution Vol. 2<br>Number 2 pg 150-174,<br>1985 | <i>Substitution rates in mammalian genes</i> pg. 8<br>For several reasons, we shall use mainly genes from mammals:<br>man, rodents (mouse, rat, and Chinese hamster), and artiodactyls<br>(cow, goat, and pig). First, the fossil record for mammals is better<br>than those for other organisms; we assume that the above<br>mammalian orders diverged 80 Myr ago. ....<br>We assume that all mammalian orders diverged at the same time,<br>i.e., 80 Myr ago.  |                 | USA            |
| 2000        | Dan Graur,<br>Wen-Hsiung Li   | Fundamentals of<br>Molecular Evolution   | Book 2000  | <i>Chapter 4</i> Table 4.1 pg 103<br>a. All rates are based on comparisons between human and mouse<br>or rat genes. The time of divergence was set at 80 million years<br>ago. Rates are in units of substitutions per site per $10^9$ years.<br><br><i>Chapter 4</i> pg 139<br>For example, let us assume that the rate of nonsynonymous<br>substitution for the $\alpha$ chain of hemoglobin is $0.56 \times 10^{-9}$<br>substitutions per site per year, and that $\alpha$ -globins from rat and<br>human differ by 0.093 substitutions per site. Then, under the<br>molecular clock hypothesis, the divergence time between the<br>human and rat lineages is estimated to be approximately<br>$0.093 / (2 \times 0.56 \times 10^{-9}) = 80$ million years ago. |                 | Israel<br>USA  |
| 2001        | Ronald M.<br>Adkins,<br>Eric L. Gelke,<br>Diane Rowe,<br>Rodney L.<br>Honeycutt | Molecular Phylogeny and<br>Divergence Time<br>Estimates for Major<br>Rodent Groups: Divergence<br>from Multiple Genes  | Molecular Biology<br>Evolution vol. 18, pg<br>777-791                      | The text does not specifically mention the Human-Mouse<br>divergence time. (only Homo-Macaca, Rattus-Mus). But there<br>are some info given in the phylogenetic tree figures.<br>Homo = Homo Sapiens => Human<br>Rattus => Rat<br>Mus => Mouse<br><br><i>Fig 1a</i> Maximum-parsimony phylogeny of GHR sequences with<br>individual sites reweighted according to their rescaled consistency<br>index.<br><i>Fig 1b</i> Maximum-likelihood (-ln likelihood = 13,155.0)<br>phylogeny of GHR sequences.<br><br><i>Fig 2a</i> Maximum-parsimony phylogeny (2,556 steps) of 12S<br>sequences (consistency index = 0.31, retention index = 0.39).<br><i>Fig 2b</i> Maximum-likelihood (-ln likelihood = 10,881.4)   |                 | USA            |

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|             |   |  |  | <p>phylogeny of 12S sequences.</p> <p><i>Fig 3a</i> Maximum-parsimony (3,937 steps, consistency index [CI] = 0.63 and retention index [RI] = 0.70) and maximum likelihood (-ln likelihood = 22,720.6) phylogenies of BRCA1 sequences.</p> <p><i>Fig 3b</i> Maximum-parsimony phylogeny (6,860 steps, CI = 0.40 and RI = 0.40) for concatenated GHR, 12S, and vWF sequences)</p>   |                 |                |
| 2001        | Masatoshi Nei,<br>Ping Xu,<br>Galina Glazko | Estimation of divergence times from multiprotein sequences for a few mammalian species and several distantly related organisms | PNAS (Proceedings of National Academy of Science) vol. 98 no. 5, pg 2497-2502 2001 | <p><i>Table 1</i> pg. 4<br/>Estimates (+- standard errors) of divergence times (MY) between mic and rats and between humans and rodents.</p> <p><i>Estimates of gamma parameter a and divergence times</i> pg 4.<br/>Therefore, if we use a small a value obtained from closely related species, it will give unduly large pairwise distances for distantly related species and consequently give overestimates of divergence times for them but may give underestimates for closely related species. Therefore, time estimates of 82 and 25 MY for the human-rodent and the mouse-rat divergence time appear to be underestimates.</p> <p><i>Table 2</i> pg. 5<br/>Estimates (+- standard errors) of divergence times (MY) of various organisms from the human lineage.</p> <p><i>Estimate of ancient divergence times</i> pg. 5<br/>Table 2 includes the estimates obtained by <math>d_3</math> with <math>a=0.54</math>, which was obtained by using only animal sequences (five species). This distance again gives a smaller estimate (115 MY) for the human-rat divergence, which is below the calibration point (310 MY). However, it gives rather high estimates for divergence times earlier than the calibration point. In particular, the estimate of the E. coli-eukaryote divergence is unrealistic, because it is older than the age of Earth (ca. 4,500 MY).</p> <p>Unlike the case of mammalian data, Lynch's distance (<math>d_L</math>) gives the smallest time estimates (62 MY) for the human-rat divergence but give large estimates for ancient divergence times. However, the standard errors of these estimates are very large.</p> |                 | USA            |

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|-------------|-------------------------------------|--|--|---|-----------------|--|
|             |                                     |  |  | <p>Discussion pg. 6</p> <p>Nevertheless, if we use a large number of protein sequences, the estimates appear to be reasonably good (11, 17, 18). Our estimate (96 MY) of the time of human-rodent divergence from d3 is somewhat smaller than a recent estimate (112 MY) obtained by Kumar and Hedges (11). This difference occurred primarily because we used the CD approach with multiprotein gamma distance, whereas Kumar and Hedges used the IP approach with PC distance.</p>  |                 |  |
| 2002        | Mouse Genome Sequencing Consortium* | <p>Initial sequencing and comparative analysis of the mouse genome</p> <p><b>MOST IMPORTANT &amp; COMPLETE FOR MOUSE/HUMAN GENOME COMPARISON</b></p> | Nature, Vol 420, pg 520-577, 5 December 2002 | <p><i>Introduction</i> pg. 1</p> <p>Metaphorically, comparative genomics allows one to read evolution's laboratory notebook. In the roughly 75 million years since the divergence of the human and mouse lineages, the process of evolution has altered their genome sequences and caused them to diverge by nearly one substitution for every two nucleotides (see below) as well as by deletion and insertion.</p> <p><i>Background to the mouse genome sequencing project</i> pg. 2</p> <p>In the analyses below, we use a divergence time for the human and mouse lineages of 75Myr for the purpose of calculating evolutionary rates, although it is possible that the actual time may be as recent as 65Myr.</p> <p><i>Conservation of synteny between mouse and human genomes</i> pg. 7</p> <p>Starting from a common ancestral genome approximately 75Myr, the mouse and human genomes have each been shuffled by chromosomal rearrangements. The rate of these changes, however, is low enough that local gene order remains largely intact.</p> <p><i>Higher substitution rate in mouse lineage</i> pg. 12</p> <p>Assuming a speciation time of 75Myr, the average substitution rates would have been <math>2.2 \times 10^{29}</math> and <math>4.5 \times 10^{29}</math> in the human and mouse lineages, respectively. This is in accord with previous estimates of neutral substitution rates in these organisms.</p> <p>Genomic outliers pg. 15</p> <p>Other repeat-poor loci in the human genome (about 100-kb regions on human chromosomes 1p36,8q21 and 18q22) have independently remained repeat-poor in mouse (2.6, 6.5 and 7%, respectively) over</p> |                 | USA<br>UK<br>Switzerland<br>Germany<br>Canada<br>Japan |

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|             |   |   |  | <p>roughly 75 million years of evolution; we speculate that this similarly reflects dense regulatory information in the region.</p> <p><i>Fine-scale alignment of genomes</i> pg. 30<br/>           In a preliminary test of this hypothesis, we identified ancestral repeats in the mouse that lay in intervals defined by orthologous landmarks. Examination of the corresponding interval in the human genome showed a rate of loss of these elements, broadly consistent with the 24% deletion rate in the human lineage assumed above (see Supplementary Information).<br/>           Such a deletion rate in the human lineage over about 75 million years is also roughly compatible with the observation that roughly 6% has been deleted over about 22 million years since the divergence from baboon, an estimate derived from the sequencing of specific regions in human and baboon (E. Green, unpublished data).</p> |   |                         |
| 2003        | Ross C. Hardison                              | Comparative Genomics  | PloS Biology vol. 1 issue 2 pg 156-160     | <p><i>What can you learn about genome evolution?</i> pg. 2<br/>           The basic observation in comparative genomics is a description of the matches between genomes. For example, in the roughly 75-80 million years since human diverged from mouse, the large-scale gene organization and gene order have been preserved (International Mouse Genome Sequencing Consortium 2002).</p>   | References<br>“Initial sequencing and comparative analysis of the mouse genome”   | USA                     |
| 2003        | Anton Nekrutenko, Wen-Yu Chung, Wen-Hsiung Li | An evolutionary approach reveals a high protein-coding capacity of the human genome | TRENDS in Genetics vol. 19 no. 6 June 2003 | <p><i>Identifying novel exons</i> pg. 2<br/>           Second, it is highly unlikely for a noncoding region to maintain the observed level of sequence conservation among three species with divergence times of ~20 Myr (rat-mouse) to ~80 Myr (human-rat, human-mouse)</p>  | References<br>“Molecular Phylogeny and Divergence Time Estimates for Major Rodent Groups: Dvidence from Multiple Genes” | USA<br>Taiwan<br>Taiwan |

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