Phylogenetic analysis of cystic fibrosis transmembrane conductance regulator gene in mammalian species argues for the development of a rabbit model for cystic fibrosis

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The species-specific pattern of cystic fibrosis transmembrane conductance regulator (CFTR) expression was investigated in order to identify species closely related to man which can be used as potential cystic fibrosis (CF) animal models. To this purpose, the nucleotide sequences of the CFTR promoter region of eight mammalian species representing four different orders (Primates, Artiodactyla, Lagomorpha, and Rodentia) were analyzed. Distance matrices and unrooted trees of the CFTR promoter region sequences yielded two deeply separated groups, one including man (*Homo sapiens*), nonhuman primates (*Hylobates lar*, *Macaca fascilularis*, *Saimiri sciureus*), cow (*Bos taurus*), and rabbit (*Oryctolagus cuniculus*) and the other including the rodents (*Rattus norvegicus*, *Mus musculus*). Divergences between rodent and nonrodent groups have been observed in putative cis transcriptional regulatory elements and can be involved in the differences of pattern of expression between these to groups. Comparison of the available CFTR cDNA sequences enabled us to root the tree with a noneutherian outgroup and to perform a phylogenetic analysis. This analysis did not detect any base composition bias and supported polyphyletic Glires. Although a long-branch attraction artifact cannot be completely excluded, these findings converge toward the recent statement (Graur, Duret, and Gouy 1996) that Lagomorpha is more closely related to Primates than to Rodentia. In addition, the phenylalanine residue in exon 10 involved in the most common CF mutation in man is conserved in rabbit. These phylogenetic analyses as well as anatomical and developmental data suggest that, once rabbit embryonic stem cells become available, the rabbit will provide a suitable tool for both gene transfer and pharmacological investigations and could lead to a better CF model than the current murine models.