Effect Of Anini Acids on Gene And Genetic Code

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Abstract

were fairly consistent across wide taxonomic groups. These two groups of amino acids share interesting features: the decreasing group are proposed to be the first amino acids to be incorporated into the genetic code, while the accumulating group entered the code later. Therefore, all genomes appear to be accumulating more of the newer amino acids at the expense of the older amino acids, in a process that began 3.4 billion years ago and continues today, even in humans.

Zooming out in scale from amino acid to a gene family, a German group led by Svante Pääbo examined the evolution of the family of olfactory receptor (OR) genes in 19 primates plus mouse. In particular, they looked at the number of OR **pseudogenes**. They randomly sampled 100 OR genes from each genome and plotted the percentage of sampled genes that were pseudogenes (Figure 3.5). The nonhuman animals fell into two categories of ≥ 30% or ~18% pseudogenes that correlated with apes and Old World monkeys (30%), as opposed to New World monkeys, a prosimian, and rodent (18%). The New World howler monkey was the lone exception to the correlation since more than 30% of its OR genes had been inactivated due to mutation. Failing to find a perfect correlation could prove disheartening, but there is a different physiological trait that clarifies the number of pseudogenes. Every species with ~30% OR pseudogenes has full, three-color vision, while males with ~18% OR pseudogenes see only two colors. With the exception of howler monkeys, Old World monkeys have two opsin (color receptor pigment) genes, with one gene on the X chromosome and two alleles (greens or reds) for this locus. Therefore, males can see only two colors (blues and either greens or reds); females can see blue, green, and red if they are heterozygous at the X-linked opsin locus. The howler monkey genome duplicated its X-linked opsin gene and therefore males and females can see all three colors. As often happens in evolution, a gain in one area leads to a loss in another, so those species with full three-color vision cannot sense odors as well. In this case of comparative genomics, we learned how families of genes co-evolve due to selective advantage offered by a second family of genes.

An American team of 72 authors at 8 different institutions zoomed out a bit further to look at a 1.8 Mb segment from human chromosome 7 (including the cystic fibrosis gene *CFTR*) and compared the human sequences to syntenic regions in 11 other species. The entire region encodes 10 genes and the investigators wanted to examine not just the coding regions, but also introns, promoters, and intergenic regions (Figure 3.6). As you would expect, the greatest conservation was in the coding regions; the closer two species were phylogenetically, the higher the DNA conservation.

Surprisingly, rodents are an exception to this trend. Mouse and rat share 10 deletions but their genomes have

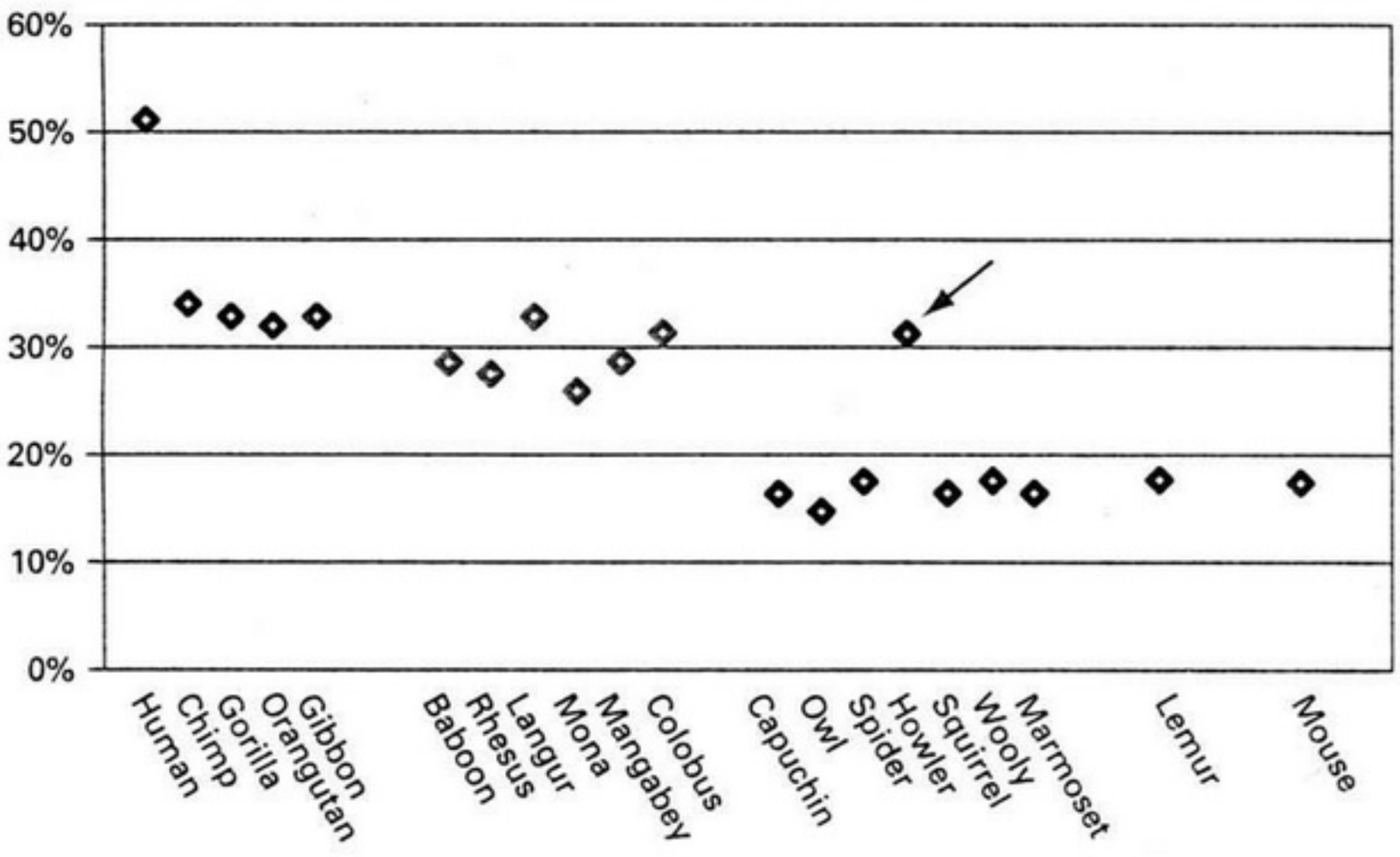
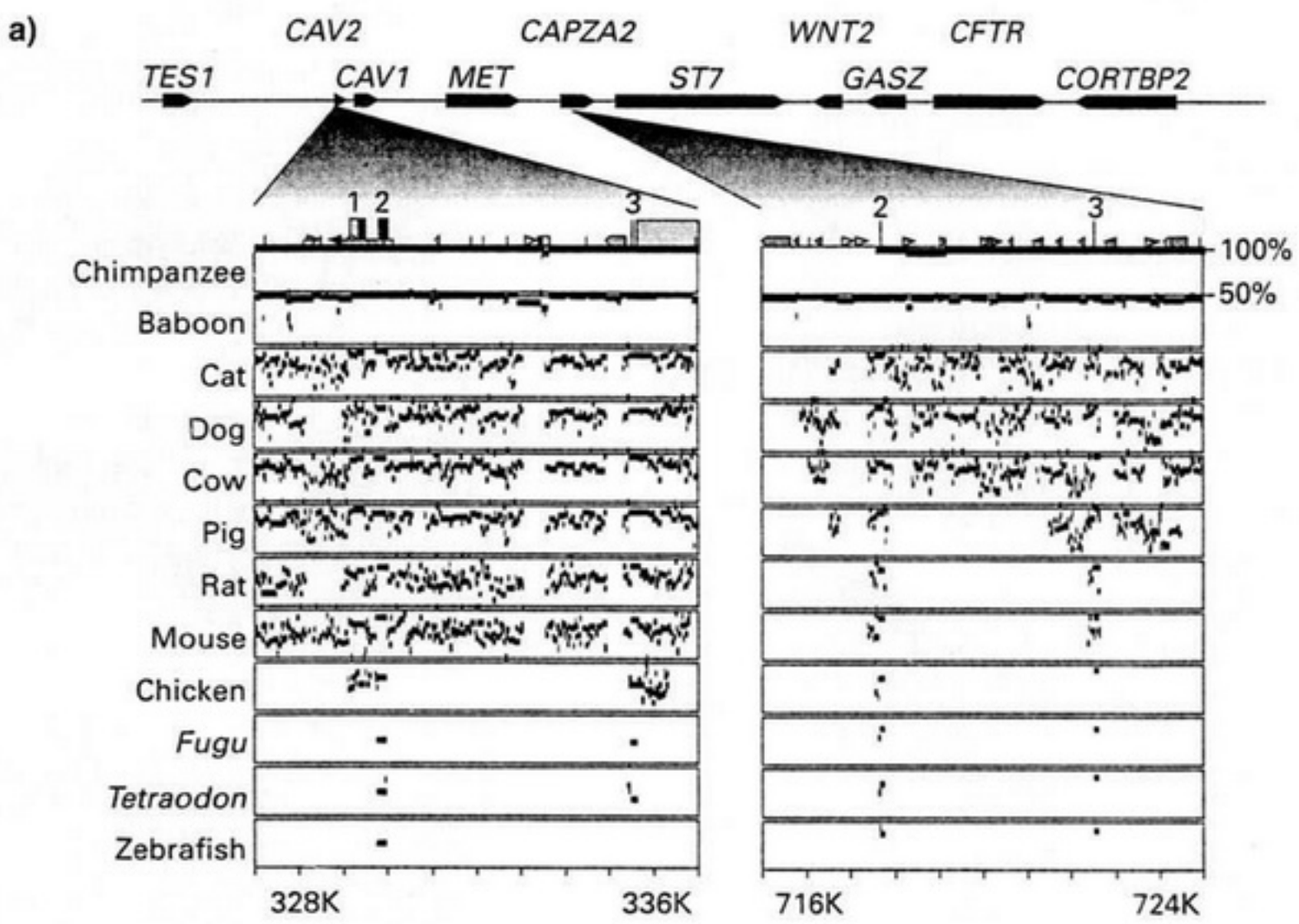


Figure 3.5 Evolution of three-color vision.

Percentage of olfactory receptor pseudogenes form a random sampling of 100 genes from each species. Species are color-coded: humans and apes (purple); Old World monkeys (black); New World monkeys, lemur, and mouse (gray).



LINKS
Evan Eichler

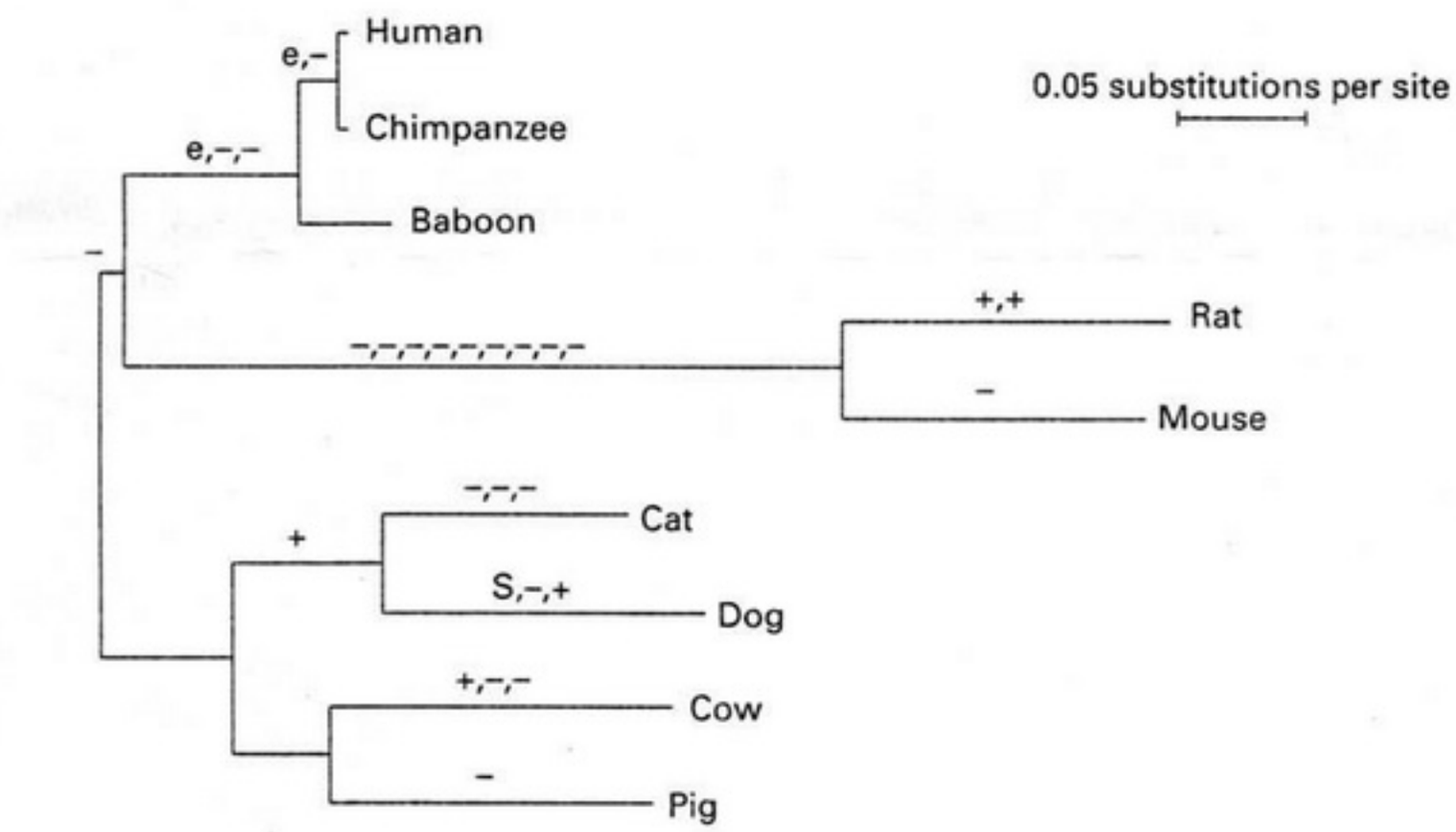


Figure 3.6 Multispecies genome conservation of CFTR region.
a) Pair-wise alignments between the human and 12 vertebrate species. The percentage identity of each gap-free alignment is indicated. Numbered boxes correspond to exons. **b)** Deduced phylogenetic tree of indicated mammalian species. Labels on branches reflect differences in exon lengths: +, insertion; −, deletion; e, extension due to alteration of splice site or stop codon; s, early stop codon.

drifted rapidly due to high nucleotide substitution rates, which may explain why they can adapt so quickly to different human environments. However, based on shared deletions, insertions, and transposons, rodents are more closely related to primates than are other mammals. Based on this analysis, rodents are better model animals for studying human physiology than other mammals.

What Can We See at the Chromosomal Perspective?

Evan Eichler at Case Western Reserve University examined human chromosome 7, and his team looked at the entire chromosome for recombination hot spots. By comparing human and mouse synteny, they were able to map locations

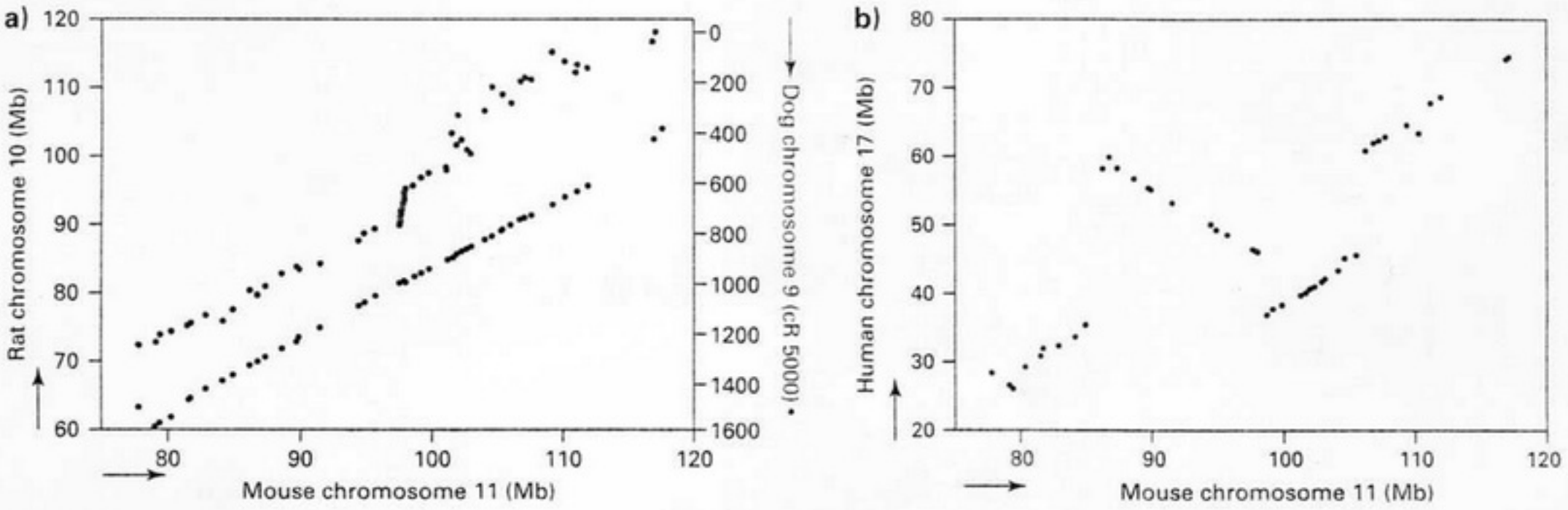


Figure 3.7 Dot plot of gene colinearity compared to mouse.
Arrows point from centromere to telomere. **a)** Rat (black, left Y-axis) genes compared to mouse (X-axis). Dog (gray, right Y-axis) genes compared to mouse (X-axis). **b)** Human genes compared to mouse.

where recombination was more frequent than expected from random recombination events. Chromosome 7 has a total of 27 hot spots for recombination, with 12 on the shorter p arm and 15 on the q arm. Locating recombination hot spots complemented related findings by the international team studying human recombination frequencies that led to common human genotypes (see Chapter 4). A team of 10 investigators from Canada, France, and the U.S. decided to map the exact recombination events that have produced syntenic regions in human, mouse, rat, and dog. Now that all of these genomes have been sequenced, we will examine just one portion of a chromosome associated with a genetic disease in dogs.

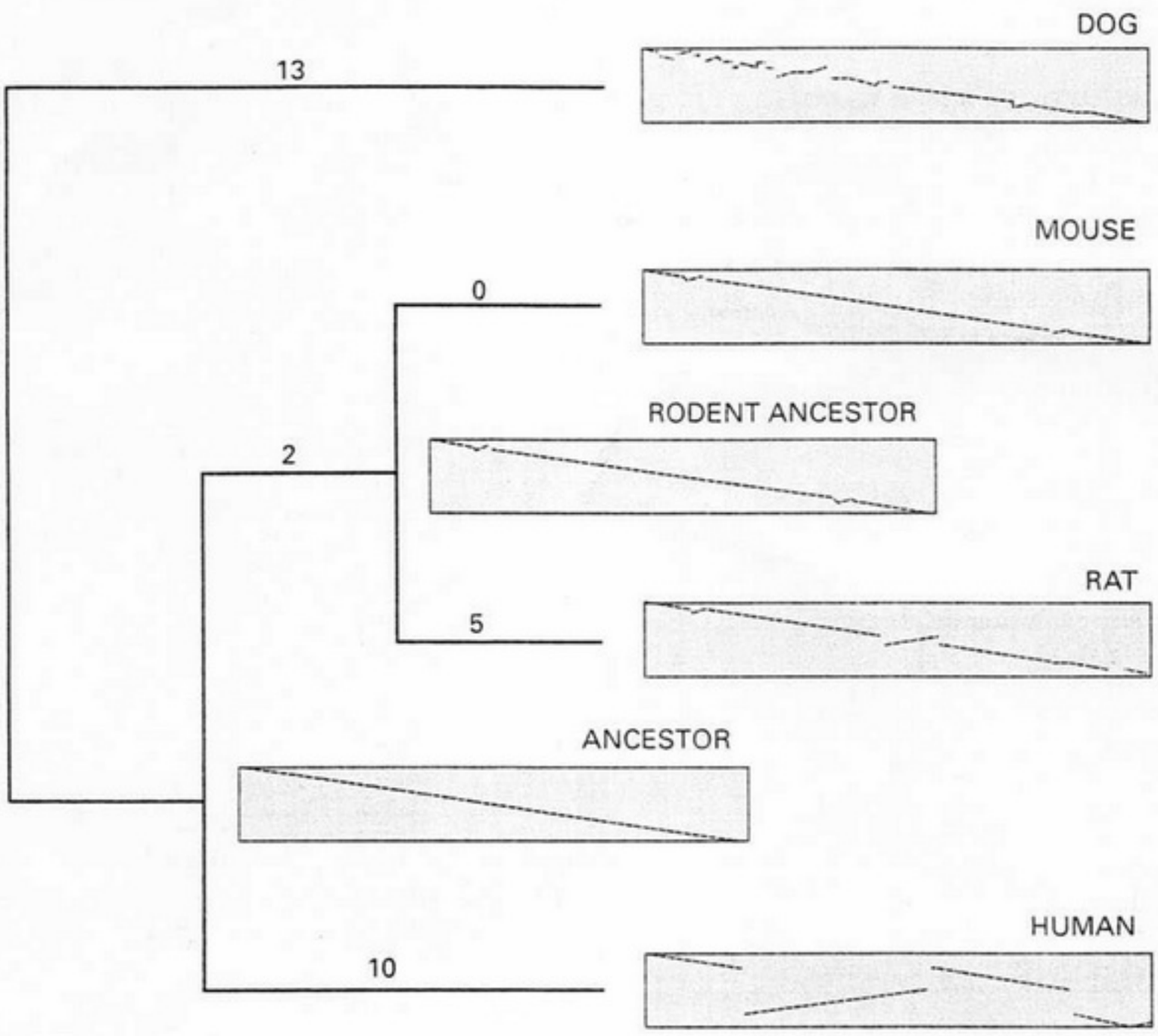
Canine tricuspid valve malformation (CTVM) is a genetic disease that leads to thickened heart valves, which stick to the ventricular septum and lead to sudden death. CTVM is especially common in Labrador retrievers, and the CTMV locus was mapped on canine chromosome 9 (dogs have a total of 78 chromosomes). Human chromosome 17 is syntenic to the region containing CTMV and over 50 Mendelian traits are mapped to this region, as well as polygenic traits such as high blood pressure, multiple sclerosis, and diabetes. The investigators looked at whole-chromosome recombination events for CTVM syntenic regions (mouse chromosome 11 and rat number 10; Figure 3.7). As you might expect, the rat and mouse comparison exhibited the fewest chromosomal recombination events. When compared to mouse, dog had one major (4 Mb) recombination event and human experienced two large recombinations (9.2 Mb and 23 Mb).

The dot plots in Figure 3.7 revealed the major recombination events, but the resolution of these figures was limiting. The authors expanded their level of detail, compared all four chromosomes simultaneously, and used lines to help us

Figure 3.8 Mammalian chromosome recombinations.
Go to www.GeneticsPlace.com to view this figure.

follow the major recombination events (Figure 3.8). They also used colored lines to highlight the recombination hot spots, with shaded regions showing the two large human recombined areas. Figure 3.8 is a good example of the power of visualizing data: it is easy to follow inversions (crossing lines) and translocations (lines bending but not crossing).

When we consider smaller recombination events, we can see dog has experienced at least 15, compared to the other mammals, with exact numbers depending on the species being compared (23 between human and dog). The site of recombination is often conserved across species, as is the site of gene loss when it happens. When the perspective is changed to correlate recombination hot spots with DNA sequence, we find highly repetitive DNA, such as Alu sequences, transposons, and RNA genes (including tRNA and rRNA), is often involved. However, the large-scale recombination allows us to create a different type of phylogenetic tree (Figure 3.9). In addition to tracking the number of chromosomal-scale changes between different species, the authors constructed two **most recent common ancestor** (MRCA) chromosomes. The mouse has undergone no new recombination events since it diverged from the rat, but rats have experienced five. Two additional recombinations separate rodents from the human MRCA, as indicated by the two small inversions in the mouse chromosome. Humans have accumulated 10 new inversions or translocations since we diverged from our rodent MRCA.



DATA GEP
Dog v. Mouse genetic code

LINKS
ECR Browser

MATH MINUTES
dot plot

Figure 3.9 Deduced, unrooted phylogenetic tree.
The number of rearrangements that occurred on each edge is shown. Rectangles represent chromosomal arms from Figure 3.8 but are not drawn to scale. A diagonal line provides a visual indication of the gene order and of the positions of rearrangements.

Dogs are placed on the outermost branch of this unrooted tree because its 13 recombinations are unrelated to those shared by the other 3 mammals.

DISCOVERY QUESTIONS

15. Go to the genetic code web page and see if there GEP is a DNA trend based on which amino acids are increasing and which are decreasing.

16. Go to the ECR Browser, choose "Human," and GEP submit this region to be aligned: "chr21:23674384-23707716." What gene have you located? Red bars indicate conserved, noncoding DNA; yellow is conserved *un*translated *r*egion (**UTR**) of exons; blue marks coding exons. Compare the first alignment with the following region: "chr21:26024345–26079899." Is this second region coding or noncoding DNA? How well is this DNA conserved compared to the first alignment?

17. Copy and paste the Dog v. Mouse sequences into GEP the dot plot web page. Describe the genomic changes that have taken place at this region. Look at Figure 3.7a and notice that the rat chromosome is shorter than the mouse one. Look at Figure 3.8 and find a deleted rat region. What visual characteristic in Figure 3.8 makes finding a deletion easier?

18. Use Figure 3.9 to calculate the total recombination distance between each of the species and fill in the following chart:

	Human	Mouse	Rat	Dog
Human	0	—	—	—
Mouse		0	—	—
Rat			0	—
Dog				0

19. Look at the number of human OR pseudogenes in Figure 3.5. Based on these data, what would you predict about human reliance on smell vs. sight for collecting information about our environment?