# Evolution and Medicine

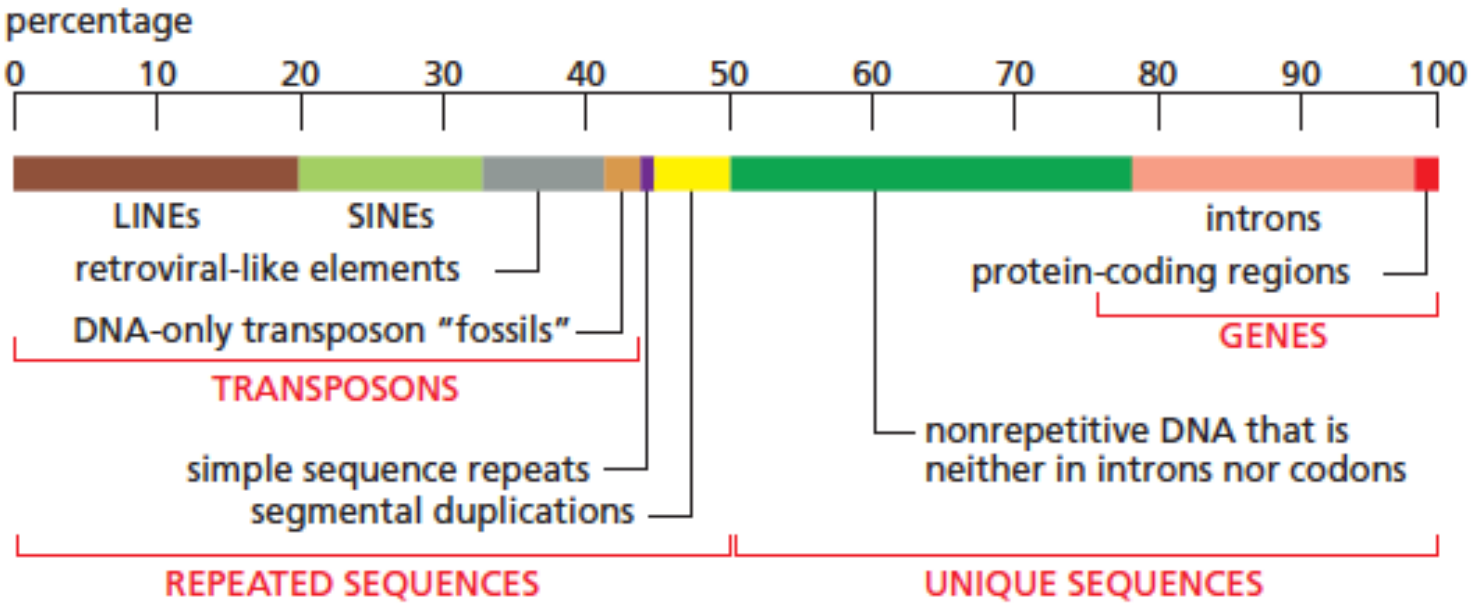
**Evolution of the Genomes**

Genetic Diversity and Polymorphism

Evolutionary Mechanisms
- Microevolution vs Macroevolution
- Population Genetics
- Evolution and Medicine

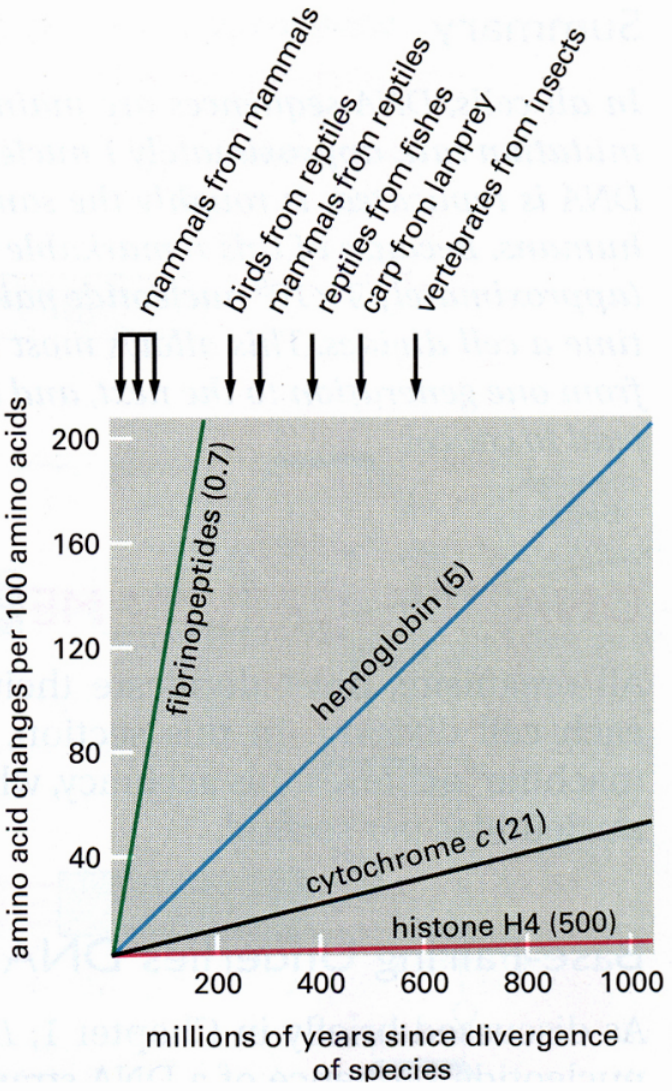
# How do Genomes Evolve?

Genome Alterations Are Caused by Failures of the Normal Mechanisms for Copying and Maintaining DNA, as well as by Transposable DNA Elements



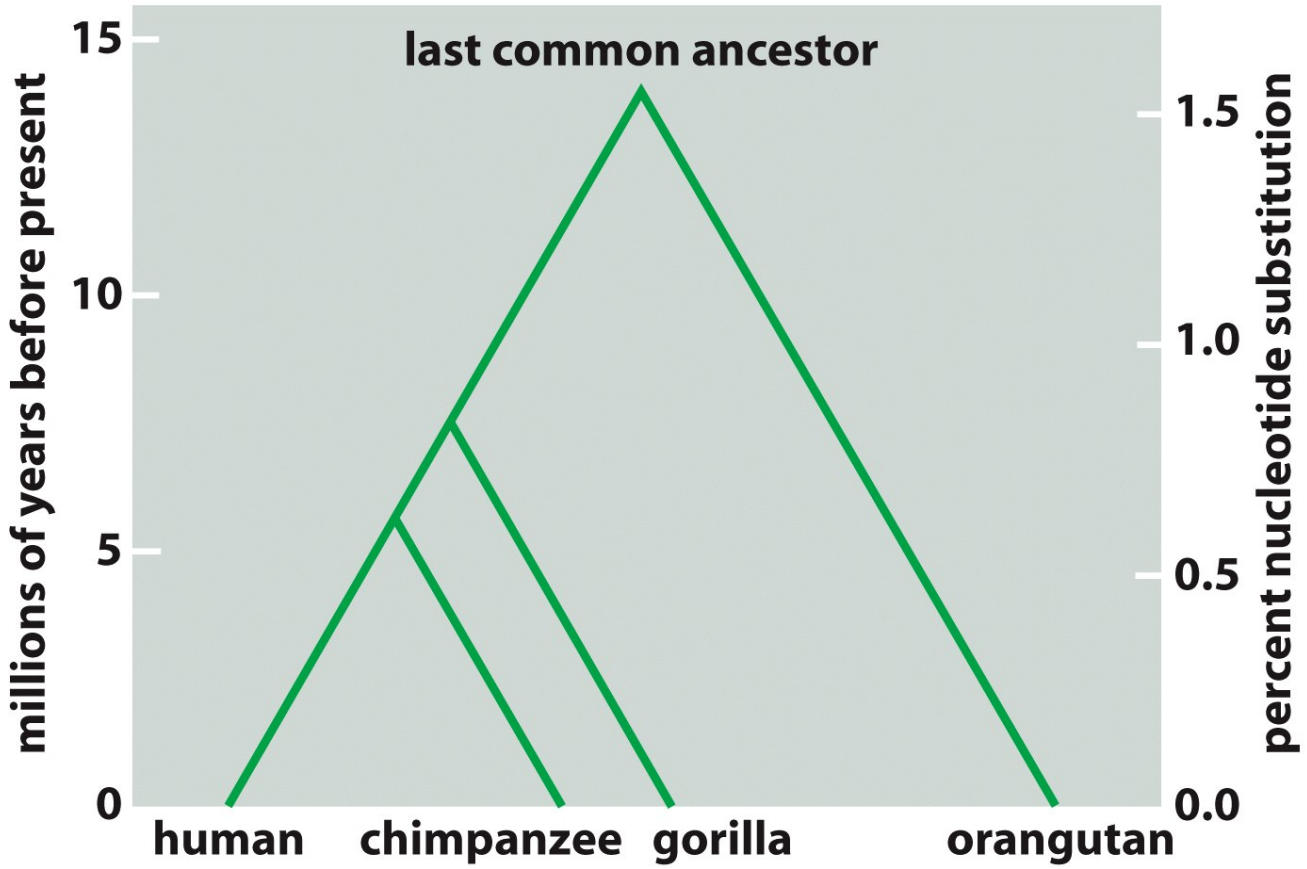

A representation of the nucleotide sequence content of the sequenced human genome.

**Figure 5–1 Different proteins evolve at very different rates.**
A comparison of the rates of amino acid change found in hemoglobin, histone H4, cytochrome *c*, and the fibrinopeptides. The first three proteins have changed much more slowly during evolution than the fibrinopeptides, the number in parentheses indicating how many million years it has taken, on average, for one *acceptable* amino acid change to appear for every 100 amino acids that the protein contains. In determining rates of change per year, it is important to realize that two species that diverged from a common ancestor 100 million years ago are separated from each other by 200 million years of evolutionary time.

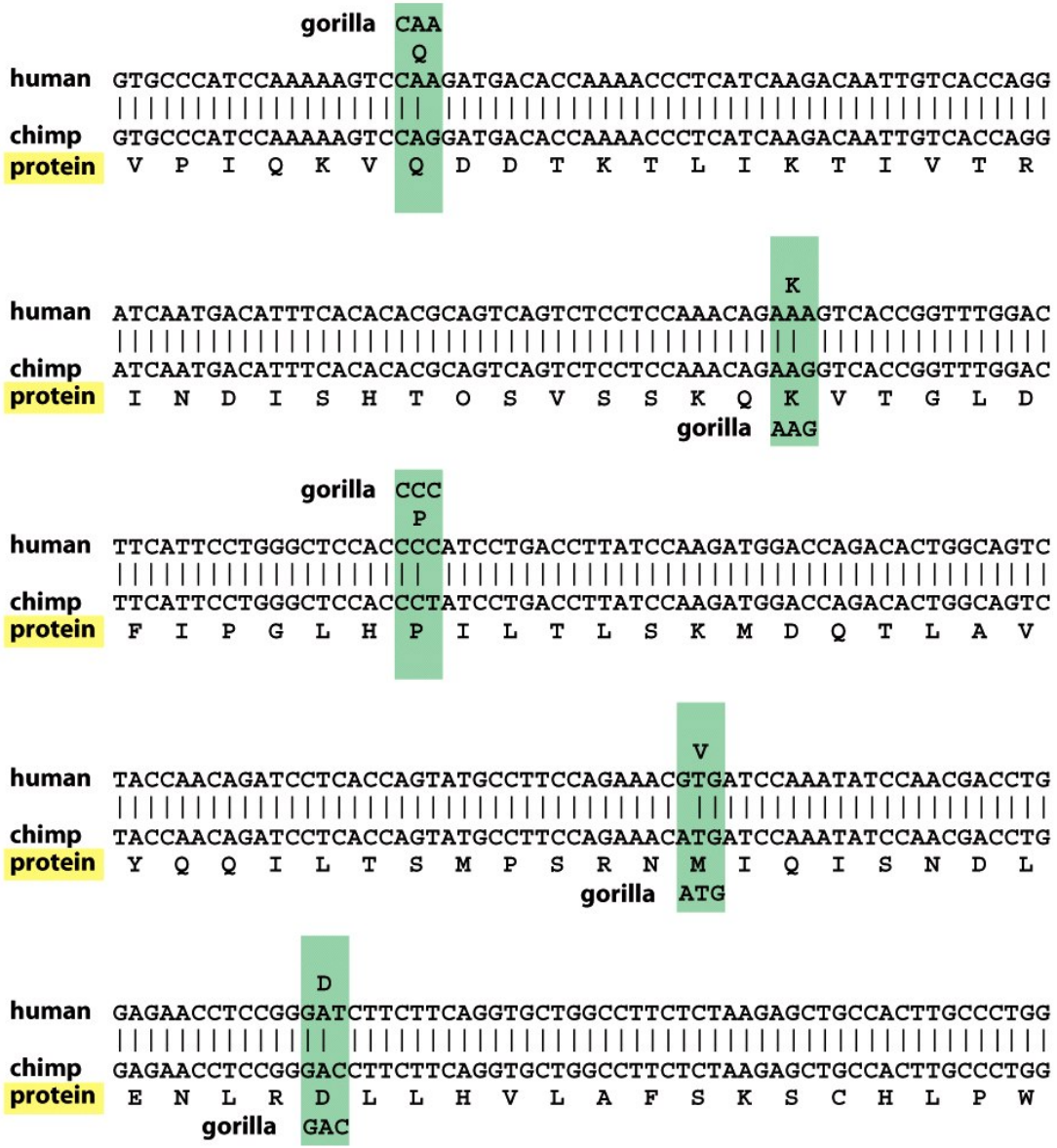



Genome Comparisons Reveal Functional DNA Sequences by their Conservation Throughout Evolution

# Phylogenetic Trees Constructed from a Comparison of DNA Sequences Trace the Relationships of All Organisms

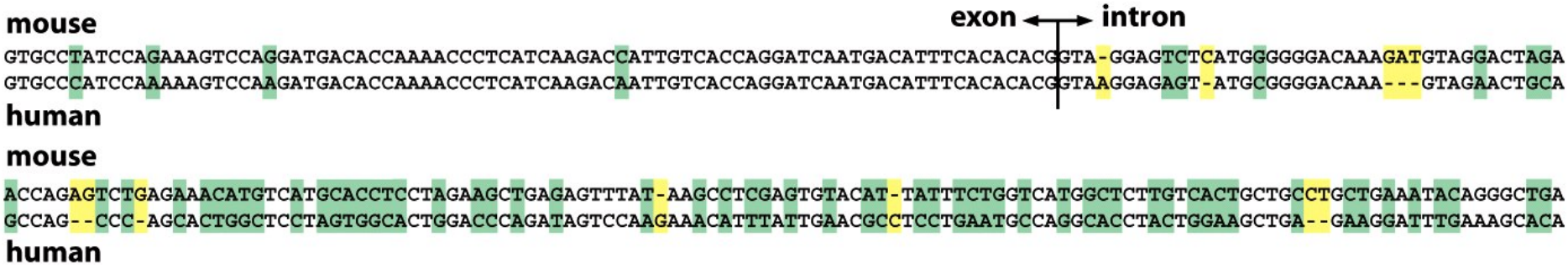



A phylogenetic tree showing the relationship between humans and the great apes based on nucleotide sequence data.



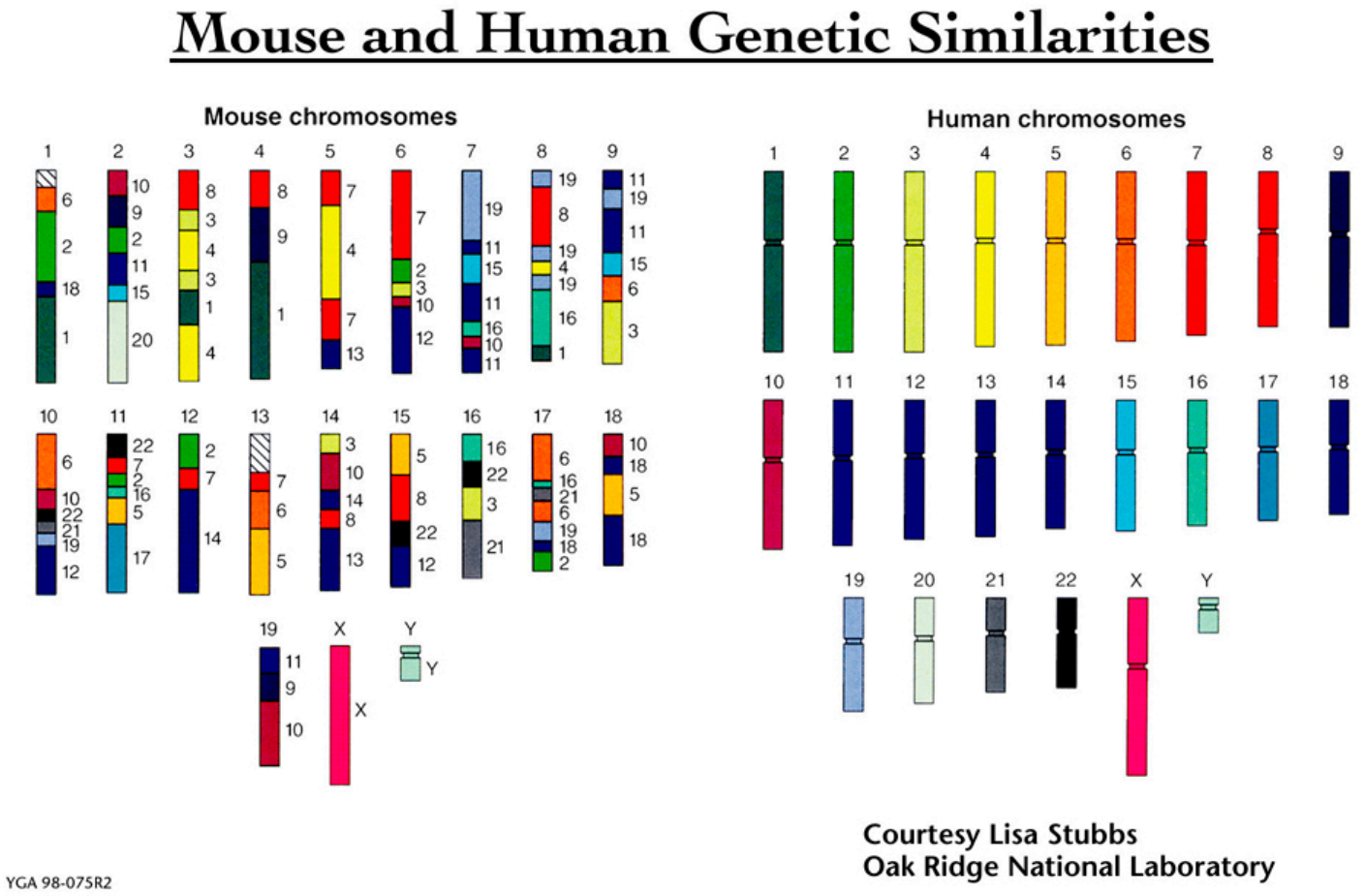

# Phylogenetic Trees Constructed from a Comparison of DNA Sequences Trace the Relationships of All Organisms

Tracing the ancestral sequence from a sequence comparison of the coding regions of human and chimpanzee leptin genes.



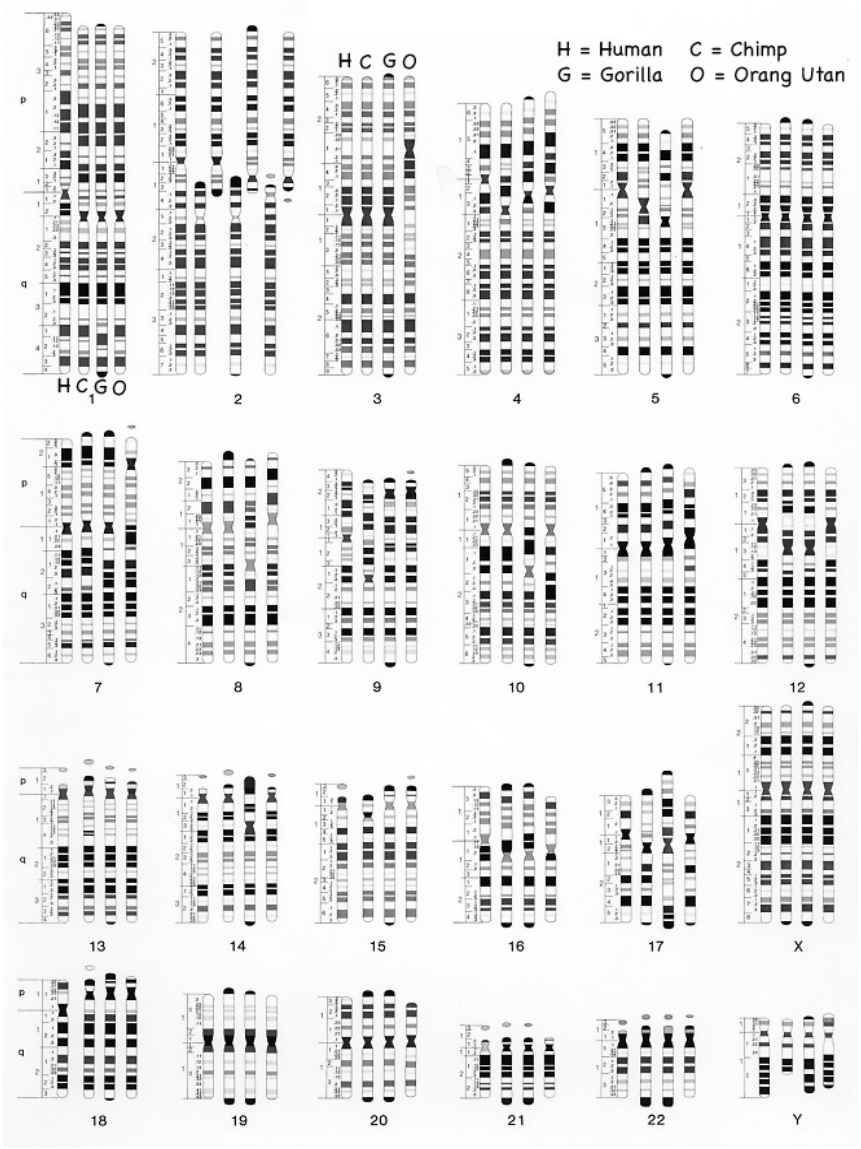

The very different rates of evolution of exons and introns, as illustrated by comparing a portion of the mouse and human leptin genes. Positions where the sequences differ by a single nucleotide substitution are boxed in green, and positions that differ by the addition or deletion of nucleotides are boxed in yellow. Note that, thanks to purifying selection, the coding sequence of the exon is much more conserved than is the adjacent intron sequence.

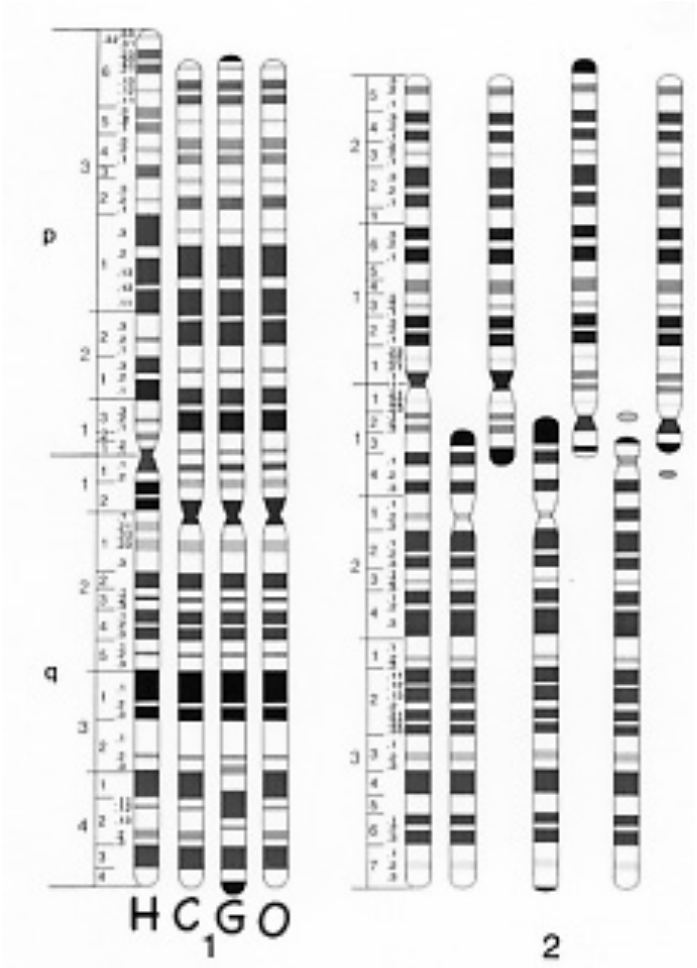
A Comparison of Human and Mouse Chromosomes Shows How the Structures of Genomes Diverge

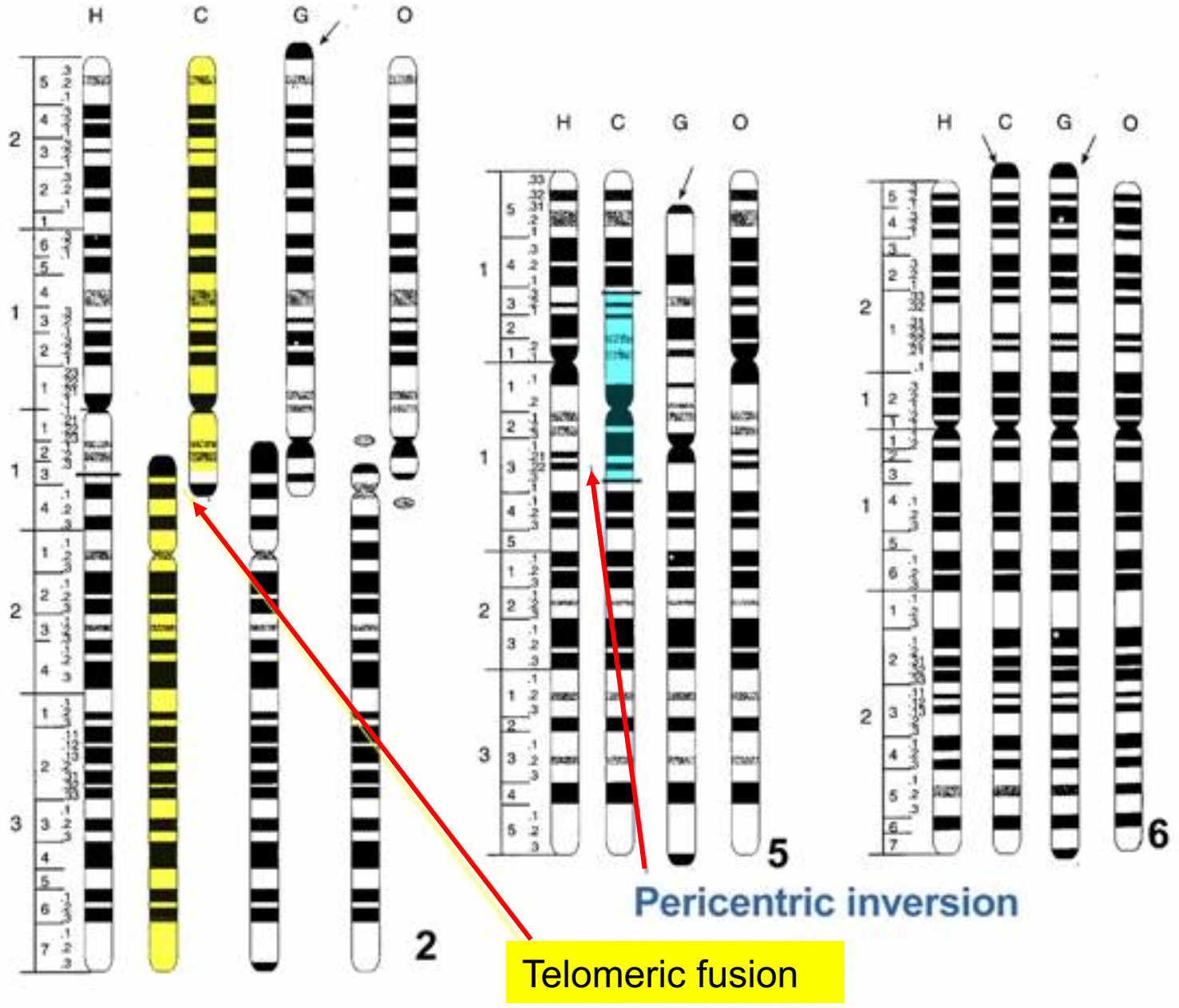



**Synteny** between human and mouse chromosomes.

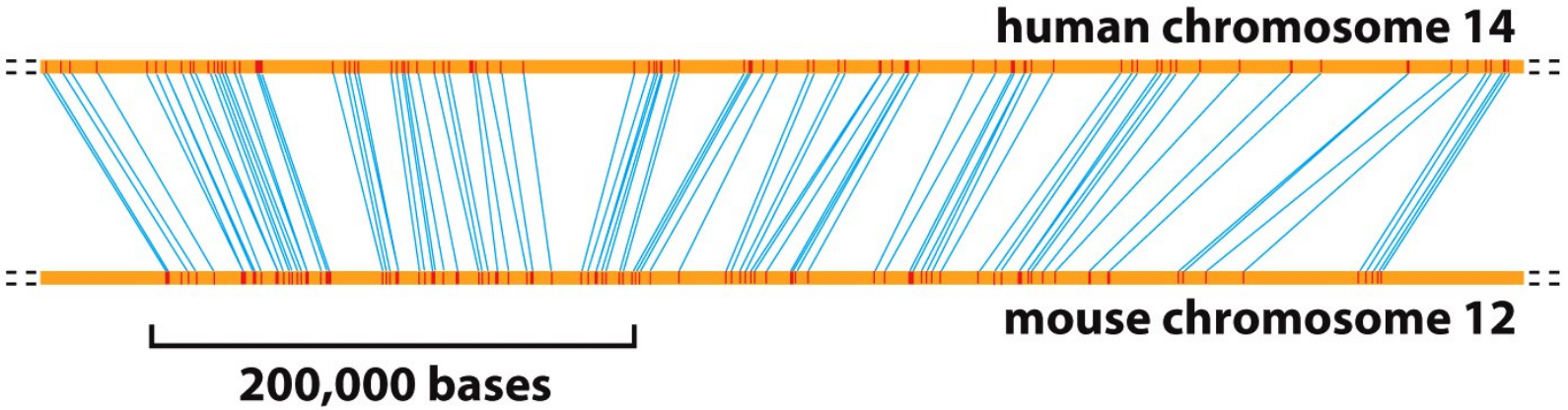
# CHROMOSOMES OF THE GREAT APES



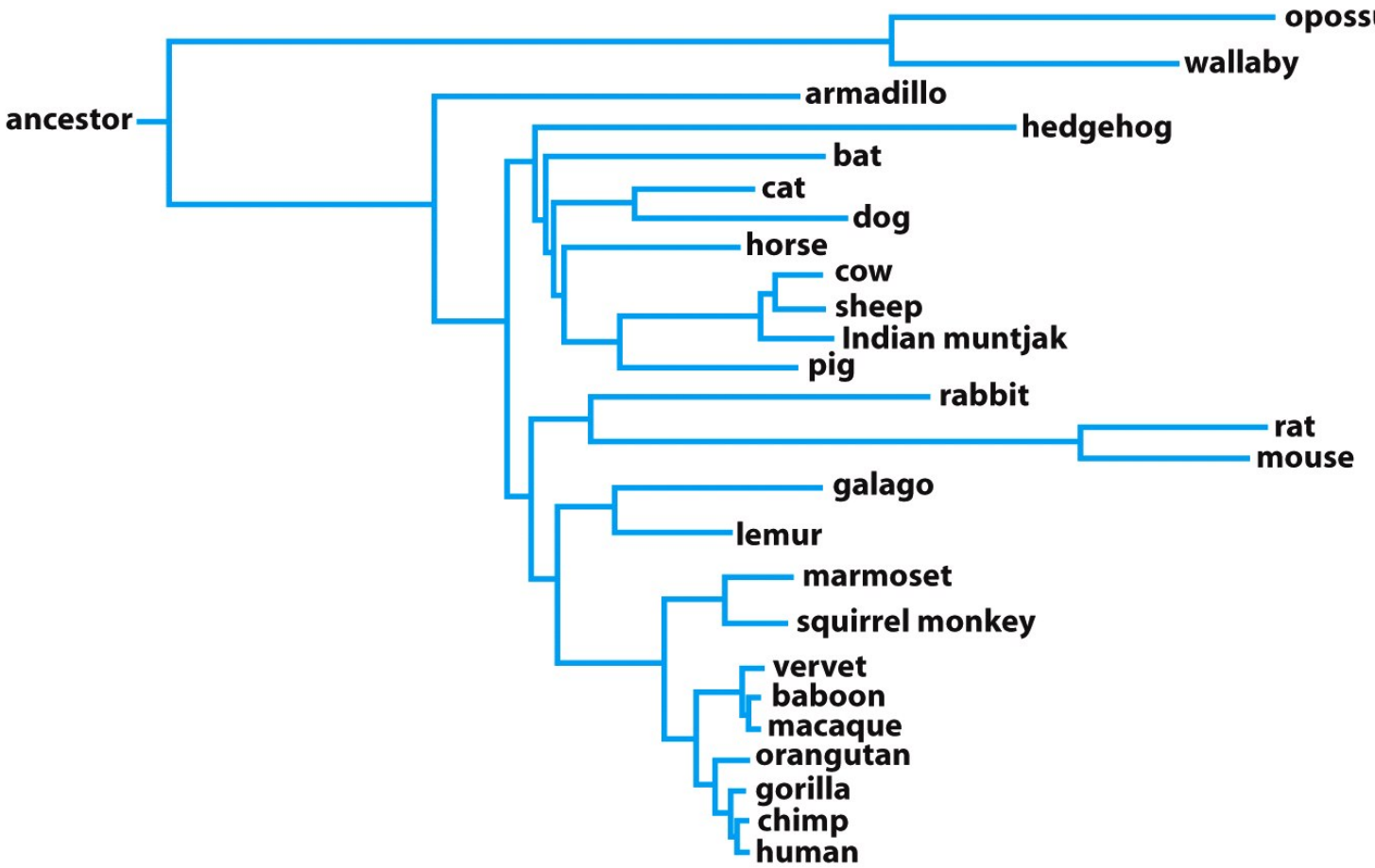

H
C
G
O
2
5
6
Pericentric inversion
Telomeric fusion

# The Size of a Vertebrate Genome Reflects the Relative Rates of DNA Addition and DNA Loss in a Lineage

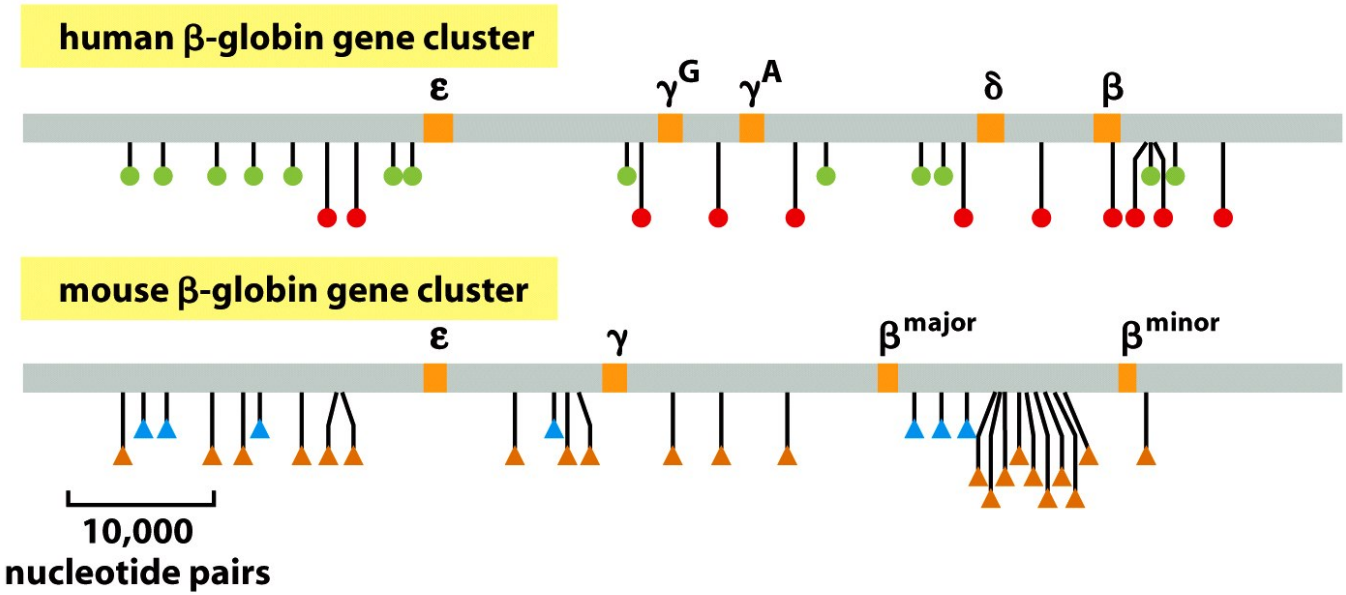



Comparison of a syntenic portion of mouse and human genomes.

About 90% of the two genomes can be aligned in this way. Note that while there is an identical order of the matched index sequences (red marks), there has been a net loss of DNA in the mouse lineage that is interspersed throughout the entire region. This type of net loss is typical for all such regions, and it accounts for the fact that the mouse genome contains 14% less DNA than does the human genome.

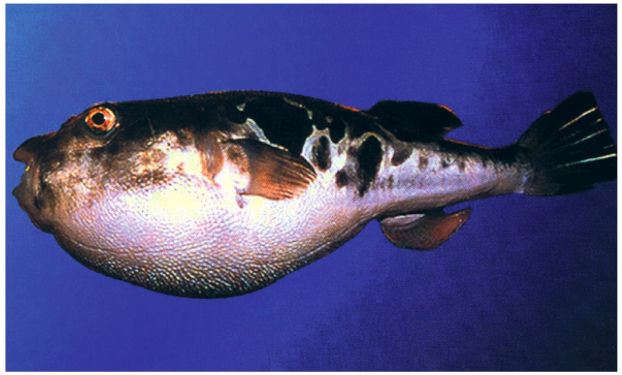



A phylogenetic tree showing the evolutionary relationships of some present-day mammals. The length of each line is proportional to the number of "neutral substitutions"—that is, nucleotide changes at sites where there is assumed to be no purifying selection.

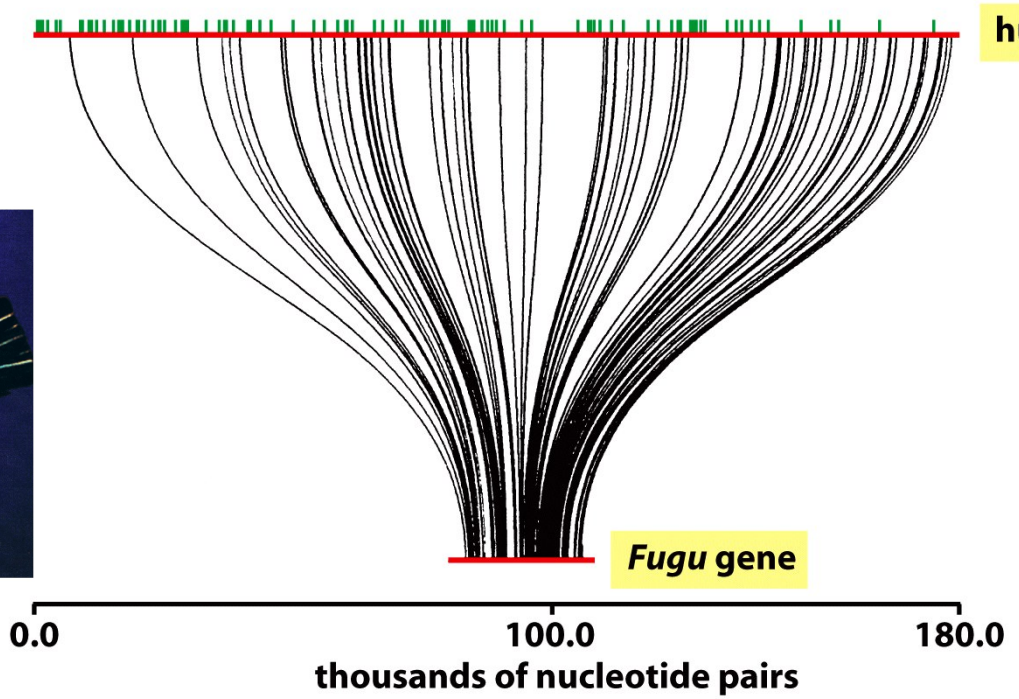



A comparison of the β-globin gene cluster in the human and mouse genomes, showing the locations of transposable elements.

The absence of transposable elements from the globin structural genes can be attributed to purifying selection, which would have eliminated any insertion that compromised gene function.

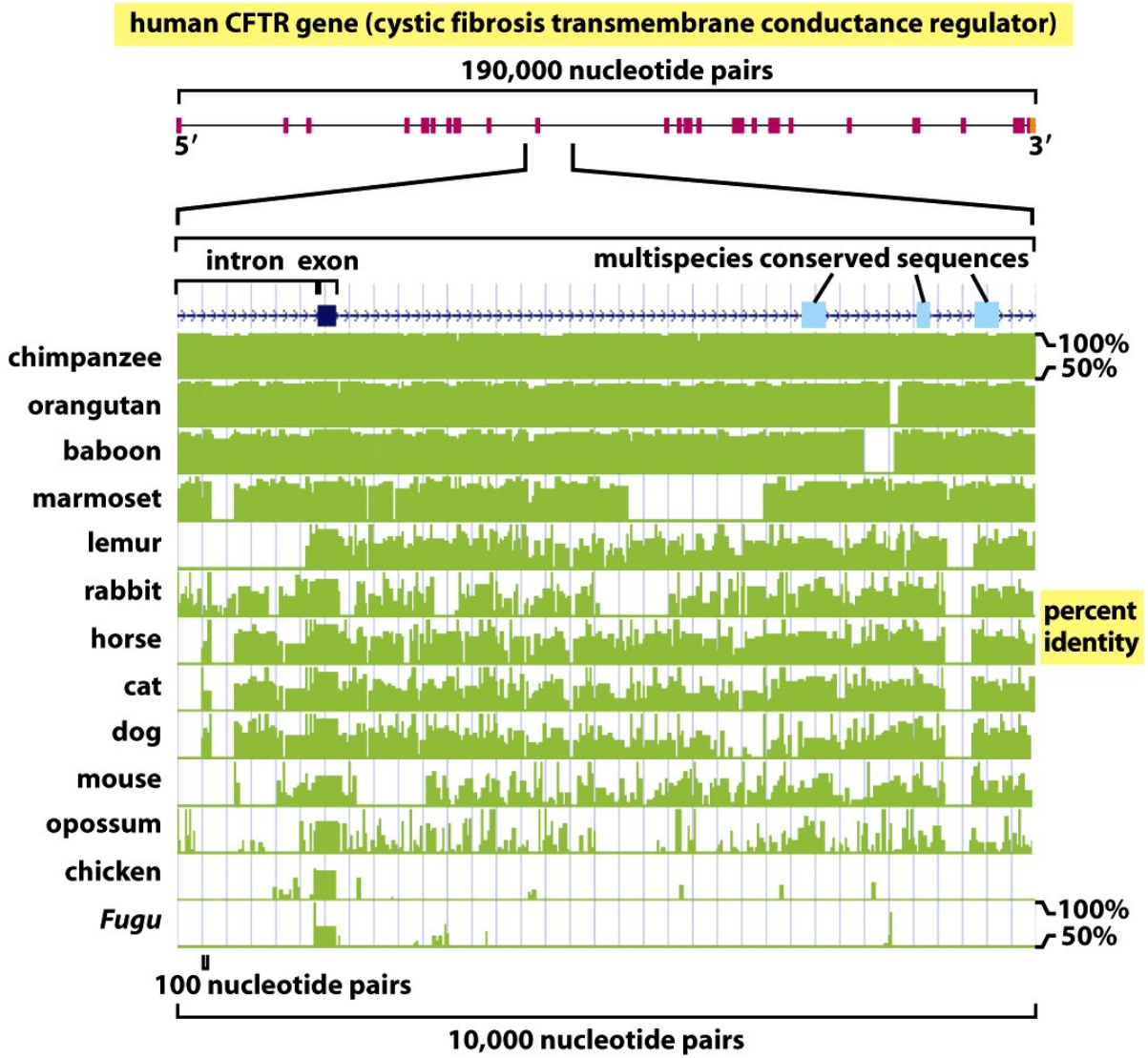


Fugu rubripes
Genome size: $4 \times 10^8$ bp



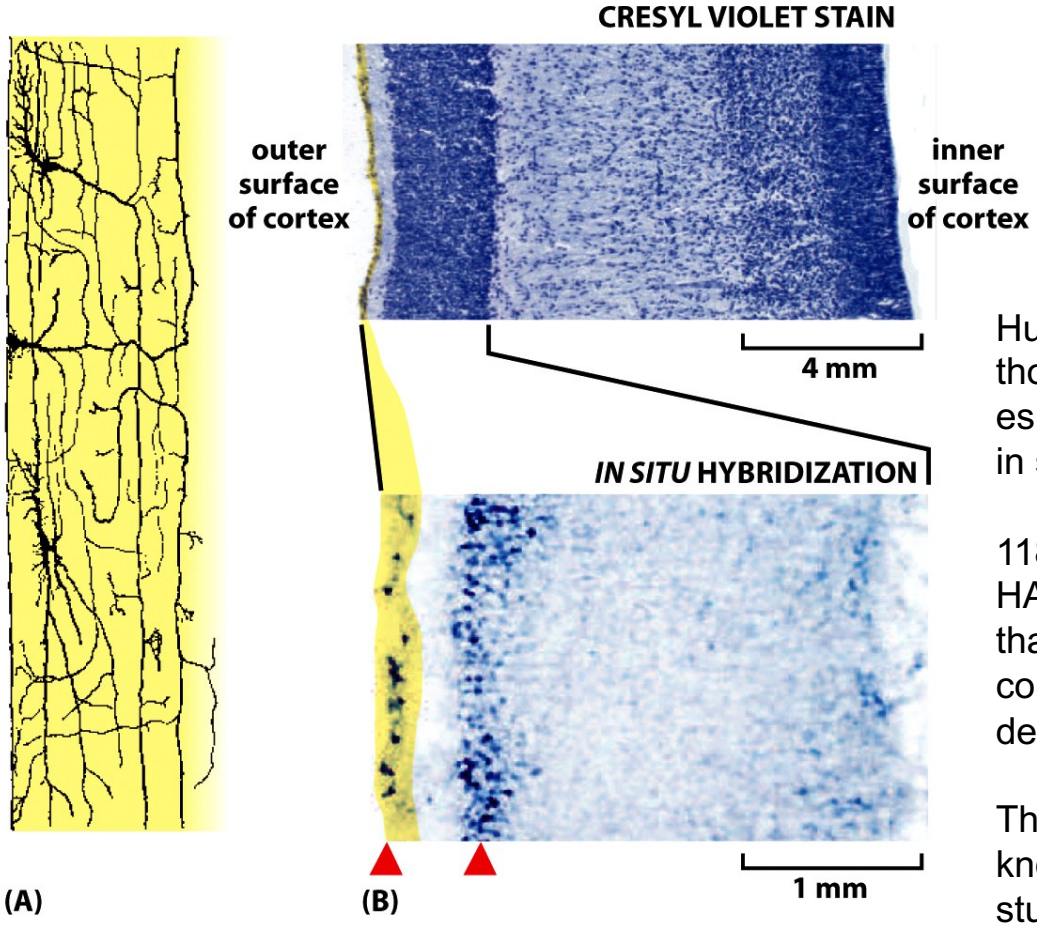

Comparison of the genomic sequences of the human and Fugu genes encoding the protein huntingtin. Both genes (indicated in red) contain 67 short exons that align in 1:1 correspondence to one another. The size difference is entirely due to larger introns in the human gene. The larger size of the human introns is due in part to the presence of retrotransposons

# Multispecies Sequence Comparisons Identify Conserved DNA Sequences of Unknown Function




The detection of multispecies conserved sequences. Besides the exon (dark blue on the line atthe top of the figure), the positions of three other blocks of multispecies conserved. sequences are indicated (pale blue). The function of most such sequences in the human genome is not known.

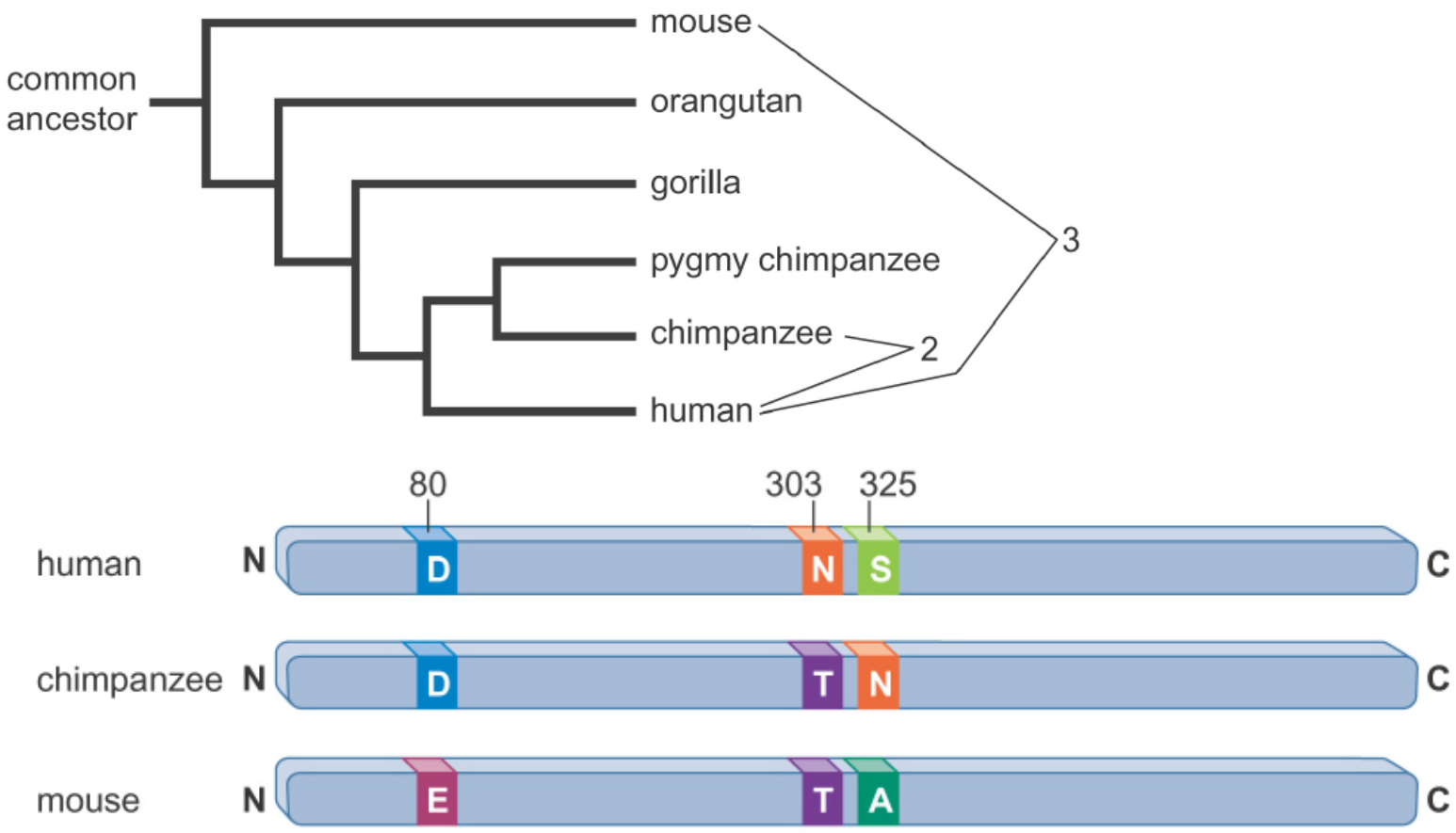
# Changes in Previously Conserved Sequences Can Help Decipher Critical Steps in Evolution




Human accelerated regions (HARs) are thought to reflect functions that have been especially important in making us different in some useful way.

118-nucleotide noncoding RNA molecule, HAR1F (human accelerated region 1F), that is produced in the human cerebral cortex at a critical time during brain development.

The function of this HAR1F RNA is not yet known. 50 such sites were identified in one study, one-fourth of which were located near genes associated with neural development.




***FOXP2*** a transcriptional regulator protein

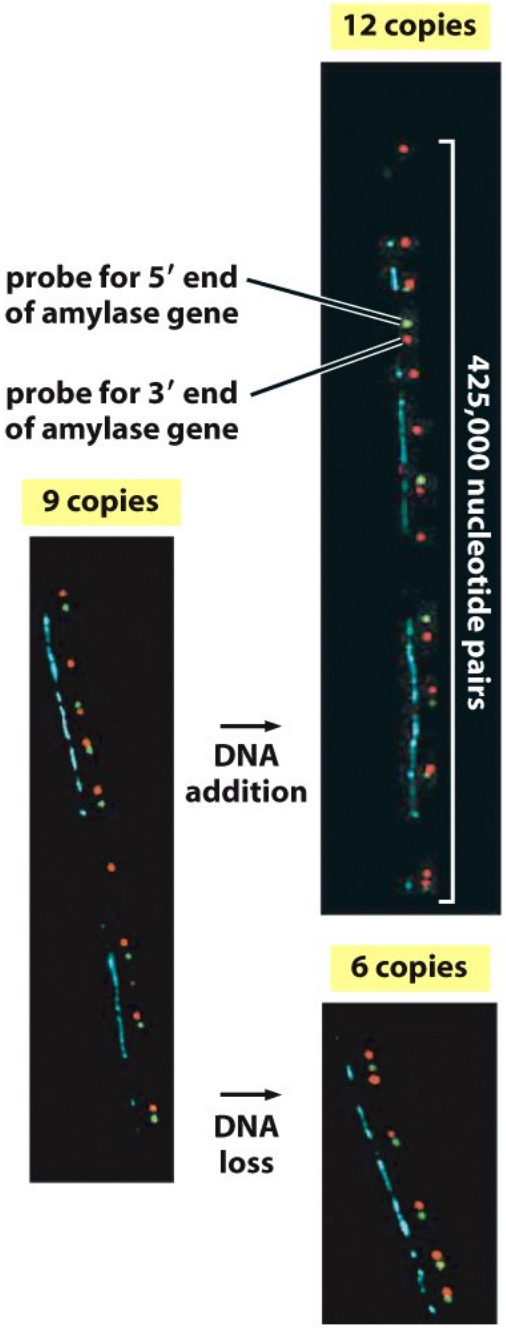
Expressed in many areas of the brain including the basal ganglia and inferior frontal cortex.
Essential for brain maturation, speechh and language development.

# A Great Deal Can Be Learned from Analyses of the Variation Among Humans

Tracing the course of human history by analyses of genome sequences. The map shows the routes of the earliest successful human migrations.

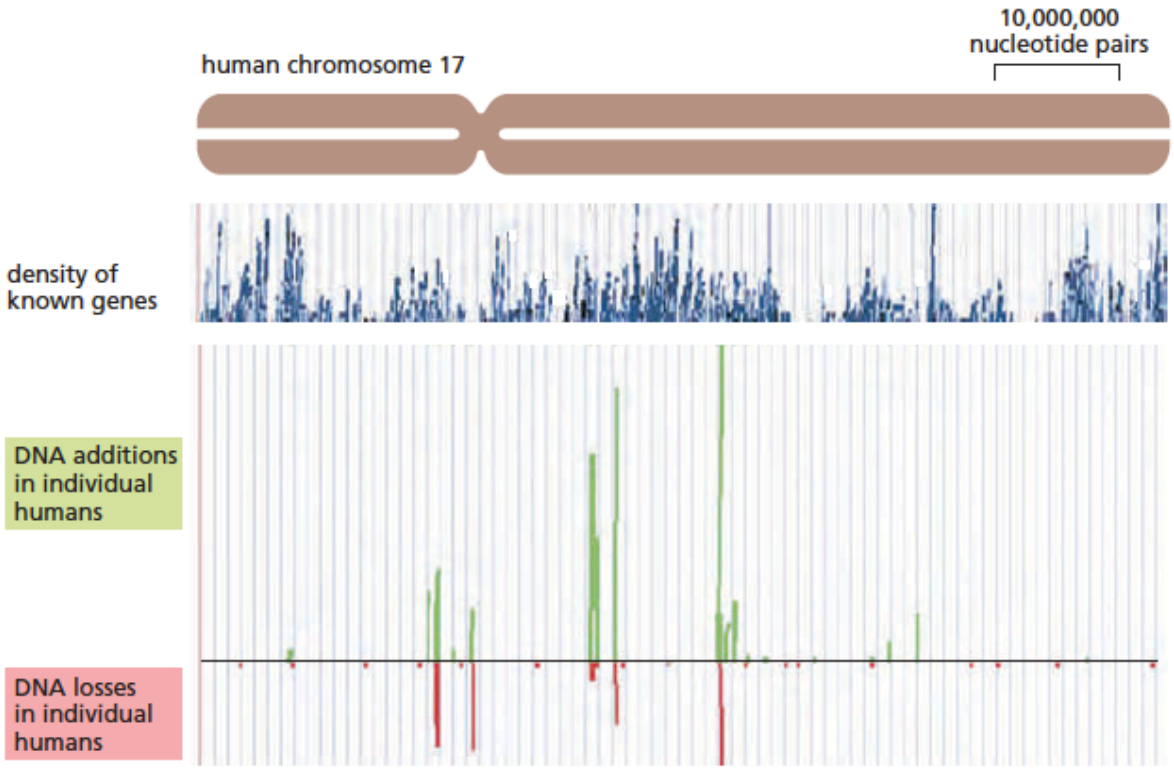
Europeans descended from a small ancestral population that existed about 30,000 to 50,000 years ago.

In agreement, archaeological findings suggest that the ancestors of modern native Australians (solid red arrows) and of modern European and Middle Eastern Populations reached their destinations about 45,000 years ago.




Copy number variation of amylase gene in humans

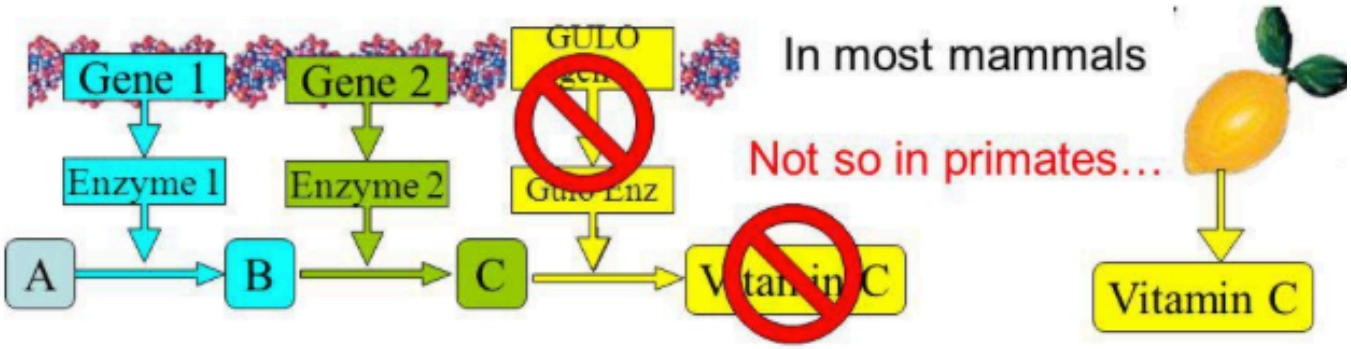
Streched human chromosomes are hybridized with single stranded nucleotide probes against amylase gene, *AMY1A*




Detection of copy number variations on human chromosome 17.
100 individuals were tested by a DNA microarray analysis that detects the copy number of DNA sequences throughout the entire length of this chromosome.

The results show regions where the variations occur tend to be in or near regions that already contain blocks of segmental duplications.

# Pseudogenes and Vitamin C




Portion of Working GULO Gene in Rat: