



To facilitate the annotation process, Jim Kent and the growing UCSC Genome Bioinformatics Group constructed the UCSC Genome Browser. This web-based tool serves as a multi-powered microscope to view all 23 chromosomes of the human genome. The coarse-level view shows early chromosome maps as determined by electron microscopy, then the browser drills down to levels of increasing detail, focusing first on chromosome bands, then on gene clusters (showing known genes—mostly those linked to diseases), then single genes, then components of genes, and finally on the nucleotides—the As, Cs, Gs, and Ts that make up the genome alphabet.

Not only does the browser show the genome sequence, it delineates known areas of the genome and offers supplementary information about the genes—in effect, providing the word breaks and punctuation. The UCSC browser brings the genome sequence to life by aligning relevant areas with experimental and computational data and images generated in the last decades by scientists from around the world. It also links to databases throughout the world, giving researchers instant access to deeper information about the genome.

The UCSC Genome Browser is available worldwide without charge, and the web site receives about 4,000 visitors per day. In a usual week, the visitors generate 1 million page requests as they explore the genome. The site has logged visitors from 44 countries throughout the world.

Since the first assembly of the human genome, the UCSC group has added a growing number of species to the UCSC Genome Browser, including roundworm, puffer fish, chicken, mouse, and chimpanzee. Interspecies alignments allow researchers to compare human genes to similar genes in other species. New features, such as VisiGene, an image library that corresponds to the genome data, expand the usefulness of the browser. Along with researchers worldwide, UCSC participates in projects to compare genomes of various species as a way to better understand gene function and the process of evolution.

### COMPARATIVE GENOMICS

Besides developing, supporting, and continuing to improve the genome browser, the UCSC Genome Bioinformatics Group conducts research into the functional elements of the human genome that have evolved under natural selection. The UCSC Genome Browser allows rapid comparisons between species, which can lead to many different types of new discoveries:

- Searching the human genome for sequences that match those with known functions in

other organisms can lead to new human gene discoveries.

- The molecular genetics behind disease development and progression in model organisms can be leveraged to discover potential disease-related genes in humans, moving us closer to diagnostic advances and targeted treatments.
- We can reconstruct the evolutionary history of the human genome by identifying the origins of interspecies differences and of short segments in the human genome that have been extremely well-conserved over millions of years of evolution.
- By searching for the highly conserved segments in the human genome—those that are unchanged from like segments in the genomes of other organisms, we can begin to understand the essential elements of the blueprint for life. Researchers suspect that these highly conserved elements must be essential to function. Genes make up only a small percentage of the unchanged elements, suggesting that other unknown regulatory elements in the genome are also important for function.
- Searching for genes that have evolved with unusual speed from one organism to another will give clues to essential interspecies differences, such as differences between the human and chimpanzee brain.

### POSSIBILITIES FOR HEALTH

As we begin to better understand the molecular mechanisms responsible for human disease, entire new avenues of treatments will be possible. We are only now getting a first glimmer of the molecular functions of a healthy human cell or organ, and we are still a long way from understanding the often subtle and complex ways that these can go awry. Yet knowledge of the human genome puts us on the brink of a revolution in medicine.

Rather than relying on trial and error to design and test new drugs, researchers will increasingly use their knowledge of the molecular causes of diseases to design new, targeted therapies. Research based on genome studies will also form the basis for new diagnoses and therapies for human disease that will transform the practice of medicine in this century.

The UCSC Genome Browser supports the latest endeavor of the National Human Genome Research Institute (NHGRI), a medical sequencing project intended to amass data relating genes to health conditions. This project sets the stage for the time when it becomes affordable for an individual's genome to be

sequenced. The information obtained will allow estimates of future disease risk and improve the prevention, diagnosis, and treatment of disease. The project focuses on rare Mendelian disorders, complex disorders, and normal human variation.

The practice of medicine will become much more individualized, with therapies tailored to be most effective given an individual's genetic makeup. Medical tests are already available to identify individual genetic variations that affect a patient's response to commonly used medications. These tests can allow doctors to avoid adverse reactions and choose medications appropriate for specific individuals. Someday we may even be able to repair or replace the disease-causing genes, re-orchestrating the molecular pathways needed for health.

**COMPARING GENOMES: human-mouse and human-chimp**

The graphs below indicate the similarity between the human genome and those of the chimpanzee and the mouse as they are mapped to identical

locations in the human genome. Since the chimpanzee genome is closer in evolutionary time to the human genome, the chimp chromosomes map very closely to human chromosomes. The mouse genome is more distant in evolutionary time from human, and thus its chromosomes do not map as closely as do the chimp chromosomes.

The white areas indicate areas of the human genome that either do not map well to the other genome, or are areas of centromeres and telomeres where the genome sequence is unknown. Chromosome numbering is purely arbitrary, based upon early microscopic estimates of chromosome length. The chimpanzee genome has 23 numbered chromosomes, the human genome has 22 numbered chromosomes (chimp chromosomes 2a and 2b map to human chromosome 2), the mouse genome has 19 numbered chromosomes. The X and Y sex chromosomes have unique names, as well as other unique characteristics.

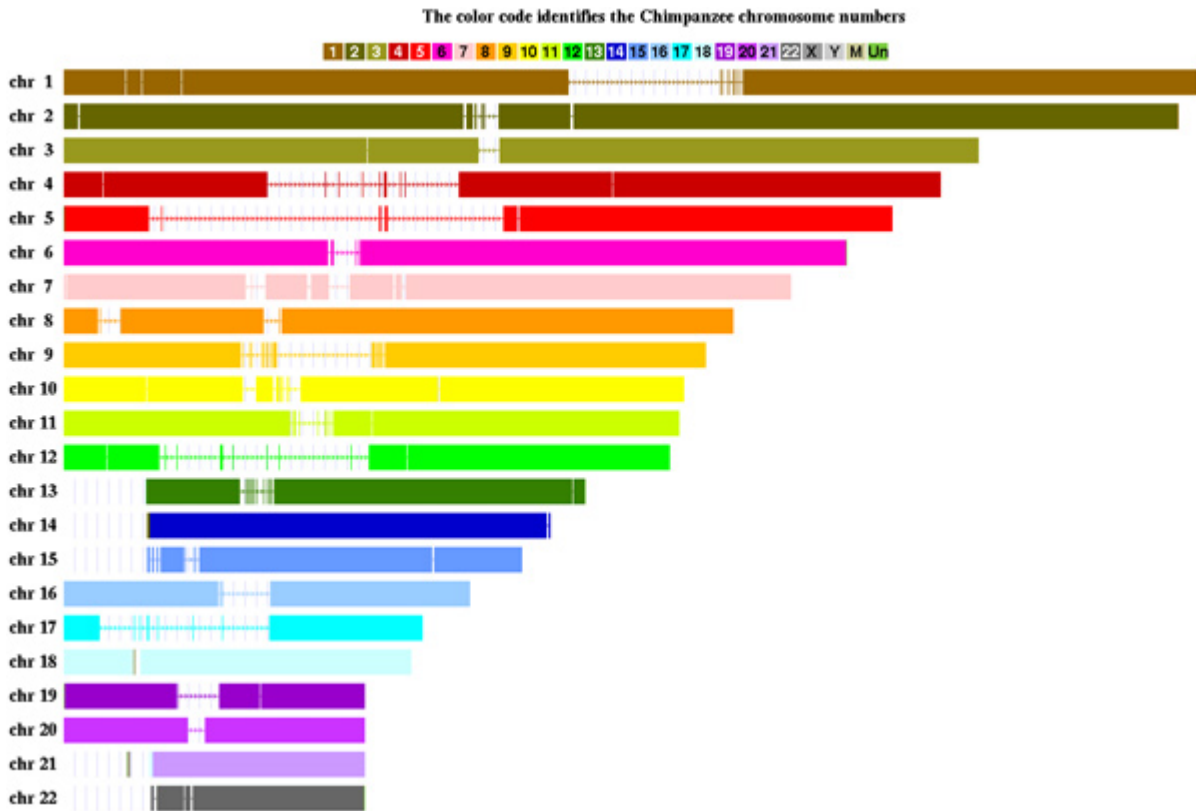
**Mouse genome mapped on the human genome**

This image shows the 34% of the mouse genome that maps to identical sequence in the human genome. The matching locations are jumbled, indicating rearrangements of the two genomes since their last common ancestor, approximately 75 million years before present.



**Chimpanzee genome mapped on the human genome**

This image shows the 95% of the chimpanzee genome that maps to identical sequence in the human genome. The consistency of the color indication demonstrates the close identity between the two genomes since their last common ancestor, approximately 5 million years before present.



Data were assembled from the UCSC Genome Browser by Hiram Clawson and Kate Rosenbloom. June 9, 2006