

## Timeline of Genomics (1977–2004)\*

Year	Event and Theoretical Implication/Extension	Reference
1977	<p><b>Frederick Sanger</b> (1980 Noble Prize Laureates for Chemistry) explores the technology of DNA sequencing. Sanger and colleagues use the technique to determine the sequence of all 5,375 nucleotides of the bacteriophage phi-X174, the first complete determination of the genome of an organism.</p> <p><b>Allan Maxam</b> and <b>Walter Gilbert</b> (1980 Nobel Prize Laureate for Chemistry) develop a new method for sequencing DNA, called Maxam-Gilbert chemical degradation method. They use the technique to determine the sequence of the operon of a bacterial genome.</p> <p><b>Louise Chow</b> and <b>Richard Roberts</b>, and independently <b>Phillip Sharp</b> (the latter two are 1993 Nobel Prize Laureates for Physiology or Medicine) show that eukarotic genes contain many interruptions, called <b>INTRONS</b>.</p> <p><b>Carl Woese</b> uses ribosomal RNA analysis to identify a third form of life, the Archea, whose genetic makeup is distinct from but related to both Bacteria and Eucaryea.</p> <p><b>Herbert Wayne Boyer</b> and colleagues synthesize a gene for the human hormone somatostatin, representing the first synthesis of a functional polypeptide product from a gene of chemically synthesized origin.</p>	<ol style="list-style-type: none"> <li>1. Sanger, F., <i>et al.</i> 1977. DNA sequencing with chain-terminating inhibitors. <i>Proc. Natl. Acad. Sci. USA</i> 74: 5463-5467.</li> <li>2. Sanger, F., <i>et al.</i> 1977. The nucleotide sequence of bacteriophage phi-X174. <i>J. Mol. Biol.</i> 125: 225-246.</li> <li>3. Sanger, F., <i>et al.</i> 1977. Nucleotide sequence of bacteriophage phi X174 DNA. <i>Nature</i> 165: 687-695.</li> </ol> <p>Maxam, A.M. and Gilbert, W. 1977. A new method for sequencing DNA. <i>Proc. Natl. Acad. Sci. USA</i> 74: 560-564.</p> <ol style="list-style-type: none"> <li>1. Chow, L.T., Gelinas, R.E., Broker, T.R., and Roberts, R.J. 1977. An amazing sequence arrangement at the 5' ends of adenovirus 2 messenger RNA. <i>Cell</i> 12: 1-8.</li> <li>2. Berget, S.M., Moore, C., and Sharp, P.A. 1977. Spliced segments at the 5'-terminus of adenovirus 2 late mRNA. <i>Proc. Natl. Acad. Sci. USA</i> 74: 3171-3175.</li> <li>1. Woese, C.R. and Fox, G.E. 1977. Phylogenetic structure of the prokaryotic domain: the primary kingdoms. <i>Proc. Natl. Acad. Sci. USA</i> 74: 5088-5090.</li> <li>2. Fox, G.E., Pechman, K.R., and Woese, C.R. 1977. Comparative cataloging of 16S ribosomal ribonucleic acid: molecular approach to procaryotic systematics. <i>Int. J. Syst. Bacteriol.</i> 27: 44-57.</li> </ol> <p>Itakura, K., Hirose, T., Crea, R., Riggs, A.D., Heyneker, H.L., Bolivar, F., and Boyer, H.W. 1977. Expression in <i>Escherichia coli</i> of a chemically synthesized gene for the hormone somatostatin. <i>Science</i> 198: 1056-1063.</p>
1978	<p><b>Michael Smith</b> (1993 Nobel Prize Laureate for Chemistry) establishes oligonucleotide-based, site-directed mutagenesis.</p> <p><b>Vasudha B. Reddy</b> and colleagues first sequence the genome of the simian virus 40.</p> <p><b>Frederick Sanger</b> and colleagues develop ultrathin gels for improved sequence analysis.</p>	<p>Smith, M. 1978. Mutagenesis at a specific position in a DNA molecule. <i>J. Biol. Chem.</i> 253: 6651-6560.</p> <p>Reddy, V.B., <i>et al.</i> 1978. The genome of simian virus 40. <i>Science</i> 200: 494-502.</p> <p>Sanger, F. and Coulson, A.R. 1978. The use of thin acrylamide gels for DNA sequencing. <i>FEBS Lett.</i> 87: 107-110.</p>

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1979	<b>H. Chaim Birnboim</b> introduces a method to isolate the plasmid DNA.	<ol style="list-style-type: none"> <li>1. Birnboim, H.C. and Doly, J. 1979. A rapid alkaline extraction procedure for screening recombinant plasmid DNA. <i>Nucleic Acids Res.</i> 7: 1513-1523.</li> <li>2. Birnboim, H.C. 1983. A rapid alkaline extraction method for the isolation of plasmid DNA. <i>Methods Enzymol.</i> 100: 243-255.</li> </ol>
1980	<b>David Botstein, Ray White, Mark Skolnick, and Ronald Davis</b> initiates the use of <b>restriction fragment length polymorphisms (RFLPs)</b> in mapping genes to indicate genetic differences among individuals. <b>Frederick Sanger</b> and colleagues develop <b>the random shotgun method</b> to prepare templates for DNA sequencing.	<p>Botstein, D., White, R., Skolnick, M., and Davis, R. 1980. Construction of a genetic linkage map in man using restriction fragment length polymorphisms. <i>Am. J. Hum. Genet.</i> 32: 314-331.</p> <p>Sanger, F., <i>et al.</i> 1980. Cloning in single-stranded bacteriophage as an aid to rapid DNA sequencing. <i>J. Mol. Biol.</i> 143: 161-178.</p>
1981	<b>Stephen Anderson</b> first reports of mtDNA sequencing, now called the Anderson or more commonly the Cambridge Reference Sequence/CRS. He also develops <b>the shotgun sequencing strategy.</b>	<ol style="list-style-type: none"> <li>1. Anderson, S. 1981. Sequence and organization of the human mitochondrial genome. <i>Nature</i> 290: 457-465.</li> <li>2. Anderson, S. 1981. Shotgun DNA sequencing using cloned DNase I-generated fragments. <i>Nucleic Acids Res.</i> 9: 3015-3027.</li> </ol>
	<b>Thomas Cech</b> finds the self-splicing RNA from Tetrahymena.	<ol style="list-style-type: none"> <li>1. Grabowski, P.J., Zaug, A.J., and Cech, T.R. 1981. The intervening sequence of the ribosomal RNA precursor is converted to a circular RNA in isolated nuclei of Tetrahymena. <i>Cell</i> 23: 467-476.</li> <li>2. Zaug, A.J. and Cech, T.R. 1982. The intervening sequence excised from the ribosomal RNA precursor of Tetrahymena contains a 5-terminal guanosine residue not encoded by the DNA. <i>Nucleic Acids Res.</i> 10: 2823-2838.</li> </ol>
	<b>Thomas Wagner</b> and colleagues produce the first transgenic animals by transferring genes from other animals into mice.	<ol style="list-style-type: none"> <li>1. Wagner, T.E., <i>et al.</i> 1981. Microinjection of a rabbit beta-globin gene into zygotes and its subsequent expression in adult mice and their offspring. <i>Proc. Natl. Acad. Sci. USA</i> 78: 6376-6380.</li> <li>2. Costantini, F. and Lacy, E. 1981. Introduction of a rabbit beta-globin gene into the mouse germ line. <i>Nature</i> 294: 92-94.</li> </ol>
	<b>J. C. Chang</b> and <b>Y. W. Kan</b> detect the sickle cell anemia by restriction enzyme analysis of the DNA, making it the first genetic illness diagnosed antenatally at the gene level directly.	<p>Chang, J.C. and Kan, Y.W. 1981. Antenatal diagnosis of sickle cell anaemia by direct analysis of the sickle mutation. <i>Lancet</i> 2: 1127-1129.</p>
	<b>Wang De-Bao</b> and coworkers first complete the synthesis of yeast alanine transfer ribonucleic acid.	<ol style="list-style-type: none"> <li>1. Wang, D.B. 1980. Synthesis of 3'-half molecule (nucleotides 36-76) of yeast alanine transfer ribonucleic acid. <i>Nucleic Acids Symp. Ser.</i> 7: 325-333.</li> <li>2. Wang, D.B., <i>et al.</i> 1983. Total synthesis of yeast alanine transfer ribonucleic acid. <i>Sci. Sin. B.</i> 26: 464-481.</li> </ol>

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1981	<b>Mary Harper</b> and colleagues map the gene for insulin. Mapping by <b>in situ hybridization</b> became a standard method.	<ol style="list-style-type: none"> <li>1. Harper, M.E. and Saunders, G.F. 1981. Localization of single copy DNA sequences of G-banded human chromosomes by <i>in situ</i> hybridization. <i>Chromosoma</i>. 83: 431-439.</li> <li>2. Harper, M.E., <i>et al.</i> 1981. Localization of the human insulin gene to the distal end of the short arm of chromosome 11. <i>Proc. Natl. Acad. Sci. USA</i> 78: 4458-4460.</li> </ol>
1982	<p><b>Frederick Sanger</b> and colleagues sequence the entire genome of bacteriophage lambda using a random shotgun technique.</p> <p><b>Stanley B. Prusiner</b> (1997 Nobel Prize Laureate for Physiology or Medicine) finds evidence that a class of infectious proteins he calls <b>PRIONS</b> cause scrapie, a fatal neurodegenerative disease of sheep.</p> <p><b>Gerald Rubin</b> and <b>Allan Spradling</b> develop methods for making transgenic <i>Drosophila</i>.</p> <p>Los Alamos National Laboratory forms <b>GenBank</b>, NIH's publicly accessible genetic sequence database.</p>	<p>Sanger, F., <i>et al.</i> 1982. Nucleotide sequence of bacteriophage lambda. <i>J. Mol. Biol.</i> 162: 729-733.</p> <p>Prusiner, S.B. 1982. Novel proteinaceous particles cause scrapie. <i>Science</i> 216: 136-144.</p> <p>Rubin, G.M. and Spradling, A.C. 1982. Genetic transformation of <i>Drosophila</i> with transposable element vectors. <i>Science</i> 218: 348-353.</p>
1983	<p><b>Kary B. Mullis</b> (1993 Nobel Prize Laureate for Chemistry) invents <b>the polymerase chain reaction (PCR)</b>, a method for rapidly and easily cloning DNA fragments.</p> <p><b>Scott D. Putney</b> and colleagues recognize that essentially random cloning and sequencing could provide rapid access to the messenger RNAs in the cell: they develop the method later called <b>EST (expressed sequence tag)</b>.</p> <p><b>James Gusella</b> maps the first disease gene linked to Huntington's disease, which is on chromosome 4.</p> <p><b>G. Schröder</b> and colleagues perform the first genetic transformation of plant cells by Ti plasmids.</p>	<ol style="list-style-type: none"> <li>1. Saiki, R.K., <i>et al.</i> 1985. Enzymatic amplification of beta-globin genomic sequences and restriction site analyses for diagnosis of sickle cell anemia. <i>Science</i> 230: 1350-1354.</li> <li>2. Mullis, K.B. and Faloona, F.A. 1987. Specific synthesis of DNA <i>in vitro</i> via a polymerase-catalyzed chain reaction. <i>Methods Enzymol.</i> 155: 335-350.</li> <li>3. Saiki, R.K., <i>et al.</i> 1988. Primer-directed enzymatic amplification of DNA with a thermostable DNA polymerase. <i>Science</i> 239: 487-491.</li> </ol> <p>Putney, S.D., <i>et al.</i> 1983. A new troponin T and cDNA clones for 13 different muscle proteins, found by shotgun sequencing. <i>Nature</i> 302: 718-721.</p> <p>Gusella, J.F., <i>et al.</i> 1983. A polymorphic DNA marker genetically linked to Huntington's disease. <i>Nature</i> 306: 234-238.</p> <ol style="list-style-type: none"> <li>1. Schröder, G., <i>et al.</i> 1983. The conserved part of the T-region in Ti-plasmids expresses four proteins in bacteria. <i>EMBO J.</i> 2: 403-409.</li> <li>2. Willmitzer, L., <i>et al.</i> 1983. The use of Ti-plasmids as plant-directed gene vectors. <i>Folia. Biol. (Praha)</i> 29: 106-114.</li> </ol>

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1983	<b>Andrew Murray</b> and <b>Jack Szostak</b> synthesize the first artificial chromosome.	1. Murray, A.W. and Szostak, J.W. 1983. Construction of artificial chromosomes in yeast. <i>Nature</i> 305: 189-193. 2. Murray, A.W. and Szostak, J.W. 1987. Artificial chromosomes. <i>Sci. Am.</i> 257: 62-68.
1984	<b>Alec Jeffreys</b> develops “genetic fingerprinting” for identifying individuals by analyzing polymorphic (variable) sequences in their DNA. <b>Richard Baer</b> and colleagues complete the entire DNA sequence of the Epstein-Barr virus. <b>William McGinnis</b> discovers homeotic ( <i>Hox</i> ) regulatory genes, and demonstrates that a single mutation in a <i>Hox</i> gene suffices to suppress all limb development in the thoracic region of fruit flies.	Jeffreys, A.J., <i>et al.</i> 1985. Individual-specific “finger-prints” of human DNA. <i>Nature</i> 316: 75-79. Baer, R., <i>et al.</i> 1984. DNA sequence and expression of the B95-8 Epstein-Barr virus genome. <i>Nature</i> 310: 207-211. 1. McGinnis, W., <i>et al.</i> 1984. A conserved DNA sequence in homeotic genes of the <i>Drosophila</i> Antennapedia and bithorax complexes. <i>Nature</i> 308: 428-433. 2. McGinnis, W., <i>et al.</i> 1984. A homologous protein-coding sequence in <i>Drosophila</i> homeotic genes and its conservation in other metazoans. <i>Cell</i> 37: 403-408.
	<b>Charles Cantor</b> and <b>David Schwartz</b> develop pulsed field gel electrophoresis.	Schwartz, D.C. and Cantor, C.R. 1984. Separation of yeast chromosome-sized DNAs by pulsed field gradient gel electrophoresis. <i>Cell</i> 37: 67-75.
1985	<b>Robert Sinsheimer</b> convenes Santa Cruz meeting, which develops idea of complete characterization of the human genome. <b>Renato Dulbecco</b> suggests sequencing the genome to help to understand cancer. <b>Charles DeLisi</b> proposes a project to sequence the genome to help understand radiation damage.	1. Sinsheimer, R.L. 1989. The Santa Cruz Workshop—May 1985. <i>Genomics</i> 5: 954-956. 2. Dulbecco, R. 1986. A turning point in cancer research: sequencing the human genome. <i>Science</i> 231: 1055-1056.
1986	<b>Brigitte Royer-Pokora</b> for the first time clones one human disease gene positionally for the chronic granulomatous disease. <b>Leroy Hood</b> invents the first automatic DNA fluorescence sequencer.	Royer-Pokora, B., <i>et al.</i> 1986. Cloning the gene for an inherited human disorder—chronic granulomatous disease on the basis of its chromosomal location. <i>Nature</i> 322: 32-38. Smith, L.M., <i>et al.</i> 1986. Fluorescence detection in automated DNA sequence analysis. <i>Nature</i> 321: 674-679.
1987	<b>Maynard Olson</b> invents “yeast artificial chromosomes” (YACs), expression vectors for large proteins. <b>Helen Donis-Keller</b> and colleagues publish the first human genetic map with 403 markers. DuPont scientists develop a system for rapid DNA sequencing with fluorescent chain-terminating dideoxynucleotides.	Burke, D.T., Carle, G.F., and Olson, M.V. 1987. Cloning of large segments of exogenous DNA into yeast by means of artificial chromosome vectors. <i>Science</i> 236: 806-812. Donis-Keller, H., <i>et al.</i> 1987. A genetic linkage map of the human genome. <i>Cell</i> 51: 319-337.

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1989	<p><b>HUGO</b> (Human Genome Organisation), an international association of researchers involved in the Human Genome Project, is created to help coordinate activities and to assist in sharing of data and resources.</p> <p><b>Francis Collins</b> and colleagues identify the gene coding for the cystic fibrosis transmembrane conductance regulator protein (CFTR) on chromosome 7, which causes cystic fibrosis when mutant.</p> <p><b>James Weber</b> and <b>Paula May</b> use <b>MI-CROSATELLITES</b> as new genetic markers, a stretch of DNA made of a two to four base-pair long sequence that is repeated in tandem.</p> <p><b>Maynard Olson</b> develops <b>sequence tagged site (STS)</b> as another marker.</p> <p><b>Stanley Fields</b> develops <b>the “two-hybrid” approach</b> for looking at interactions between pairs of proteins by expressing them in yeast.</p> <p><b>Thomas P. Beebe Jr.</b> and colleagues first observe the DNA double-helix structure directly by <b>scanning tunneling microscope (STM)</b>.</p>	<ol style="list-style-type: none"> <li>1. Drumm, M.L., <i>et al.</i> 1988. Physical mapping of the cystic fibrosis region by pulse-field gel electrophoresis. <i>Genomics</i> 2: 346-354.</li> <li>2. Iannuzzi, M.C., <i>et al.</i> 1989. Isolation of additional polymorphic clones from the cystic fibrosis region, using chromosome jumping from D7S8. <i>Am. J. Hum. Genet.</i> 44: 695-703.</li> <li>3. Dean, M., <i>et al.</i> 1990. Approaches to localizing disease genes as applied to cystic fibrosis. <i>Nucleic Acids Res.</i> 18: 345-350.</li> </ol> <p>Weber, J.L. and May, P.E. 1989. Abundant class of human DNA polymorphisms which can be typed using the polymerase chain reaction. <i>Am. J. Hum. Genet.</i> 44: 388-396.</p> <p>Olson, M.V., <i>et al.</i> 1989. A common language for physical mapping of the human genome. <i>Science</i> 245: 1434-1435.</p> <p>Fields, S. and Song, O. A novel genetic system to detect protein-protein interactions. <i>Nature</i> 340: 245-246.</p> <p>Beebe, T.P. Jr., <i>et al.</i> 1989. Direct observation of native DNA structures with the scanning tunneling microscope. <i>Science</i> 243: 370-372.</p>
1990	<p>US Department of Energy and NIH officially launch the Human Genome Project (HGP).</p> <p><b>Sydney Brenner</b> proposes sequencing human cDNAs to provide rapid access to human genes.</p> <p>Three groups develop <b>capillary electrophoresis</b>, one team led by <b>Lloyd Smith</b>, the second by <b>Barry Karger</b>, and the third by <b>Norman Dovichi</b>.</p>	<ol style="list-style-type: none"> <li>1. Watson, J.D. 1990. The Human Genome Project: past, present, and future. <i>Science</i> 248: 44-49.</li> <li>2. Cantor, C.R. 1990. Orchestrating the Human Genome Project. <i>Science</i> 248: 49-51.</li> </ol> <p>Brenner, S. 1990. The human genome: the nature of the enterprise. In <i>Human Genetic Information: Science, Law and Ethics. Ciba Found. Symp.</i> 149: 6-12.</p> <ol style="list-style-type: none"> <li>1. Luckey, J.A., <i>et al.</i> 1990. High-speed DNA sequencing by capillary electrophoresis. <i>Nucleic Acids Res.</i> 18: 4417-4421.</li> <li>2. Guttman, A., Cohen, A.S., Heiger, D.N., and Karger, B.L. 1990. Analytical and micropreparative ultrahigh resolution of oligonucleotides by polyacrylamide gel high-performance capillary electrophoresis. <i>Anal. Chem.</i> 62: 137-141.</li> </ol> <p>(to next page)</p>

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1990		(Continued)
	<b>David Lipman, Eugene Myers</b> , and colleagues publish the BLAST (basic local alignment search tool) algorithm for aligning sequences.	3. Swerdlow, H., Wu, S.L., Harke, H., and Dovichi, N.J. 1990. Capillary gel electrophoresis for DNA sequencing. Laser-induced fluorescence detection with the sheath flow cuvette. <i>J. Chromatogr.</i> 516: 61-67. Altschul, S.F., Gish, W., Miller, W., Myers, E.W., and Lipman, D.J. 1990. Basic local alignment search tool. <i>J. Mol. Biol.</i> 215: 403-410.
1991	<b>Mark Adams</b> and colleagues propose the concept of expressed sequence tag ( <b>EST</b> ).  <b>Mary-Claire King</b> finds evidence that a gene on human chromosome 17 causes the inherited form of breast cancer and also increases the risk of ovarian cancer.  <b>Edward Uberbacher</b> and <b>Richard Mural</b> develop <b>GRAIL</b> , the first of many gene-finding programs.	Adams, M.D., <i>et al.</i> 1991. Complementary DNA sequencing: expressed sequence tags and human genome project. <i>Science</i> 252: 1651-1656. King, M.C. 1991. Localization of the early-onset breast cancer gene. <i>Hosp. Pract.</i> 26: 121-126. Uberbacher, E.C. and Mural, R.J. 1991. Locating protein-coding regions in human DNA sequences by a multiple sensor-neural network approach. <i>Proc. Natl. Acad. Sci. USA</i> 88: 11261-11265.
1992	<b>David Page</b> and colleagues complete the first physical map of the human Y chromosome.  <b>Helen Donis-Keller</b> and colleagues publish the low-resolution genetic linkage map of the entire human genome.  <b>Jean Weissenbach</b> and colleagues complete a genetic map of human genome.  <b>Andrew Collins</b> and colleagues publish gene maps of human chromosome 1.  <b>Kathleen Mills</b> and colleagues construct genetic and physical maps of human chromosome 4.  <b>Ilya Chumakov</b> and colleagues complete a physical map of human chromosome 21.	1. Vollrath, D., <i>et al.</i> 1992. The human Y chromosome: a 43-interval map based on naturally occurring deletions. <i>Science</i> 258: 52-59. 2. Foote, S., <i>et al.</i> 1992. The human Y chromosome: overlapping DNA clones spanning the euchromatic region. <i>Science</i> 258: 60-66. NIH/CEPH Collaborative Mapping Group. 1992. A comprehensive genetic linkage map of the human genome. <i>Science</i> 258: 67-86, 148-162. Weissenbach, J., <i>et al.</i> 1992. A second-generation linkage map of the human genome. <i>Nature</i> 359: 794-801. Collins, A., <i>et al.</i> 1992. Integration of gene maps: chromosome 1. <i>Proc. Natl. Acad. Sci. USA</i> 89: 4598-4602. Mills, K.A., <i>et al.</i> 1992. Genetic and physical maps of human chromosome 4 based on dinucleotide repeats. <i>Genomics</i> 14: 209-219. Chumakov, I., <i>et al.</i> 1992. Continuum of overlapping clones spanning the entire human chromosome 21q. <i>Nature</i> 359: 380-387.

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1992	<p><b>Eric Lander</b> and colleagues complete a genetic map of the mouse.</p> <p><b>Steve Oliver</b> and colleagues identify the entire sequence of 315 kb of one of the sixteen chromosomes of the yeast <i>Saccharomyces cerevisiae</i>, representing a major advance toward the sequencing of all the chromosomes of yeast.</p> <p><b>Mark Adams, Craig Venter</b>, and colleagues describe a fast new approach to gene discovery using ESTs.</p> <p><b>Mel Simon</b> and colleagues develop <b>bacterial artificial chromosomes (BACs)</b> for cloning.</p> <p><b>Kousaku Okubo</b> uses a method based on single-strand partial sequencing of cDNAs from libraries enriched in the 3' end portions to establish tissue expression profiles.</p>	<p>Dietrich, W., <i>et al.</i> 1992. A genetic map of the mouse suitable for typing intraspecific crosses. <i>Genetics</i> 131: 423-447.</p> <p>Oliver, S.G., <i>et al.</i> 1992. The complete DNA sequence of yeast chromosome III. <i>Nature</i> 357: 38-46.</p> <ol style="list-style-type: none"> <li>Adams, M.D., <i>et al.</i> 1992. Sequence identification of 2,375 human brain genes. <i>Nature</i> 355: 632-634.</li> <li>Adams, M.D., <i>et al.</i> 1995. Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of DNA sequence. <i>Nature</i> 377: 3-174.</li> </ol> <p>Shizuya, H., <i>et al.</i> 1992. Cloning and stable maintenance of 300-kilobase-pair fragments of human DNA in <i>Escherichia coli</i> using an F-factor-based vector. <i>Proc. Natl. Acad. Sci. USA</i> 89: 8794-8797.</p> <ol style="list-style-type: none"> <li>Okubo, K., <i>et al.</i> 1992. Large scale cDNA sequencing for analysis of quantitative and qualitative aspects of gene expression. <i>Nat. Genet.</i> 2: 173-179.</li> <li>Matsubara, K. and Okubo, K. 1993. cDNA analyses in the human genome project. <i>Gene</i> 135: 265-274.</li> </ol>
1993	<p><b>Daniel Cohen, Ilya Chumakov</b>, and <b>Jean Weissenbach</b> produce a rough map of all 23 pairs of human chromosomes.</p> <p><b>Maynard Olson</b> and colleagues publish physical maps of six chromosomes of <i>Saccharomyces cerevisiae</i>.</p>	<p>Cohen, D., Chumakov, I, and Weissenbach, J. 1993. A first-generation physical map of the human genome. <i>Nature</i> 366: 698-701.</p> <p>Riles, L., <i>et al.</i> 1993. Physical maps of the six smallest chromosomes of <i>Saccharomyces cerevisiae</i> at a resolution of 2.6 kilobase pairs. <i>Genetics</i> 134: 81-150.</p>
1994	<p><b>Jeffrey Murray</b> and colleagues complete a comprehensive genetic linkage map of the human genome.</p> <p><b>Marc Wilkins</b> coins the term <b>PROTEOME</b> to mean all the proteins expressed by the genome.</p>	<p>Murray, J.C., <i>et al.</i> 1994. A comprehensive human linkage map with centimorgan density. Cooperative Human Linkage Center (CHLC). <i>Science</i> 265: 2049-2054.</p> <p>Wilkins, M.R., <i>et al.</i> (eds.) 1997. <i>Proteome Research: New Frontiers in Functional Genomics</i>. Springer-Verlag, Berlin, Germany.</p>
1995	<p><b>John Sulston</b> and <b>Robert Waterston</b> propose to produce a draft sequence of the human genome by 2000.</p> <p><b>Ilya Chumakov</b> and colleagues map the human genome using yeast artificial chromosomes (YACs), and some chromosomes, notably 22, are mapped in finer detail. The map is an important step toward clone-based sequencing.</p>	<p>Marshall, E. 1995. A strategy for sequencing the genome 5 years early. <i>Science</i> 267: 783-784.</p> <p>Chumakov, I.M., <i>et al.</i> 1995. A YAC contig map of the human genome. <i>Nature</i> 377: 175-297.</p>

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1995	<b>Thomas Hudson</b> and colleagues publish a physical map of the human genome containing 15,000 markers.	Hudson, T.J., <i>et al.</i> 1995. An STS-based map of the human genome. <i>Science</i> 270: 1945-1954.
	<b>Craig Venter</b> and colleagues publish the first genome sequence of a free-living organism, <i>Haemophilus influenzae</i> (1.8 Mb).	Fleischmann, R.D., <i>et al.</i> 1995. Whole-genome random sequencing and assembly of <i>Haemophilus influenzae</i> Rd. <i>Science</i> 269: 496-512.
	<b>Craig Venter</b> and colleagues complete the genome sequence of <i>Mycoplasma genitalium</i> (0.58 Mb), the smallest known genome of any free-living organism.	Fraser, C.M., <i>et al.</i> 1995. The minimal gene complement of <i>Mycoplasma genitalium</i> . <i>Science</i> 270: 397-403.
	<b>Michael Reeve</b> and <b>Carl Fuller</b> find a novel thermostable polymerase for DNA sequencing.	Reeve, M.A. and Fuller, C.W. 1995. A novel thermostable polymerase for DNA sequencing. <i>Nature</i> 376: 796-797.
	<b>Patrick Brown</b> and colleagues publish the first paper using a printed glass microarray of complementary DNA (cDNA) probes.	Schena, M., <i>et al.</i> 1995. Quantitative monitoring of gene expression patterns with a complementary DNA microarray. <i>Science</i> 270: 467-470.
1996	<b>Richard Mathies</b> and colleagues develop improved sequencing dyes.	Ju, J., <i>et al.</i> 1995. Fluorescence energy transfer dye-labeled primers for DNA sequencing and analysis. <i>Proc. Natl. Acad. Sci. USA</i> 92: 4347-4351.
	<b>Shizhen Qin</b> and colleagues construct a high-resolution physical map of human chromosome 11.	Qin, S, <i>et al.</i> 1996. A high-resolution physical map of human chromosome 11. <i>Proc. Natl. Acad. Sci. USA</i> 93: 3149-3154.
	<b>Lee Rowen, Ben Koop, and Leroy Hood</b> complete the sequence of the human T-cell receptor region.	Rowen, L., Koop, B.F., and Hood, L. 1996. The complete 685-kilobase DNA sequence of the human beta T cell receptor locus. <i>Science</i> 272: 1755-1762.
	<b>William Dietrich</b> and colleagues complete a comprehensive genetic map of the mouse genome.	Dietrich, W.F., <i>et al.</i> 1996. A comprehensive genetic map of the mouse genome. <i>Nature</i> 380: 149-152.
	<b>Yoshihide Hayashizaki</b> and colleagues complete the first set of full-length mouse cDNAs.	Carninci, P., <i>et al.</i> 1996. High-efficiency full-length cDNA cloning by biotinylated CAP trapper. <i>Genomics</i> 37: 327-336.
	<b>Craig Venter</b> and colleagues complete the genome sequence of <i>Methanococcus jannaschii</i> (1.7 Mb).	Bult, C.J., <i>et al.</i> 1996. Complete genome sequence of the methanogenic archaeon, <i>Methanococcus jannaschii</i> . <i>Science</i> 273: 1058-1073.
	<b>Steve Oliver</b> and colleagues sequence the yeast <i>Saccharomyces cerevisiae</i> genome (12.1 Mb), the first sequenced eukaryotic genome.	1. Bradbury, J. 1996. Yeast genome sequenced completely. <i>Lancet</i> 347: 1175. 2. Goffeau, A., <i>et al.</i> 1996. Life with 6000 genes. <i>Science</i> 274: 546, 563-567. 3. Mewes, H.W. 1997. Overview of the yeast genome. <i>Nature</i> 387: 7-65.
1997	<b>Ian Wilmut</b> creates the first somatocytal clone sheep (Dolly).	Wilmut, I., <i>et al.</i> 1997. Viable offspring derived from fetal and adult mammalian cells. <i>Nature</i> 385: 810-813.
	<b>Frederick Blattner</b> and colleagues complete the genome sequence of <i>Escherichia coli</i> (4.6 Mb).	Blattner, F.R., <i>et al.</i> 1997. The complete genome sequence of <i>Escherichia coli</i> K-12. <i>Science</i> 277: 1453-1462.



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1997	<b>Joe DeRisi, Vishy Iyer, and Patrick Brown</b> publish the first complete eukaryotic genome ( <i>Saccharomyces cerevisiae</i> ) on a microarray.  Molecular Dynamics introduces a capillary sequencing machine called <b>MegaBACE</b> .	DeRisi, J.L., Iyer, V.R., and Brown, P.O. 1997. Exploring the metabolic and genetic control of gene expression on a genomic scale. <i>Science</i> 278: 680-686.
1998	<b>Panos Deloukas</b> and colleagues produce a rough draft of the human genome map, showing the locations of more than 30,000 genes.  <b>Craig Venter</b> and colleagues publish "Shotgun sequencing of the human genome".  <b>Francis Collins</b> proposes SNPs initiative beginning.  <b>Bart Barrell</b> and colleagues complete the genome sequence of <i>Mycobacterium tuberculosis</i> (4.4 Mb).  <b>John Sulston, Robert Waterston,</b> and colleagues complete the genome sequence of <i>Caenorhabditis elegans</i> (97 Mb).  <b>Phil Green, Brent Ewing,</b> and colleagues publish a program called <b>phred</b> for automatically interpreting sequencer data.  <b>Phil Green</b> and colleagues publish a program called <b>consed</b> for sequence finishing.  <b>ABI Prism 3700 sequencing machine</b> reaches market.	Deloukas, P., <i>et al.</i> 1998. A physical map of 30,000 human genes. <i>Science</i> 282: 744-746.  Venter, J.C., <i>et al.</i> 1998. Shotgun sequencing of the human genome. <i>Science</i> 280: 1540-1542.  Collins, F.S., Brooks, L.D., and Chakravarti, A. 1998. A DNA polymorphism discovery resource for research on human genetic variation. <i>Genome Res.</i> 8:1229-1231.  Cole, S.T., <i>et al.</i> 1998. Deciphering the biology of <i>Mycobacterium tuberculosis</i> from the complete genome sequence. <i>Nature</i> 393: 537-544.  The <i>C. elegans</i> Sequencing Consortium. 1998. Genome sequence of the nematode <i>Caenorhabditis elegans</i> : a platform for investigating biology. <i>Science</i> 282: 2012-2018.  1. Ewing, B., Hillier, L., Wendl, M.C., and Green, P. 1998. Base-calling of automated sequencer traces using phred. I. Accuracy assessment. <i>Genome Res.</i> 8: 175-185. 2. Ewing, B. and Green, P. 1998. Base-calling of automated sequencer traces using phred. II. Error probabilities. <i>Genome Res.</i> 8: 186-194.  Gordon, D., Abajian, C., and Green, P. 1998. Consed: a graphical tool for sequence finishing. <i>Genome Res.</i> 8: 195-202.
1999	<b>Ian Dunham</b> and colleagues produce the first one of many DNA sequences of human chromosomes, chromosome 22, which is about 34 Mb and includes at least 550 genes.	Dunham, I., <i>et al.</i> 1999. The DNA sequence of human chromosome 22. <i>Nature</i> 402: 489-495.
2000	<b>Masahira Hattori</b> and colleagues complete the DNA sequence of human chromosome 21 (33 Mb).	1. Hattori, M. <i>et al.</i> 2000. The DNA sequence of human chromosome 21. <i>Nature</i> 405: 311-319. 2. Hattori, M., <i>et al.</i> 2000. The DNA sequence of human chromosome 21. <i>Am. J. Ophthalmol.</i> 130: 383.

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2000	<b>Mark Adams, Eugene Myers,</b> and colleagues publish the genome sequence of <i>Drosophila melanogaster</i> (137 Mb).	<ol style="list-style-type: none"> <li>1. Adams, M.D., <i>et al.</i> 2000. The genome sequence of <i>Drosophila melanogaster</i>. <i>Science</i> 287: 2185-2195.</li> <li>2. Myers, E.W., <i>et al.</i> 2000. A whole-genome assembly of <i>Drosophila</i>. <i>Science</i> 287: 2196-2204.</li> </ol>
	The Arabidopsis Genome Initiative completes the sequencing of the first plant genome of <i>Arabidopsis thaliana</i> (115 Mb).	The Arabidopsis Genome Initiative. 2000. Analysis of the genome sequence of the flowering plant <i>Arabidopsis thaliana</i> . <i>Nature</i> 408: 796-815.
2000	<b>Julian Parkhill, Herve Tettelin,</b> and colleagues respectively publish sequences of different strains of <i>Neisseria meningitidis</i> (2.2–2.3 Mb), the bacterium that causes many cases of meningitis.	<ol style="list-style-type: none"> <li>1. Parkhill, J., <i>et al.</i> 2000. Complete DNA sequence of a serogroup A strain of <i>Neisseria meningitidis</i> Z2491. <i>Nature</i> 404: 502-506.</li> <li>2. Tettelin, H., <i>et al.</i> 2000. Complete genome sequence of <i>Neisseria meningitidis</i> serogroup B strain MC58. <i>Science</i> 287: 1809-1815.</li> </ol>
	2001	The International Human Genome Sequencing Consortium produces a draft sequence of the human genome and makes it freely available.
2001	<b>Craig Venter</b> and colleagues publish their version of the human genome draft sequence.	Venter, J.C., <i>et al.</i> 2001. The sequence of the human genome. <i>Science</i> 291: 1304-1351.
	<b>Charles Tilford, Kate Montgomery, Thomas Bruls,</b> and colleagues produce the physical map of human chromosomes Y, 12, and 14, respectively.	<ol style="list-style-type: none"> <li>1. Tilford, C.A., <i>et al.</i> 2001. A physical map of the human Y chromosome. <i>Nature</i> 409: 943-945.</li> <li>2. Montgomery, K.T., <i>et al.</i> 2001. A high-resolution map of human chromosome 12. <i>Nature</i> 409: 945-946.</li> <li>3. Bruls, T., <i>et al.</i> 2001. A physical map of human chromosome 14. <i>Nature</i> 409: 947-948.</li> </ol>
2001	<b>Panos Deloukas</b> and colleagues produce the sequence of human chromosome 20.	Deloukas, P., <i>et al.</i> 2001. The DNA sequence and comparative analysis of human chromosome 20. <i>Nature</i> 414: 865-871.
	<b>Stewart Cole</b> and colleagues sequence the genome of <i>Mycobacterium leprae</i> (3.3 Mb), the causative agent of leprosy.	Cole, S.T., <i>et al.</i> 2001. Massive gene decay in the leprosy bacillus. <i>Nature</i> 409: 1007-1011.
2001	<b>Barbara May</b> and colleagues complete the genome sequence of <i>Pasteurella multocida</i> (5.6 Mb).	May, B.J., <i>et al.</i> 2001. Complete genomic sequence of <i>Pasteurella multocida</i> , Pm70. <i>Proc. Natl. Acad. Sci. USA</i> 98: 3460-3465.

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2002	<b>Jun Yu</b> and colleagues finish a draft sequence of the rice ( <i>Oryza sativa</i> L. ssp. <i>indica</i> ) genome (420 Mb).	Yu, J., <i>et al.</i> 2002. A draft sequence of the rice genome ( <i>Oryza sativa</i> L. ssp. <i>indica</i> ). <i>Science</i> 296: 79-92.
	<b>Stephen Goff</b> and colleagues finish a draft sequence of the rice ( <i>Oryza sativa</i> L. ssp. <i>japonica</i> ) genome (420 Mb).	Goff, S.A., <i>et al.</i> 2002. A draft sequence of the rice genome ( <i>Oryza sativa</i> L. ssp. <i>japonica</i> ). <i>Science</i> 296: 92-100.
	<b>Simon Gregory</b> and colleagues publish a physical map of the mouse genome.	Gregory, S.G., <i>et al.</i> 2002. A physical map of the mouse genome. <i>Nature</i> 418: 743-750.
	The Mouse Genome Sequencing Consortium publishes its draft sequence of the mouse genome.	Mouse Genome Sequencing Consortium. 2002. Initial sequencing and comparative analysis of the mouse genome. <i>Nature</i> 420: 520-562.
	<b>Robert Holt</b> and colleagues finish the genome sequence of the malaria mosquito, <i>Anopheles gambiae</i> (278 Mb).	Holt, R.A., <i>et al.</i> 2002. The genome sequence of the malaria mosquito <i>Anopheles gambiae</i> . <i>Science</i> 298: 129-149.
	<b>Malcolm Gardner</b> and colleagues publish the genome sequence of the human malaria parasite <i>Plasmodium falciparum</i> (22.9 Mb).	Gardner, M.J., <i>et al.</i> 2002. Genome sequence of the human malaria parasite <i>Plasmodium falciparum</i> . <i>Nature</i> 419: 498-511.
	<b>Ian Paulsen</b> and colleagues publish the genome sequence of <i>Brucella suis</i> (3.3 Mb).	Paulsen, I.T., <i>et al.</i> 2002. The <i>Brucella suis</i> genome reveals fundamental similarities between animal and plant pathogens and symbionts. <i>Proc. Natl. Acad. Sci. USA</i> 99: 13148-13153.
	<b>Samuel Aparicio</b> and colleagues publish the genome sequence of <i>Fugu rubripes</i> (400 Mb).	Aparicio, S., <i>et al.</i> 2002. Whole-genome shotgun assembly and analysis of the genome of <i>Fugu rubripes</i> . <i>Science</i> 297: 1301-1310.
	<b>Paramvir Dehal</b> and colleagues publish the genome sequence of <i>Ciona intestinalis</i> (116.7 Mb).	Dehal, P., <i>et al.</i> 2002. The draft genome of <i>Ciona intestinalis</i> : insights into chordate and vertebrate origins. <i>Science</i> 298: 2157-2167.
	2003	<b>Roland Heilig, Helen Skaletsky, LaDeana Hillier, Andy Mungall</b> , and colleagues publish the sequences of human chromosomes 14, Y, 7, and 6, respectively.
<b>Ewen Kirkness</b> and colleagues publish a survey sequencing of the dog genome.		Kirkness, E.F., <i>et al.</i> 2003. The dog genome: survey sequencing and comparative analysis. <i>Science</i> 301: 1898-1903.
<b>James Galagan</b> and colleagues publish the genome sequence of <i>Neurospora crassa</i> (bread mold) (43 Mb).		Galagan, J.E., <i>et al.</i> 2003. The genome sequence of the filamentous fungus <i>Neurospora crassa</i> . <i>Nature</i> 422: 859-868.

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2003	<b>Lincoln Stein</b> and colleagues publish the genome sequence of <i>Caenorhabditis briggsae</i> (104 Mb).	Stein, L.D., <i>et al.</i> 2003. The genome sequence of <i>Caenorhabditis briggsae</i> : a platform for comparative genomics. <i>PLoS Biol.</i> 1: E45.
2004	The International Human Genome Sequencing Consortium finishes the euchromatic sequence of the human genome.	International Human Genome Sequencing Consortium. 2004. Finishing the euchromatic sequence of the human genome. <i>Nature</i> 431: 931-945.
	<b>Andrew Dunham, Jane Grimwood, Sean Humphray, Panos Deloukas, Jeremy Schmutz, Joel Martin,</b> and colleagues publish the sequences of human chromosomes 13, 19, 9, 10, 5, and 16, respectively.	<ol style="list-style-type: none"> <li>1. Dunham, A., <i>et al.</i> 2004. The DNA sequence and analysis of human chromosome 13. <i>Nature</i> 428: 522-528.</li> <li>2. Grimwood, J., <i>et al.</i> 2004. The DNA sequence and biology of human chromosome 19. <i>Nature</i> 428: 529-535.</li> <li>3. Humphray, S.J., <i>et al.</i> 2004. DNA sequence and analysis of human chromosome 9. <i>Nature</i> 429: 369-374.</li> <li>4. Deloukas, P., <i>et al.</i> 2004. The DNA sequence and comparative analysis of human chromosome 10. <i>Nature</i> 429: 375-381.</li> <li>5. Schmutz, J., <i>et al.</i> 2004. The DNA sequence and comparative analysis of human chromosome 5. <i>Nature</i> 431: 268-274.</li> <li>6. Martin, J., <i>et al.</i> 2004. The sequence and analysis of duplication-rich human chromosome 16. <i>Nature</i> 432: 988-994.</li> </ol>
	<b>Richard Gibbs</b> and colleagues complete the rat genome sequence.	Gibbs, R.A., <i>et al.</i> 2004. Genome sequence of the Brown Norway rat yields insights into mammalian evolution. <i>Nature</i> 428: 493-521.
	The International Chicken Genome Sequencing Consortium publishes the chicken genome sequence.	<ol style="list-style-type: none"> <li>1. Hillier, L.W., <i>et al.</i> 2004. Sequence and comparative analysis of the chicken genome provide unique perspectives on vertebrate evolution. <i>Nature</i> 432: 695-716.</li> <li>2. Wong, G.K., <i>et al.</i> 2004. A genetic variation map for chicken with 2.8 million single-nucleotide polymorphisms. <i>Nature</i> 432: 717-722.</li> <li>3. Wallis, J.W., <i>et al.</i> 2004. A physical map of the chicken genome. <i>Nature</i> 432: 761-764.</li> </ol>
	<b>Kazuei Mita, Qingyou Xia,</b> and colleagues independently publish the genome sequence of silkworm, <i>Bombyx mori</i> (530 Mb).	<ol style="list-style-type: none"> <li>1. Mita, K., <i>et al.</i> 2004. The genome sequence of silkworm, <i>Bombyx mori</i>. <i>DNA Res.</i> 11: 27-35.</li> <li>2. Xia, Q., <i>et al.</i> 2004. A draft sequence for the genome of the domesticated silkworm (<i>Bombyx mori</i>). <i>Science</i> 306: 1937-1940.</li> </ol>
	<b>Motomichi Matsuzaki</b> and colleagues complete the genome sequence of the ultrasmall unicellular red alga, <i>Cyanidioschyzon merolae</i> (16.5 Mb).	Matsuzaki, M., <i>et al.</i> 2004. Genome sequence of the ultrasmall unicellular red alga <i>Cyanidioschyzon merolae</i> 10D. <i>Nature</i> 428: 653-657.

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