

Index

- Acid** Precipitation Task Force, 120
acquired immune **deficiency syndrome**, 64, 72, 96, 117
adenosine, 21-22
adenosine deaminase, 61
agriculture, genome mapping implications for, 73
alanine, codon, 23
Alberts, Bruce, 107
albinism, 149
albumin, 61
alcoholism, 86
aldolase, chromosome assignment of, 33
Alexander, Duane, 94 n.1
alleles, 27, 28, 58
alpha globin, 61
alpha interferon, 64
.Alzheimer's disease, 65, 95, 146
American Society for Biochemistry and Molecular Biology, 127
American Type Culture Collection, 101, 141, 190, 192
amino acids
 codon, 23
 databases, 97, 98, 190-191
 generation of, 22-23
anemias, 64, 136
antibodies, 21
apolipoprotein E, 61
Applied Biosystems, Inc., automated DNA sequencer, 47, 108, 138
applied research, government controls on, 87
arginine, codon, 23
Argonne National Laboratory, 122
Armed Forces Institute of Pathology, 103
arthritis, 64
Ashburner, Michael, 42
Asian nations, interest in genome projects, 8
asparagine, codon, 23
aspartic acid, codon, 23
atria] natriuretic factor, 64
Australia, genome research, 8, 133, 148, 195
automation of DNA sequencing
 DOE initiative for, 7-8
 by Japan, 9, 47-48, 137-138
 new technologies, 46-48
 robotic devices, 48, 137-138
 standard setting for equipment for, 103
autoradiography/autoradiographs
 automated scanning of, 48
 use in DNA sequencing, 46
 use in physical mapping, 32, 40, 45
 use in RFLP mapping, 29
autosomes
 karyotyping of, 32
 mapping of genetic loci on, 27, 30, 33-34
bacteria
 DNA sequencing of, 45
 E. coli, 41, 45, 47, 100
 genome mapping, 4, 40, 41
 haploid DNA content, 25
 mitochondria similarities to, 71
 S. typhimurium, 45
bacteriophage T4, genomic map of, 40
Baltimore, David, 124
basic research
 government restriction of, 87
 value of, 81
Baylor College of Medicine, 97
bears, 36, 69
behavior, human, genetic factors in, 85-86
Berg, Paul, 126
beta globin, 61, 65, 70
beta interferon, 64
Billings, John Shaw, 97
Bio-Rad Laboratories, automated DNA sequencer, 47-48
biomedical research
 HHMI support for, 8
 NIH funding, 6, 95
Bimolecular Engineering Programme, 140
BIONET™, 193
biotechnology
 databases, 97
 European research programs in, 140-141
 international competitiveness in, 11
 NBS support for, 103
Biotechnology Action Program, 140-141
Biotechnology Research and Innovation for Development and Growth in Europe, 140-141
bison, 72
blood pressure disorders, 64
Brenner, Sydney, 147
burn treatment, 64
Botstein, David, 126
Bush, Vannevar, 102
C-value paradox, 24-25
Caenorhabditis elegans
 amount sequenced, 47
 genome mapping, 42
 genome size, 47
California Biotechnology, probe development, 58
California Institute of Technology, automated DNA sequencer, 47, 102
Cambridge University, genome mapping project, 42
Canada, genome research, 8, 133, 148, 195
cancer
 mutation-induced, 25
 polygenic nature, 62
 treatment, therapeutic agents, 64
catalase, 61
cataract surgery, 64
cDNA
 clones, 59-63, 67
 libraries, 59
 mapping, 30, 32, 44, 63
 restriction enzyme cutting, 35
cell culture, see somatic cell hybridization

- Cell Line Two-Dimensional Gel Electrophoresis Database, 97
- cell receptors, 21-22
- Center for the Study of Human Polymorphism
 collaborative efforts of, 8, 106, 143-144, 146, 149
 family pedigree data set, 58, 143, 146
 funding for, 106
 mission, 145
- Centers for Disease Control, 103
- chicken, haploid DNA content, 25
- Chiles, Lawton, 97
- cholesterol, lowdensity lipoprotein, 58
- chromosome markers
 for single-gene diseases, 57
 funding for research on, 6
 mapping through family inheritance patterns, 27
 maps, low-resolution, 4
 use for genetic linkage studies, 6, 27, 28, 44
- chromosomes
 banding patterns, 30, 33, 34-35, 40, 42, 45, 56
 crossing over (recombination), 26, 27
 deletion of, 25, 31, 32
 diploid number, 21
Drosophila melanogaster salivary gland, 30, 32
 duplication, 25
E. Coli, 41
 gene assignment to, 31
 haploid number, 21
 hybrids, single, 31
 inversion, 26
 isolation techniques, 31-32, 43
 of clinical significance, 44
 phage lambda, 36, 39, 42, 56, 100
 polytene, 42
 sorting, 31-32, 37, 47, 56, 97, 100
 species similarities in, 34-35, 36
 translocation, 25-26, 31, 32
 yeast artificial, 36-37, 39, 43, 56
- chromosomes, human
 1, 27
 4, 28
 6, 148
 7, 31, 44, 62
 9, 33, 148
 10, 32, 33
 11, 32
 13, 34
 16, 31, 44, 100, 148
 17/ 31, 33
 19, 31, 44, 100
 21, 35, 44, 95, 100, 145-146
 22, 44, 145
 average size, 37
 number, 3
 resemblance to primate chromosomes, 34-35
 X, 24, 27, 30, 31, 44, 63, 100, 148
 Y, 24, 30, 31, 145
- chronic granulomatous disease, 57, 59, 62
- Church, George, 44-45
- cloning/clones
 access to and ownership of, 147
 automation of, 47, 48
 banding patterns, 40
 cDNA, 59-63
 disease-associated genes, 57, 59, 60
 of DNA fragments, 39, 72
 drug development through, 62-63
E. coli, 41
 fingerprinting method for ordering, 42
 fruit fly chromosomes, 42
 gene isolation by, 31, 59
 libraries of, 39, 42, 59, 62-63; see also contig maps
 microdissection, 42
 NIH grants for, 94
 ordering of, 38-40, 41, 42
 overlapping, 39, 42, 62, 100
 phage lambda chromosomes, 36, 39, 42, 56, 100
 repositories, 97, 101, 115
S. cerevisiae, 42
 vectors, 35-37, 38-39, 42, 56, 67, 100
 yeast artificial, 36-37, 39, 43, 56, 157
- Cold Spring Harbor Laboratories Conference, 6
- collaboration on genome research
 by Australia, 148
 by Center for the Study of Human Polymorphism, 8, 106, 143, 146, 149, 157
 center-based vs. networking, 156
 databases and repositories, 8, 139, 158-159
 DOE, 157
 existing frameworks, 155-157
 European, 142, 150
 International Human Gene Mapping Workshops, 29, 157
 international] journals, 157-158
 organizational options, 152-155
 precedents for international scientific programs, 150-152
 views on, 152-153
 Washington University -RIKEN, 157
- Collaborative Research, Inc.
 DNA probe development, 58, 108
 RFLP linkage map, 6, 30
- collagen, 61, 67
- color-blindness, 21
- Columbia University
 mapping of *E. coli* genome, 41
 mapping of human chromosome 21, 44, 100
- Compton, Arthur Holly, 99
- computers, computational methods, and software
 artificial intelligence, 96
 costs, 180-181
 for DNA sequencing, 65, 97
 gene mapping applications to, 57, 146
 networking, 156
 NIH funding for improvements in, 95, 96
 see also databases; informatics
- Concertation Unit for Biotechnology in Europe, 140
- consortia
 of Federal/private interests, authority for, 16, 121
 funding, 122
 goals, 121
 intellectual property rights, 122

- Midwest Plant Biotechnology Consortium, 122
 national, to administer genome projects, 14-15, 121-123
 peer review, 122
 two-tiered system, 122
- contig mapping/maps
 construction, 39, 40
 correlation with large-fragment restriction maps, 42
 forward genetics applications, 61
 nematode, 42, 43
 reverse genetics applications, 62
 strategies, 43-44
 yeast, 42
- controversial issues
 Big Science vs. small science, 125-128
 DNA sequencing, extent of, 4, 6, 44, 57, 79, 81
 feasibility of genome mapping, 4
 quotes on, 126
 resolution of genome mapping, 3, 79, 81, 88
 see also ethical issues
- corn, haploid DNA content, 25
- Coulson, Alan, 44-45, 147-148
- Crick, Francis H.C., 3, 21
- cysteine, codon, 23
- cystic fibrosis, 57, 58, 62, 149
- cytidine, 21-22
- Dana Farber Cancer Institute, 97
- databases
 access, to and ownership of, 12, 82, 102, 128, 134, 139, 146; see also technology transfer
 Cell Line Two-Dimensional Gel Electrophoresis, 97
 CODATA Hybridoma Databank, 141
 DNA Data Bank of Japan, 139, 158
 DNA fingerprints, 80
 European support of, 141
 funding for, 7, 12, 96-97, 141, 190
 Genatlas, 157
 GenBank[®], 46, 96, 98, 109, 115, 139, 142, 154, 158, 190
 genetic maps, 24, 98, 106, 189-190
 government protection of, 87
 HHMI, 7, 8, 98, 106
 Human Gene Mapping Library, 106, 189-190
 importance, 4, 9
 international collaboration on, 8, 139, 158-159
 Japan Protein Information Database, 159
 linking of, 98
 management of, 12
 Martinsreid Institute for Protein Sequence data, 159
 MEDLARSIMEDLINE, 97
 mouse genetics, 106
 National Library of Medicine, 7, 8, 12, 96, 97
 needs for, 191-192
 nucleotide sequence data, 46, 96, 98, 141, 158, 190
On-Line Mendelian Inheritance in Man, 24, 98, 106, 189-190
 Protein Data Bank, 190-191
 Protein Identification Resource, 97, 98, 158-159, 190-191
- Dausset, Jean, 145-146
- DeLisi, Charles, 100, 153
- Denmark, national genome research efforts, 133, 143, 195
- deoxyribonucleic acid, see DNA listings
- Department of Defense, biomedical research resources, 104
- Department of Energy
 funding for genome projects, 7, 96, 100
 Health and Environmental Research Advisory Committee report, 101-102
 interest in massive sequencing, 9
 international research collaboration, 157
 as lead agency for genome projects, 12, 14, 116, 117
 mission, 7, 99-100
 Office of Health and Environmental Research, 99-101
 organization, 99, 117-118
 peer review, 101, 118
 recommendations for genome projects, 4, 11, 100
 research supported by, 100, 117
 workshops sponsored by, 6, 100
 see also Human Genome Initiative
- determinism, effect of genome mapping on, 86
- development, see human physiology and development
- diabetes, 62
- diseases
 infectious, 64
 linking mapping and sequencing data to, 104
 see also genetic diseases; and specific diseases
- DNA
 amount relative to organism complexity, 24-25
 C-value paradox, 24-25
 cloning in plasmids, 36-37, 39
 complementary, see cDNA
 discovery, 3
 electrophoretic separation of, 37-39
 expendable fraction, 25, 57
 fingerprints, 89; see also genetic screening
 fragmentation of, 37-39
 mitochondrial, 71
 oldest human samples, 72
 polymerase, 45
 recombinant technology, see recombinant DNA technology
 replication process, 21-22
 structure, 3, 21-22
 transcription to mRNA, 23-24
 see also chromosomes
- DNA markers, see chromosome markers
- DNA probes
 automated synthesis of, 47, 48
 cDNA, 28-29, 32, 33, 59-61, 63
 companies developing, 58
 fluorescently labeled, 46-48
 for genetic disease diagnosis, 58-59
 in *in situ* hybridization, 33
 number needed to complete human linkage map, 29
 oligonucleotides, 48
 radioactively labeled, 28-29, 32-33, 40, 44-46, 58
 reliability, 58
 for RFLP markers, 28-29, 56, 58, 61-62

- synthetic, 48, 59-60
 use to clone genes, 60
 DNA Segment Library, 97
 DNA sequence/sequencing
 automation of, 47-48
 commercialization, 82-83, 133, 138-139
 computer-assisted, 65
 controversies, 4, 6, 44, 79; see *also* ethical issues
 costs, 6, 182-183
 database, 46, 96, 98, 190
 definition, 3, 21
 directly from genomic DNA, 45
 E. coli, 41, 100
 enhanced fluorescence detection method, 46, 47
 exons, 59, 61, 63, 65, 69
 expenditures, federal, 8
 facilities for, 13
 government role in, 87
 homeo box, 67-68
 importance, 9
 introns, 25, 30, 61, 65, 69-70
 longest stretch determined, 46
 of mitochondria, 71
 mukiplex, 44-46
 mutation detection applications, 56
 NIH funding for, 8
 rate, 46
 repeated, 25, 28, 43, 57
 RFLP mapping required for, 37-39
 scanning tunneling microscopy for, 46
 selective amplification without prior cloning, 45-46
 species comparisons, 68-70
 steps, 47
 strategies, 44-45
 technologies, 44-47
 variations, 28, 29
 VNTR, 29
 Domestic Policy Council, 8, 105, 109, 119
 Donis-Keller, Helen, 30
 Down's syndrome, 32, 35, 58, 95, 146
Drosophila melanogaster
 amount sequenced, 47
 genome mapping, 42-43
 genome size, 47
 salivary gland chromosomes, 30, 33
 drugs and pharmaceuticals, development, 62-63
 Duchenne muscular dystrophy, 57-59, 61-63
 Duffy blood group, 27
 Dulbecco, Renato, 100, 126, 145
 dwarfism, 64
 dystrophin, 63

 EG&G Bimolecular) automated DNA sequencer, 47
 E.I. du Pont de Nemours & Co., automated DNA sequencer, 47
 electrophoresis, see gel electrophoresis
 England, see United Kingdom
 enzymes
 functions, 22
 see *also* specific enzymes

 epidermal growth factor, 64
 Epstein-Barr virus, 46
 erythropoietin, 64
Escherichia coli
 amount sequenced, 47
 genome mapping, 41, 43, 100
 genome size, 47
 ethical issues
 academic freedom, 87
 access to and ownership of databases and repositories, 16, 82, 88
 access to and use of genetic information, 79-80
 attitudes and perceptions of ourselves and others, 85-86
 commercialization, 16, 82-83, 133
 diagnostic/therapeutic gap, 83
 eugenics, 81, 84-85, 88, 143-144
 genetic fingerprinting, 80
 government role in mapping and sequencing, 87, 88
 international competitiveness, 87-88, 133
 physician practice, 83
 reproductive choices, 83-84, 88
 responsibility for considering, 123-124
 eugenics
 negative, 85, 143-144
 of normalcy, 85
 positive, 84-85
 eukaryotes, 70-71
 Europe, Eastern, interest in genome projects, 8, 133, 143, 195
 Europe, Western, genome sequencing and mapping activities, 139-148; see *also* specific countries and organizations
 European Economic Community, genome research, 139-141, 153
 European Molecular Biology Laboratory, 8, 139, 141-142, 158
 European Molecular Biology Organization, 8, 141
 European Research Coordination Agency, 142, 145-146
 European Science Foundation, 142, 156
 evolution, see molecular evolution

 facilities for genome research
 bioprocess engineering, 102
 data handling, European needs, 142
 DOE funding for, 100
 flow cytometry, 32, 97; see *also* specific national laboratories
 need for, 10, 128
 NSF biology centers, 8, 102-103, 109
 factor IX, 61
 factor VII, 61
 factor VIII:C, 64
 familial hypercholesterolemia, 56, 58, 149
 family pedigree projects
 CEPH data set on, 58, 136, 146
 Danish, 143
 Egyptian, 134, 136
 on mental illness, 156
 South African, 149

- use in genetic linkage mapping**, 27, 33, 58, 61
 Venezuelan, Huntington's disease, 63-64, 134-136, 143, 146
- fatalism, 86
- Federal Advisory Committee Act, 124
- Federal Republic of Germany, genetics research, 8, 133, 143-144, 195
- fibroblast growth factor, 64
- Finland, national genome research effort, 133, 144
- flow cytometry
 enhanced fluorescence detection in, for DNA sequencing, 46
 extraction of whole chromosomes by, 37
- facility**, 32
- France
 Center for the Study of Human Polymorphism, 33, 58, 144-146
 genome projects, 8, 144-145
 published genome research, 133, 195
- fruit fly
 developmental regulation in, 67
Drosophila melanogaster, 30, 33, 42-43, 47
genome mapping, 42-43
 haploid DNA content, 25
 human DNA sequences compared with, 68
 lethal mutations in larval stage, 42
- funding for genome projects**
 advisory body for determining, 124
 of consortia, 122
 databases, 7, 12, 96-97, 190
 determinants, 98
 determinants of congressional appropriations, 11-12
 DNA marker studies, 6
 DOE, 7, 96, 100, 118, 190
 European Economic Community, 139-143
 HHMI, 7, 190
 international, 8
 NIH, 6, 7, 94-98, 117, 155, 190
 NSF, 7, 8, 96, 190
 pluralism in, 13, 15, 119
 priority setting, 10
 private vs. federal, 79, 83
 recommendations, 4, 11-12, 107
 through a lead agency, effects of, 12-13
 through a national consortium, 14
 USDA, 190
 West German, 144
- Gall, Joseph, 126
- Galton, Francis, 84
- gamma interferon, 64
- gel electrophoresis
 database, 97
 DNA separation for physical mapping, 37, 39, 45
 polyacrylamide, 45 "
 pulsed-field, 37, 44, 56
 in RFLP mapping, 28, 37, 58
- GenBank", 46, 96, 98, 109, 115, 139, 142, 154, 158, 190
- gene expression
 control of, 57
 steps in, 23-24
 study centers, 144
- gene products**
 functions of, 67
 with potential as therapeutic agents, 62, 64
- gene therapy**, 64, 141
- genes**
 biochemical identification, 62
 in a chromosome band, number, 33
 color-blindness, 21
 definition, 3, 21, 24
 dosage mapping, 34
 encoding ribosomal RNAs, detection, 33
 expressed, 24, 30
 families of, 25, 70
 functions, approaches to understanding, 66-67, 73
 homeotic, 68
 isolation techniques, 31, 33, 59-62
 largest, 63
 linked, 26, 34; see *also* genetic linkage mapping/maps
 mapping, see genetic linkage maps
 species similarities in, 34
 structure/function relationships, study of, 144
 see *also* human genes
- genes, human**
 aldolase, 33
 chromosomal locations known, 4
 number of loci identified, 24, 30
 number per haploid genome, 24
 sizes, 61
- genetic code**
 definition, 21--24
 for amino acids, 23
- genetic diseases**
 chromosomal locations of genes for, 4
 clinical services for, 100
 companies developing DNA probes for diagnosis of, 58
 correlating gross chromosomal abnormalities with, 32
 diagnostic information, physician handling of, 83
 family pedigree studies, 61, 63
 HHMI support of research on, 8
 isolation of genes associated with, 59-62
 mechanisms, 4
 not associated with biochemical defects, 61
 polygenic, 62
 RFLP markers for, 28, 56, 58
 single-gene, 57, 88
 see *also* specific diseases
- genetic information**
 access to and use of, 79-80, 82, 84
 causes of changes in, 25-26
 insurer use of, 81, 83
 organization and function, 21-26
- genetic linkage mapping/maps**
 autoradiography use in, 29
 autosomes, 27
 costs, 181-182
 databases, 24, 98, 106, 189-190
 disease diagnosis applications, 56, 58, 62
 distance measurements on, 27

- early attempts, 4, 6, 21
- electrophoretic technology in, 28
- family pedigree data in, 27, 33, 58, 61
- HHMI funding for, 7
- medical applications, 56, 58, 62-64
- number of markers needed to complete, 29-30
- projects to link physical maps with, 181-182
- purpose, 26-27
- recombinant DNA technology use in, 28
- resolution, 62
- reverse genetics applications, 62
- of RFLP, 28-30, 62
- somatic cell hybridization for, 27
- X chromosome, 27
- genetic locus, see chromosome marker
- genetic screening
 - ethical questions about, 80, 88
 - for missing children, 80
 - for proof of paternity, 80
- genetic selection, see eugenics
- genetics
 - definition, 21
 - forward, 59-61, 62-63
 - HHMI funding for, 7
 - molecular, NIH research resources activities related to, 97
 - NIH funding for, 95
 - population, 72-73
 - reverse, 59, 61-62
- Genetics Institute, robotic devices for DNA sequencing, 48, 108
- Genome Corp., physical mapping project, 108
- genome mapping
 - agricultural applications, 73
 - application in developmental studies, 42, 65
 - automation, 47
 - determinism and, 86
 - distance measurements in, 40
 - evolutionary applications, 68-72
 - facilities, 13
 - importance, 9
 - international efforts and cooperation, 8, 9, 150-159; see also specific countries
 - resolution levels in, 56, 79
 - see also genetic linkage mapping/maps; physical mapping
- genome mapping, human
 - commercialization, 82-83, 138-139
 - controversies, 3, 4, 6, 9, 44, 55, 57, 102
 - government role in, 87
 - priorities for, 88
 - scale of efforts, 5, 24
 - strategies, 43-46
- genome mapping, nonhuman
 - bacteria, 4, 40, 41, 44
 - fruit fly, 42-43, 44
 - importance, 9, 44, 107
 - international efforts, 8, 42
 - nematodes, 4, 42, 44
 - plants, 73, 136, 149
 - yeast, 4, 41-42, 44
- genome projects
 - accountability to Congress, 13, 14, 124
 - administration of, 12-15, 115-123, 184
 - advisory board structure for, 123-124
 - appropriations for, see funding
 - benefits, 11, 55, 56, 133, 172-174
 - Big Science v. small science approach, 120, 125, 127-128
 - center-based vs. networking, 156
 - collaboration on, 150-159, see also collaboration on genome research
 - commercialization potential, 82-83, 133, 138-139, 151, 165
 - common features, 7
 - component nature, 4, 6, 10
 - congressional oversight, 15-17
 - congressional role in, 11-17
 - consortium structure for, 14-15, 121-122
 - cooperation among agencies, 9, 15, 118-119
 - costs, 11-12, 4, 47, 180-185
 - definition, 4
 - displacement of other research by, 102, 125
 - duplication of efforts, 13, 82, 105
 - early estimates of costs for, 184-186
 - economic impacts, 165, 172
 - ethical considerations, 79-88
 - expenditures, Federal, 8
 - facilities, 10, 13
 - focus, 7-9
 - funding, see funding for genome projects
 - interagency coordination and communications, 8, 11, 123
 - interagency task force oversight of, 14, 119-121
 - international efforts on, 133-159; see also specific countries
 - lead agency concept, 12-14, 115, 116-118
 - legislation, 12, 14, 123
 - manpower availability, 10
 - medical applications, 56-64; see also disease; medicine
 - military applications, 174
 - misconceptions about, 9-10
 - national prestige associated with, 174
 - objectives, 7, 9, 55
 - organization of, 12-15
 - organizations involved in, 6, 7
 - policy development for, 134
 - political interference with, 127-128
 - quality control and reference standards, 103, 127, 183
 - resource allocation for, 10; see also funding for genome projects
 - scope of, 10, 134
 - training of personnel, 183-184
 - U.S. competitiveness and, 11, 133
 - see also genome mapping; DNA sequencing; sequencing; Human Genome Initiative; pilot projects
- genome, human
 - amount sequenced, 46-47

- bibliometric analysis of research on, 133, 157-158, 195
 size, 24, 43, 46-47
- genomes**
 bacteriophage T4, 40
 definition, 3, 21
 Epstein-Barr virus, 46
 mitochondrial, 71
 organization, 21
 regeneration, 21
 size, 21, 24-25, 43
 smallest, 148
- genomic library, 35**
- Germany, see Federal Republic of Germany**
- Gilbert, Walter, 44-46, 126, 153, 156**
- glutamic acid, codon, 23
- glutamine, codon, 23
- glycine, codon, 23
- granulocyte colony stimulating factor, 64
- guanosine, 21-22
- Gusella, James, 136**
- Harvard University, DNA sequencing, 44, 100**
- heart disease, 58, 62, 64**
- hemophilia, 56, 57, 58, 64**
- high-mobility group COA reductase, 61**
- Hill, Lister, 97**
- histidine, codon, 23**
- Hitachi, Ltd., automated DNA sequencer, 47
- Hood, Leroy, 47, 126
- hormones, 21
- Howard Hughes Medical Institute**
 as lead agency for genome projects, 13
 budget, 8
 collaboration with CEPH, 146
 databases, 7, 8, 98, 106
 expenditures, 102, 106
 funding, 7, 105, 109
 genome initiatives, 8, 105-106, 109
 mission, 7
 RFLP mapping project, 6, 29
 university centers, 106
- Hpa I, 28**
- Human Gene Mapping Library, 106, 189-190**
- Human Gene Mapping Workshop, 29, 106, 144, 157**
- Human Genetic Mutant Cell Repository, 31, 96, 190, 192-193**
- Human Genome Initiative**
 budget, 7-8, 101
 expenditures, 7-8
 justification for, 102
 management, 6
 objectives, 6, 7, 14
 recommendations on, 101
 stages, 101
 workshops, 6
- human growth hormone, 59, 62, 64**
- human physiology and development**
 genome mapping applications to, 65
 NICHD-supported research, 95
- Huntington's disease, 28, 57, 58, 64, 83, 134-136, 146, 149**
- hybridization, see *in situ* hybridization; somatic cell hybridization
- hypercholesterolemia, 56, 58, 149
- hypertension, 64
- Imperial Cancer Research Fund, 148**
- in situ* hybridization**
 cDNA mapping by, 30, 33-34
 in mapping genes to whole chromosomes, 56
 localization of fruit fly clones by, 42, 43
- Index Medicus, 97***
- Industrial Biotechnology Association, opinions on Federal initiatives in mapping and sequencing, 108**
- informatics**
 Advanced Informatics in Medicine, 141
 Bioinformatics: Collaborative European Programs and Strategy, 141
 BIONET™, 193
 Contextual Measures for R&D in Biotechnology, 140-141
 National Biotechnology Information Center, 193
- infrastructure for genome projects**
 European, 141
 Federal support, 8, 102
 resource allocation, 10
- Institute for Medical Research, somatic cell hybrid line repository, 31**
- insulin, 21, 59, 61, 62, 64**
- Integrated Genetics, DNA probe development, 58, 108**
- intellectual property, protection of, see patent and copyright policies**
- IntelliGenetics Corp., 96**
- interleukin-2, 62, 64**
- International efforts on genome projects**
 collaboration and cooperation, 150-159; see *also* collaboration on genome research
 see *also* specific countries
- International Geophysical Year, 150-151**
- isoleucine, codon, 23
- Italy, human genome research, 8, 133, 145-147, 195**
- Japan**
 automation of DNA sequencing equipment, 47-48, 137
 basic science expertise, 137
 collaboration on research, 157
 commercialization of mapping and sequencing technologies, 133, 138
 competitiveness with U. S., 133, 137-139
 cooperation with U.S., 139
 databases and repositories, 139
 expenditures on genome projects, 8-9, 138
 funding for genome research, 137
 grants program in genetics, 9
 Human Frontiers Science Program, 9, 137-138
 mapping and sequencing research, 136-138
 Ministry of Education, Science, and Culture, 9, 136-137
 Ministry of International Trade and Industry, 137-138

- peer review, 136
 - physical mapping of *E. coli* genome, 41
 - policy development on genome research, 136-137
 - published genome research, 133, 195
 - robotics technology, 137
 - Science and Technology Agency, 8-9, 137
 - workshop on DNA sequencing technologies, 47
- karyotypes, human female, 34
- karyotyping, 32-33, 56
- Kennedy, John, 97
- kidney diseases, 57, 58, 64
- Kirschstein, Ruth, 94 n.1, 117
- Koshland, Daniel, 126
- Lalouel, Jean-Marc, 146
- Latin America, genome research, 149
- Lawrence Livermore National Laboratory
- chromosome sorting, 100
 - mapping of chromosome 19, 44, 100
 - ordering of DNA clones, 100, 108
- Lederberg, Joshua, 126
- leucine, codon, 23
- leukemia, 64
- Levinson, Rachel, 94 n.1
- libraries
- of DNA fragments, construction of, 39
 - of overlapping clones, 38-39
 - see *also* repositories
- life sciences
- DOE funding for, 7
 - HHMI funding for, 7
 - NIH funding for, 7
 - NSF funding for, 7, 8
- Lifecodes, DNA probe development, 58
- ligase, 39
- lily, haploid DNA content, 25
- Lindberg, Donald A. B., 94 n.1
- Los Alamos National Laboratory
- chromosome sorting at, 32, 100-101
 - mapping of chromosome 16, 44, 100
 - ordering of DNA clones, 100
 - see *also* GenBank "
- Lovell, Joseph, 97
- lowdensity lipoprotein receptor, 58, 61
- lysine, codon, 23
- microphage colony stimulating factor, 64
- Massachusetts Institute of Technology, bioprocess engineering center, 102
- Maxam, Alan, 44-46
- Max Planck Society, 144
- McKusick, Victor, 24, 98
- medicine
- diagnostic tool development, 56, 58-59
 - drug development, 62-63
 - human gene therapy prospects, 64
 - isolation of genes associated with diseases, 59-62
 - see *also* genetic diseases
- meiosis, 26-27
- Mendel, Gregor, 3, 73
- Mendelian Inheritance in Man*, 24, 98, 106, 189
- Merriam, John, 42
- messenger RNA
- function, 23
 - size of human genes, 61
 - translation into protein, 23, 30
- methionine
- codon, 23
- mitochondrial genome, human origin clues from, 71
- molecular anthropology, 72
- molecular biology
- Big Science vs. small science, 125, 126-127
 - of human development, 65, 95
 - manpower in, 10
 - plant, genome mapping applications to, 73
- molecular evolution
- genome mapping and DNA sequencing applications to, 57, 68-72
 - human origins, 71
 - primate, 70
 - unanswered questions in, 69-70
- monoamine oxidase, 86
- Moskowitz, Jay, 94 n.1
- Mount Sinai Medical Center Institute of Human Genomic Studies, 100
- mouse
- beta globin gene, 65
 - cell hybridization, see somatic cell hybridization
 - genetic similarities to humans, 34, 67
 - genetics database, 106
 - haploid DNA content, 25
 - Mus musculus*, amount sequenced and genome size, 47
- muscular dystrophy
- Becker's, 63
 - Duchenne, 57-59, 61-63
- mutations
- artificially induced, 25
 - cancer from, 25
 - chromosome structural changes involved in, 25-26
 - deletion, 25, 31
 - detection of, 42, 56, 58, 59
 - duplication, 25
 - in fruit flies, 42, 68
 - Human Genetic Mutant Cell Repository, 31, 96, 190, 192-193
 - human rates, 72
 - inversion, 26
 - lethal, 42
 - in nucleotide sequence, 23
 - saturating screen technique for, 42
 - in sex cells, 25
 - in somatic cells, 25, 31
 - translocation, 25-26, 31
- National Academy of Sciences
- recommendations on genome projects, 107
 - role in genome project oversight, 14, 15, 124
 - views on international cooperation, 153
 - see *also* National Research Council

- National Aeronautics and Space Administration, 150-151
National Biotechnology Information Center, 193
National Bureau of Standards, 103
National Cancer Institute, 93-94, 96, 98, 117
National Center for Biotechnology Information Act of 1986, 97
National Flow Cytometry Resource, 32, 97
National Institute of Allergy and Infectious Diseases, 93-94
National Institute of Child Health and Human Development, 93-94, 95,
National Institute of General Medical Sciences, 93, 95, 94
National Institute of Neurological and Communicative Disorders and Stroke, 93-94, 95
National Institute on Aging, 95
National Institute on Mental Health, 95
National Institutes of Health
 budgets for **genome projects**, 8, 93
 databases, see **National Library of Medicine**
 expenditures for genome projects, 8, 93, 109
 funding for genome projects, 6, 7, 14, 93-94, 95-97, 109, 155
 genome project objectives, 8, 93-95
 as lead agency for genome projects, 12, 13-14, 116-117
 mission, 7, 93
 organization, 93-94, 99, 116
 origin, 93
 peer review, 98-99, 109
 research infrastructure, 96-98
 research resources activities related to molecular genetics, 97
 see *also* specific institutes
 working group on human genome, 94
national laboratories, see specific laboratories
National Library of Medicine, 7, 8, 12, 97-98, 117
National Research **Council**
 physical mapping strategies, 44
 recommendations for genome projects, 4, 11, 107, 116
 sequencing strategies, 44
National Science Foundation
 as lead agency for genome projects, 14
 funding for genome-related research, 7, 8, 96, 102-103, 109
 mission, 7, 102
 role on genome projects, 116
nematodes
 Caenorhabditis elegans, 42, 47, 147-148
 genome mapping, 4, 42, 147-148
 haploid DNA content, 25
 human DNA sequences compared with, 68
 mutant, 67
neurofibromatosis, 149
nucleotides
 base order, 3, 21-22; see *also* DNA sequence/sequencing
 bonding between base pairs, 21
 dideoxynucleotide, 45
 mutations in sequence of, 23
 number of base pairs in human cells, 5
 substitution and recombination rates, 70
 total sequenced, 46
Office of Science and Technology Policy
 Biotechnology Science Coordination Committee, 104
 Committee on Life Sciences, 15, 104
 interagency coordination of genome projects under, 8, 104, 109, 124
 mission, 104
Office of Management and Budget, role in genome projects, 105
Office of Technology Assessment
 cost estimates for human genome projects, 180-185
 workshop on genome projects, 4
oncogenes, 67
Organization of American States, 149
Oudtshoorn skin disease, 134, 149

Palade, George, 94 n.1
pandas, 36, 69
parasites, 64
parathroid, 61
Pardue, Mary Lou, 33
Pasteur Institute, 145, 157
patent and copyright policies, 16-17, 82, 88, 166-170
Patent and Trademark Amendments of 1980, 16, 187
peer review
 at DOE, 101, 109, 118
 by Japan, 136
 in a national consortium, 122
 at NIH, 98-99, 109, 118
Pepper, Claude, 97
Perkin-Elmer Cetus Instruments
 DNA sequencing technology, 45-46, 47
 probe development, 58
phenylalanine, codon, 23
phenylalanine hydroxylase, 61
phenylketonuria, 57
Philipson, Lennart, 142, 152
physical mapping/maps
 automation of, 47
 bacterial genome, 41
 bottom-up, 43
 chromosome sorting for, 31-32, 56
 comparative mapping of species, 34
 construction of libraries of DNA fragments for, 38-39
 contig, 30, 39, 40, 41, 43-44, 61
 costs, 181-182
 detail possible on, 37
 distance measurements, 27, 40
 forward genetics applications, 61
 fragmentation of DNA for, 37-39
 fruit fly, 42-43
 gene dosage technique, 34
 high-resolution, 30, 35-46, 56
 human genome, 35-41, 43-46
 in situ hybridization in, 33-34, 56
 karyotyping in, 32-33, 56
 linking of genetic maps with, 181-182
 low-resolution, 30-35, 41, 43, 56
 medical applications, 64
 nematode genome, 42
 NIH **grants** for, 84
 nonhuman genomes, 41--43

- ordering of clones for, 39, 40
- private enterprises, 108
- purification of chromosomal DNA for, 37
- rapid, mass-analysis approach, 41
- of restriction enzyme sites, 37-41
- size determinants, 43, 81
- somatic cell hybridization in, 27, 30-32, 33, 56
- strategies, 43-44
- time required for, 40-41
- topdown, 43
- yeast genome, 41-42
- physicians' attitudes and practice, effects of genetic information on, 83
- physiology, see human physiology and development
- Pickett, Betty, 94 n.1
- pilot programs
 - DNA sequencing, 44
 - European, 140, 145, 147
 - importance, 4
 - NRC recommendations for, 107
 - yeast chromosome sequencing, 140
- plants, genome mapping of, 73
- polycystic kidney disease, 57, 58
- polymerase, 45
- population biology, genome mapping applications in, 72-73, 134
- President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, 85
- private sector
 - foundation support, 109, 137, 147, 148
 - funding of genome projects, 14-15, 108, 109
 - genome mapping efforts, 9
 - government formation of consortia with, 14-15
 - role in genome projects, 107-108
 - technology development, 108; see also automation; robotics
 - see also specific companies
- prokaryotes, lack of introns in, 69-70
- proline, codon, 23
- protein
 - classification by period of invention, 68-69
 - coding sequences, identification of, 65, 67
 - databases, 97, 98, 158-159, 190-191
 - engineering, 63, 142, 148
 - folding, 66
 - functions, 21-24, 67
 - kinase C, 61
 - life cycle regulator, 67
 - for single-gene diseases, identification of, 57, 59
 - structure/function relationship, 63, 65
 - synthesis, 23-24, 30
 - see also amino acids; enzymes; and other specific proteins
- publications
 - international, 157-158, 195
- quagga, 72
- recombinant DNA technology
 - cloning vector development through, 36, 38
 - definition, 24
 - use to create genetic linkage maps, 3, 24, 28
- repositories for research materials
 - access to, 58, 134
 - American Type Culture Collection, 101, 141, 190, 192
 - Armed Forces Institute of Pathology, 104
 - Center for the Study of Human Polymorphism, 33, 58
 - clones, 97, 101, 115
 - costs, 182
 - DNA Segment Library, 97
 - family pedigrees, 58-59
 - Federal support, 8, 12, 96
 - Human DNA Probes and Libraries, 96
 - Human Genetic Mutant Cell Library, 31, 96, 190, 192-193
 - importance, 4, 9
 - international collaboration on, 158
 - tissue, 104
- reproductive choices, ethical considerations in, 83-84, 85
- restriction enzyme cutting
 - automation of, 47
 - infrequent, 41
 - partial, 39
- restriction enzyme cutting sites
 - on bacteriophage T4 genomic map, 40
 - high-resolution physical mapping with, 35, 37-41
 - polymorphisms, see restriction fragment length polymorphisms
- restriction enzymes
 - cDNA cutting with, 35
 - Hpa I, 28
 - Not I, 41
- restriction fragment length polymorphisms (RFLP)
 - allelic forms, 28
 - diagnostic uses, 58, 59, 62
 - DNA probe detection of, 28-29, 61-62
 - linkage maps of, 28-30, 62
 - mapping of, 28-29, 62, 73
 - markers for genetic diseases, 28, 58, 62
- retinoblastoma, 57, 59, 62
- ribonucleic acid, see RNA
- ribosomes
 - functions, 23
- RIKEN-Washington University collaboration, 157
- RNA
 - functions, 23-24
 - ribosomal, 23, 30, 33
 - see also messenger RNA; transfer RNA
 - structure, 22
- robotics
 - devices for DNA sequencing, 48, 137
 - DNA extraction devices, 108
 - DOE initiative in, 7-8
 - microchemical, 48, 137
- Saccharomyces cerevisiae*
 - amount sequenced, 47
 - genome mapping, 41-42
 - genome size, 47
- salamander, haploid DNA content, 24-25
- Salmonella typhimurium*, 45

- Sanger, Fred, 44-45, 47
 scanning tunneling microscopy, for DNA sequencing, 46
 scleroderma, 64
 Seiko, automation of DNA sequencing, 48, 138
 Sendai virus, 31
 SeQ, Ltd., physical mapping project, 108
 serine, codon, 23
 sex cells
 mutations, 25
 progenitors, 26
 sickle cell disease, 4, 28, 56, 57, 58, 88
 Singer, Maxine, 126
 Sinsheimer, Robert, 100, 126
 Smith, Cassandra, 41
 Smith, Lloyd, 126
 somatic cell hybrid lines, 31 n.2, 37
 somatic cell hybridization
 cDNA mapping by, 30
 genome mapping applications, 27, 30-31, 33, 56
 of single copies of chromosomes, 31
 somatic cells
 definition, 21
 mutations in, 25, 31 n.2
 South Africa, genome research, 133, 149, 195
 Soviet Union, genome research, 133, 149, 195
 Sulston, John, 147-148
 superoxide dismutase, 64
- Task Force for Biotechnology Information, 141
 Tay-Sachs disease, 4
 technology development
 costs, 183
 NIH grants for, 94-95
 NRC recommendations for, 107
 private sector role in, 108
 see also automation; robotics
 technology transfer
 advantages of national consortium for, 14-15, 121-122
 congressional encouragement of, 166
 economic implications, 165, 122, 172
 ethical issues, 87-88, 173-174
 international, 172-174
 military applications, 174
 national prestige issue, 174
 patent/copyright policies, 16-17, 82, 88, 122, 166-170
 strategies for improving, 16
 trade secrets, 170-172
 Technology Transfer Act of 1986, 14, 16, 167
 thalassemias, 57, 134
 threonine, codon, 23
 thymidine, 21-22
 thyroglobulin, 61
 Tinoco, Ignacio, 101
 tissue plasminogen activator, 64
 Trademark Clarification Act of 1984, 167
 transcription
 of DNA into mRNA, 23-24, 25, 30
 of introns, 25, 30
 transfer RNA
 functions, 23, 30
 structure, 23
 translation of mRNA into protein, 23-24, 30
 Trivelpiece, Alvin, 101
 tryptophan, codon, 23
 tumor necrosis factor, 62, 64
 Turner's syndrome, 32, 64
 tyrosine, codon, 23
- United Kingdom
 DNA sequencing, 44
 equipment development, 48, 147-148
 expenditures, 147
 Medical Research Council, 42, 44, 147
 national genome research effort, 147-148
 nonhuman genome mapping, 8, 42, 147
 published genome research, 133, 195
 University of California at Los Angeles, clone library, 42
 University of California at Santa Cruz, workshop, 6, 100
 University of Copenhagen Institute of Medical Genetics, 143
 University of Helsinki, 144
 University of Manchester Institute of Science and Technology, 48, 148
 University of Wisconsin at Madison, physical mapping of *E. coli* genome, 41
- valine, codon, 23
 vectors
 cloning of, 36, 38-39
 cosmid, 36-37, 38, 42, 56, 101
 plasmid, 36-37, 38, 47, 56, 67, 101
 robotic devices for producing, 47
 viral infections, 64
- Wada, Akiyoshi, 152, 156
 Walsh, James, 126
 Washington University
 collaboration with RIKEN, 157
 physical mapping of yeast genome, 41
 Watson, James D., 3, 21, 126, 152
 Weinberg, Robert, 126
 Wexler, Nancy, 135-136
 White, Raymond, 29, 126, 146
 Wilson, Allan, 126
 workshops
 on automation of DNA sequencing, 47
 on collaboration for genome projects, 187
 on costs of genome projects, 188
 DOE-sponsored, 6, 97
 European Economic Community, 141
 International Human Gene Mapping, 29, 106, 144, 157
 information management system applications, 97
 on materials repositories and databases, 97
 Matrix of Biological Knowledge, 193-194
 NIH-supported, 96-97
 OTA, 187-188
 University of California at Santa Cruz, 6, 100
 wound healing, 64
 Wyngaarden, James, 93

yeast chromosomes

artificial, 36, 39, 43, 56, 157
electrophoretic separation of, 37
genome mapping, 4, 41-42, 157
haploid DNA content, 25

lack of introns in, 69

pilot project on sequencing, 140
Saccharomyces cerevisiae, 41-42, 47
similarities to other organisms, 67
use to isolate human gene functions, 67, 68