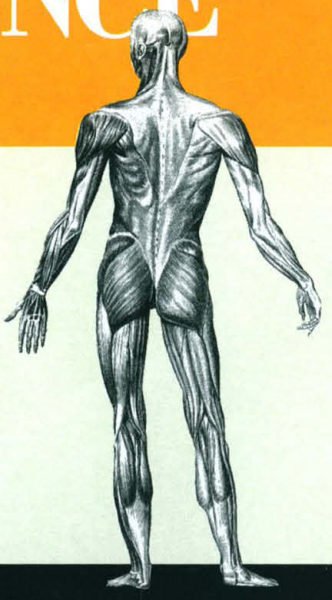
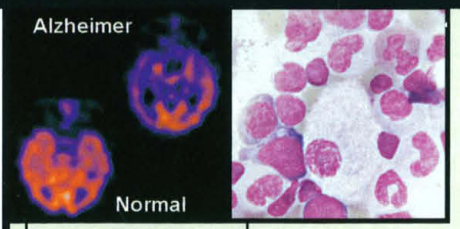
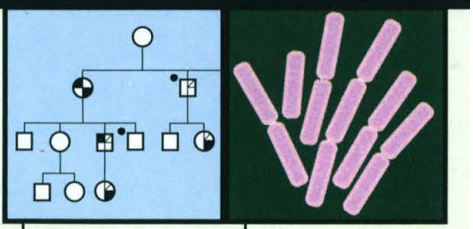
# SCIENCE

# The H



The Human Genome Project is expe
of DNA representing the functiona
history of the human species. How
sequence is thought to specify the portio
genes that encode proteins. Thus an impo
genomics is to identify and localize these
transcript mapping. When genes are expr
converted into messenger RNA transcrip
form of complementary DNAs (cDNAs). A
human genes had been sampled as of 15



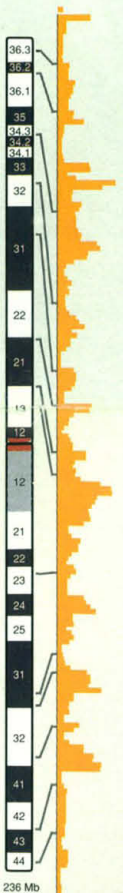



**GBA** In Gaucher disease, the defective enzyme is unable to metabolize glucocerebrosides which accumulate in characteristic, distended phagocytic cells.

IMAGE: E. BEUTLER, SCRIPPS RES. INST.

**AD4** Brain scans of a healthy elderly person and a patient with Alzheimer's disease.

IMAGE: K. JOHNSON, BRIGHAM AND WOMEN'S HOSP.




**MSH2** A human gene mutated in some familial colon cancers is homologous to an enzyme in the DNA mismatch repair pathway in bacteria.

IMAGE: G.SCHULER, NCBI

**PAX3** Portion of a pedigree of Waardenburg syndrome, indicating the occurrence of deafness and changes in pigmentation, including a white forelock.

IMAGE: V. McKUSICK, JOHNS HOPKINS HOSP.

# Human Tran

bject is expected to produce a sequence
ne functional blueprint and evolutionary
pecies. However, only about 3% of this
y the portions of our 50,000 to 100,000
nus an important part of basic and applied
calize these genes in a process known as
nes are expressed, their sequences are first
A transcripts, which can be isolated in the
s (cDNAs). Approximately half of all
ed as of 15 June, 1996.

A small portion of each cDNA sequence is all that is need
develop unique gene markers, known as sequence-tagged site
which can be detected in chromosomal DNA by assays based
polymerase chain reaction (PCR). To construct this transcript
cDNA sequences from a master catalog of human genes were
uted to mapping laboratories in North America, Europe, and
These cDNAs were converted to STSs and their physical locat
chromosomes determined on one of two radiation hybrid (RH
or a yeast artificial chromosome (YAC) library containing hu
genomic DNA. This mapping data was integrated relative to t

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**SCLC1** Deletion of a tumor suppressor gene is associated with one type of lung cancer. A large tumor (Ca) of the lung is visible in this CT scan.

IMAGE: P. CONNELLY, MIAMI VALLEY HOSP.

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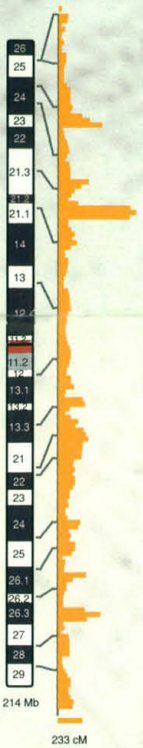


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IMAGE: K. A. ROT
R. E. SCHMIDT, W
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community.

IMAGE: C. D. ERHARDT, JR., BALTIMORE, MD

# nscript Map

that is needed to
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ssays based on the
s transcript map,
genes were distrib-
Europe, and Japan.
nysical locations on
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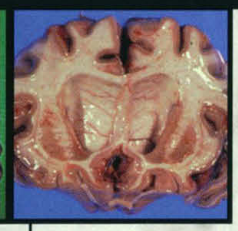
genetic map and then cross-referenced to cytogenetic band maps of the chromosomes. (Further details are available in the accompanying article in the 25 October issue of *SCIENCE* and on the World Wide Web at **http://www.ncbi.nlm.nih.gov/SCIENCE96/**).

The histograms (■) reflect the distributions and densities of genes along the chromosomes. Because the individual genes (>16,000) are too numerous to represent, images have been chosen to illustrate the myriad aspects of human biology, pathology, and relationships with other organisms that can be revealed by analysis of genes and their protein products.



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**HD** Brain section from a patient with Huntington's disease showing dilatation of ventricles and atrophy of caudate nucleus.

IMAGE: K. A. ROTH & R. E. SCHMIDT, WASH. U. SCH. MED.

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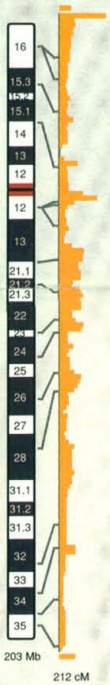


**SRD5A1** Discovery of the plant homolog of human steroid 5-alpha reductase links botany to endocrinology and may lead to new drugs.

IMAGE: J. CHORY, SALK INST.; BY PERMISSION, *THE PLANT CELL*


**DTD** X-ray of the hand of a patient with diastrophic dysplasia, caused by mutations in a gene encoding a sulfate transport protein.

IMAGE: E. LANDER, WHITEHEAD CTR. GENOME RES.; BY PERMISSION, *CELL* PRESS

MAPS

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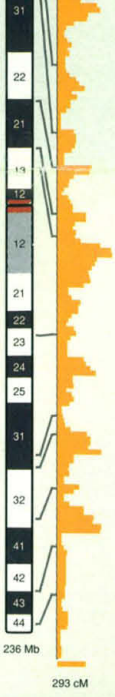


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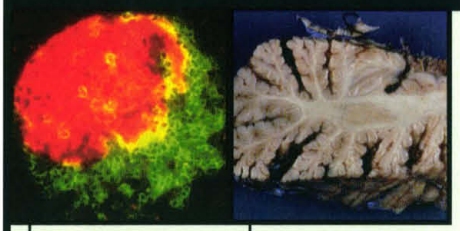

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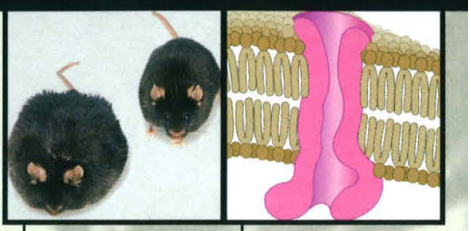
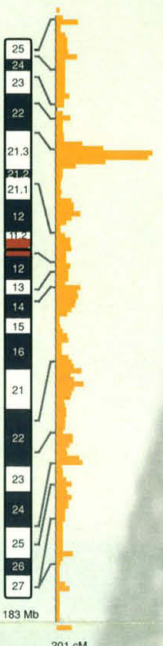


**SCA1** Degeneration of the cerebellum leads to loss of muscle coordination in patients with spinocerebellar atrophy.

IMAGE: K. A. ROTH AND R. E. SCHMIDT, WASH. U. SCH. MED.




**IDDM1** Juvenile onset diabetes, in which the body's own T lymphocytes infiltrate and destroy insulin-producing, pancreatic islet cells, is associated with the major histocompatibility complex.

IMAGE: A. COOKE & J. TODD, WELLCOME TRUST CTR. HUMAN GENET.

**CFTR** The gene encoding a chloride ion channel is defective in patients with cystic fibrosis.

IMAGE: Q. AL-AWQATI, COLUMBIA U., K. SUTLIFF, ADAPTED FROM *SCIENCE*

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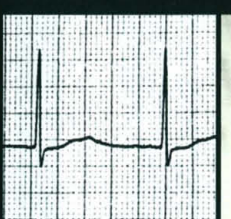

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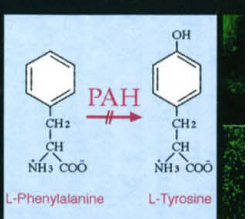

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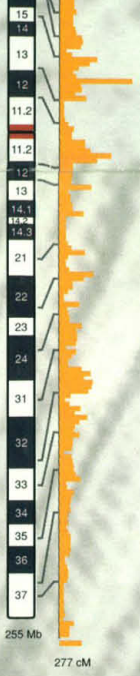


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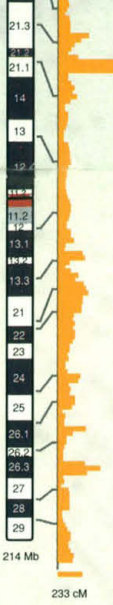


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IMAGE: K. A. ROT
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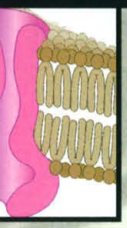

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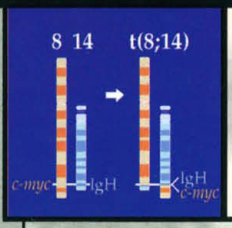


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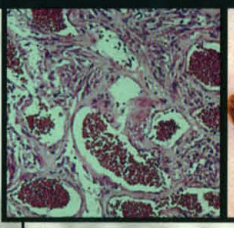

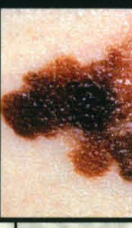

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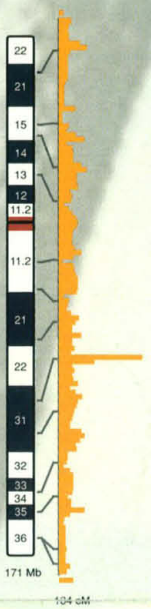



**WRN** Werner's syndrome is a disease of premature and accelerated aging associated with defects in a DNA unwinding enzyme.

IMAGE: WILLIAMS AND WILKINS PUBLISHING CO.


**MYC** A reciprocal chromosome translocation involving the c-myc oncogene is associated with Burkitt lymphoma.

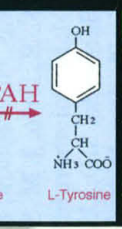
IMAGE: G.SCHULER, NCBI

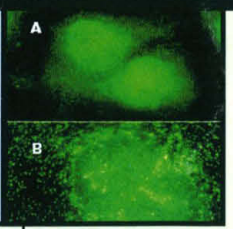
**CDKN2** Mal
melanoma is
with mutatio
tumor suppr
involved in c
control.

IMAGE: NATIONA
INSTITUTE

**TSC1** Microscopic section of angion a benign tumor of the kidney preser patients with tuberous sclerosis.

IMAGE: M. SMITH, JOHNS HOPKINS U.

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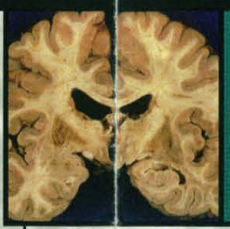

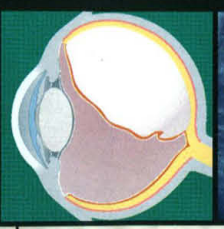

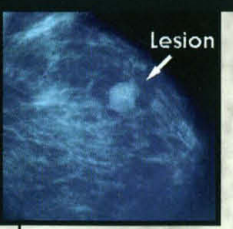


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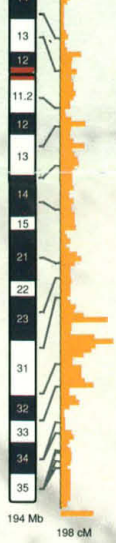


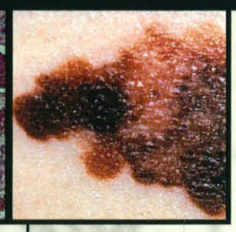

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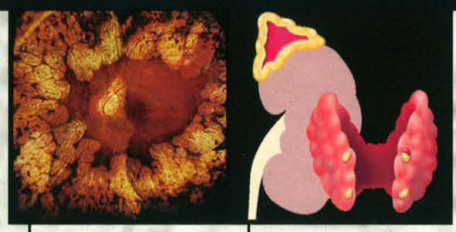

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**CDKN2** Malignant melanoma is associated with mutation of a tumor suppressor gene involved in cell cycle control.

IMAGE: NATIONAL CANCER INSTITUTE


ection of angiomyolipoma,
e kidney present in many
us sclerosis.

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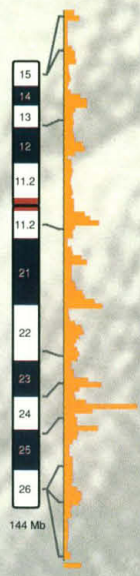
**MEN2A** The syndrome of multiple endocrine neoplasia (type 2A) is characterized by tumors in the pituitary, thyroid, parathyroid, and adrenal glands.

IMAGE: K. SUTLIFF, *SCIENCE*

**OAT** The retina of a patient with gyrate atrophy of the choroid and retina of the eye caused by ornithine aminotransferase deficiency.

IMAGE: M. KAISER-KUPFER, NEI,NIH, & D. VALLE, JOHNS HOPKINS U.

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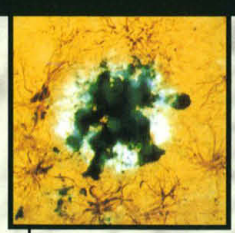

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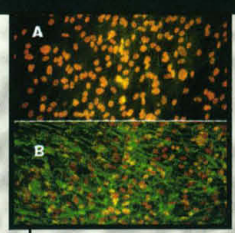


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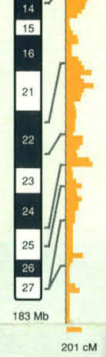


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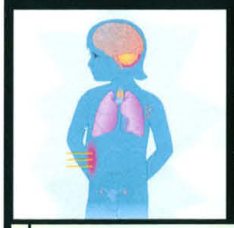

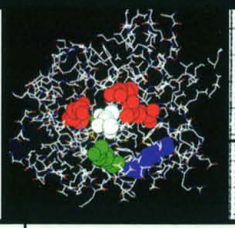

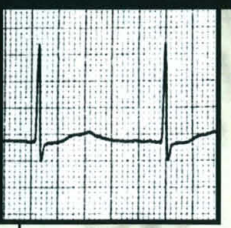

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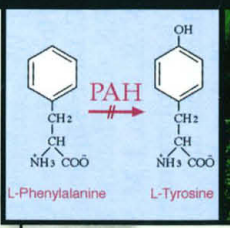



**HRAS**
Three-dimensional structure of Ras, the product of an oncogene that is mutated in many human cancers.

IMAGE: M. BOGUSKI, NCBI

**LQT1**
Portion of an EKG used to diagnose long-QT syndrome, an inherited cardiac arrythmia associated with mutations in an ion channel protein.

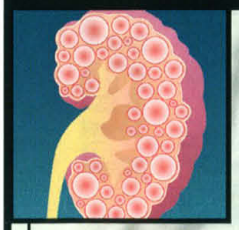
IMAGE: J. T. COCKERHAM, GEORGETOWN U. HOSP.


**PAH** Millions of newborns per year are screened for deficiency of phenylalanine hydroxylase to identify those susceptible to phenylketonuria.

IMAGE: G.SCHULER, NCBI

**ATM** Ataxia-telangiectasia is a multi-system disease characterized by cerebellar degeneration, immunodeficiency, radiosensitivity, and predisposition to cancer.

IMAGE: K. SUTLIFF, *SCIENCE*



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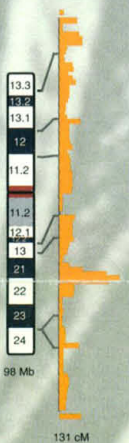
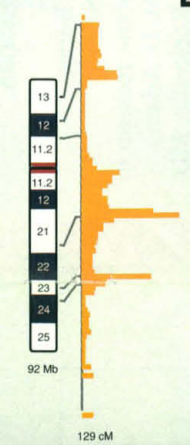
**PKD1** Adult polycystic kidney disease is characterized by large cysts; patients eventually die from renal failure or consequences of hypertension.

IMAGE: K. SUTLIFF, *SCIENCE*




**TP53** Yellow dots indicate some of the many types of tumors that carry mutations in the p53 gene.

IMAGE: K. SUTLIFF & C. FABER SMITH, REPRINTED FROM *SCIENCE*




**BRCA1** Distribution of mutations in the BRCA1 gene, which is associated with early-onset breast and ovarian cancer.

IMAGE: L. BRODY, NCHGR; S. GAYTHER, ADDENBROOKES HOSPITAL; BIC

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171 Mb

104 cM

accelerated aging associated with defects in a DNA unwinding enzyme.

IMAGE: WILLIAMS AND WILKINS PUBLISHING CO.

**MYC** A reciprocal chromosome translocation involving the c-myc oncogene is associated with Burkitt lymphoma.

IMAGE: G.SCHULER, NCBI

155 Mb

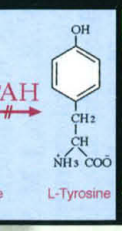
166 cM

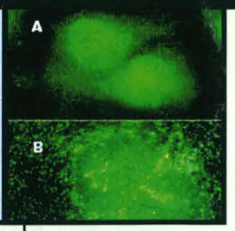
control.

IMAGE: NATIONAL INSTITUTE

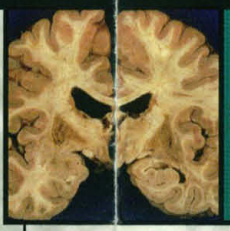
**TSC1** Microscopic section of angiom a benign tumor of the kidney preser patients with tuberous sclerosis.

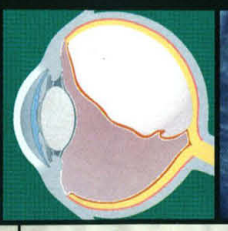
IMAGE: M. SMITH, JOHNS HOPKINS U.

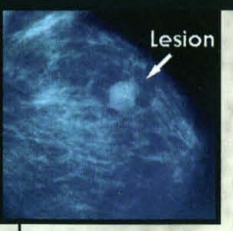



12








13

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SCHULER, NCBI

**PXR1** Peroxisomes are not detected in Zellweger syndrome fibroblasts (A) but can be reconstituted by transfection with the PXR1 gene (B).

IMAGE: N. BRAVERMAN, G. DODT, S. J. GOULD, & D. VALLE, JOHNS HOPKINS U.

143 Mb

169 cM

**RB1** Childhood tumors of the retina are associated with inactivation of the retinoblastoma gene.

IMAGE: K. SUTLIFF, *SCIENCE*

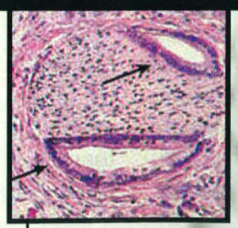
**BRCA2** Mammogram showing breast cancer.

IMAGE: P. CONNELLY, MIAMI VALLEY HOSP.

**ATP7B** In Wilson's disease, toxic levels of copper accumulate and damage many tissues and organs, including the basal ganglia of the brain.

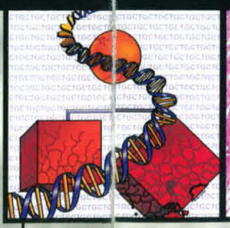
IMAGE: K. A. FOTH & R. E. SCHMIDT, WASH. U. SCH. MED.

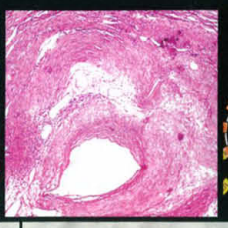
114 Mb

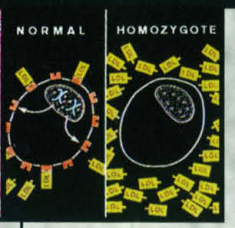


17

18








19

**DPC4** Loss of this gene causes pancreatic cancers to grow aggressively, as seen by tumor cells invading a nerve bundle.

IMAGE: R. H. HRUBAN, JOHNS HOPKINS HOSP.

85 Mb

124 cM

**DM** Myotonic dystrophy is a muscular disease associated with an unstable nucleotide repeat that is amplified between generations.

IMAGE: M. A. DE LA FLOR, REPRINTED FROM *SCIENCE*

**APOE** Atherosclerotic coronary artery disease is associated with the gene encoding apolipoprotein E, a ligand for the LDL receptor.

IMAGE: M. BOGUSKI, NCBI

**LDLR** Mutations in the receptor for low density lipoprotein lead to extracellular accumulation of cholesterol and heart attacks.

IMAGE: J. GOLDSTEIN & M.S. BROWN, U. TEXAS SW MED. CTR.; BY PERMISSION, EXCERPTA MEDICA INC.

129 cM

67 Mb

control.

IMAGE: NATIONAL CANCER INSTITUTE

ection of angiomyolipoma, e kidney present in many us sclerosis.

PKINS U.

145 Mb

167 cM

of multiple endocrine neoplasia (type 2A) is characterized by tumors in the pituitary, thyroid, parathyroid, and adrenal glands.

IMAGE: K. SUTLIFF, *SCIENCE*

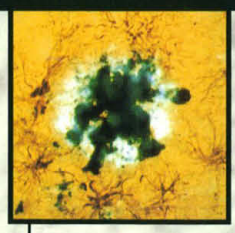
**OAT** The retina of a patient with gyrate atrophy of the choroid and retina of the eye caused by ornithine aminotransferase deficiency.

IMAGE: M. KAISER-KUPFER, NEI,NIH, & D. VALLE, JOHNS HOPKINS U.

144 Mb

182 cM

# 13



**AD3** Neuritic plaques and neurofibrillary tangles are the major microscopic abnormalities in the brains of patients with Alzheimer's disease.

IMAGE: P. McGEER, UNIV. OF BRITISH COLUMBIA

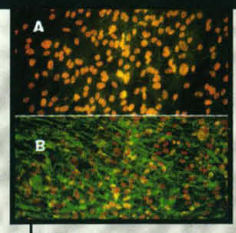
114 Mb

118 cM

109 Mb

129 cM

# 14




**FBN1** Extracellular fibrillin-1 microfibrils (stained green) are absent in Marfan syndrome (A) compared to a control sample (B).

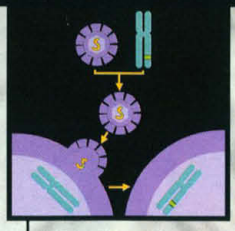
IMAGE: H. DIETZ, JOHNS HOPKINS U.; BY PERMISSION, ELSEVIER SCIENCE IRELAND LTD.

106 Mb

110 cM

# 15

# 19



**ADA** Gene therapy has been attempted to treat severe combined immunodeficiency caused by a missing enzyme, adenosine deaminase.

IMAGE: NATIONAL CANCER INSTITUTE

67 Mb

110 cM

72 Mb

97 cM

# 20

**SOD1** Amyotrophic lateral sclerosis, known as Lou Gehrig's disease, is caused in some cases by a deficiency in the enzyme superoxide dismutase.

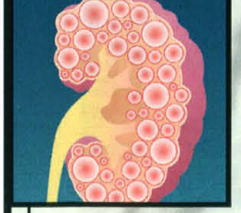
IMAGE: T. E. SMITH, CROFTON, MD

50 Mb

60 cM

# 21

GENOME



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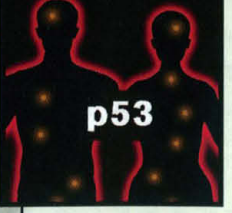



17

**PKD1** Adult polycystic kidney disease is characterized by large cysts; patients eventually die from renal failure or consequences of hypertension.

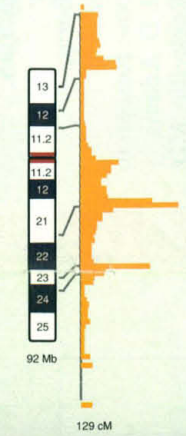
IMAGE: K. SUTLIFF, *SCIENCE*

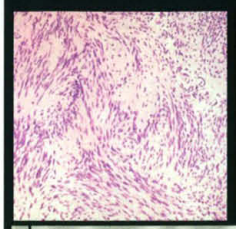

**TP53** Yellow dots indicate some of the many types of tumors that carry mutations in the p53 gene.

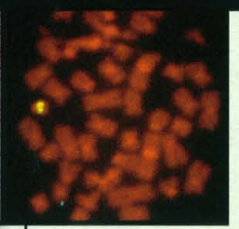
IMAGE: K. SUTLIFF & C. FABER SMITH, REPRINTED FROM *SCIENCE*

**BRCA1** Distribution of mutations in the BRCA1 gene, which is associated with early-onset breast and ovarian cancer.

IMAGE: L. BRODY, NCHGR; S. GAYTHER, ADDENBROOKES HOSPITAL; BIC





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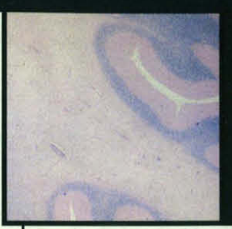
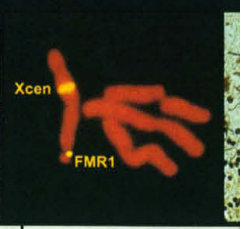


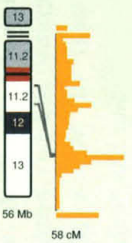



**NF2** Microscopic section of a schwannoma, a tumor commonly found in patients with neurofibromatosis, type 2.

IMAGE: K. A. ROTH & R. E. SCHMIDT, WASH. U. SCH. MED.

**DGS/VCFS** Deletion of genes in DiGeorge syndrome is visualized by a fluorescent signal on only one of the two copies of chromosome 22.

IMAGE: D. I. WILSON, UNIVERSITY OF NEWCASTLE UPON TYNE; BY PERMISSION BMJ PUBLISHING GROUP




**ALD** Myelin-stained section of brain in adrenoleukodystrophy, characterized by defective catabolism of long-chain fatty acids.

IMAGE: K. A. ROTH & R. E. SCHMIDT, WASH. U. SCH. MED.

**FMR1** An unstable nucleotide repeat is associated with a common form of mental retardation known as the Fragile X syndrome.

IMAGE: S. WARREN, EMORY U. SCH. MED.

**Gene Specific STSs and Matching cDNA Clones for Each Mapped Transcript • BAC and YAC Librari**
**Radiation Hybrid Mapping Panels • I.M.A.G.E. Consortium (LLNL) cDNA Cl**

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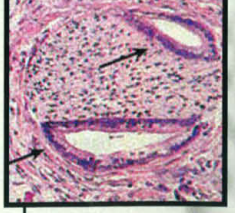

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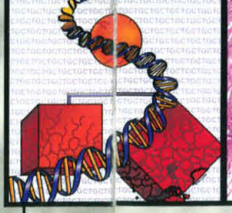
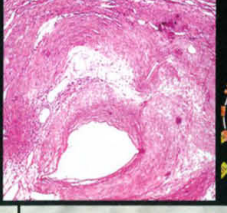
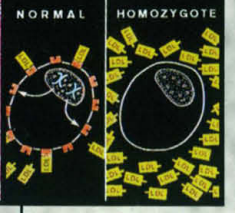


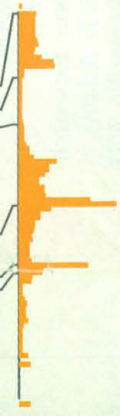





19

**DPC4** Loss of this gene causes pancreatic cancers to grow aggressively, as seen by tumor cells invading a nerve bundle.

IMAGE: R. H. HRUBAN, JOHNS HOPKINS HOSP.





**DM** Myotonic dystrophy is a muscular disease associated with an unstable nucleotide repeat that is amplified between generations.

IMAGE: M. A. DE LA FLOR, REPRINTED FROM *SCIENCE*

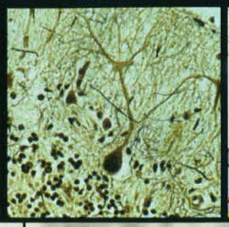
**APOE** Atherosclerotic coronary artery disease is associated with the gene encoding apolipoprotein E, a ligand for the LDL receptor.

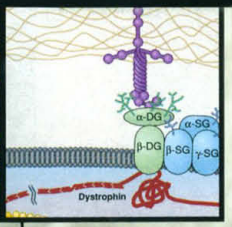
IMAGE: M. BOGUSKI, NCBI

**LDLR** Mutations in the receptor for low density lipoprotein lead to extracellular accumulation of cholesterol and heart attacks.

IMAGE: J. GOLDSTEIN & M.S. BROWN, U. TEXAS SW MED. CTR.; BY PERMISSION, EXCERPTA MEDICA INC.








X

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An unstable
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non form of
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as the
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WARREN,
. SCH. MED.

**ATP7A** Abnormal Purkinje cell dendrites in the brain of a patient with Menkes disease.

IMAGE: K. A. ROTH & R. E. SCHMIDT, WASH. U. SCH. MED.

**DMD** Defects in the dystrophin gene cause Duchenne muscular dystrophy, a fatal progressive degeneration of muscle tissue.

IMAGE: R. WORTON, OTTAWA GEN. HOSP., K. SUTLIFF REPRINTED FROM *SCIENCE*


**TDF** Testis-determining factor (also known as SRY) binds to DNA and regulates genes controlling the development of the testis.

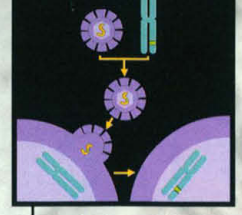
IMAGE: G.SCHULER, NCBI


**Legend**

Physical and genetic lengths are given under the ideogra and histograms respectively. Markers mapping telomeric the most distal reference genetic markers are placed in separate bins above and below each histogram.

— 10 genes per cM

19



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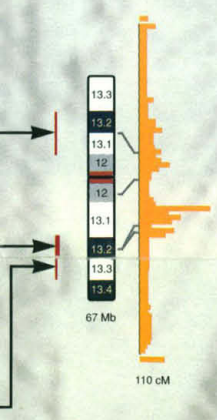
21

**ADA** Gene therapy has been attempted to treat severe combined immunodeficiency caused by a missing enzyme, adenosine deaminase.

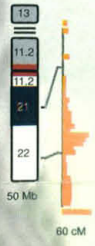
IMAGE: NATIONAL CANCER INSTITUTE





**SOD1** Amyotrophic lateral sclerosis, known as Lou Gehrig's disease, is caused in some cases by a deficiency in the enzyme superoxide dismutase.

IMAGE: T. E. SMITH, CROFTON, MD

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gram.

**Credits:** **Science Coordinator:** Barbara R. Jasny **Authors:** G. D. Schuler, M. S. Boguski, National Center for Biotechnology Information, Bethesda, MD, USA T. J. Hudson, L. Hui, J. Ma, A. B.Castle, X. Wu, J. Silva, H. C. Nusbaum, B. B. Birren, D. K. Slonim, S. Rozen, L. D. Stein, D. Page, E. S. Lander, Center for Genome Research, Whitehead Institute, Cambridge, MA, USA; E. A. Stewart, A. Aggarwal, E. Bajorek, S. Brady, A. Chu, N. Fang, D. Hadley, M. Harris, S. Hussain, A. Maratukulam, S. Perkins, M. Piercy, F. Qin, T. Reif, C. Sanders, X. She, W.-L. Sun, P. Tabar, S. Voyticky, C. Mader, K. B. McKusick, J.-B. Fan, S. Cowles, J. Quackenbush, D. Vollrath, R. M. Myers, D. R. Cox, Stanford Human Genome Center, Stanford, CA USA; A. Butler, C. Clee, T. Dibling, C. East, C. Edwards, C. Garrett, L. Green, P. Harrison, A. Hicks, E. Holloway, S. Ranby, A. MacGilvery, A. Mungall, A. Peck, T. Wilmer, C. Soderlund, K. Rice, I. Dunham, D. Bentley, P. Deloukas, The Sanger Center, Cambridge, UK; G.Gyapay, N. Chiannilkulchai, C. Fizames, S. Bentolila, S. Duprat, N. Vega-Czarny, D. Muselet, N. Drouot, J. Morissette, J. Beckmann, J. Weissenbach, Généthon, CNRS, Evry, FRANCE; J. Morissette, Centre de Recherche du Centre Hospitalier de l'Université Laval, Québec, CANADA; M. R. James, R. E. White, T. Thangarajah, C. Louis-Dit-Sully, P. J. R. Day, Wellcome Trust Centre for Human Genetics, Oxford, UK; P.N. Goodfellow, K. Schmitt, Cambridge University, Cambridge, UK; N. A. R. Walter, R. Berry, K. R. Iorio, J. M. Sikela, University of Colorado Health Sciences Center, Denver, CO, USA; M. H. Polymeropoulos, R. Torres, S. E. Ide, A. Dehejia, National Center for Human Genome Research, Bethesda, MD, USA; R. Houlgatte, C. Auffray, Genexpress, CNRS, Villejuif, FRANCE; M. D. Adams, C. Phillips, R. Brandon, M. Sandusky, J. C. Venter, The Institute for Genomic Research, Rockville, MD, USA; N. Seki, T. Nagase, K. Ishikawa, N. Nomura, Kazusa DNA Research Institute, Kisarazu, JAPAN; P. Rodriguez-Tome, The EMBL Outstation, The European Bioinformatics Institute, Cambridge, UK; T. C. Matise, The Rockefeller University, New York, NY, USA; W. Y. Lee, K. A. Swanson, J. R. Hudson Jr., Research Genetics, Huntsville, AL, USA; **Reviewers:** R. Kucherlapati, Albert Einstein College of Medicine, New York, NY, USA; V. McKusick, Johns Hopkins Hospital, Baltimore, MD, USA. **Art Director,** Amy Decker Henry; **Design,** Tracy Keaton-Drew; **Production,** Linda Hannigan.