Figure 9.15 TD Gelehrter, FS Collins, D Ginsburg. 
Figure 9.31  TD Gelehrter, FS Collins, D Ginsburg. Principles of Medical Genetics. 1997.
NORMAL

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CYSTIC FIBROSIS

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</tbody>
</table>
A SAMPLING OF COOL THINGS ABOUT THE GENOME

Humans have fewer genes than expected

Human genes make more proteins than those of other critters

Male mutation rate is twice that of females

“Junk” DNA contains the remnants and raw materials for evolution

Big Events in April 2003

• 50th Anniversary of Watson and Crick
• Completion of the sequence of all the human chromosomes
• Announcement of bold new research plan for genomics
**Fulfilling the Promise of Genomics for Better Health**

Positional cloning of a gene for a highly penetrant Mendelian disorder is now straightforward –

but tracking genetic susceptibility factors for non-Mendelian disorders continues to be vexing.
Finding genetic variants that contribute to common disease is critically important. Here association (case control) studies have greater power than family linkage studies.

N. Risch and K. Merikangas.
Science 273: 1516-1517, 1996

Sequence from chromosome 7

Three variants are present
These three variants could theoretically occur in 8 different haplotypes

...C...A...A...
...C...A...G...
...C...C...A...
...C...C...G...
...T...A...A...
...T...A...G...
...T...C...A...
...T...C...G...

But in practice, only two are observed

...C...A...A...
...C...A...G...
...C...C...A...  
...C...C...G...
...T...A...A...
...T...A...G...
...T...C...A...
...T...C...G...
These three variants are said to be in linkage disequilibrium

...C...A...A...
...C...A...G...
...C...C...A...
...C...C...G...
...T...A...A...
...T...A...G...
...T...C...A...
...T...C...G...
A Haplotype Map of Human Variation

- Goal is to define all common haplotypes in the human genome
- Genome-wide association studies can then be done with 30 – 50 times less work
- Project was initiated in October 2002, using samples of African, Asian, and European origin

Association of the ADAM33 gene with asthma and bronchial hyperresponsiveness

Paul Van Eerdewegh*,†, Randall D. Little*†, Josée Dupuis*†,
Richard G. Del Mastro*†, Kathy Falls*, Jason Simon*†, Dana Torrey*†,
Sunil Pandit†, Joyce McKenny†, Karen Braunschweiger†, Alison Walsh†,
Ziyong Liu*, Brooke Hayward*, Colleen Folz*†, Susan P. Manning*,
Alicia Bawa*, Lisa Saracino*, Michelle Thackston*,
Youssef Benchekroun*, Neva Capparell*, Mei Wang*, Ron Adair*,
Yun Feng*, JoAnn Dubois*, Michael G. FitzGerald*, Hui Huang*,
René Gibson*, Kristina M. Allen*, Alex Pedan†, Melvyn R. Danzig‡,
Shelby P. Umland‡, Robert W. Egan§, Francis M. Cuss§, Steuart Rorke||,
Joanne B. Clough||, John W. Holloway||, Stephen T. Holgate||
& Tim P. Keith†

With these resources, it is likely that many of the major contributing genes for diabetes, heart disease, cancer, mental illness, Alzheimer’s disease, Parkinson’s disease, asthma, etc. will be identified within the next 5 – 10 years.
Gleevec™ – Specifically Targets An Abnormal Protein, Blocking Its Ability To Cause Chronic Myeloid Leukemia

Chromosome 9;22 translocation → Bcr-Abl fusion protein → CML

Gleevec™ → Bcr-Abl fusion protein → Normal
Ethical, Legal, and Social Implications

An integral component of the Human Genome Project

Will effective legislative solutions to genetic discrimination be found?
Can health care providers and the public become genetically literate in time?

Will the benefits of the advances in genetics only be available to a privileged few?
Will knowledge of human variation reduce prejudice, or increase it?
Will we arrive at consensus about the limits of genetic technology for trait enhancement?

Will we succumb to genetic determinism, neglecting the role of the environment, and undervaluing the power of the human spirit and our need for God?