

Genomics, Medicine, and Society

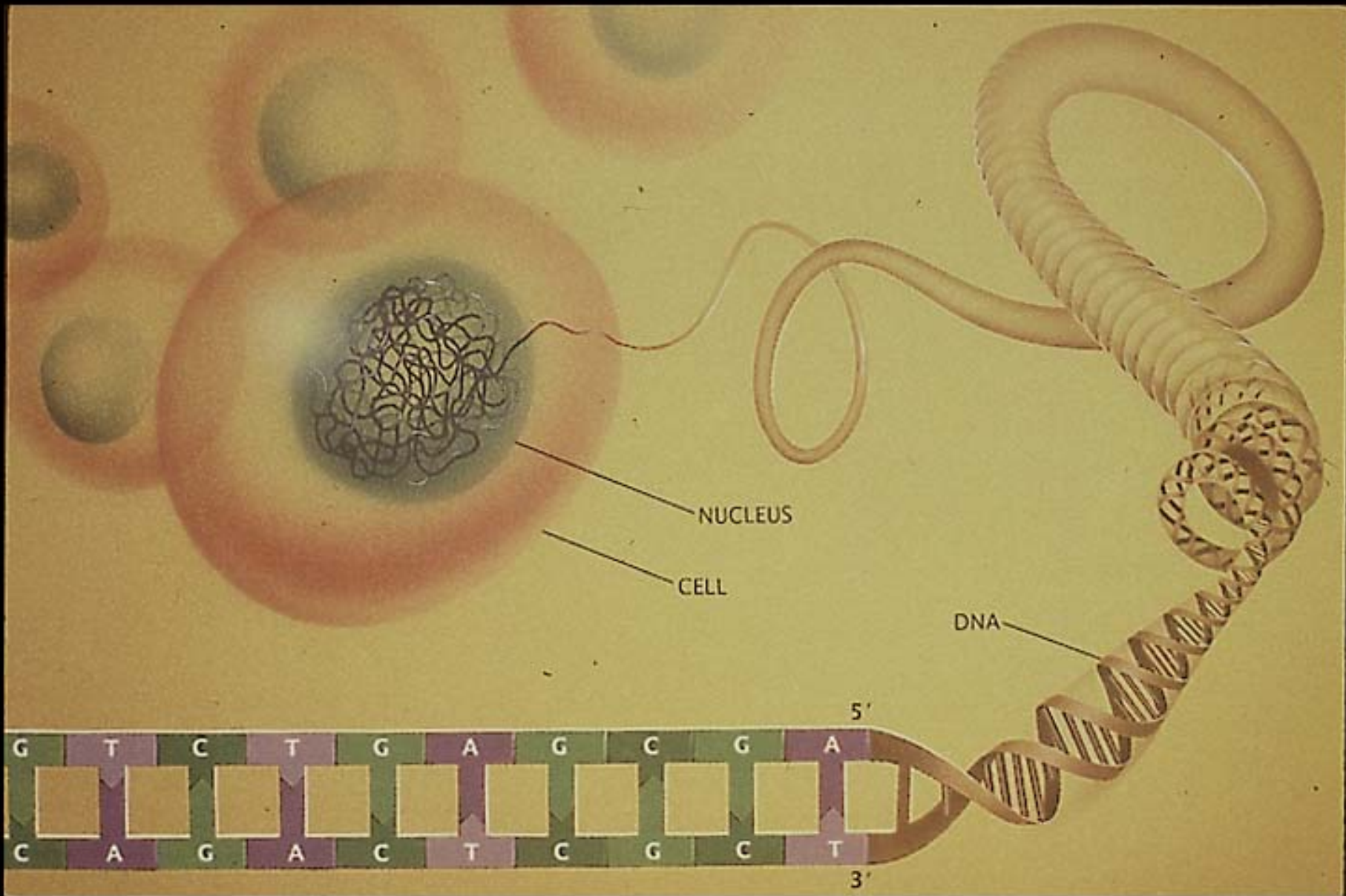
Francis S. Collins, M.D., Ph.D.

National Human Genome Research Institute

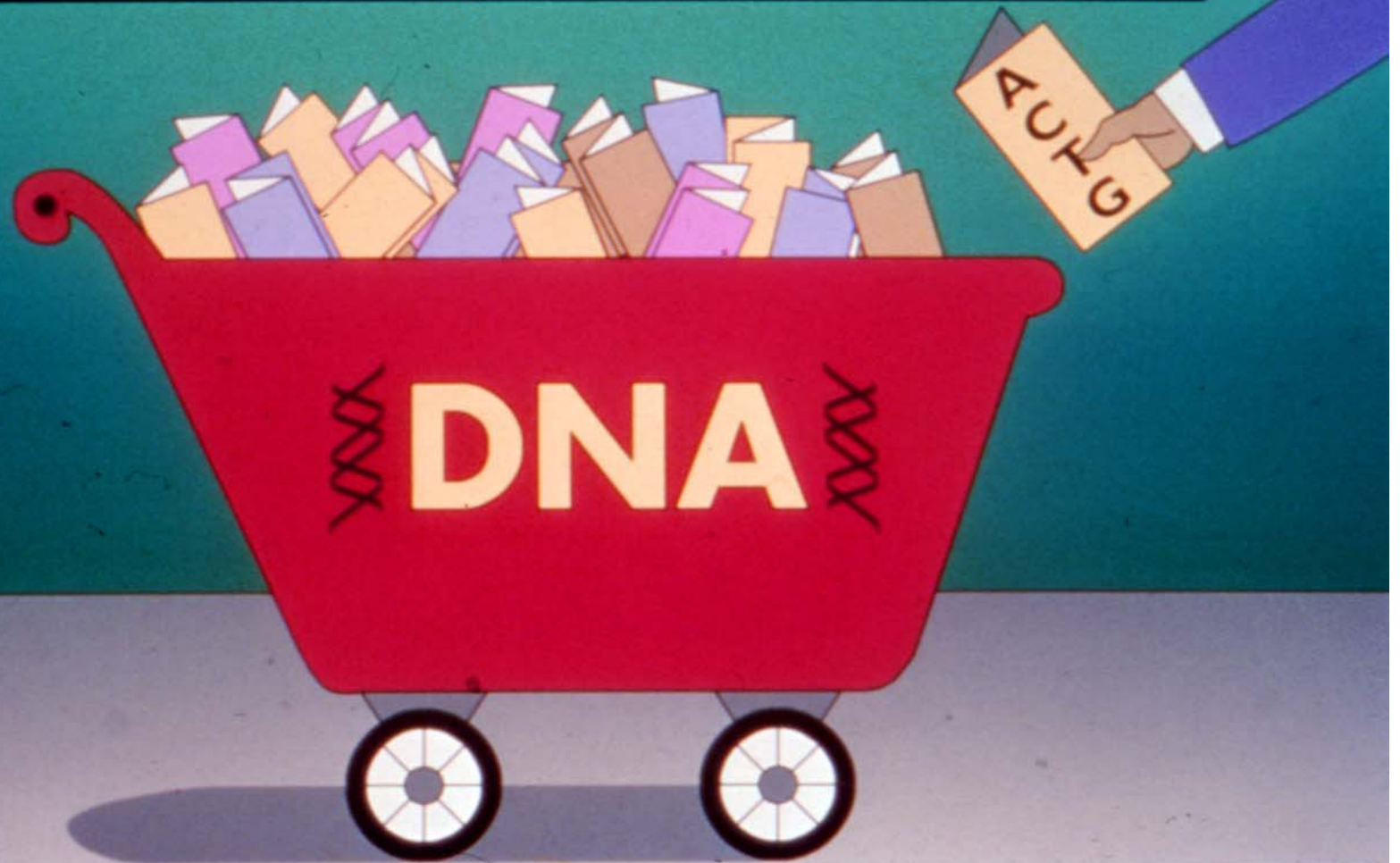
Presentation for House of Lords Visit

June 4, 2008





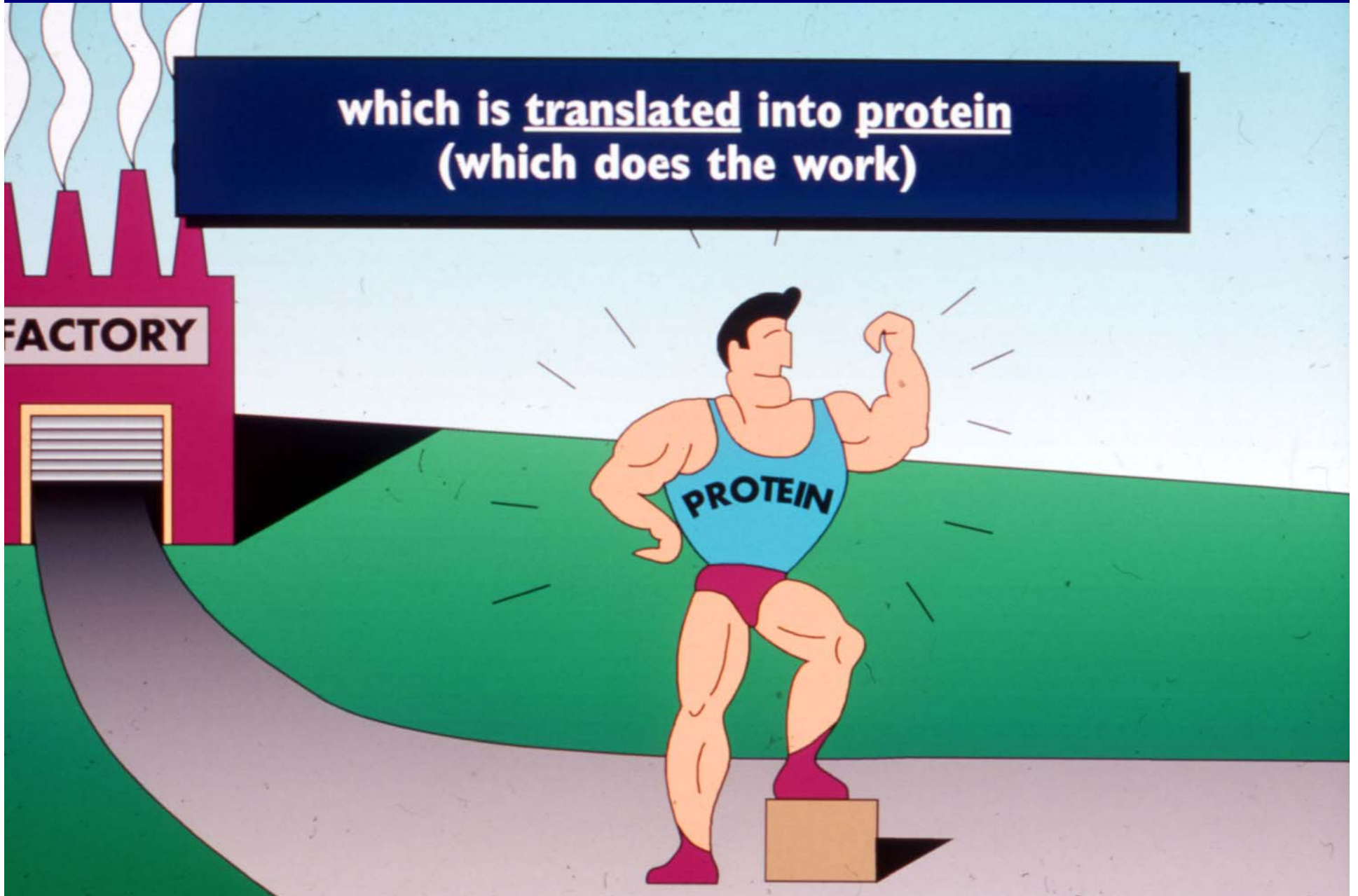
Instructions are transcribed into RNA



RNA is a messenger that carries the message



which is translated into protein
(which does the work)



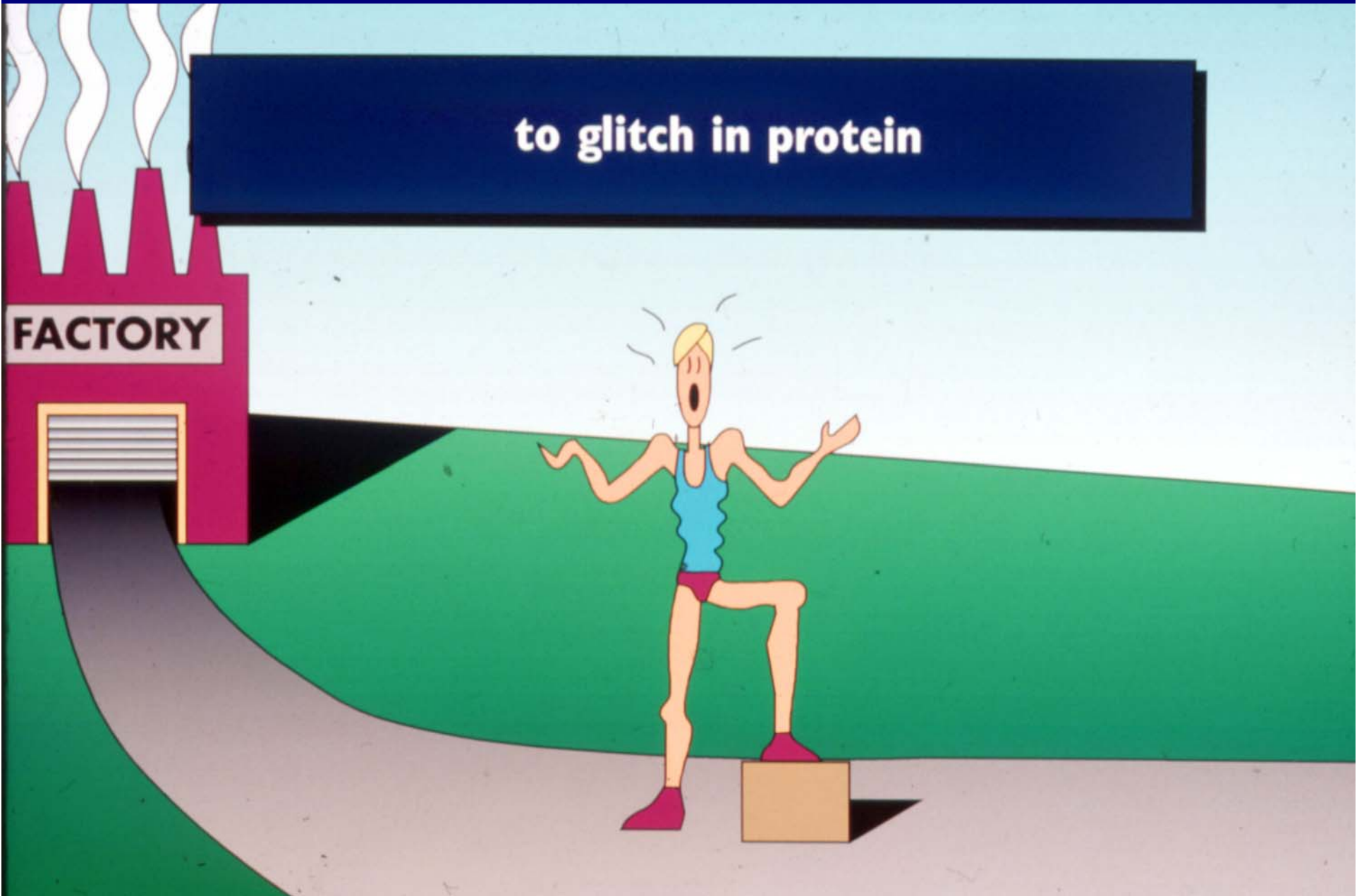
Misspelling of DNA...



Leads to glitch in RNA...



to glitch in protein



April, 1953



April, 2003

No. 4356 April 25, 1953 NATURE

MOLECULAR STRUCTURE OF
NUCLEIC ACIDS
A Structure for Deoxyribose Nucleic Acid



J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the
Study of the Molecular Structure of
Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.



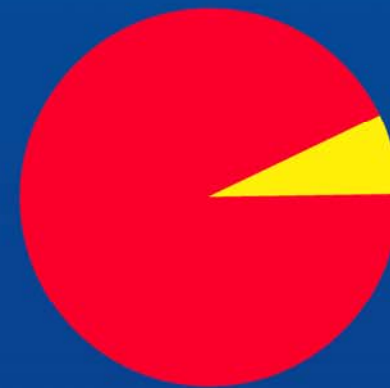
Virtually All Diseases (Except Maybe Trauma) Have a Genetic Component



Cystic fibrosis



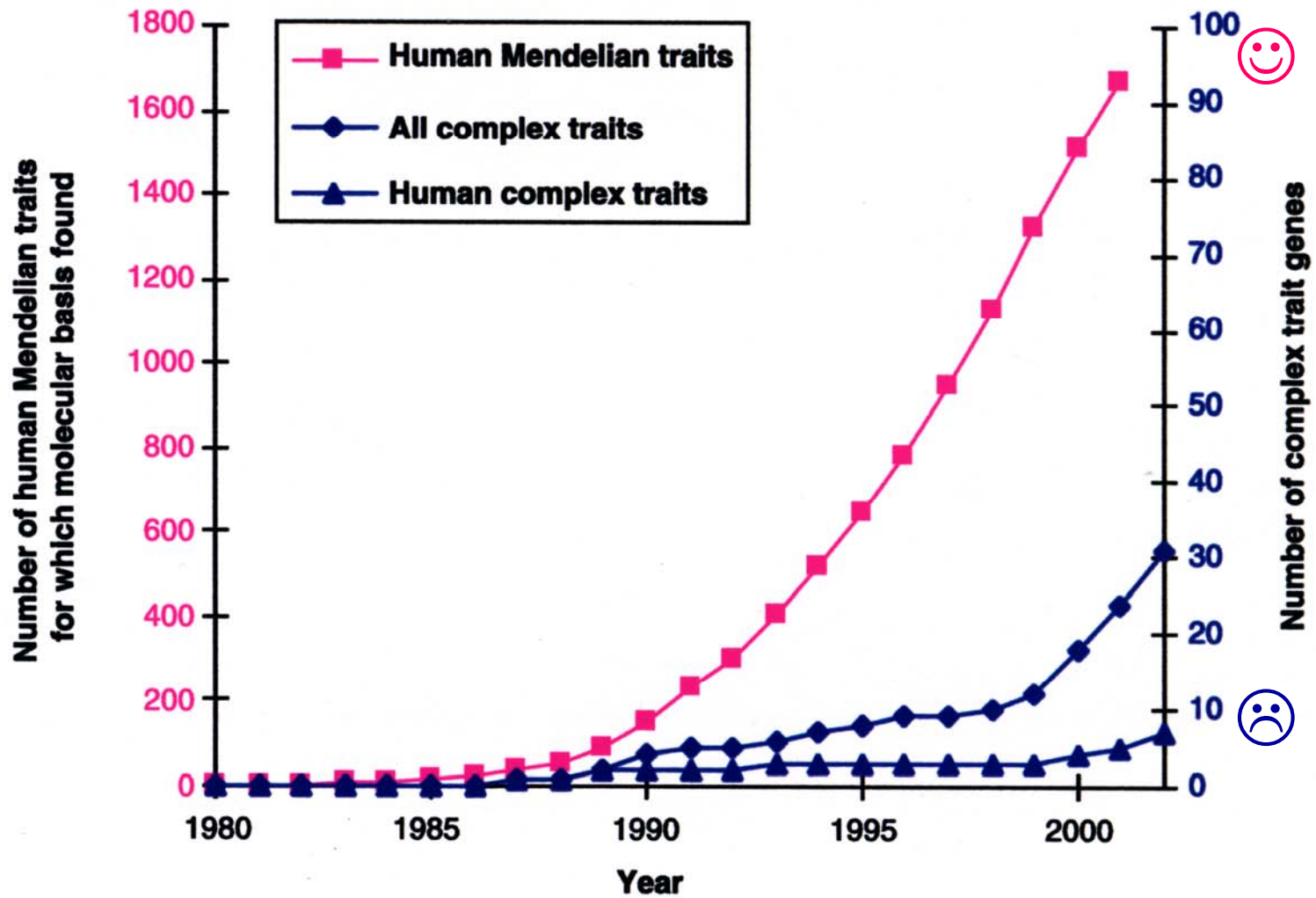
Adult onset diabetes



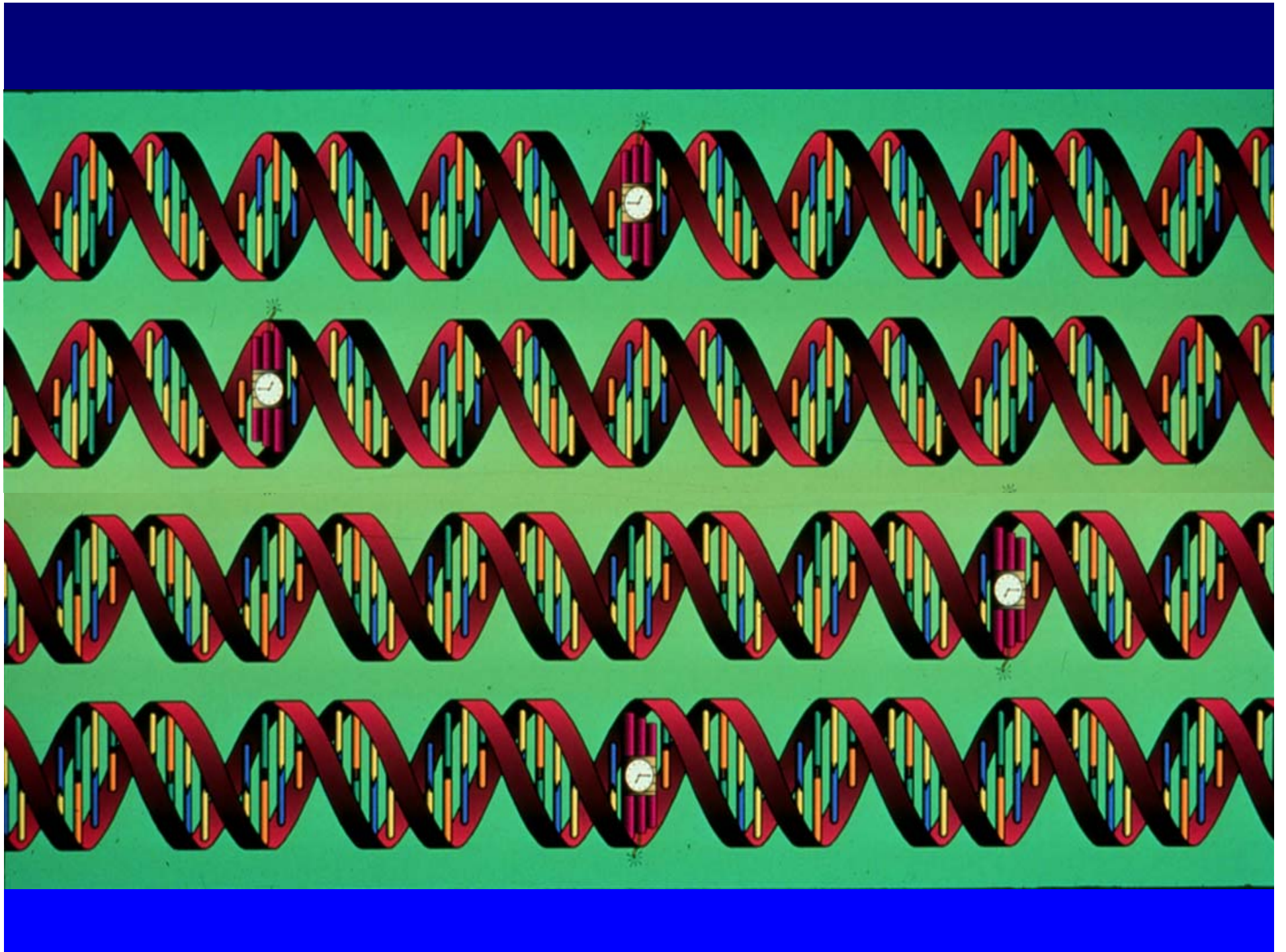
AIDS

Genetic Component 

Environmental Component 



Glazier et al., Science 298:2345-9, 2002



C

G

A

C

T

C

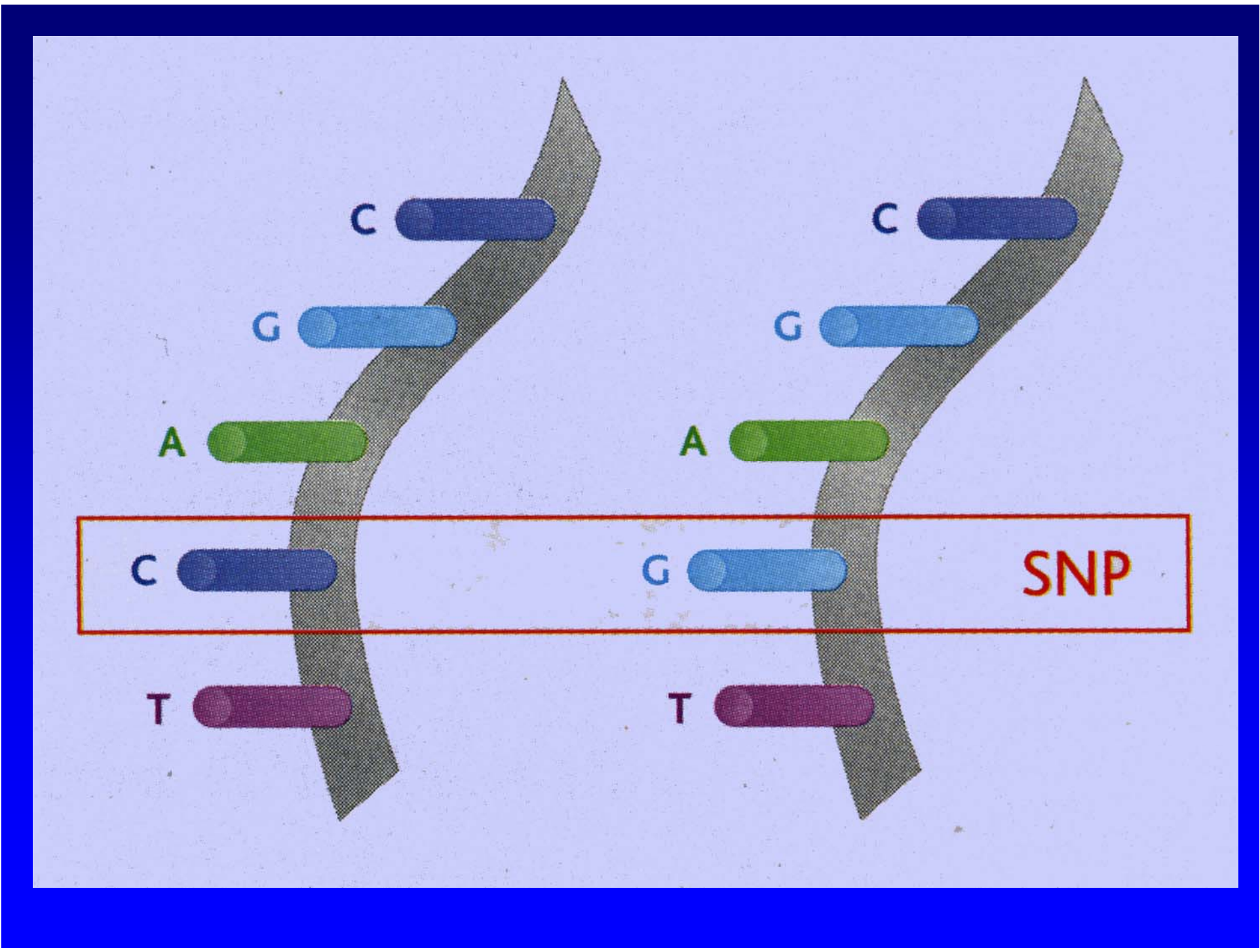
G

A

G

T

SNP



SNP A

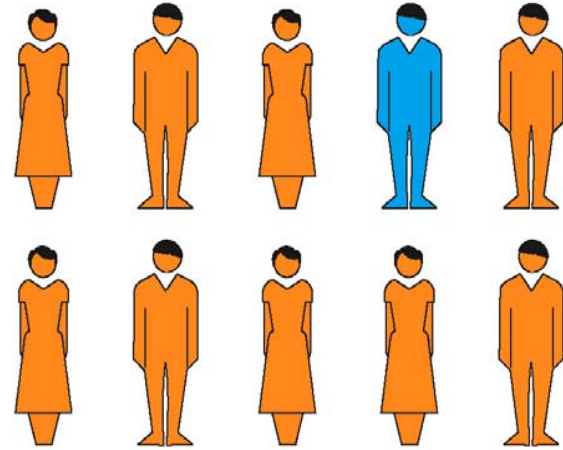


Diabetes

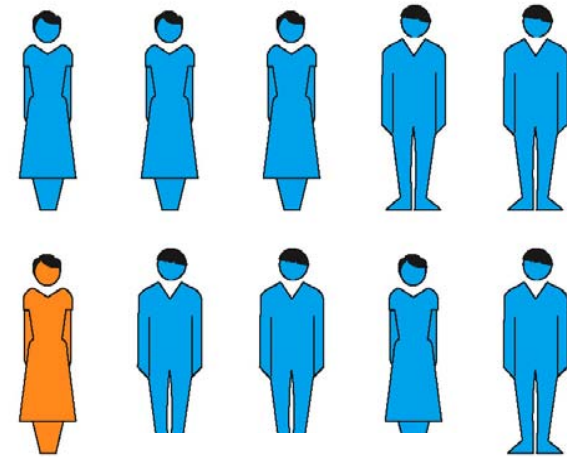


Unaffected

SNP B



Diabetes



Unaffected



“Genome Wide Association” Approach to Common Disease: The View from 2002

- **Identify all 10 million common SNPs**
- **Collect 1000 cases and 1000 controls**
- **Genotype all DNAs for all SNPs**
- **That adds up to 20 billion genotypes**
- **At 50 cents a genotype, that’s \$10 billion for each disease – completely out of the question**

Sequence from chromosome 7

GAAATAATTAATGTTTTCTTCCTTCTCCTATTTTGCCTTTACTTCAATTTATTTATTTATTATTAATATTATTATTTTTG
AGACGGAGTTTCACTCTTGTGGCCAACCTGGAGTGCAGTGGCGTGATCTCAGCTCACTGCACACTCCGCTTTCCTGG
TTTCAAGCGATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGACTACAGTCACACACCACCACGCCCGGCTAATTTTTG
TATTTTAGTAGAGTTGGGGTTTACCATGTTGGCCAGACTGGTCTCGAACTCCTGACCTTGTGATCCGCCAGCCTCT
GCCTCCCAAAGAGCTGGGATTACAGGCGTGAGCCACCGCGCTCGGCCCTTGCATCAATTTCTACAGCTTGTTCCTT
TGCCTGGACTTTACAAGTCTTACCTTGTCTGCCTTCAGATATTTGTGTGGTCTCATTCTGGTGTGCCAGTAGCTAAAA
ATCCATGATTTGCTCTCATCCACTCCTGTTGTTTCATCTCCTCTTATCTGGGGTCCACACTATCTCTTCGTGATTGCATTC
TGATCCCCAGTACTTAGCATGTGCGTAACAACCTCTGCCTCTGCTTCCAGGCTGTTGATGGGGTGTCTGTTTCATGCCT
CAGAAAAATGCATTGTAAGTTAAATTATTAAGATTTTAAATATAGGAAAAAAGTAAGCAAACATAAGGAACAAAAAG
GAAAGAACATGTATTCTAATCCATTATTTATTATACAATTAAGAAATTTGGAAACTTTAGATTACACTGCTTTTAGAGAT
GGAGATGTAGTAAGTCTTTTACTCTTTACAAAATACATGTGTTAGCAATTTTGGGAAGAATAGTAACCTCACCCGAACA
GTGTAATGTGAATATGCACTTACTAGAGGAAAGAAGGCACTTGAAAACATCTCTAAACCGTATAAAAACAATTACA
TCATAATGATGAAAACCCAAGGAATTTTTTTAGAAAACATTACCAGGGCTAATAACAAAGTAGAGCCACATGTCATTT
ATCTTCCCTTTGTGTCTGTGTGAGAATTCTAGAGTTATATTTGTACATAGCATGGAAAAATGAGAGGCTAGTTTATCAA
CTAGTTCATTTTTAAAAGTCTAACACATCCTAGGTATAGGTGAACTGTCCTCCTGCCAATGTATTGCACATTTGTGCC
AGATCCAGCATAGGGTATGTTTGCCATTTACAAACGTTTATGTCTTAAGAGAGGAAATATGAAGAGCAAAACAGTGCA
TGCTGGAGAGAGAAAGCTGATACAAATATAAATGAAACAATAATTGGAAAAATTGAGAACTACTCATTTTCTAAATT
ACTCATGATTTTCTAGAAATTTAAGTCTTTTAAATTTTTGATAAATCCCAATGTGAGACAAGATAAGTATTAGTGATGGT
ATGAGTAATTAATATCTGTTATATAATATTCATTTTCATAGTGAAGAAATAAAATAAAGGTTGTGATGATTGTTGATTA
TTTTTTCTAGAGGGGTTGTCAGGGAAAGAAATTGCTTTTTTTCATTCTCTTTCCACTAAGAAAGTTCAACTATTAATT
TAGGCACATACAATAACTTCCATTCTAAAATGCCAAAAGGTAATTTAAGAGACTTAAACTGAAAAGTTTAAAGATA
GTCACACTGAACTATATTAATAATCCACAGGGTGGTTGGAAGTGGCCTTATATTAAGAGGCTAAAAATTGCAATA
AGACCACAGGCTTTAAATATGCTTTTAAACTGTGAAAGGTGAACTAGAATGAATAAAATCCTATAAATTTAAATCAA
AAGAAAGAAACAACTAAGAAATTAAGTTAATATACAAGAATATGGTGGCCTGGATCTAGTGAACATATAGTAAAGA
TAAACAGAATATTTCTGAAAATCCTGAAAATCTTTTGGGCTAACCTGAAAACAGTATATTTGAAACTATTTTTAAA

Three single nucleotide polymorphisms (SNPs) are present

Sequence from chromosome 7

GAAATAATTAATGTTTTCTTCCTTCTCCTATTTTGTCTTTACTTCAATTTATTTATTTATTATTAATATTATTATTTTTG
AGACGGAGTTTCACTCTTGTGGCCAACCTGGAGTGCAGTGGCGTGATCTCAGCTCACTGCACACTCCGCTTTC**C/T**G
TTTCAAGCGATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGACTACAGTCACACACCACCACGCCCGGCTAATTTTTG
TATTTTAGTAGAGTTGGGGTTTCACCATGTTGGCCAGACTGGTCTCGAACTCCTGACCTTGTGATCCGCCAGCCTCT
GCCTCCCAAAGAGCTGGGATTACAGGCGTGAGCCACCGCGCTCGGCCCTTTCATCAATTTCTACAGCTTGTTCCTT
TGCCTGGACTTTACAAGTCTTACCTTGTTCCTCAGATATTTGTGTGGTCTCATTCTG**G/T**GTGCCAGTAGCTAAAA
ATCCATGATTTGCTCTCATCCACTCCTGTTGTTTCATCTCCTCTTATCTGGGGT**CAC/A**CTATCTCTTCGTGATTGCATTC
TGATCCCCAGTACTTAGCATGTGCGTAACAACCTCTGCCTCTGCTTCCAGGCTGTTGATGGGGTGTCTGTTTCATGCCT
CAGAAAAATGCATTGTAAGTTAAATTATTAAGATTTTAAATATAGGAAAAAGTAAGCAAACATAAGGAACAAAAAG
GAAAGAACATGTATTCTAATCCATTATTTATTATACAATTAAGAAATTTGGAAACTTTAGATTACACTGCTTTTAGAGAT
GGAGATGTAGTAAGTCTTTTACTCTTTACAAAATACATGTGTTAGCAATTTTGGGAAGAATAGTA**ACT**CACCCGAACA
GTGTAATGTGAATATGCACTTACTAGAGGAAAGAAGGCACTTGAAAACATCTCTAAACCGTATAAAAACAATTACA
TCATAATGATGAAAACCCAAGGAATTTTTTTAGAAAACATTACCAGGGCTAATAACAAAGTAGAGCCACATGTCATTT
ATCTTCCCTTTGTGTCTGTGTGAGAATTCTAGAGTTATATTTGTACATAGCATGGAAAAATGAGAGGCTAGTTTATCAA
CTAGTTCATTTTTAAAGTCTAACACATCCTAGGTATAGGTGA**ACT**GTCCTCCTGCCAATGTATTGCACATTTGTGCC
AGATCCAGCATAGGGTATGTTTGCCATTTACAAACGTTTATGTCTTAAGAGAGGAAATATGAAGAGCAAAACAGTGCA
TGCTGGAGAGAGAAAGCTGATACAAATATAAATGAAACAATAATTGGAAAAATTGAGAACTACTCATTCTTCTAAATT
ACTCATGATTTTTCTAGAAATTTAAGTCTTTTAATTTTTGATAAATCCCAATGTGAGACAAGATAAGTATTAGTGATGGT
ATGAGTAATTAATATCTGTTATATAATATTCATTTTCATAGTGGAAGAAATAAAATAAAGGTTGTGATGATTGTTGATTA
TTTTTTCTAGAGGGGTTGTCAGGGAAAGAAATTGCTTTTTTTTATTCTCTCTTTCCACTAAGAAAGTTCAACTATTAATT
TAGGCACATACAATAACTCCATTCTAAAATGCCAAAAGGTAATTTAAGAGACTTAA**ACT**GAAAAGTTTAAGATA
GTCACACTGA**ACT**TATTA**AAAAAT**CCACAGGGTGGTTGGA**ACT**AGGCCTTATATTAAGAGGCTAAA**AAATT**GCAATA
AGACCACAGGCTTTAAATAT**G**GCTTTAA**ACT**GTGAAAGGTGAA**ACT**AGAATGAATAAAATCCTATAAATTTAAATCAA
AAGAAAGAAACAA**ACT****A/G**AAATTAAGTTAATATACAAGAATATGGTGGCCTGGATCTAGTGAACATATAGTAAAGA
TAAACAGAATATTTCTGAAAATCCTGAAAATCTTTTGGGCTAACCTGAAAACAGTATATTTGAAACTATTTTTAA

Are the SNPs correlated with their neighbors?

These three SNPs 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...

27 October 2005 | www.nature.com/nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

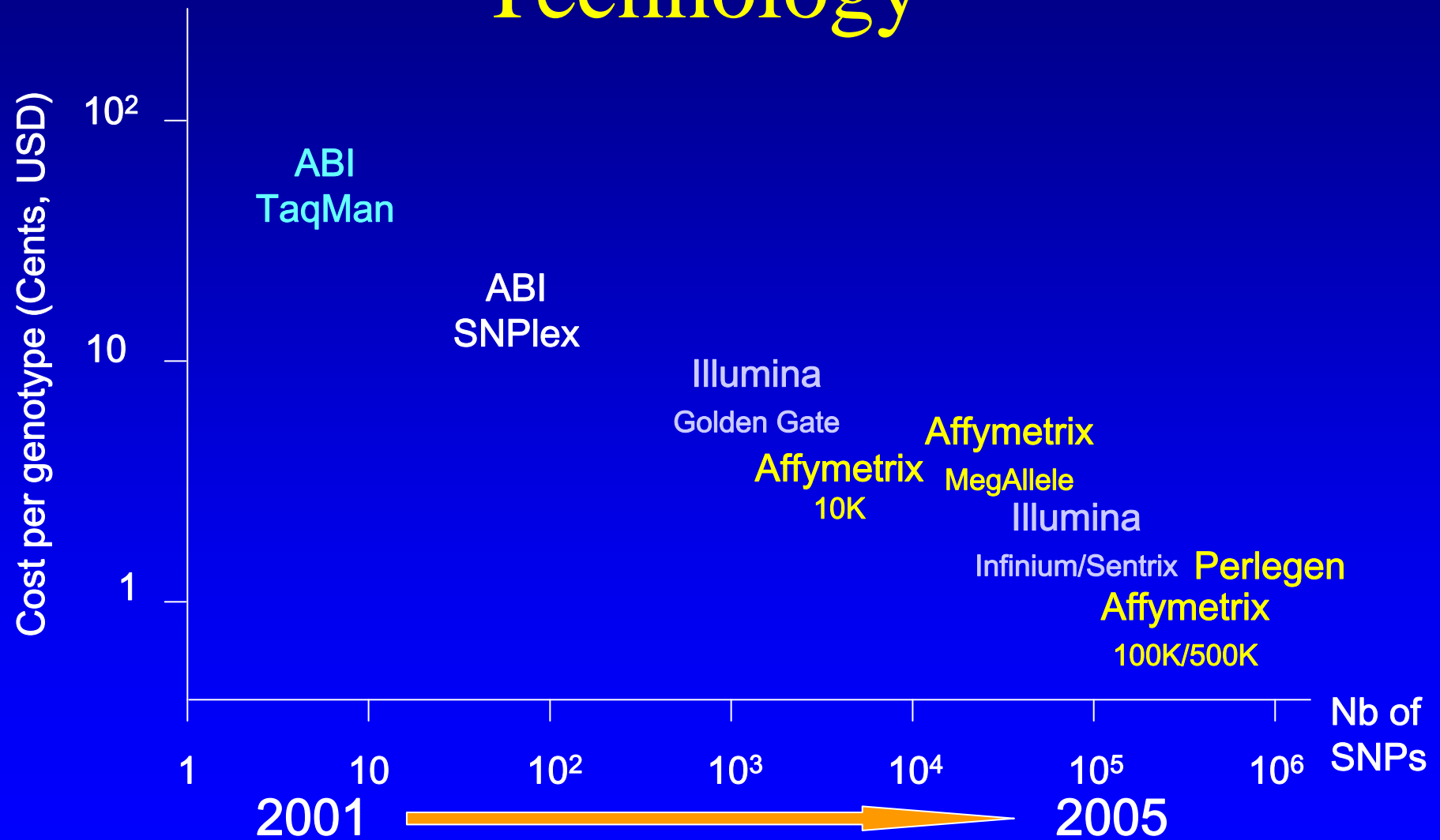
nature



THE HAPMAP PROJECT

Chapter and verse on
human genetic variation

Progress in Genotyping Technology



Courtesy S. Chanock, NCI

Genome Wide Association Approach to Common Disease: The View from 2008

- Identify an optimum set of 300,000 tag SNPs
- Collect 1000 cases and 1000 controls
- Genotype all DNAs for all SNPs
- That adds up to 600 million genotypes
- Genotyping just dropped to \$0.0010, so that's \$600,000 for each disease



First quarter 2008



**What will be the impact
of genomics on the
practice of medicine?**

Disease with Genetic Component



Identify Genetic Risk Factors



Diagnostics



**Preventive
Medicine**

**Accelerated
by Human
Genome Project
and HapMap**

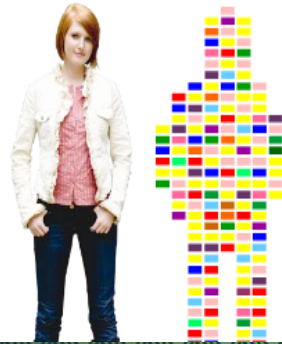
Time





Home

What is deCODEme?



deCODE genetics
the pioneers in gene discovery

deCODEme
the most comprehensive genome scan
with information on more diseases and genes

Login to myCODE

Navigenics

About

Leadership

Policies

Contact

Replay



Welcome to Navigenics

We are in the midst of an exciting era of discoveries about the connections between our individual genetic composition and our personal health and wellness. These discoveries are providing a detailed map of thousands of genes that instruct the body how to grow, live and thrive – and a better understanding of how variations in these genes may influence our health over time.

and traits

sign up now

But genetics just get personal. But the information will de- yo live

our service

genetics 101

for the experts

store

about us

Your genes offer a road map to optimal health

profile.

»More

scie
gen
»Mo

discover your genome at 23:

1866: Gregor Mendel discovers the laws of inheritance.

200,000 years ago: *Homo sapiens* walks the Earth.

2003: The Human Genome Project maps a single person's gen

2007: 23andMe introduces the first Personal Genome Service.

Unlock the secrets of your own DNA. Today.

175,000 years ago: The mother of all present-day humans is born in Africa.

1953: Watson and Crick uncover the double-helix structure of DNA.

Welcome to 23andMe, a web-based service that helps you read and understand your DNA. After providing a saliva sample using an at-

Disease with Genetic Component

**Accelerated
by Human
Genome Project
and HapMap**

Identify Genetic Risk Factors

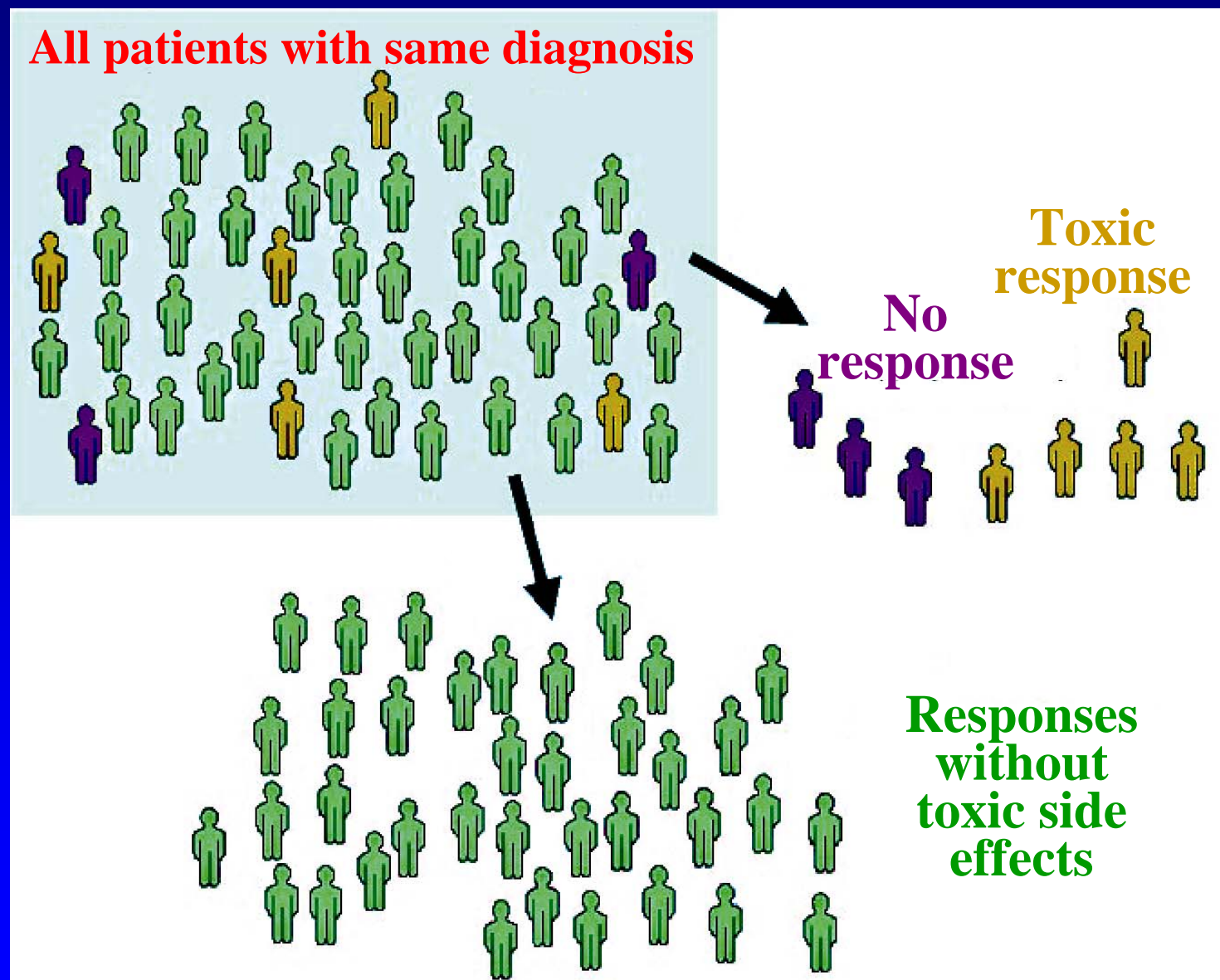
Diagnostics

Pharmacogenomics

**Preventive
Medicine**

Time

Pharmacogenomics: Unlocking the Human Genome for Better Drug Therapy



Disease with Genetic Component

**Accelerated
by Human
Genome Project
and HapMap**

Identify Genetic Risk Factors

Diagnostics

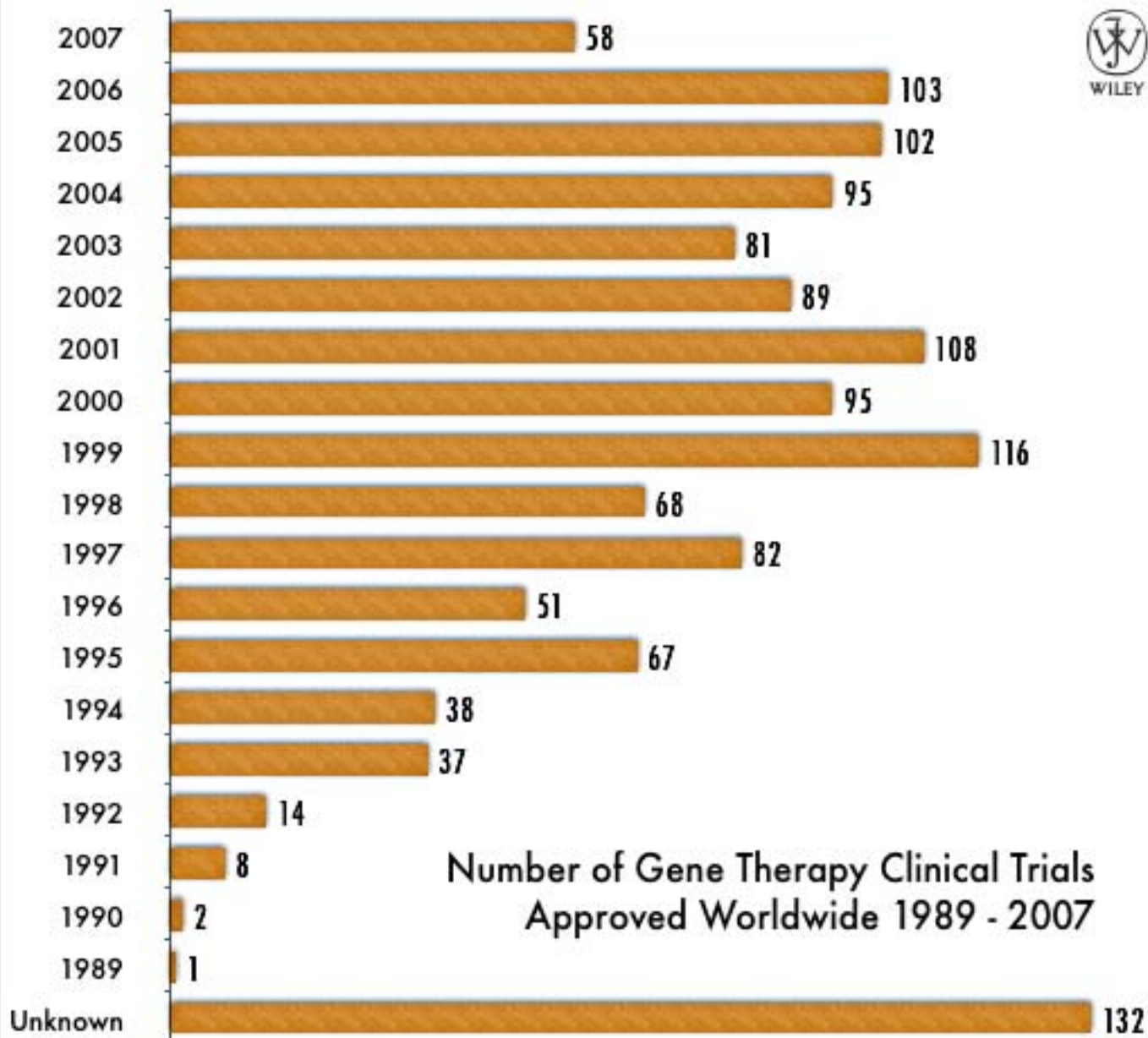
Pharmacogenomics

**Preventive
Medicine**

**Therapeutic
Developments**

- Gene Therapy
- Drug Therapy

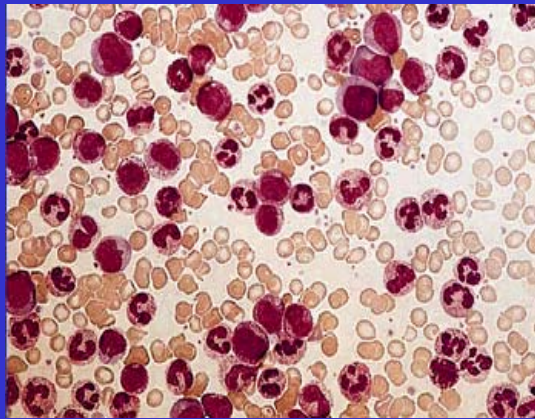
Time



Gleevec™ – Specifically Targets an Abnormal Protein, Blocking Its Ability to Cause Chronic Myeloid Leukemia

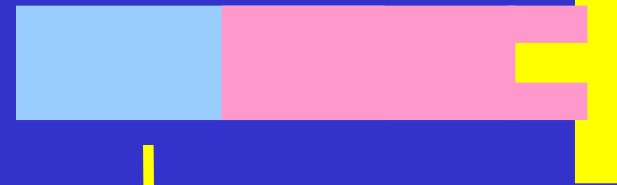
Leukemia arises in mutated blood cell

Leukemia Protein

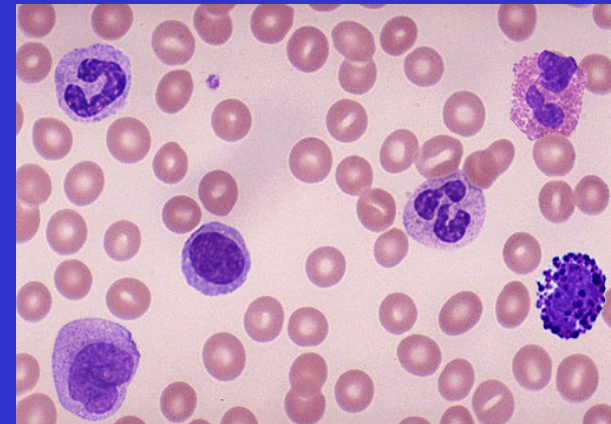


Leukemia

Leukemia Protein



Gleevec™



Remission

