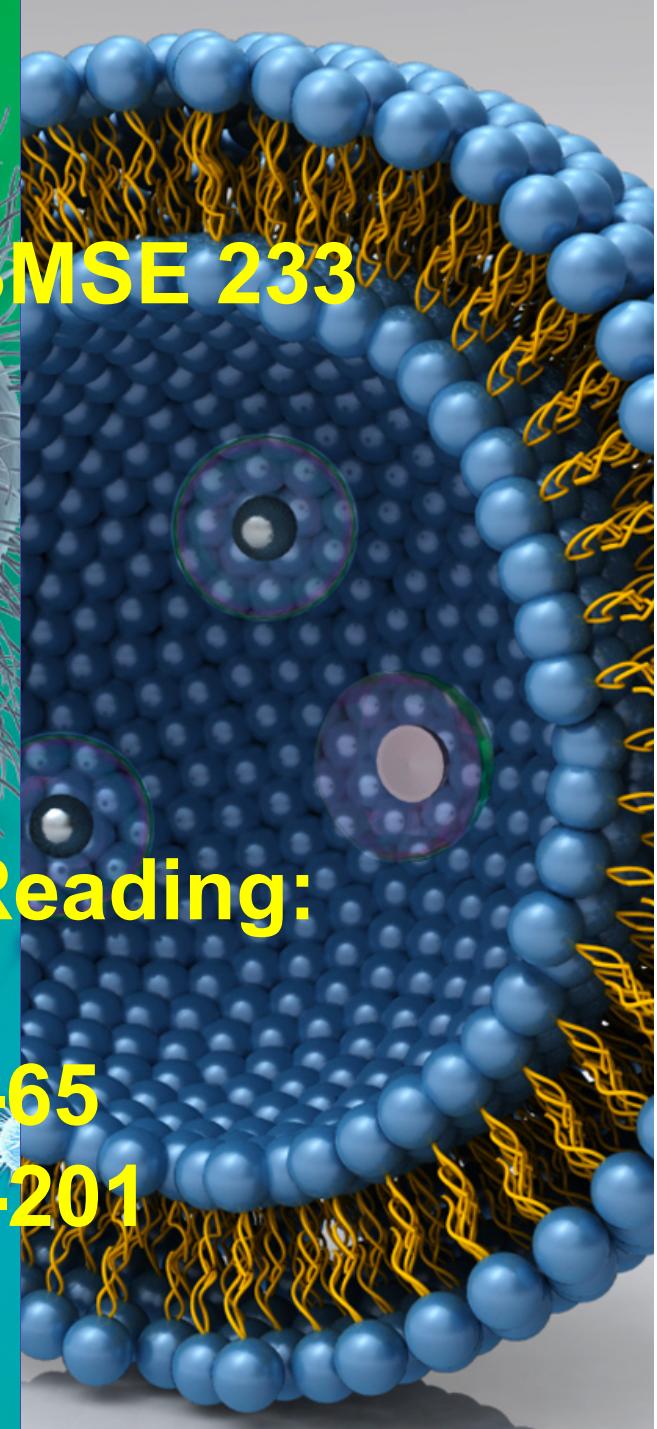
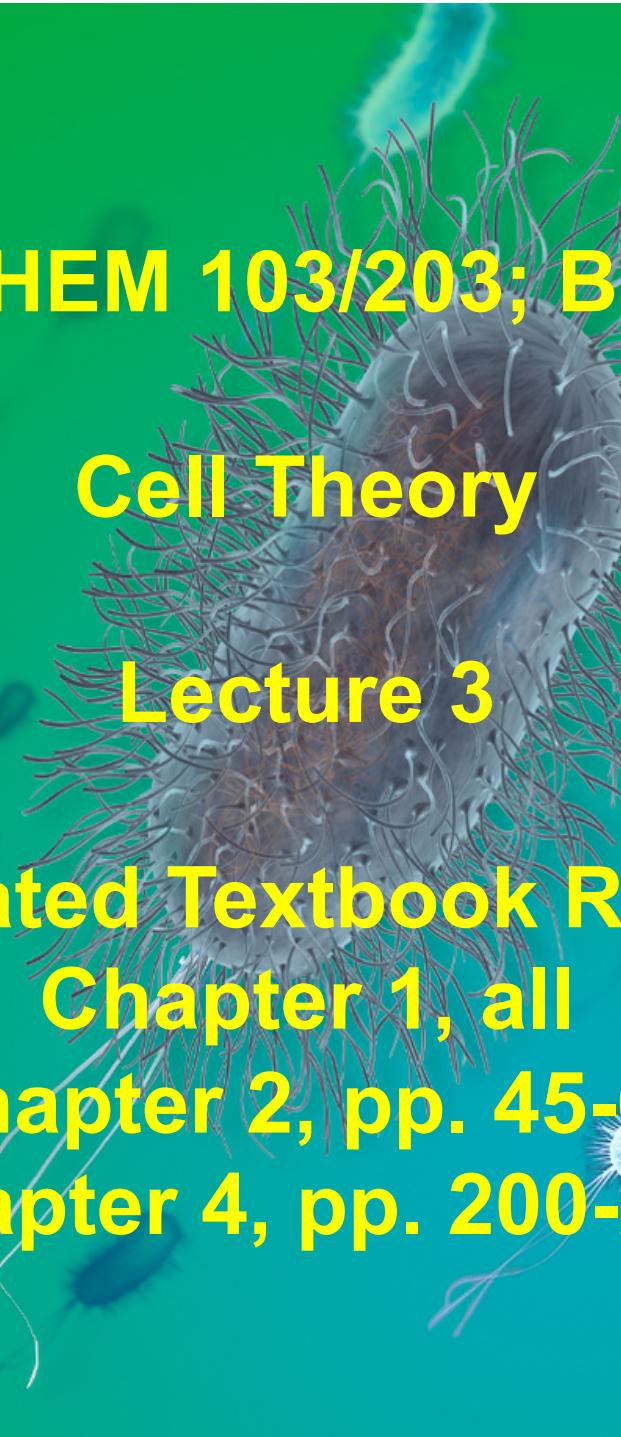


MCDB/CHEM 103/203; BMSE 233

Cell Theory

Lecture 3

Associated Textbook Reading:
Chapter 1, all
Chapter 2, pp. 45-65
Chapter 4, pp. 200-201



**The Scientific Method May Be
the Greatest Accomplishment of
the Human Species.**

**Constructing its foundations
started very early.....**



The Scientific Method



Abū ‘Alī al-Ḥasan ibn al-Ḥasan ibn al-Haytham (Alhazen), 965–1039 Iraq.
The Arab scholar who lived during the Islamic golden age is considered the father of modern scientific methodology

The Scientific Method refers to a body of techniques for investigating phenomena, acquiring new knowledge, or correcting and integrating previous knowledge. To be termed “scientific”, a method of inquiry must be based on gathering empirical and measurable evidence subject to specific principles of reasoning.

The definition in the Oxford English Dictionary states that the scientific method is a method or procedure consisting in systematic observation, measurement, and experiment, and the formulation, testing and modification of hypotheses.

The Scientific Method Generates Hypotheses, Theories and Laws

Hypothesis: A hypothesis is a testable idea. Scientists do not set out to “prove” hypotheses, but to test them. Often multiple hypotheses are posed to explain phenomena and the goal of research with the scientific method is to eliminate the incorrect ones.

Theory: A theory is an explanation of phenomena. The validity of a Theory rests upon its ability to explain phenomena. Theories may be supported, rejected, or modified, based on new evidence often gathered from experiments to test hypotheses. Hypotheses come and go by the thousands, but theories often remain to be tested and modified for decades or centuries.

Law: An empirical generalization; a statement or principles that are Universally applicable, appearing without exception and consolidated by repeated successful testing. Laws describe phenomena, often mathematically. Theories, however, explain phenomena.

The Scientific Method Provides the Means to Distinguish Between an Opinion and a Fact

Fact versus Opinion Tutorials: a statement of opinion is sometimes *disguised as a fact*.

<http://www.montgomerycollege.edu/~steuben/factopinion.htm>

www.bcps.org/offices/lis/models/biog/images/factopinion.ppt

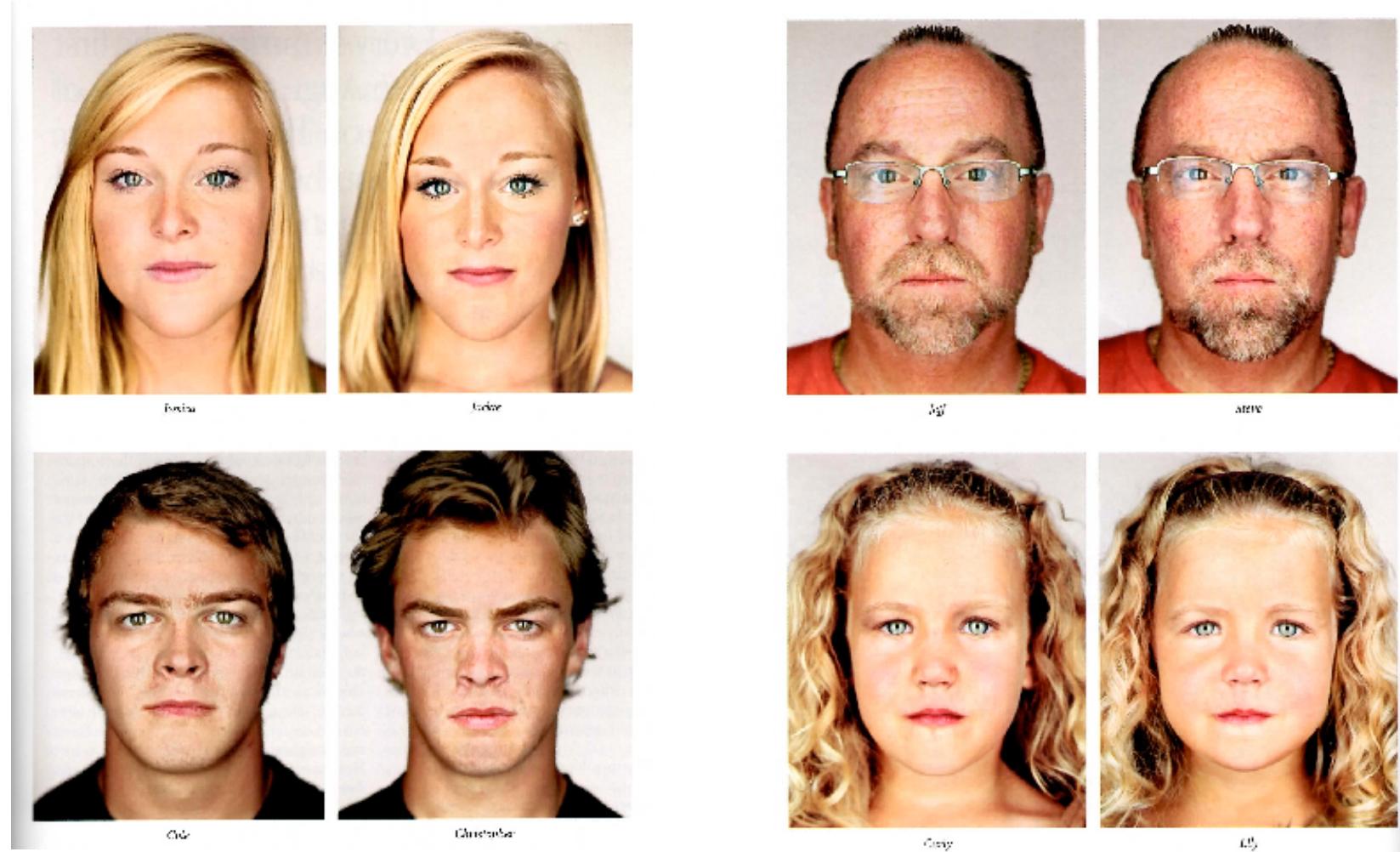
<http://www.classroomtech.org/credibility/Fact.Opinion.PDF>

“Do you believe in evolution?” is a question often asked of biology teachers by their students. The answer is, “No, I accept the fact that the Earth is very old and life has changed over billions of years because that is what the evidence reveals.” Science is not about belief—it is about making inferences based on evidence.

All Organisms Can Exist as Clones



There are Clones Among Us!



(but don't be worried- they are almost always nice people like us)

What are clones?

Any organism whose genetic information is identical to that of a parent organism from which it was created.

A group of identical cells naturally derived from a common parent cell.

An exact replica of all or part of a macromolecule.

NGM.COM JANUARY 2012

NATIONAL GEOGRAPHIC



TWINS

ALIKE BUT NOT ALIKE

The Golden Past of Panama 66

Denmark's Daring Dogsledders 82

Cambodia Heals From Land Mines 96

The Earth Goes Wild in Africa 116

Montana's Modern Homesteaders 128

NGM.COM JANUARY 2012

NATIONAL GEOGRAPHIC



TWINS

ALIKE BUT NOT ALIKE

The Golden Past of Panama 66

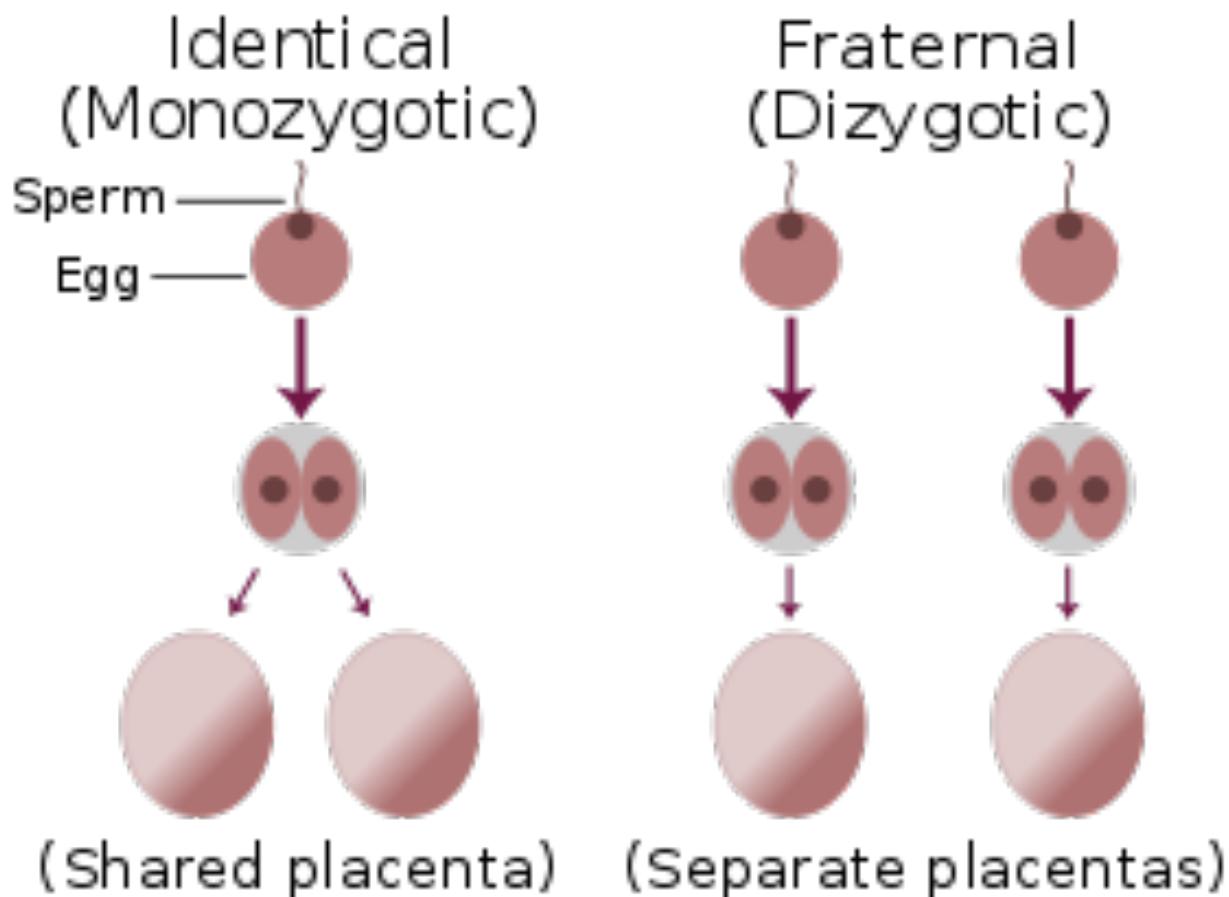
Denmark's Daring Dogsledders 82

Cambodia Heals From Land Mines 96

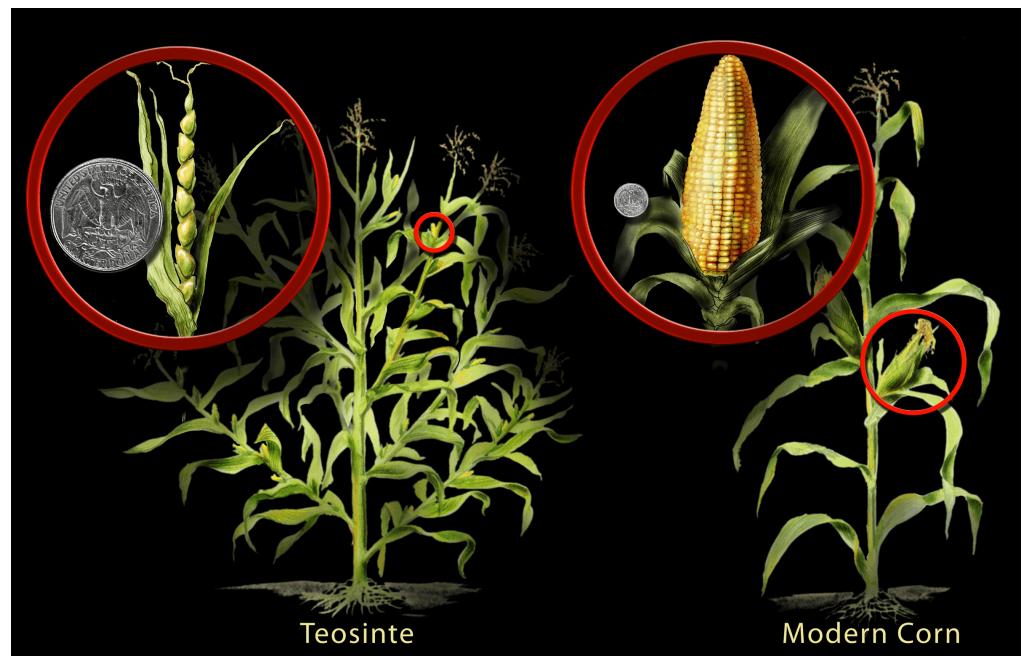
The Earth Goes Wild in Africa 116

Montana's Modern Homesteaders 128

Twins are Not Always Identical



Clones May Be a Genetically Modified Organism (GMO), But Not All GMOs are Clones



Corn is genetically engineered teosinte and a clone (engineered by selective breeding and laboratory cloning). It did not even exist as a recognizable corn plant before 10,000 BC.

Bananas are also clones.

THE NEW YORK TIMES BESTSELLER

CARL SAGAN

THE DEMON-HAUNTED WORLD



SCIENCE AS A CANDLE IN THE DARK

"A glorious book...From the first page to the last, this book is a manifesto for clear thought." —*Los Angeles Times*
"Wonder-saturated." —*The Washington Post*

“.....Scientists, like other human beings, have their hopes and fears, their passions and despondencies-and their strong emotions may sometimes interrupt the course of clear thinking and sound practice. But science is self-correcting. The most fundamental axioms and conclusions may be challenged. The prevailing hypotheses must survive confrontation.....

Appeals to authority are impermissible. The steps in a reasoned argument must be set out for all to see.....”

“.....Vigorous criticism of new ideas is a commonplace in science. While the style of the critique may vary with the character of the critic, overly polite criticism benefits neither the proponents of new ideas nor the scientific enterprise. Any substantive objection is permissible and encouraged; the only exception being that *ad hominem attacks on the personality or motives of the author are excluded*. *It does not matter what reason the proponent has for advancing his ideas or what prompts his opponents to criticize them; all that matters is whether the ideas are right or wrong; promising or retrogressive.....”*

“.....Vigorous criticism is more constructive in science than in some other areas of human endeavor because in science there are adequate standards of validity that can be agreed upon by competent practitioners the world over. The objective of such criticism is not to suppress but rather to encourage the advance of new ideas: those that survive a firm skeptical scrutiny have a fighting chance of [success].....

Carl Sagan

Michael Specter (journalist): The danger of science denial

Technology, Entertainment, and Design (TED) talk, 2010

Vaccine-autism claims, "Frankenfood" bans, the herbal cure craze: All point to the public's growing fear (and, often, outright denial) of science and reason, says Michael Specter. He warns the trend spells disaster for human progress.

Michael Specter is a staff writer for the New Yorker. His new book, *Denialism*, asks why we have increasingly begun to fear scientific advances instead of embracing them.

"People sometimes wrap themselves in their beliefs so tight that not even the truth will set them free."



How Do Organisms Become Genetically ‘Modified’?

Genetically Modified: Genetically distinct from original organism source

Random mutation: (ex. cosmic rays, X-rays)

Selective breeding: (ex. domesticated plants and animals)

Transgenesis: (ex. plants and animals, research and industrial applications)

Transgenic organism: (McGraw-Hill Dictionary of Scientific and Technical Terms, fourth edition)

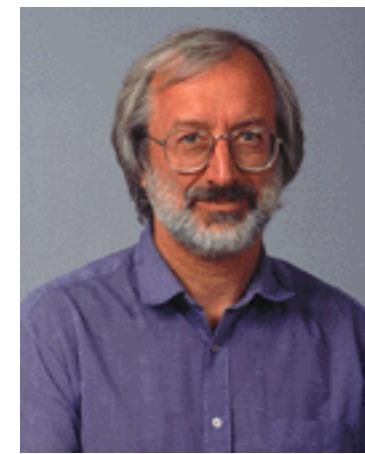
an organism in which genetic material from another organism has been experimentally transferred, so that the host acquires the genetic traits of the transferred genes in its chromosomal composition.

Transgenesis in Mammals: Developed in late 70s and early 80s

The first transgenic mouse was made in 1974 by Rudy Jaenisch (left) and Beatrice Mintz (right), but the first transgenic mice capable of passing foreign DNA onto their offspring were not made until 1981.



Ralph Brinster (left) and Richard Palmiter (right) pioneered the development of heritable methods of transgenesis in mammals.



Transgenesis

Procedure uses single cell fertilized embryos (zygotes).

Microinjection needle
with transgene DNA

Male and female
pronuclei

Holding pipet



When transgene DNA integrates into one or more chromosomes at this embryonic stage, all cells of the resulting organism have the same transgenic modification to all of their cells.

Transgenesis



Requires a microscopic imaging system combined with hydraulic micromanipulators, and microsyringes to enable microinjection of the embryo.



Transgenesis: Enormously Successful Applications in Research

GENE REGULATION

MORPHOGENESIS

IMMUNOLOGY

DISEASE MECHANISMS

VIRAL & BACTERIAL PATHOGENESIS

TOXICOLOGY

TUMORIGENESIS AND CANCER

Some Cells can Become Other Types of Cells: They are called Stem Cells

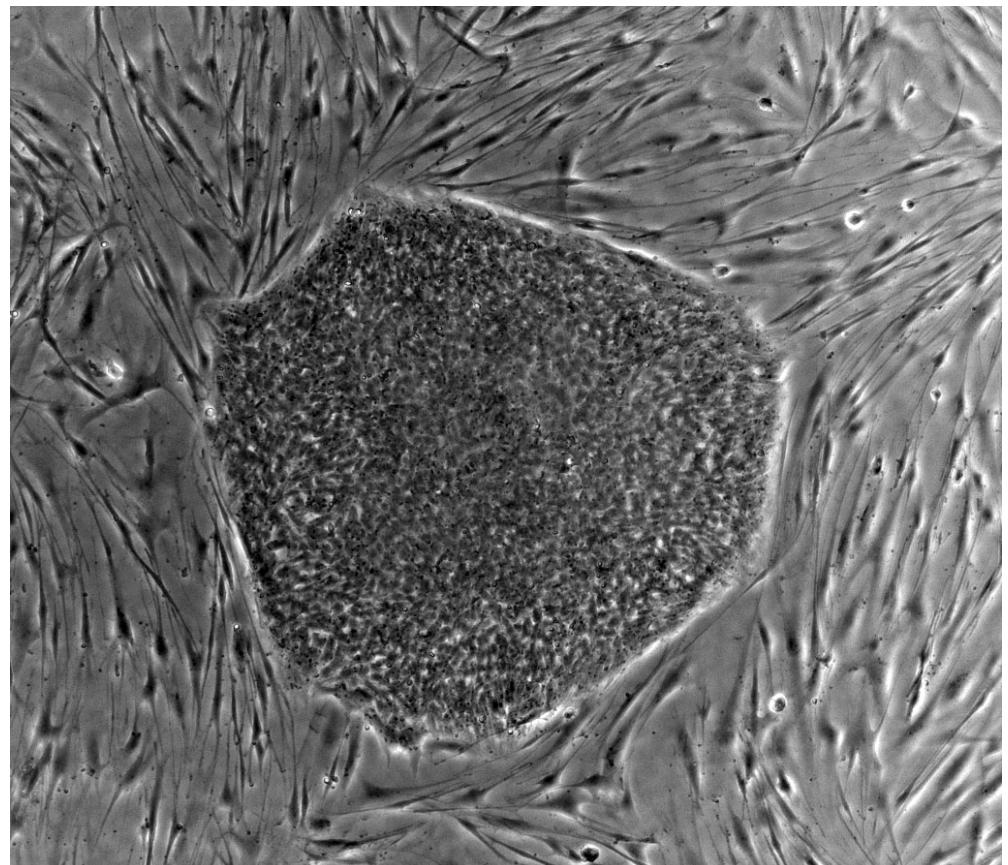
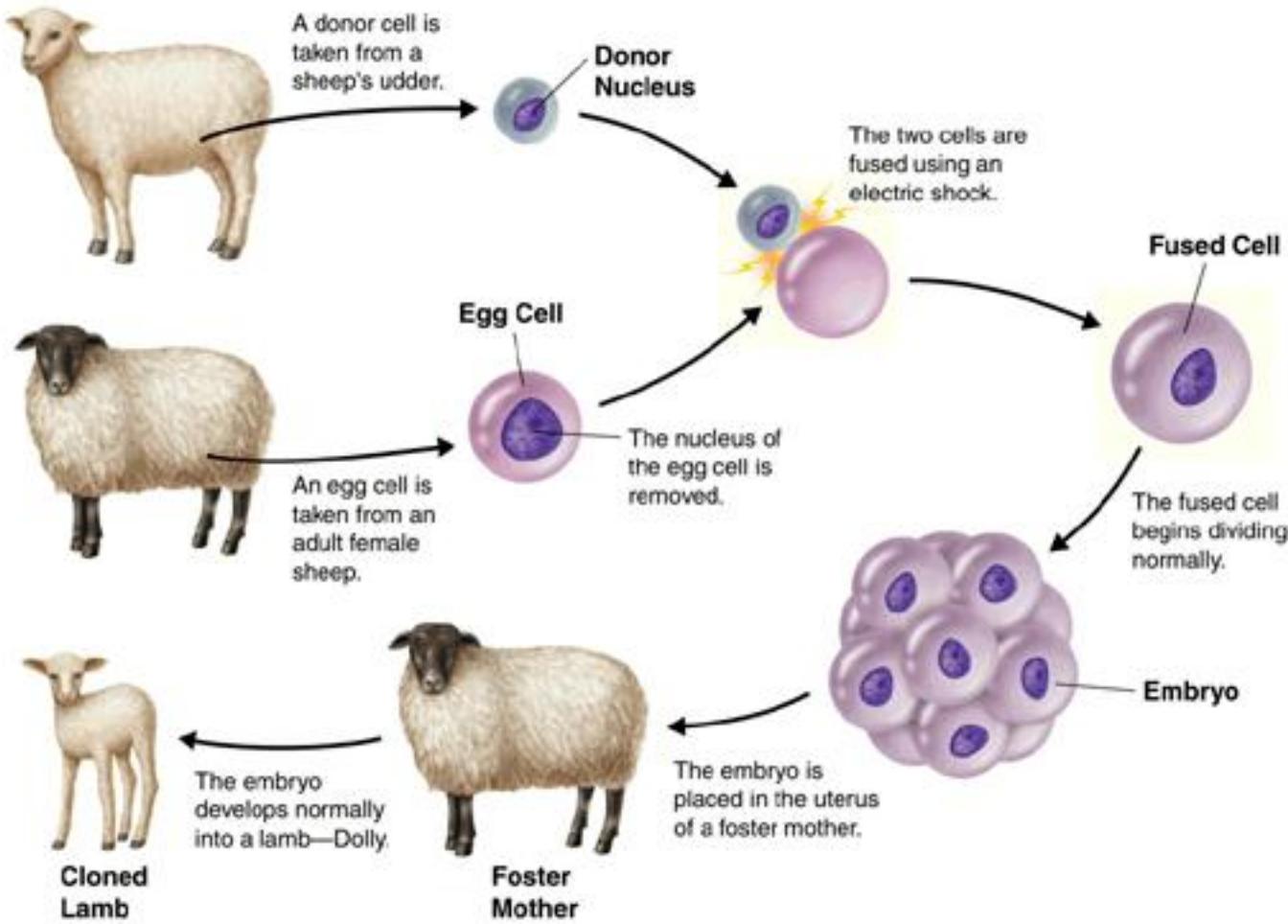




Figure 1-8
Molecular Cell Biology, Sixth Edition
© 2008 W.H. Freeman and Company

Cloning in the Agricultural/Livestock Industry



Gene-Targeting: A Remarkable Achievement that Opened the Door to a Revolution in Biology



Photo: U. Montan

Mario R. Capecchi



Photo: U. Montan

Sir Martin J. Evans

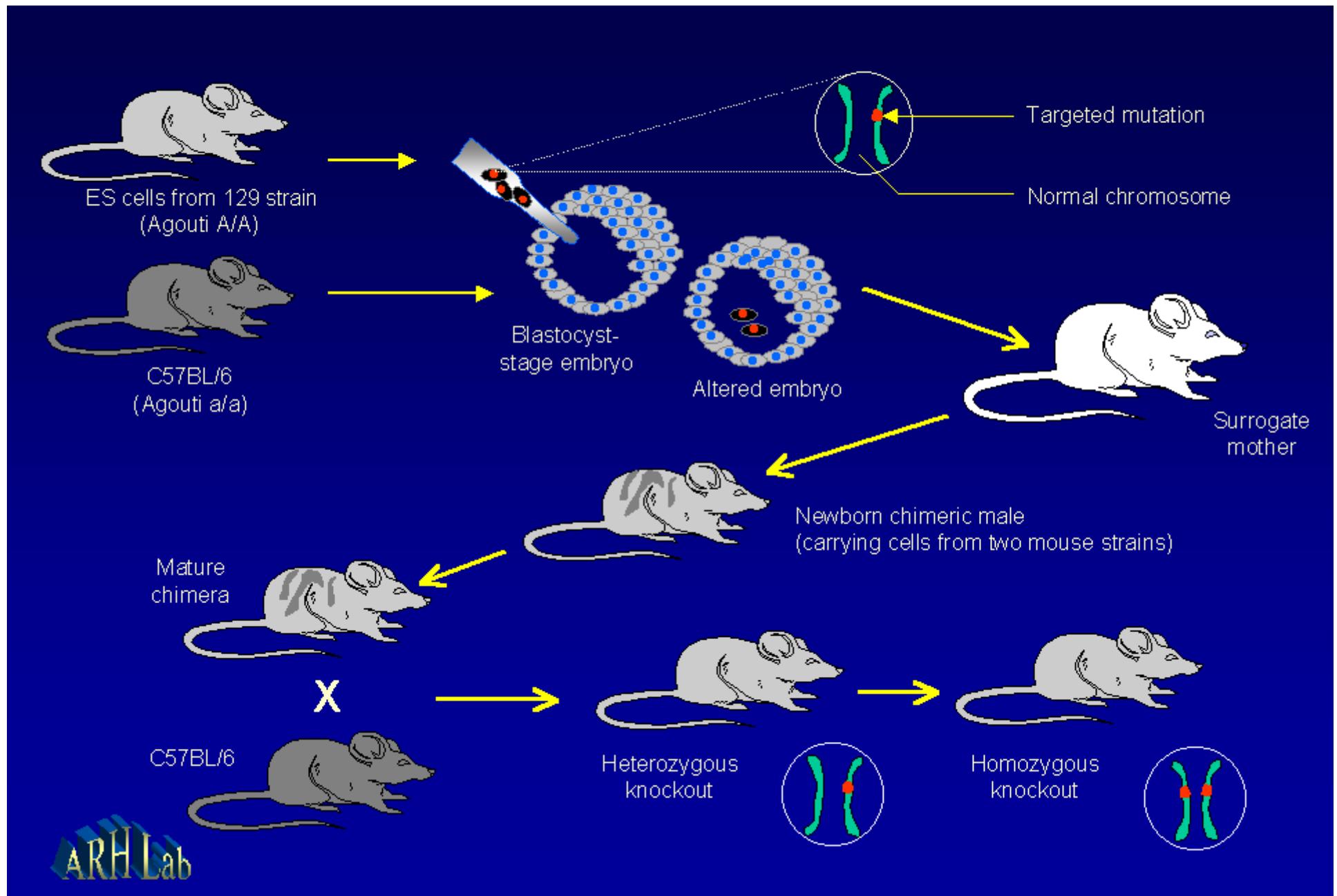


Photo: U. Montan

Oliver Smithies

The Nobel Prize in Physiology or Medicine 2007 was awarded jointly to Mario R. Capecchi, Sir Martin J. Evans and Oliver Smithies "for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells".

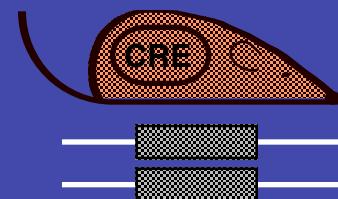
Gene Targeted Mutagenesis in Mammals



Conditional Mutagenesis Extends Gene-Targeting

G1

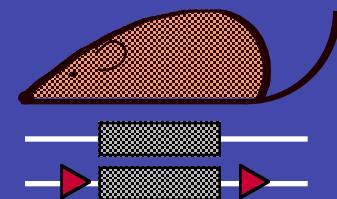
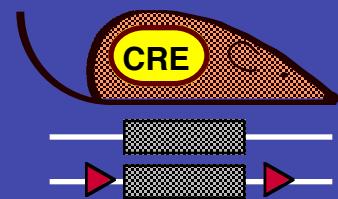
Inherited and
cell-type
regulated
recombinase
transgene
(circled region)



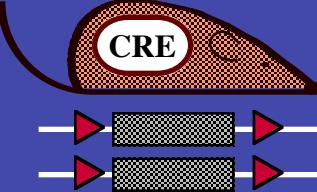
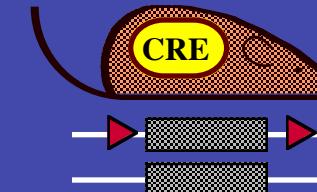
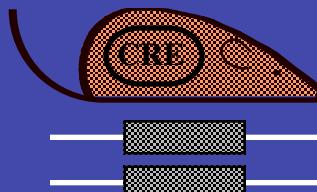
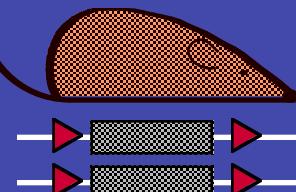
Inherited (all cells)
recombinase
target elements
(red arrowheads)

G2

Recombinase
deletes flanked
DNA segments



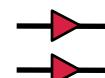
G3



Wild-type function



Heterozygous-null



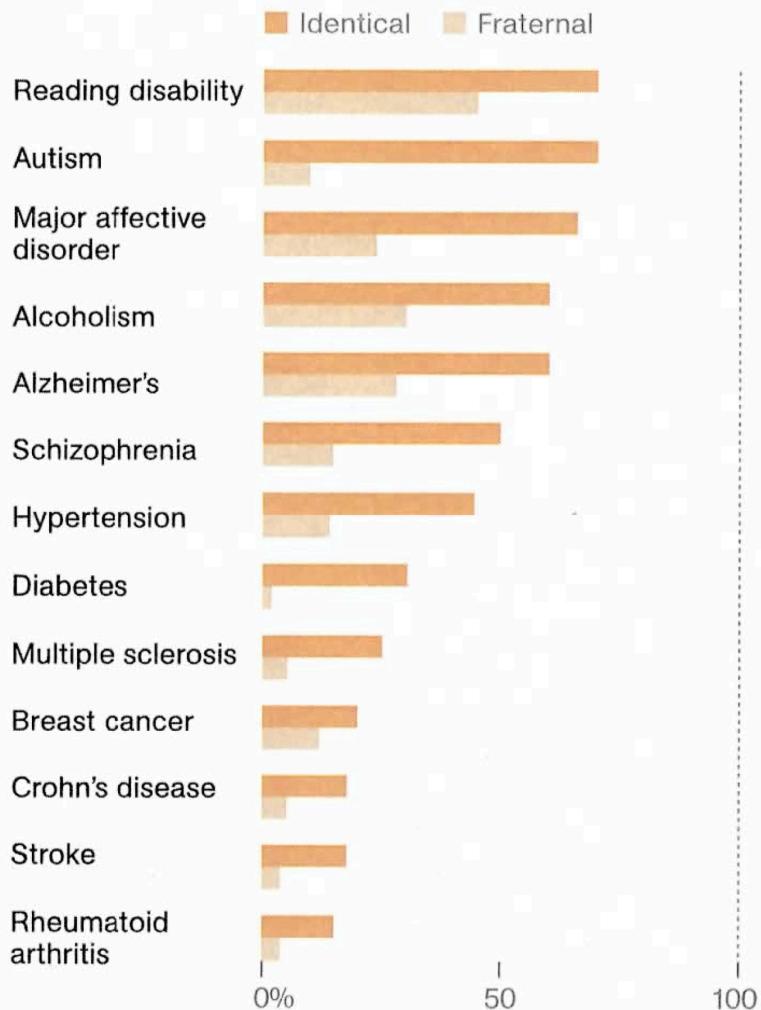
Homozygous-null

There is More to the Story About Human Clones...

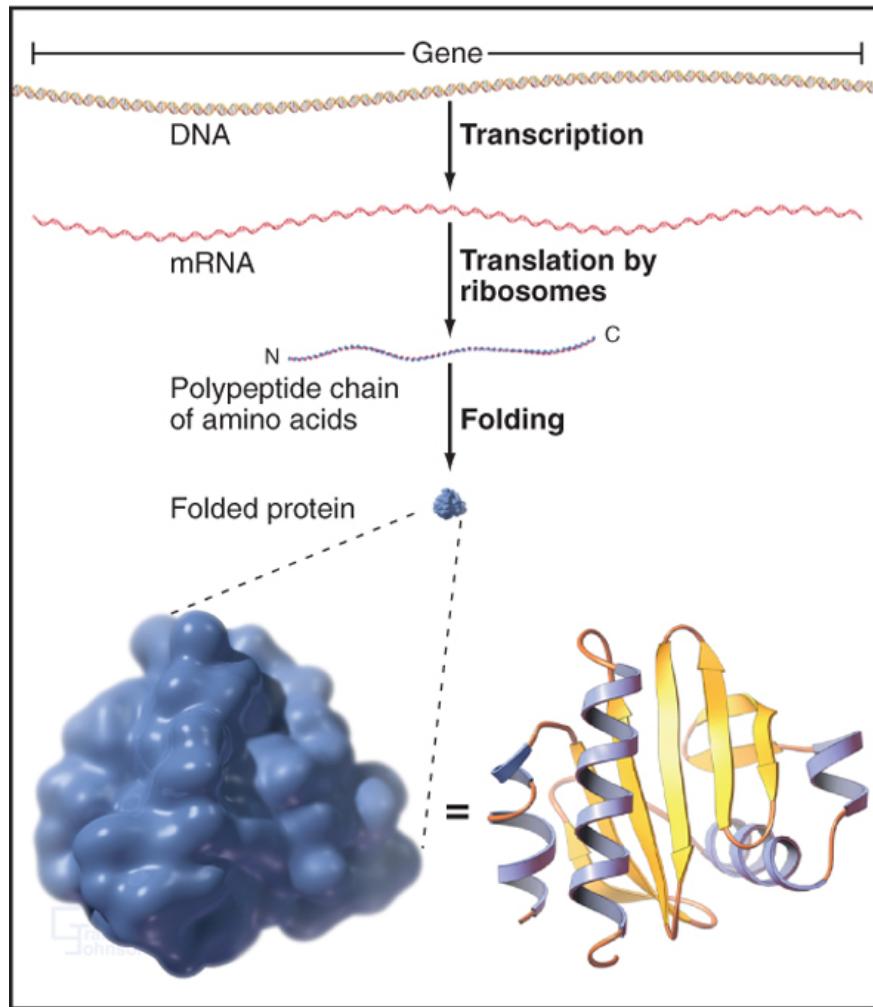
So, Clones Are Not Identical in Every Way

SHARED TRAITS

Identical twins share certain disorders, such as autism, much more often than fraternal twins do, suggesting the strong influence of heredity.



But genetics plays a minor role in many major diseases



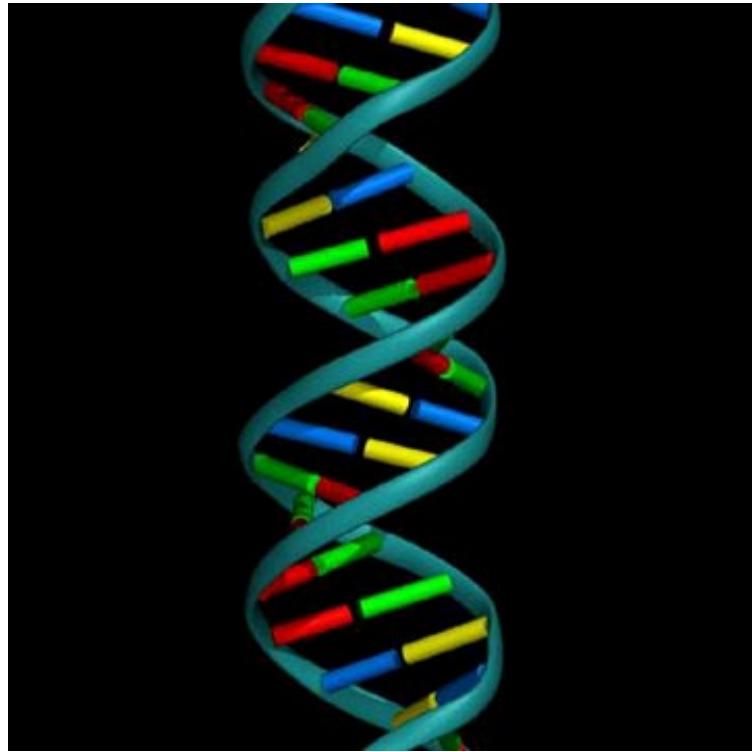
© Elsevier. Pollard et al: Cell Biology 2e - www.studentconsult.com

The Central Dogma of 20th Century Biology:

**DNA to RNA to Protein
has transformed our
understanding of life
and the cell.**

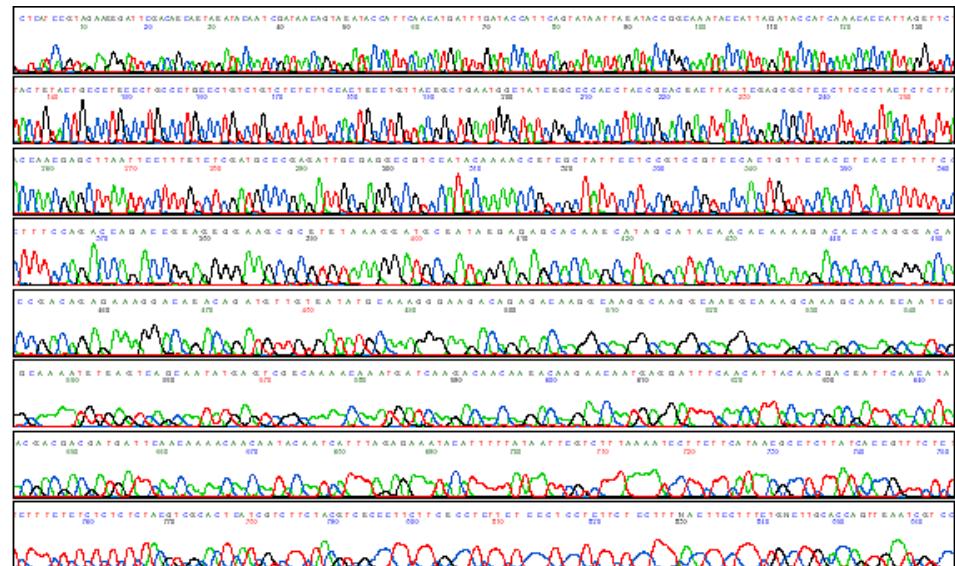
**Is the DNA to RNA to Protein Paradigm
Sufficient to Explain All of Biology and Disease?**

Is DNA a Blueprint or a Parts List of Life?



Blueprint (definition):

- 1) All the information that is needed to build or make something
 - 2) A detailed outline or plan of action



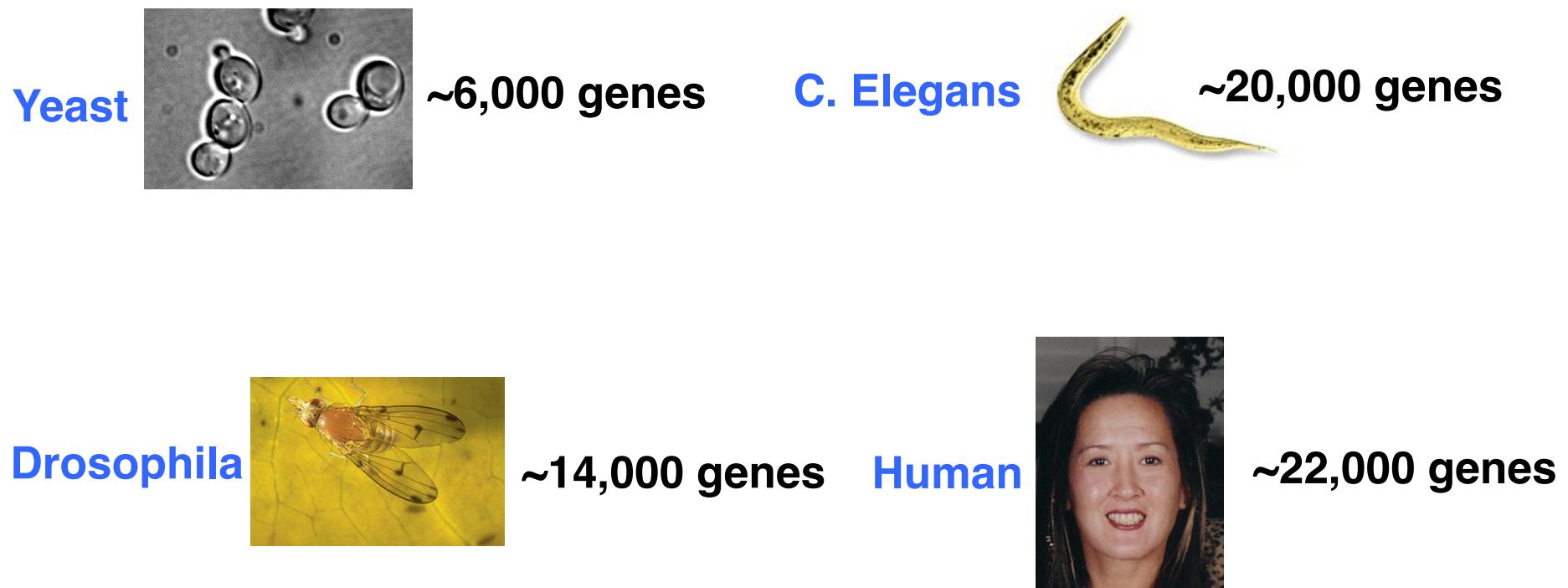
Widely Different Gene Number Among Similar Organisms

Table 1–1 Some Genomes That Have Been Completely Sequenced

SPECIES	SPECIAL FEATURES	HABITAT	GENOME SIZE (1000s OF NUCLEOTIDE PAIRS PER HAPLOID GENOME)	ESTIMATED NUMBER OF GENES CODING FOR PROTEINS
BACTERIA				
<i>Mycoplasma genitalium</i>	has one of the smallest of all known cell genomes	human genital tract	580	468
<i>Synechocystis</i> sp.	photosynthetic, oxygen-generating (cyanobacterium)	lakes and streams	3573	3168
<i>Escherichia coli</i>	laboratory favorite	human gut	4639	4289
<i>Helicobacter pylori</i>	causes stomach ulcers and predisposes to stomach cancer	human stomach	1667	1590
<i>Bacillus anthracis</i>	causes anthrax	soil	5227	5634
<i>Aquifex aeolicus</i>	lithotrophic; lives at high temperatures	hydrothermal vents	1551	1544
<i>Streptomyces coelicolor</i>	source of antibiotics; giant genome	soil	8667	7825
<i>Treponema pallidum</i>	spirochete; causes syphilis	human tissues	1138	1041
<i>Rickettsia prowazekii</i>	bacterium most closely related to mitochondria; causes typhus	lice and humans (intracellular parasite)	1111	834
<i>Thermotoga maritima</i>	organotrophic; lives at very high temperatures	hydrothermal vents	1860	1877

Genome size and gene number vary between strains of a single species, especially for bacteria and archaea. The table shows data for particular strains that have been sequenced. For eucaryotes, many genes can give rise to several alternative variant proteins, so that the total number of proteins specified by the genome is substantially greater than the number of genes.

How Does Complexity Emerge Among Cells and Organisms?



Complexity does not appear to be directly related to gene number

How Does Complexity Emerge Among Cells and Organisms?

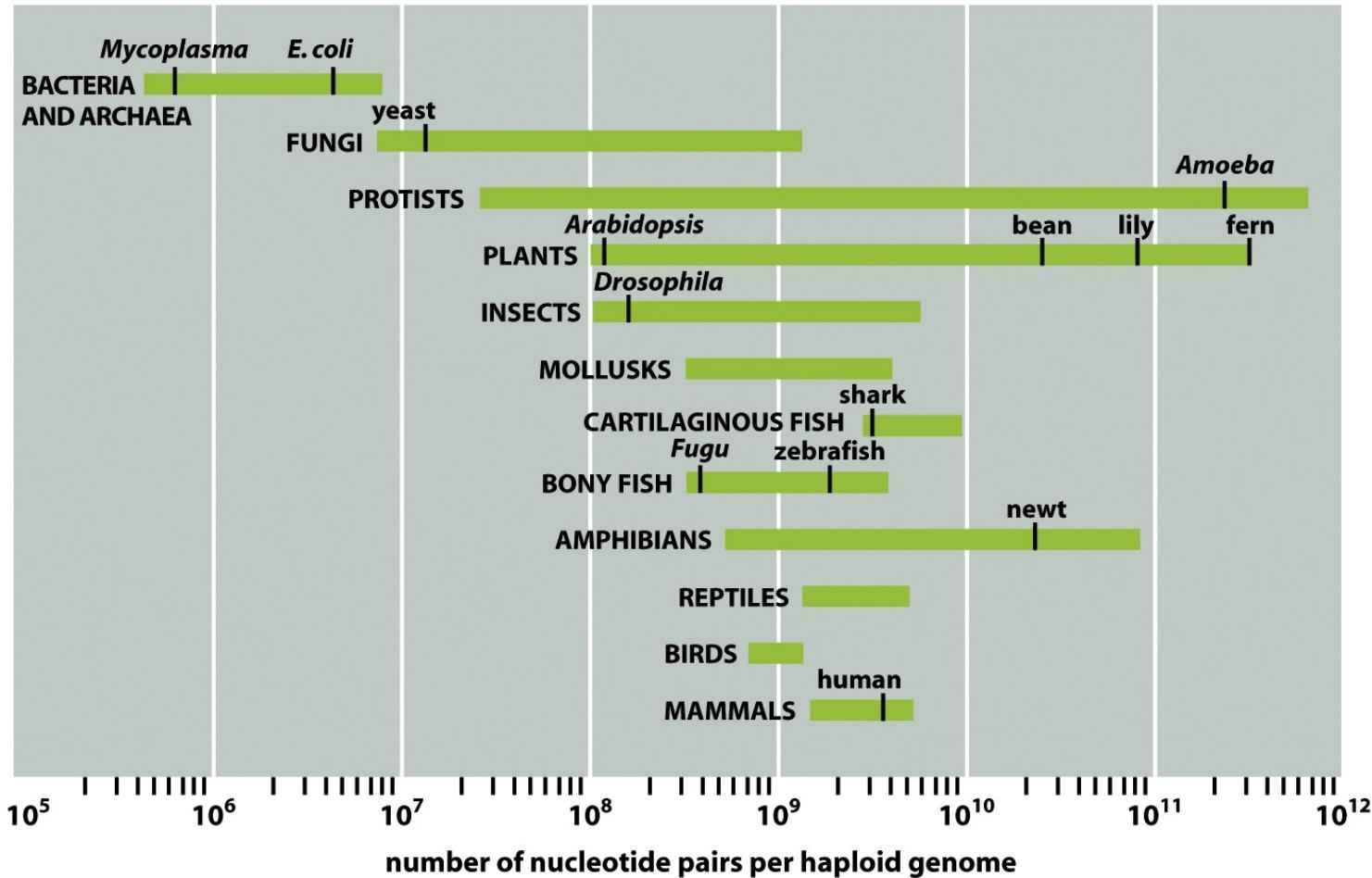


Figure 1-37 Molecular Biology of the Cell 5/e (© Garland Science 2008)

And...Genome size does not directly relate to organism complexity

Looking for the Investment in Organism Complexity

Table 1–2 The Numbers of Gene Families, Classified by Function, That Are Common to All Three Domains of the Living World

GENE FAMILY FUNCTION	NUMBER OF “UNIVERSAL” FAMILIES
Information processing	
Translation	63
Transcription	7
Replication, recombination, and repair	13
Cellular processes and signaling	
Cell cycle control, mitosis, and meiosis	2
Defense mechanisms	3
Signal transduction mechanisms	1
Cell wall/membrane biogenesis	2
Intracellular trafficking and secretion	4
Post-translational modification, protein turnover, chaperones	8
Metabolism	
Energy production and conversion	19
Carbohydrate transport and metabolism	16
Amino acid transport and metabolism	43
Nucleotide transport and metabolism	15
Coenzyme transport and metabolism	22
Lipid transport and metabolism	9
Inorganic ion transport and metabolism	8
Secondary metabolite biosynthesis, transport, and catabolism	5
Poorly characterized	
General biochemical function predicted; specific biological role unknown	24

For the purpose of this analysis, gene families are defined as “universal” if they are represented in the genomes of at least two diverse archaea (*Archaeoglobus fulgidus* and *Aeropyrum pernix*), two evolutionarily distant bacteria (*Escherichia coli* and *Bacillus subtilis*) and one eucaryote (yeast, *Saccharomyces cerevisiae*). (Data from R.L. Tatusov, E.V. Koonin and D.J. Lipman, *Science* 278:631–637, 1997; R.L. Tatusov et al., *BMC Bioinformatics* 4:41, 2003; and the COGs database at the US National Library of Medicine.)

Sequencing the Human Genome

An Astonishing Advance in Human Achievement



2.9 - 3.0 Billion Base Pairs

**Estimated Intergeneration
Mutation rate: 1.1×10^{-8}
per position, haploid genome**

Intractable Diseases of Mysterious Origins

Autoimmune Disease

5% of living population

Diabetes

10% of living population

Complications of infection

15% of living population

Neurodegeneration

1% of living population

Cardiovascular Disease

20% of living population

Cancer

0.5% of living population

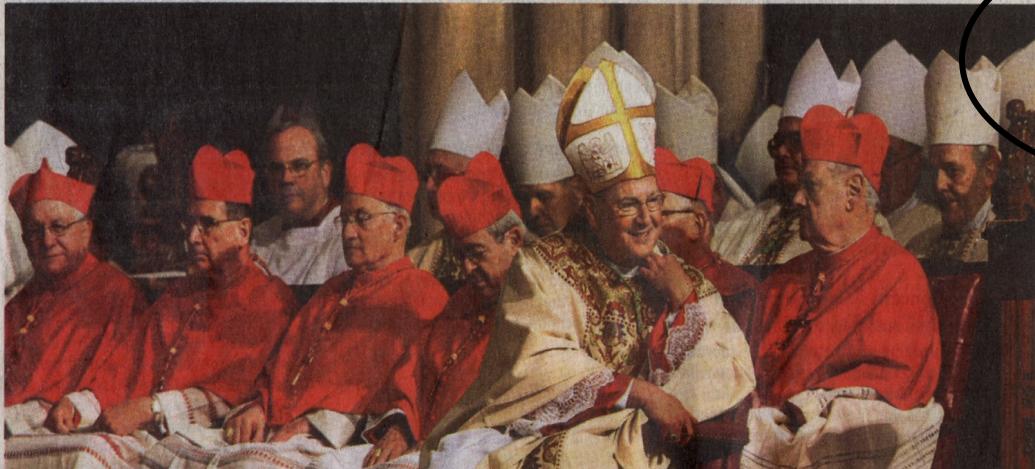
In Search of the Origins of Disease

"All the News
That's Fit to Print"

The New York Times

VOL. CLVIII . . . No. 54,647 © 2009 The New York Times THURSDAY, APRIL 16, 2009

National Edition Printed in Dallas \$1.50



**Study of Genes
And Diseases
At an Impasse**

**Scientists Split on Ways
to Hasten Results**

By NICHOLAS WADE

The era of personal genomic medicine may have to wait. The genetic analysis of common disease is turning out to be a lot more complex than expected.

Since the human genome was decoded in 2003, researchers

**DEALS HELP CHINA
EXPAND ITS SWAY
IN LATIN AMERICA**

OFFERS OF ECONOMIC AID

**Quiet Bid for Influence
as U.S. Tries to Mend
Frayed Relations**

By SIMON ROMERO
and ALEXEI BARRIONUEVO



The NEW ENGLAND
JOURNAL of MEDICINE

The Curious Cases of Penetrance and Expressivity of Organism Traits (Phenotypes).

Penetrance refers to the proportion of individuals carrying a particular variant of a gene (an allele or genotype) that also expresses the associated trait (Phenotype).

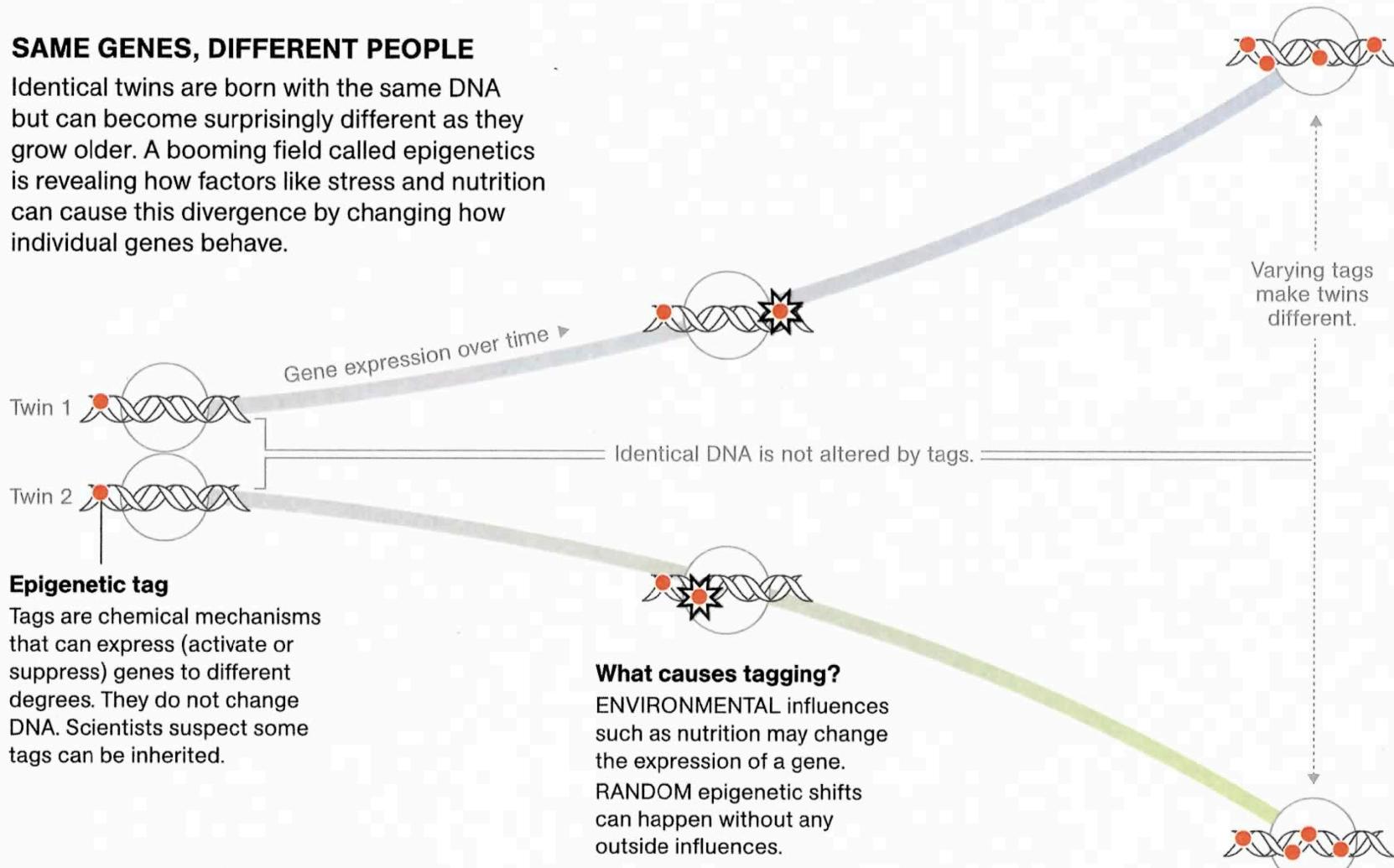
Penetrance only considers whether individuals express the trait or not. Variation in the degree of expression of the trait is termed **Expressivity**.

Expressivity: Variations in a phenotype among individuals carrying the same genotype.

Epigenetics: A Metabolic Mechanism of Gene Regulation

SAME GENES, DIFFERENT PEOPLE

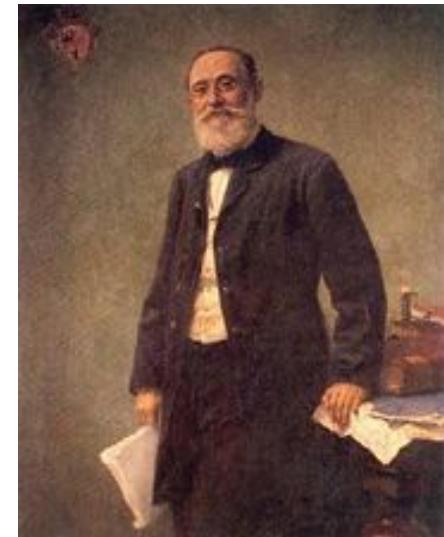
Identical twins are born with the same DNA but can become surprisingly different as they grow older. A booming field called epigenetics is revealing how factors like stress and nutrition can cause this divergence by changing how individual genes behave.



AMANDA HOBBS AND LAWSON PARKER, NGM STAFF
SOURCE: ARTURAS PETRONIS, CENTRE FOR ADDICTION AND MENTAL HEALTH, TORONTO

"All diseases are reducible to active or passive disturbances in cells."

Rudolf Virchow (1821-1902)
pathologist (father of pathology),
biologist, anthropologist, politician

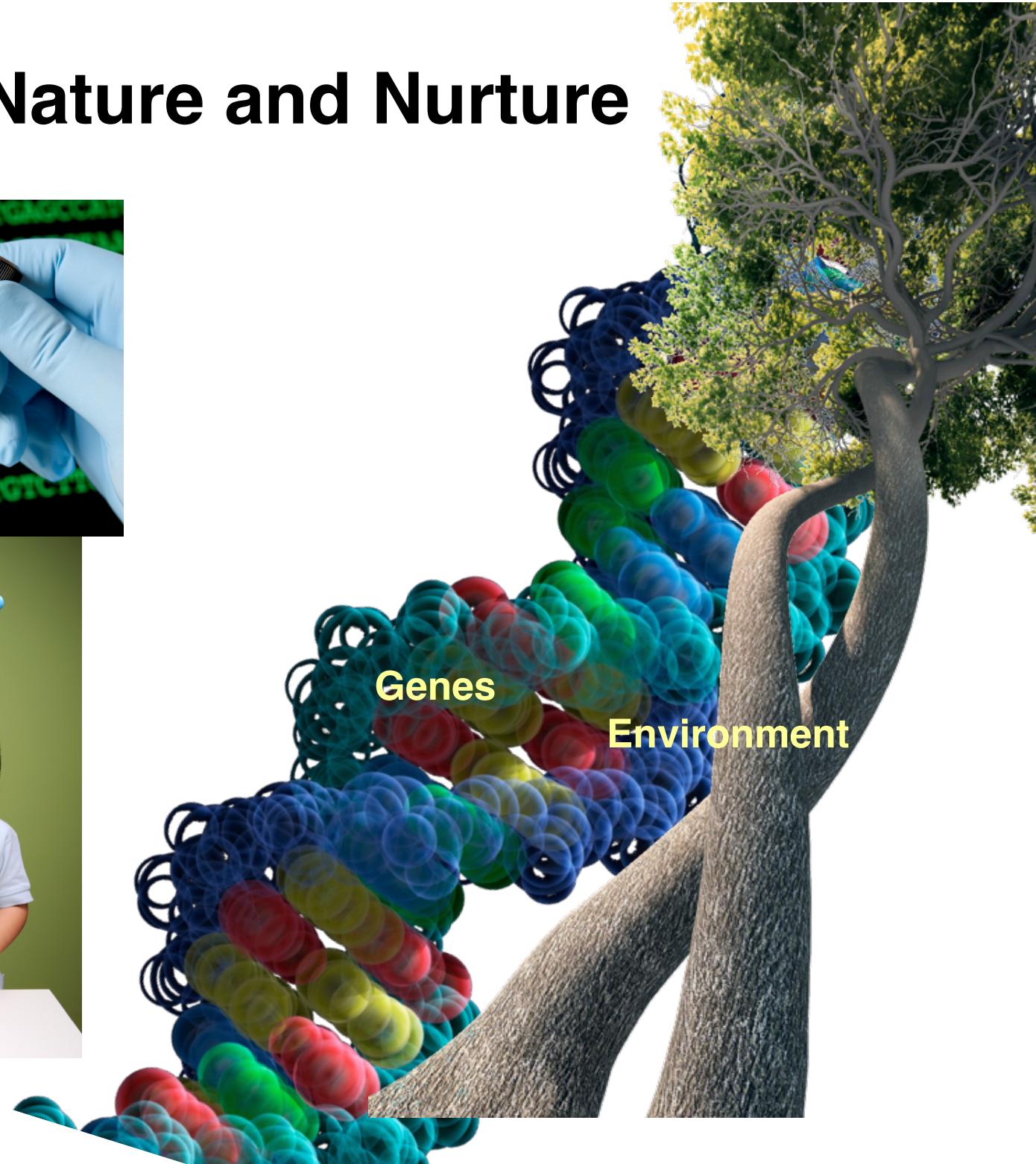


"The key to every biological problem must finally be sought in the cell."

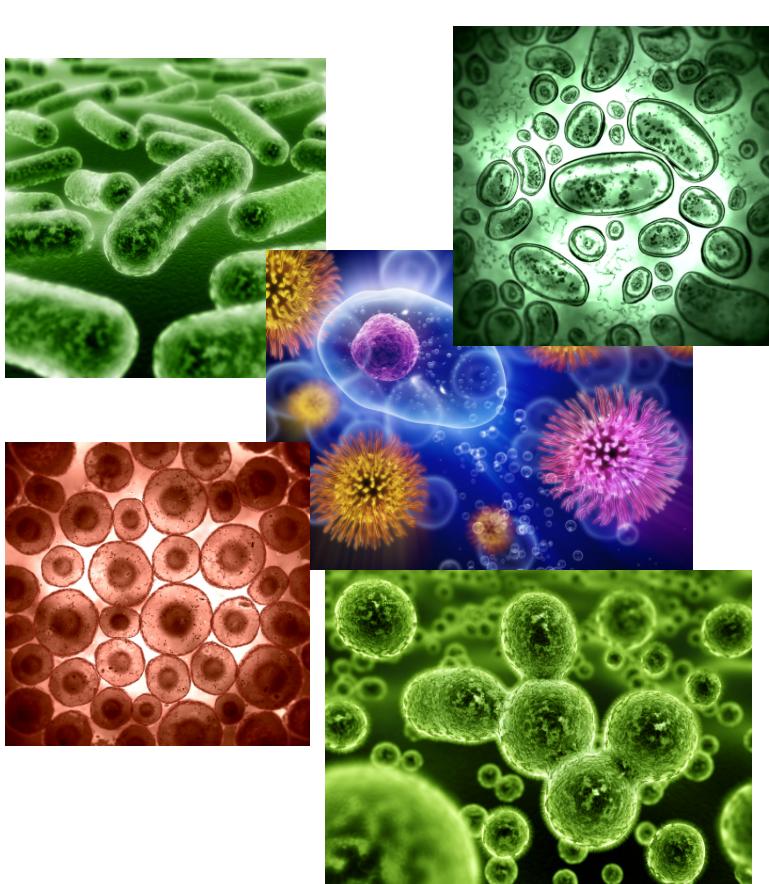
Edmund Beecher Wilson (1856-1939)
geneticist, zoologist,
first cell biologist



Factors of Nature and Nurture



Environmental Factors (an example): The Microbial Community Within Us

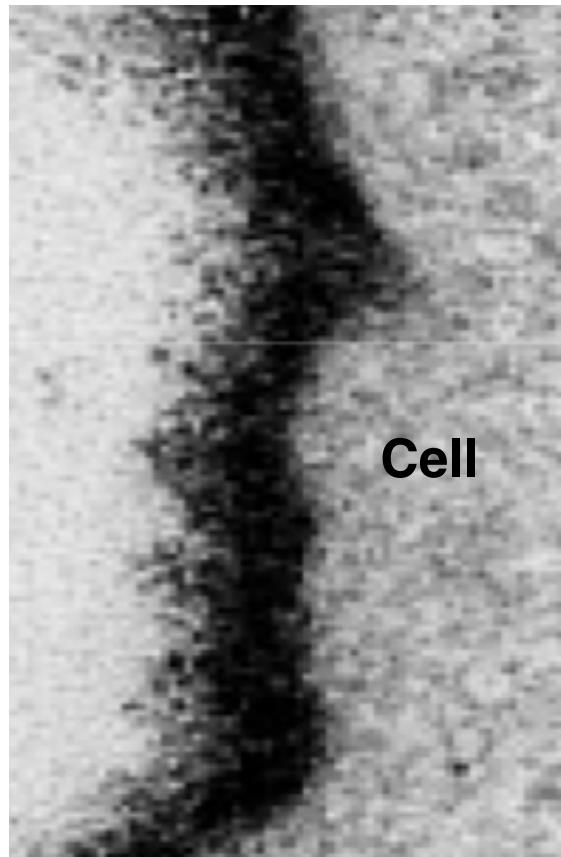


**What are they?
What are they doing?**



Cellular Factors: The Extracellular Matrix and Glycocalyx (the“Dark Matter”) of Cells: Products of Metabolism

Outside on Cell Surface



In Between Cells

