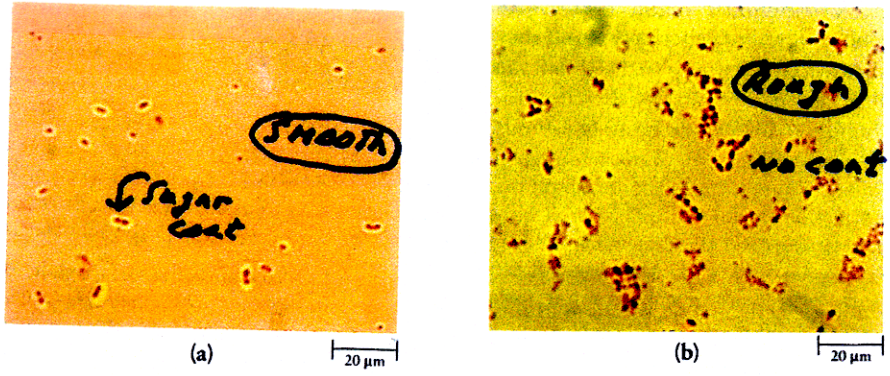
1927!!

GRIFFITH'S PNEUMONIA BACTERIA EXPERIMENT



14–2 (a) *Encapsulated and* (b) *nonencapsulated forms of pneumococci. The capsule is made up of polysaccharides deposited outside the cell wall. The encapsulated form, which is resistant to phagocytosis by white blood cells, produces pneumonia; the mutant, nonencapsulated form is harmless.*

What is BASIS OF AVIRULENCE?

SMOOTH/VIRULENT STRAIN → MUTATION → Rough/AVIRULENT STRAIN

~1927 GRIFFITH Experiment

Streptococcus pneumoniae – Genome Sequenced 2001 2.1 Mb 2236 genes

GRIFFITH'S DEMONSTRATION OF TRANSFORMATION

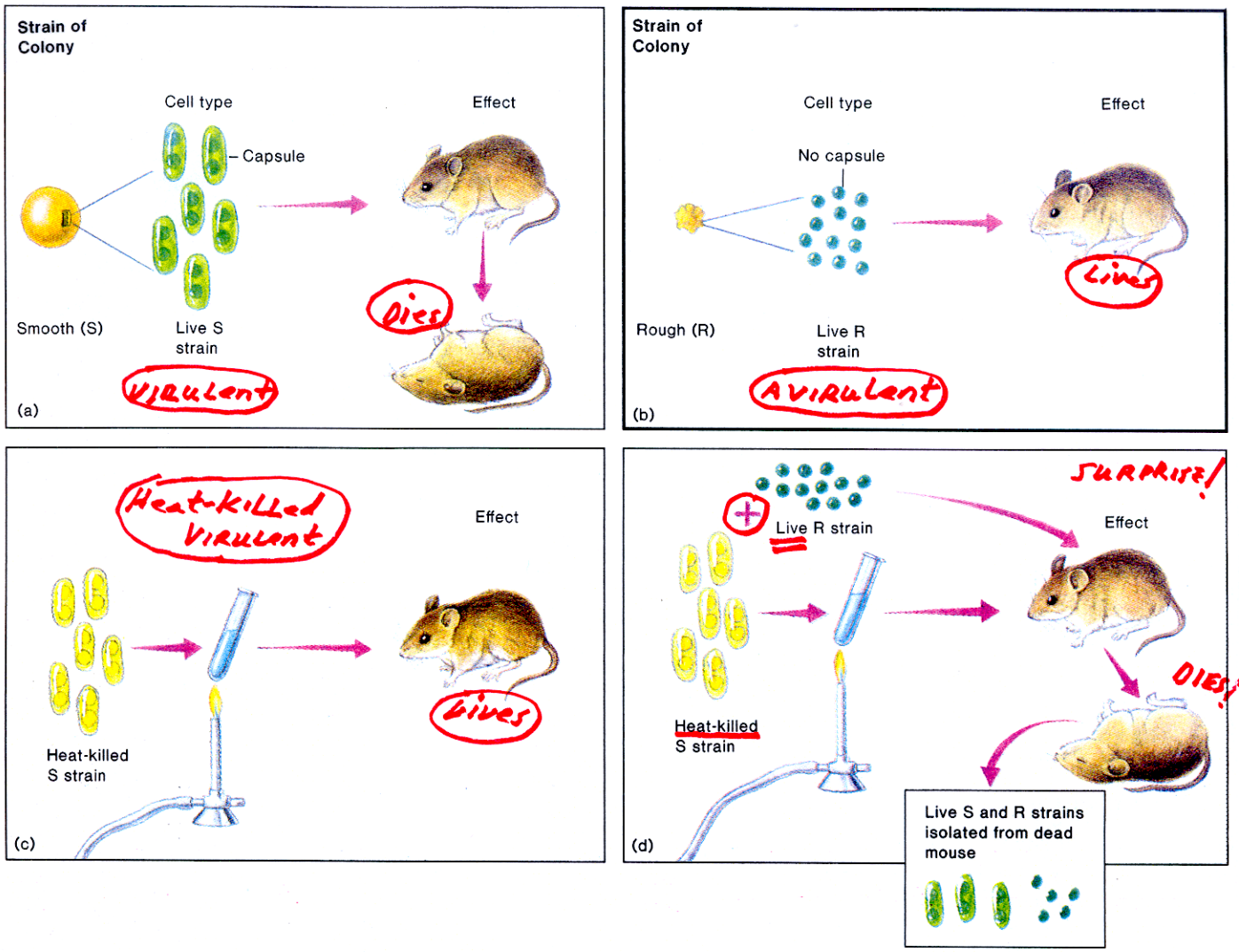


Figure 2.2 Griffith's transformation experiments. (**a**) Virulent strain S *S. pneumoniae* bacteria kill their host; (**b**) avirulent strain R bacteria cannot infect successfully, so the mouse survives; (**c**) strain S bacteria that are heat-killed can no longer infect; (**d**) a mixture of strain R and heat-killed strain S bacteria kills the mouse. The killed virulent (S) bacteria have transformed the avirulent (R) bacteria to virulent (S).

LIVE R WAS TRANSFORMED BY DEAD S!

HOW?

LARGE MOLECULES in ALL CELLS

Table 3.1 Macromolecules

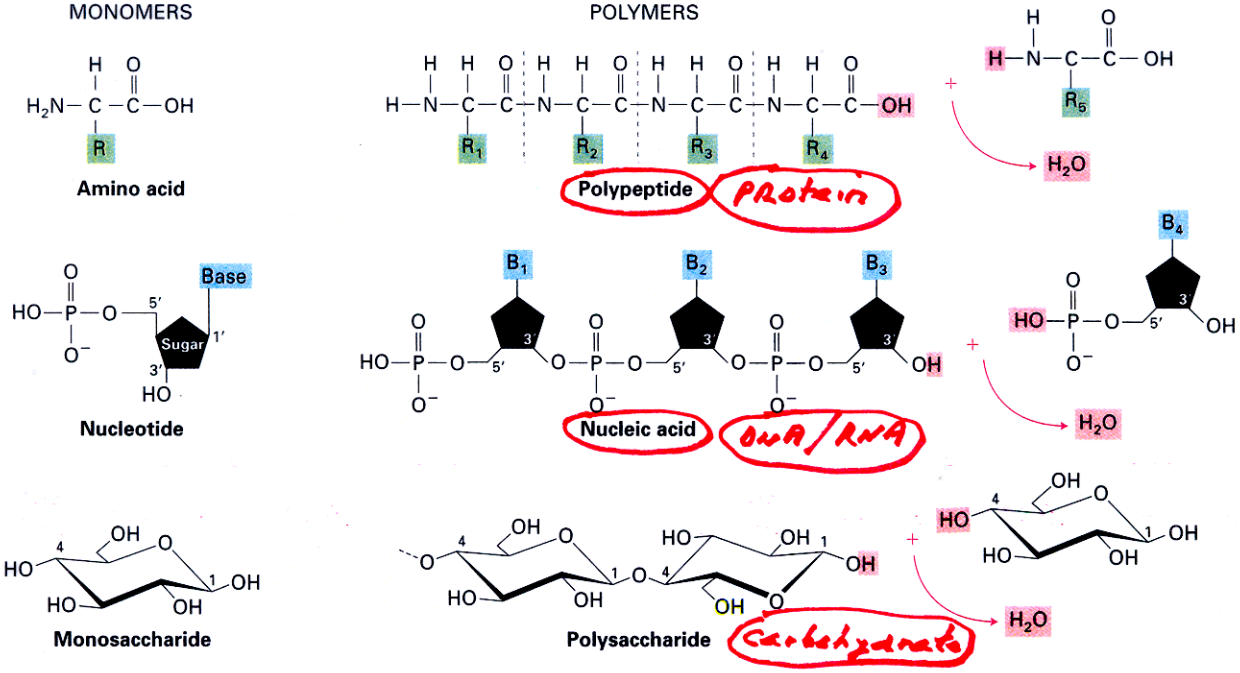
Macromolecule	Subunit	Function	Example
PROTEINS			
Globular	Amino acids	Catalysis; transport	Hemoglobir
Structural	Amino acids	Support	Hair; silk
NUCLEIC ACIDS			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
LIPIDS			
Fats	Glycerol and three fatty acids	Energy storage	Butter; corn oil; soap
Phospholipids	Glycerol, two fatty acids, phosphate, and polar R groups	Cell membranes	Lecithin
Prostaglandins	Five-carbon rings with two nonpolar tails	Chemical messengers	Prostaglandin E (PGE)
Steroids	Four fused carbon rings	Membranes; hormones	Cholesterol; estrogen
Terpenes	Long carbon chains	Pigments; structural	Carotene; rubber
CARBOHYDRATES			
Starch, glycogen	Glucose	Energy storage	Potatoes
Cellulose	Glucose	Cell walls	Paper; strings of celery
Chitin	Modified glucose	Structural support	Crab shells

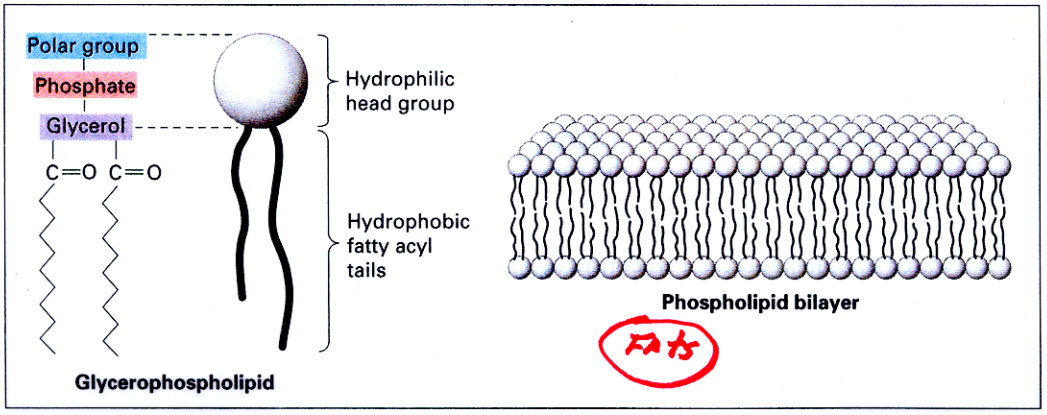
Which is the TRANSFORMING PRINCIPLE?
And the Genetic Material?

(1) What is Predicted if DNA is the Genetic Material?

(2) How Test Hypothesis?

LARGE Molecules in Cells Have Different Structure





Chemistry → Biology!

What Predict if DNA the Genetic Material?

FIRST "NAKED" DNA TRANSFORMATION
OR Genetic Engineering Experiment!

Avery, McLeod, & McCarty Experiment
SHOWING DNA is the Genetic Material

MESSAGE

The demonstration that DNA is the transforming principle was the first demonstration that genes are composed of DNA.

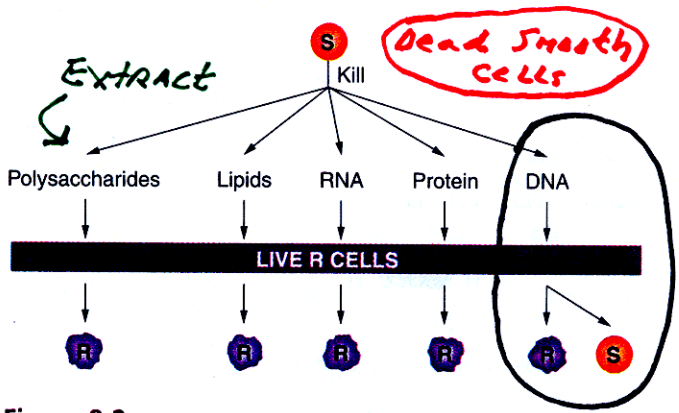


Figure 8-2 Demonstration that DNA is the transforming agent. DNA is the only agent that produces smooth (S) colonies when added to live rough (R) cells.

1. Hypothesis?
2. Predictions?
3. Experiment?
4. Results?
5. Conclusions?

DNA from Dead Smooth/Virulent cells CAN TRANSFORM Live/Avirulent cells → LIVE VIRULENT CELLS

∴ DNA taken up by Live Smooth cells & causes TRANSFORMATION

GRIFFITH & AVERY's Experiments Showing DNA is the Genetic Material

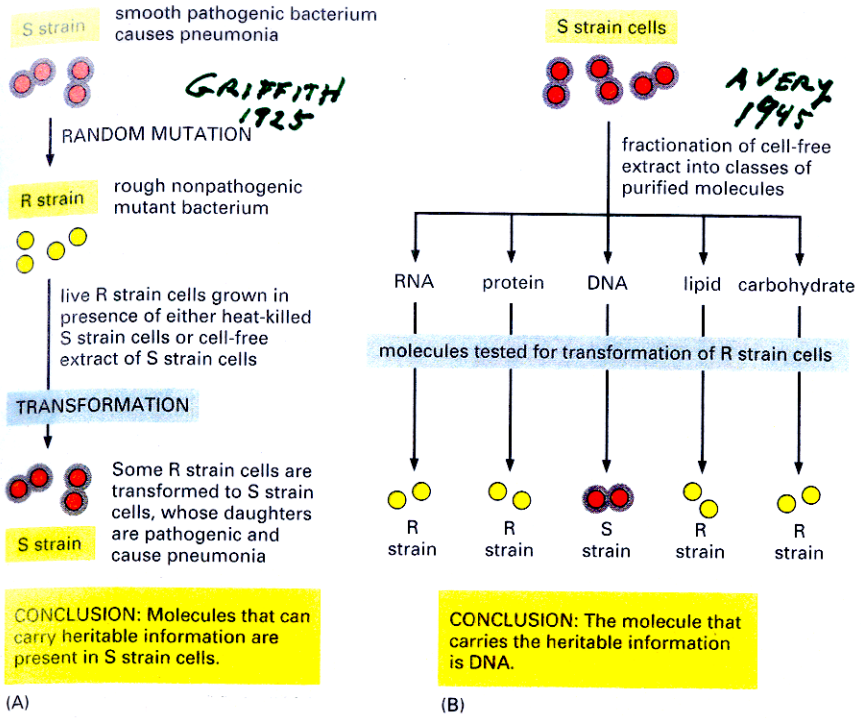
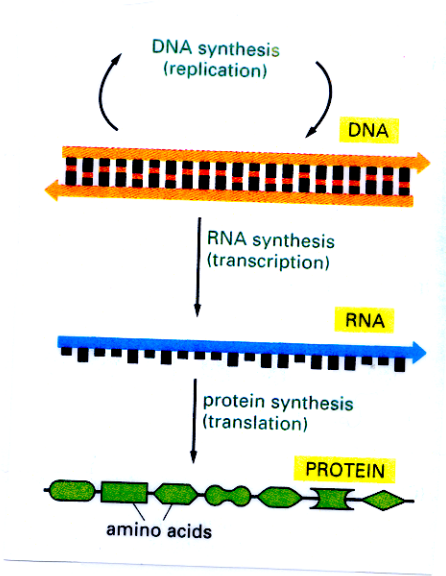


Figure 4–2 Experimental demonstration that DNA is the genetic material. These experiments, carried out in the 1940s, showed that adding purified DNA to a bacterium changed its properties and that this change was faithfully passed on to subsequent generations. Two closely related strains of the bacterium *Streptococcus pneumoniae* differ from each other in both their appearance under the microscope and their pathogenicity. One strain appears smooth (S) and causes death when injected into mice, and the other appears rough (R) and is nonlethal. (A) This experiment shows that a substance present in the S strain can change (or transform) the R strain into the S strain and that this change is inherited by subsequent generations of bacteria. (B) This experiment, in which the R strain has been incubated with various classes of biological molecules obtained from the S strain, identifies the substance as DNA.

HOW DID Avery's Experiment Verify the Hypothesis That DNA is the Gene?

Predictions	Results
Replication	yes
Phenotype	yes
Stable	yes



CELL PROCESSES

S DNA Taken up by R cells

↓ S "gene"

TRANSCRIPTION

↓ S "RNA"

TRANSLATION

↓ S "protein"

↓ Smooth/Virulent cell

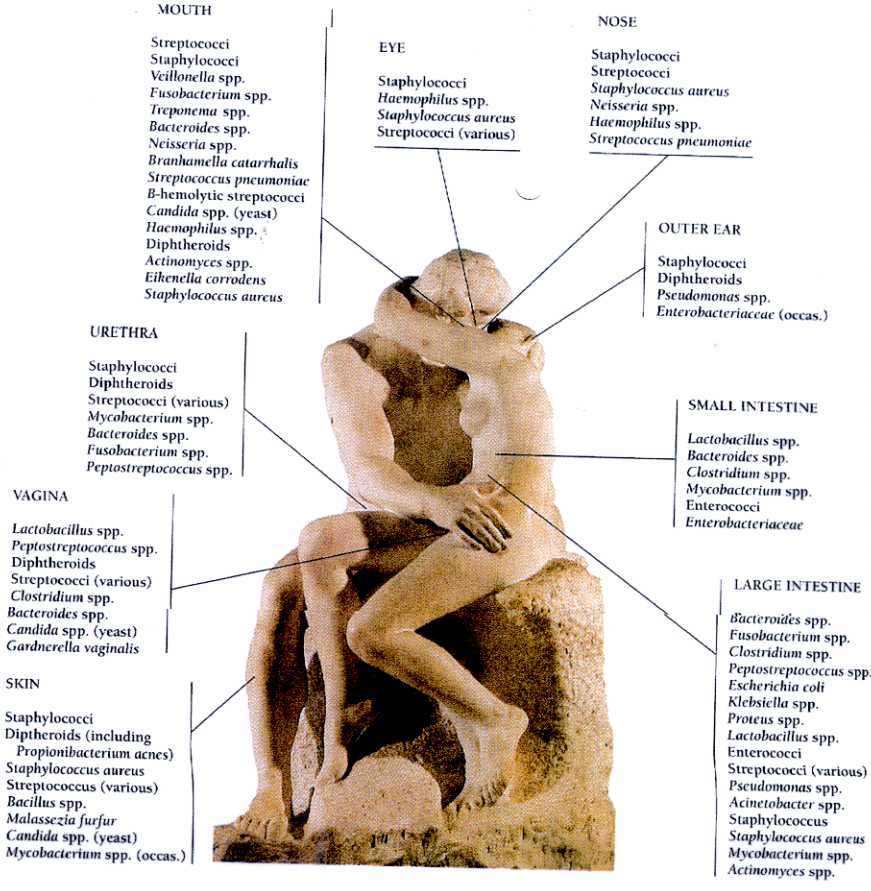
Phenotype

TRANSFORMATION used as a Genetic Engineering Process to Present Day!

TRANSFORMATION? Ability of a cell phenotype to be changed/TRANSFORMED by DNA!

CAN BACTERIA BE TRANSFORMED WITH OTHER GENES/TRAITS?

Figure 20-3 **Microorganisms that normally inhabit the human body.** All of the microorganisms listed here live—usually harmoniously—on the surfaces and in the interiors of human bodies. *Candida albicans*, commonly known as yeast, is a fungus that lives on the skin and in the mouth and vagina. *Candida* is, of course, a eukaryote, not a prokaryote. *(Erich Lessing/Art Resource)*



What are Antibiotics?

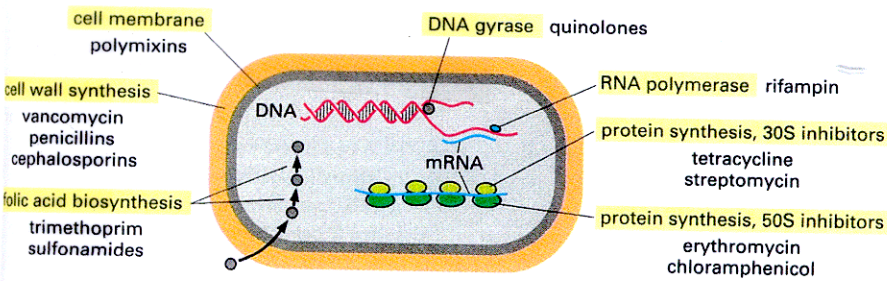
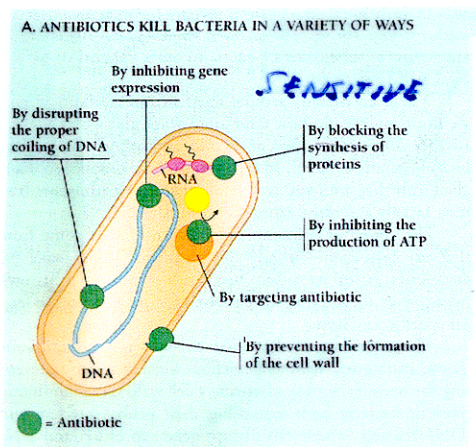


Figure 25–8 Antibiotic targets. Despite the large number of antibiotics available, they have a narrow range of targets, which are highlighted in *yellow*. A few representative antibiotics in each class are listed. All antibiotics used to treat human infections fall into one of these categories. The vast majority inhibit either bacterial protein synthesis or bacterial cell wall synthesis.



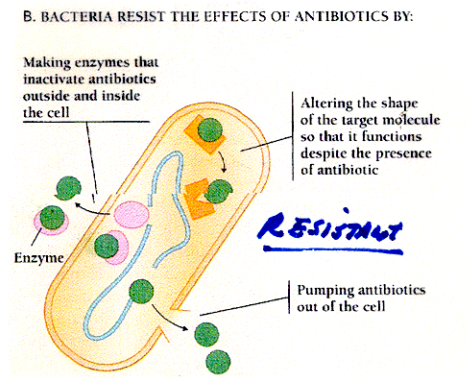


Figure 20-5 How does it work? A. Every antibiotic has a distinctive way of preventing bacteria from reproducing. B. Bacteria have different ways of resisting the effects of antibiotics.

Antibiotic Resistance is Encoded by Genes on Xtra chromosomal DNA called PLASMIDS

The First Genetic Engineering Experiment used Antibiotic Resistance

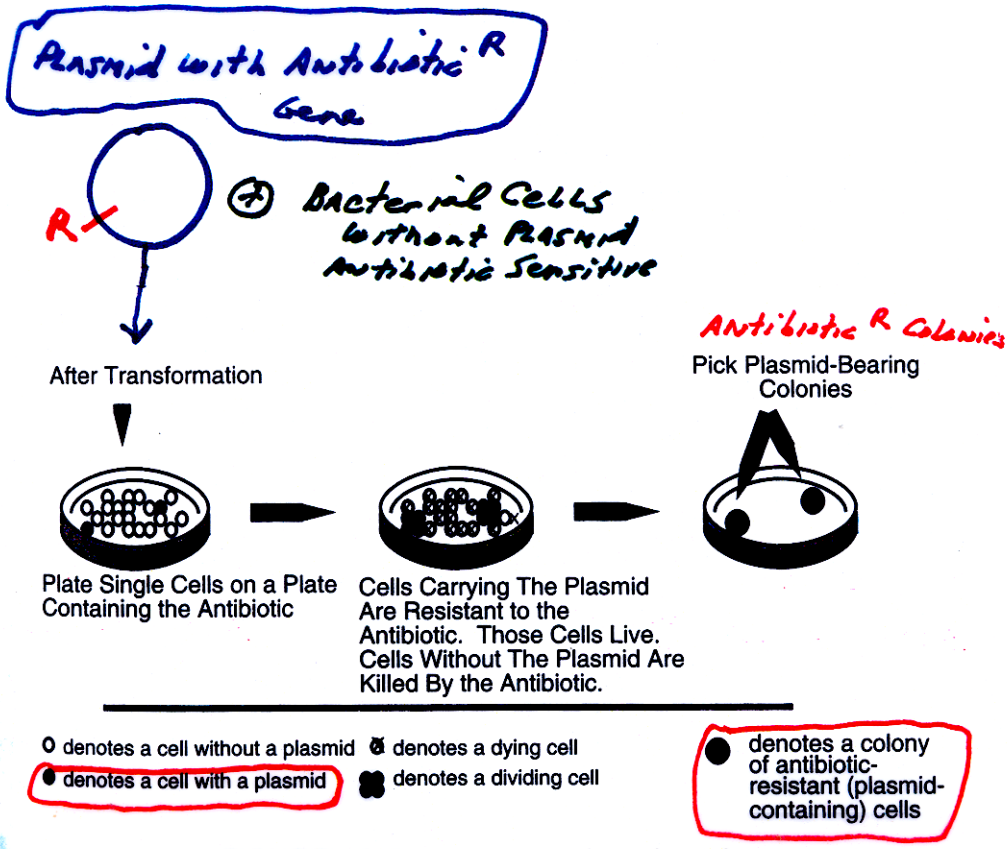
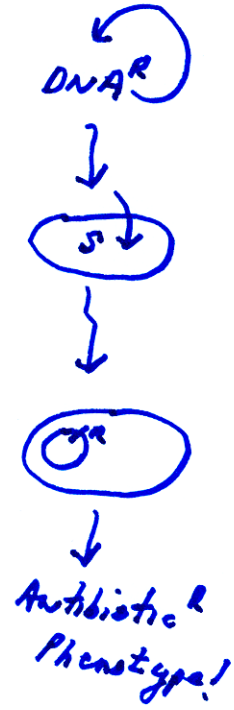


FIGURE 12.3 The process of transformation.

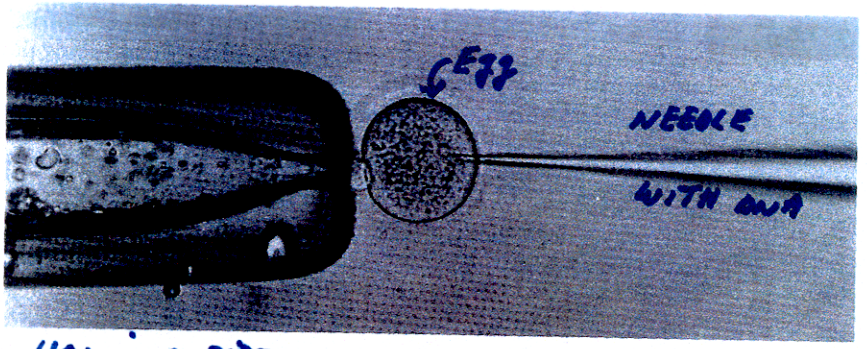


Antibiotic R DNA + Antibiotic S Cells

TRANSFORMATION → Antibiotic R cells

Stanley Cohen & Herb Boyer → 1973

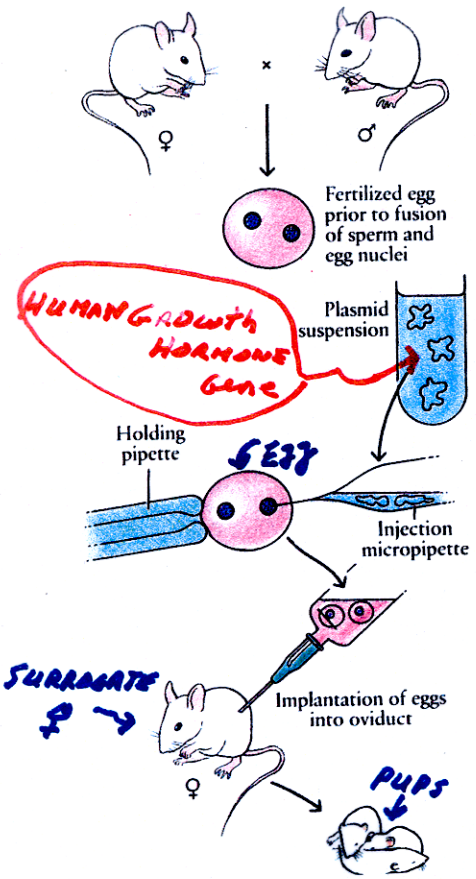
CAN Higher Organisms Be TRANSFORMED?
Genetically Engineered?



(b)

Recall GLo Fish  Experiment!

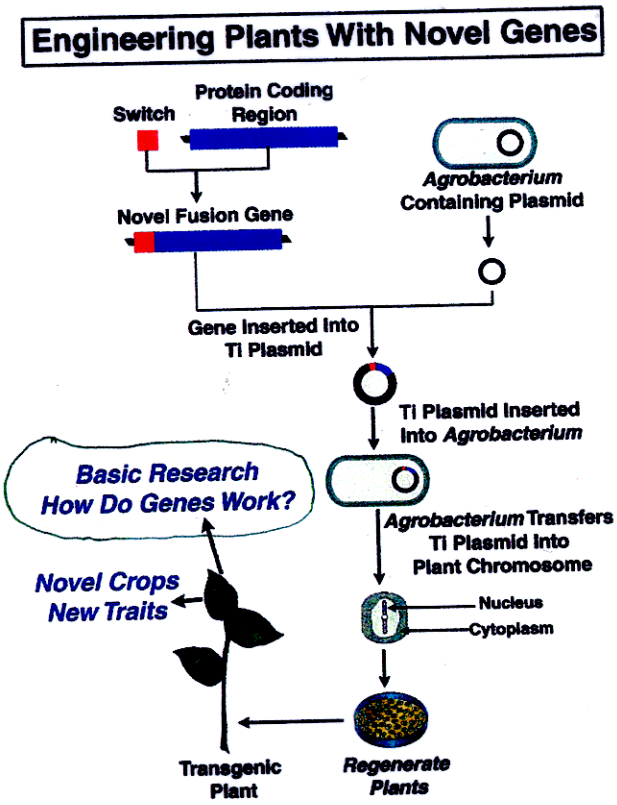
THE MAKING OF A MIGHTY MOUSE!



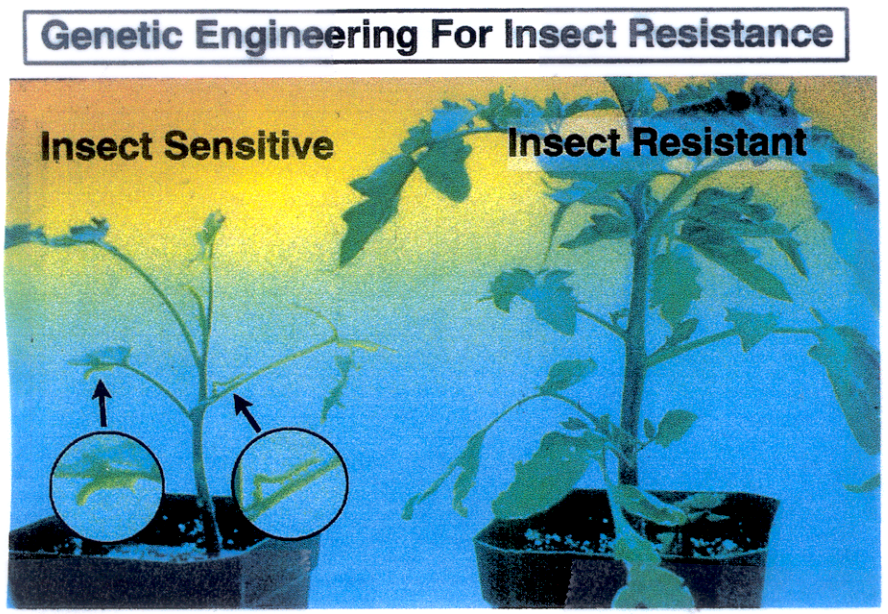
DNA → Growth Hormone → Mighty Mouse Phenotype

Yo! It's all in the DNA

CAN PLANTS BE Genetically Engineered or TRANSFORMED WITH DNA?



The MAKING OF AN Insect Resistant PLANT



Bacteria Insect® Gene / DNA → PLANT cells → PLANT®

∴ DNA is the genetic material of all organisms

Bacteria → Animals + PLANTS

HOW WAS DNA SHOWN TO BE THE GENETIC MATERIAL?

Genetic Engineering / TRANSFORMATION Involves INCORPORATING Engineered DNA or Genes Into Different ORGANISMS

genotype

↓

phenotype

Engineered Gene MUST

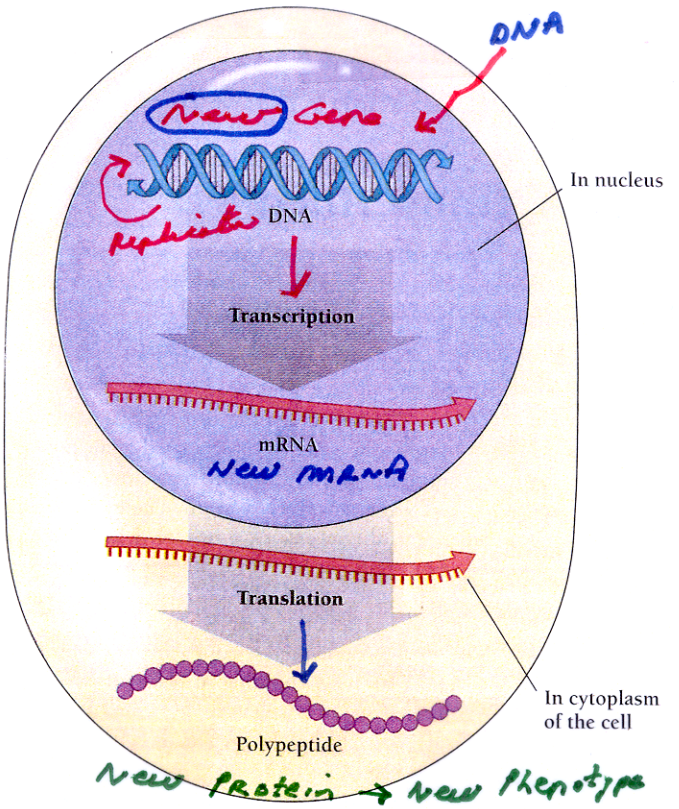
1. Enter Target Cell
2. Use Target Cell Machinary enzymes to become Part of Chromosome
3. Replicate with Target cell Chromosome
4. Use Target Cell Protein Synthesis Machinery to make a New Protein → Phenotype trait!

Engineered Gene Can Be

1. From Same Organism
2. From Different Organism
3. From a Combination of organisms stitched together by genetic engineering

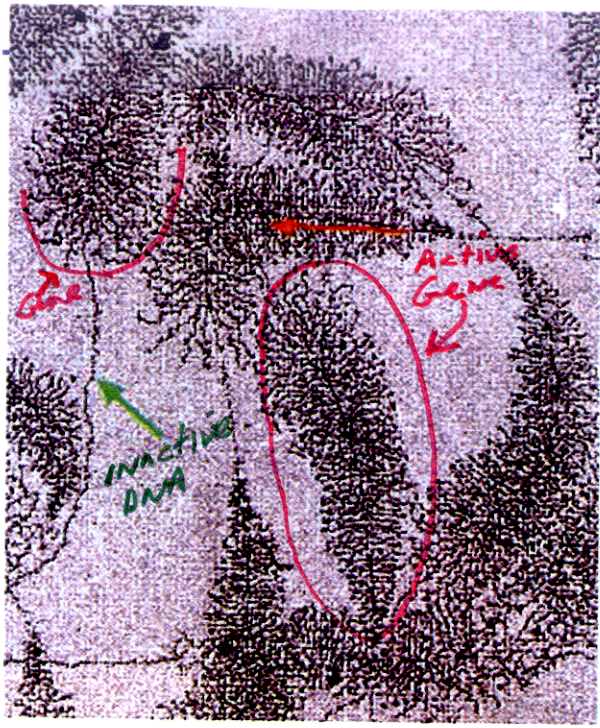
Gene Engineering Shows that Gene Processes Are Universal!

Genetic Engineering Does not Involve Any "Hocus Pocus"



IT's ALL in the DNA & CELL PROCESSES – ultimate in "Organic" Biology

What are Genes?



Electron micrograph of DNA (green arrow) being transcribed into RNA (red arrow). [O. L. Miller, Jr., and Barbara R. Beatty, Oak Ridge National Laboratory.]

Visualization of a Gene in Action

Genes + Genomes Differ
Because the Sequence
of DNA Differs

DNA Sequence

Beginning → End → Biological Uniqueness

5' 3'

If you know the DNA Sequence, you can
Engineer Anything! Even Make
New Genes + Genomes!

What is a Gene?

Begin 5'

```
CCCTGTGGAGCCACACCCTAGGGTTGGCCA
ATCTACTCCCAGGAGCAGGGAGGGCAGGAG
CCAGGGCTGGGCATAAAAGTCAGGGCAGAG
CCATCTATTGCTTACATTTGCTTCTGACAC
AACTGTGTTCACTAGCAACTCAAACAGACA
CCATGGTGCACCTGACTCCTGAGGAGAAGT
CTGCCGTTACTGCCCTGTGGGGCAAGGTGA
ACGTGGATGAAGTTGGTGGTGAGGCCCTGG
GCAGGTTGGTATCAAGGTTACAAGACAGGT
TTAAGGAGACCAATAGAAACTGGGCATGTG
GAGACAGAGAAGACTCTTGGGTTTCTGATA
GGCACTGACTCTCTCTGCCTATTGGTCTAT
TTTCCCACCCTTAGGCTGCTGGTGGTCTAC
CCTTGGACCCAGAGGTTCTTTGAGTCCTTT
GGGGATCTGTCCACTCCTGATGCTGTTATG
GGCAACCCTAAGGTGAAGGCTCATGGCAAG
AAAGTGCTCGGTGCCTTTAGTGATGGCCTG
GCTCACCTGGACAACCTCAAGGGCACCTTT
GCCACACTGAGTGAGCTGCACTGTGACAAG
CTGCACGTGGATCCTGAGAACTTCAGGGTG
AGTCTATGGGACCCTTGATGTTTTCTTTCC
CCTTCTTTTCTATGGTTAAGTTCATGTCAT
AGGAAGGGGAGAAGTAACAGGGTACAGTTT
AGAATGGGAAACAGACGAATGATTGCATCA
GTGTGGAAGTCTCAGGATCGTTTTAGTTTC
TTTTATTTGCTGTTCATAACAATTGTTTTC
TTTTGTTTAATTCTTGCTTTCTTTTTTTTT
CTTCTCCGCAATTTTTACTATTATACTTAA
TGCCTTAACATTGTGTATAACAAAAGGAAA
TATCTCTGAGATACATTAAGTAACTTAAAA
AAAAACTTTACACAGTCTGCCTAGTACATT
ACTATTTGGAATATATGTGTGCTTATTTGC
ATATTCATAATCTCCCTACTTTATTTTCTT
TTATTTTTAATTGATACATAATCATTATAC
ATATTTATGGGTTAAAGTGTAATGTTTTAA
TATGTGTACACATATTGACCAAATCAGGGT
AATTTTGCATTTGTAATTTTAAAAAATGCT
TTCTTCTTTTAATATACTTTTTTGTTTATC
TTATTTCTAATACTTTCCCTAATCTCTTTC
TTTCAGGGCAATAATGATACAATGTATCAT
GCCTCTTTGCACCATTCTAAAGAATAACAG
TGATAATTTCTGGGTTAAGGCAATAGCAAT
ATTTCTGCATATAAATATTTCTGCATATAA
ATTGTAACTGATGTAAGAGGTTTCATATTG
CTAATAGCAGCTACAATCCAGCTACCATTC
TGCTTTTATTTTATGGTTGGGATAAGGCTG
GATTATTCTGAGTCCAAGCTAGGCCCTTTT
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CCACAAGTATCACTAAGCTCGCTTTCTTGC
TGTCCAATTTCTATTAAAGGTTCCTTTGTT
CCCTAAGTCCAACTACTAAACTGGGGGATA
TTATGAAGGGCCTTGAGCATCTGGATTCTG
CCTAATAAAAAACATTTATTTTCATTGCAA
TGATGTATTTAAATTATTTCTGAATATTTT
ACTAAAAAGGGAATGTGGGAGGTCAGTGCA
TTTAAAACATAAAGAAATGATGAGCTGTTC
AAACCTTGGGAAAATACACTATATCTTAAA
CTCCATGAAAGAAGGTGAGGCTGCAACCAG
CTAATGCACATTGGCAACAGCCCCTGATGC
CTATGCCTTATTCATCCCTCAGAAAAGGAT
TCTTGTAGAGGCTTGATTTGCAGGTTAAAG
TTTTGCTATGCTGTATTTTACATTACTTAT
TGTTTTAGCTGTCCTCATGAATGTCTTTTC
```

End 3'

Sequence or order of nucleotides

Coding DNA strand

The β-globin Gene

Blood protein carries Oxygen to all cells from lungs → energy

A gene is a unique sequence of nucleotides specifying a function

SEQUENCE = BIOLOGY!

What if sequence changed?

DNA and Genes Consist of Nucleotides Joined By Bonds

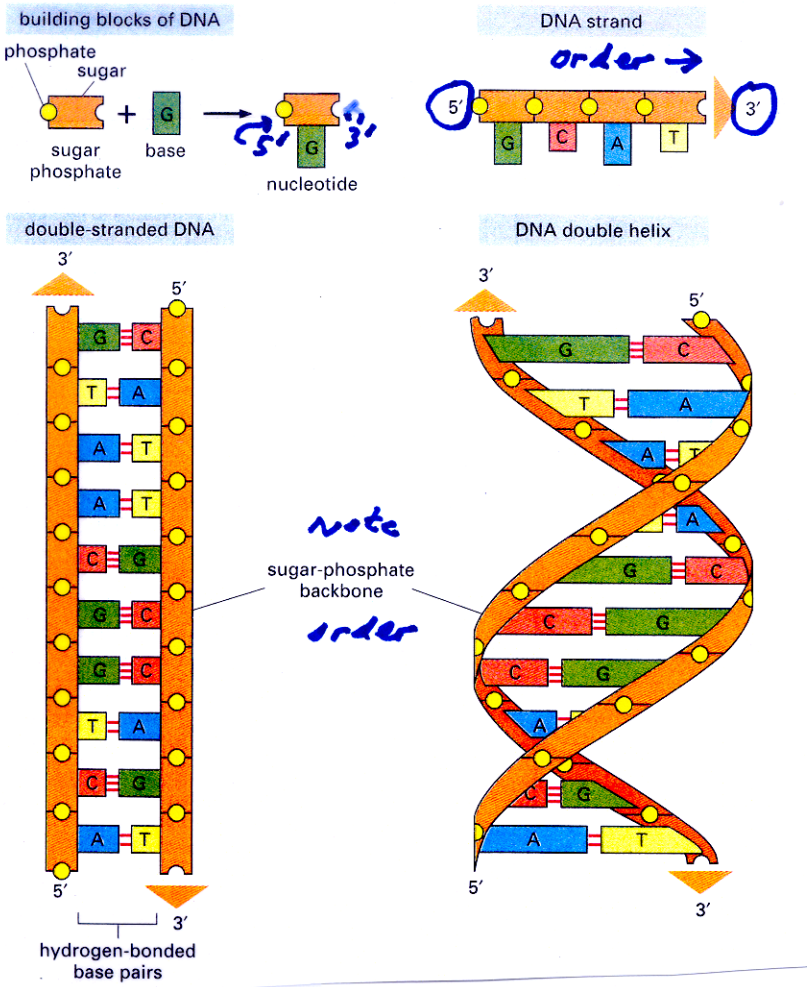

Figure 4–3 DNA and its building blocks. DNA is made of four types of nucleotides, which are linked covalently into a polynucleotide chain (a DNA strand) with a sugar-phosphate backbone from which the bases (A, C, G, and T) extend. A DNA molecule is composed of two DNA strands held together by hydrogen bonds between the paired bases. The *arrowheads* at the ends of the DNA strands indicate the polarities of the two strands, which run antiparallel to each other in the DNA molecule. In the diagram at the bottom left of the figure, the DNA molecule is shown straightened out; in reality, it is twisted into a double helix, as shown on the right. For details, see Figure 4–5.

① A nucleotide = sugar + base + phosphate

② Nucleotides are linked IN ORDER 5′→3′ by Phosphodiester Bonds