Life's Genetic Material???

Transformation or Resurrection: **Fred Griffith**'s Research Discovery

Directions:

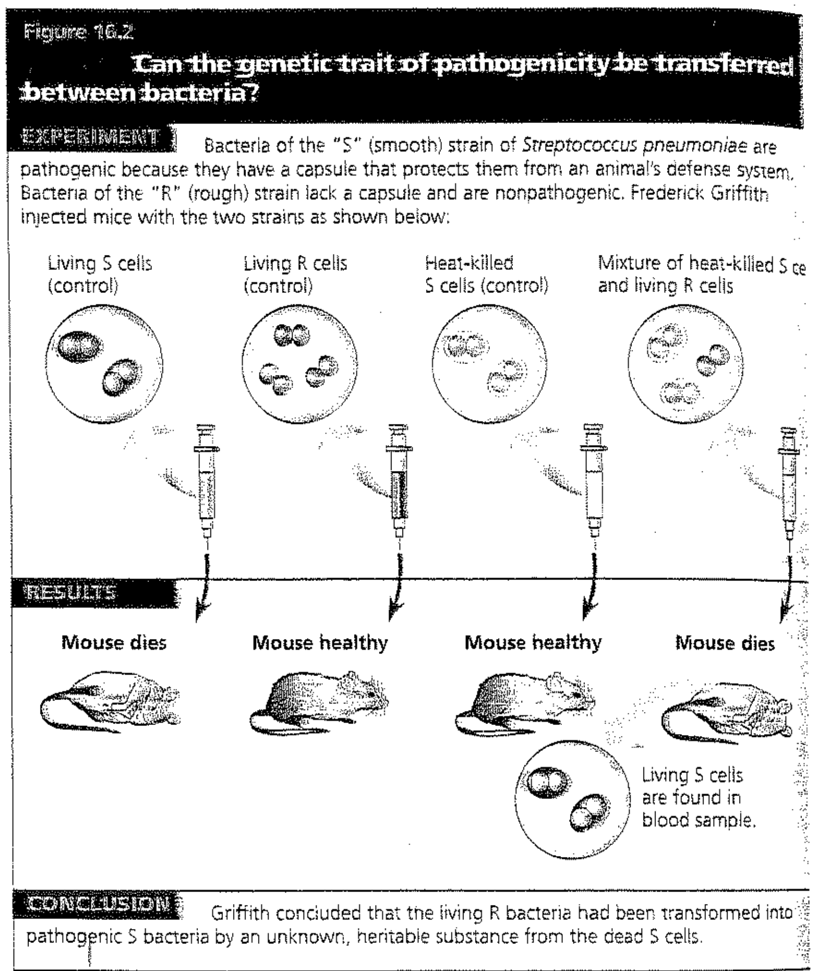
- Read the information about **Fred Griffith's** classic experiments with mice
- Summarize with pictures and words his step by step experiment
- Summarize his experimental conclusion …. What was his BIG discovery?

The Experiment:

The Conclusion:

Evidence That DNA Can Transform Bacteria

We can trace the discovery of the genetic role of DNA back to 1928. Frederick Griffith, a British medical officer, was studying *Streptococcus pneumoniae*, a bacterium that causes pneumonia in mammals. Griffith had two strains (varieties) of the bacterium, a pathogenic (disease-causing) one and a nonpathogenic (harmless) strain. He was surprised to find that when he killed the pathogenic bacteria with heat and then mixed the cell remains with living bacteria of the nonpathogenic strain, some of the living cells became pathogenic **(Figure 16.2)**. Furthermore, this new trait of pathogenicity was inherited by all the descendants of the transformed bacteria. Clearly, some chemical component of the dead pathogenic cells caused this heritable change, although the identity of the substance was not known. Griffith called the phenomenon **transformation**, now defined as a change in genotype and phenotype due to the assimilation of external DNA by a cell. (This use of the word *transformation* should not be confused with the conversion of a normal animal cell to a cancerous one, discussed in Chapter 12.)



Griffith's work set the stage for a 14-year search for the identity of the transforming substance by American bacteriologist Oswald Avery. Avery purified various types of molecules from the heat-killed pathogenic bacteria, then tried to transform live nonpathogenic bacteria with each type. Only DNA worked. Finally, in 1944, Avery and his colleagues Maclyn McCarty and Colin MacLeod announced that the transforming agent was DNA. Their discovery was greeted with interest but considerable skepticism, in part because of the lingering belief that proteins were better candidates for the genetic material. Moreover, many biologists were not convinced that the genes of bacteria would be similar in composition and function to those of more complex organisms. But the major reason for the continued doubt was that so little was known about DNA.

how researchers discovered that **deoxyribonucleic acid** (DNA), a nucleic acid once thought unremarkable, is the molecular basis of inheritance. We explore the unique features of DNA, including its replication (see photograph), that enable it to carry out this role. ■

EVIDENCE OF DNA AS THE HEREDITARY MATERIAL

Learning Objective

1 Summarize the evidence that accumulated during the 1940s and early 1950s demonstrating that DNA is the genetic material.

PROCESS OF SCIENCE

During the 1930s and early 1940s, most geneticists paid little attention to DNA, convinced that the genetic material must be protein. Given the accumulating evidence that genes control production of proteins (discussed in Chapter 12), it certainly seemed likely that genes themselves must also be proteins. Scientists knew proteins consisted of more than 20 different kinds of amino acids in many different combinations, which conferred unique properties on each type of protein. Given their complexity and diversity compared with other molecules, proteins seemed to be the "stuff" of which genes are made.

In contrast, scientists had established that DNA and other nucleic acids were made of only four nucleotides, and what was known about their arrangement made them relatively uninteresting to most researchers. For this reason, several early clues to the role of DNA were not widely noticed.

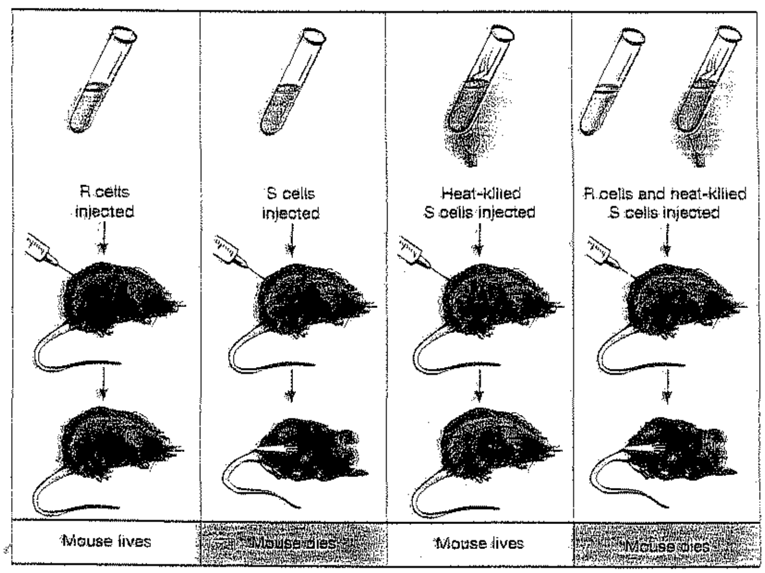
DNA is the transforming principle in bacteria

One of these clues had its origin in 1928, when Frederick Griffith, a British medical officer, made a curious observation concerning two strains of pneumococcus bacteria (Fig. 11-1). A smooth (S) strain, named for its formation of smooth colonies on a solid growth medium, was known to exhibit **virulence**, the ability to cause disease, and often death, in its host. When living cells of this strain were injected into mice, the animals contracted pneumonia and died. Not surprisingly, the injected animals survived if the cells were first killed with heat. A related rough (R) strain of bacteria, which forms colonies with a rough surface, was known to exhibit **avirulence**, or inability to produce pathogenic effects; mice injected with either living or heat-killed cells of this strain survived. However, when Griffith injected mice with a mixture of *heat-killed* virulent S cells and live avirulent R cells, a high proportion of the mice died. Griffith then isolated living S cells from the dead mice.

Because neither the heat-killed S strain nor the living R strain could be converted to the living virulent form when injected by itself in the control experiments, it seemed that something in the heat-killed cells converted the avirulent cells to the lethal form. This type of permanent genetic change in which the properties of one strain of dead cells are conferred on a different strain of living cells became known as **transformation**. Scientists hypothesized that some chemical substance (the "transforming principle") was transferred from the dead bacteria to the living cells and caused transformation.

In 1944, American biologist Oswald T. Avery and his colleagues Colin M. MacLeod and Maclyn McCarty chemically identified Griffith's transforming principle as DNA. They did this through a series of careful experiments in which they lysed (split open) S cells and separated the cell contents into several fractions: lipids, proteins, polysaccharides, and nucleic acids (DNA and RNA). They tested each fraction to see if it could transform living R cells into S cells. The experiments using lipids, polysaccharides, and proteins did not cause transformation. However, when Avery treated living R cells with nucleic acids extracted from S cells, the R cells were transformed into S cells.

FIGURE 11-1 Griffith's transformation experiments.
Although neither the rough (R) strain nor the heat-killed smooth (S) strain could kill a mouse, a combination of the two did. Autopsy of the dead mouse showed the presence of living S-strain pneumococci. These results indicated that some substance in the heat-killed S cells had transformed the living R cells into a virulent form. Avery and his colleagues later showed that purified DNA isolated from the S cells confers virulence on the R cells, establishing that DNA carries the necessary information for bacterial transformation.



Other DNA Researchers of Interest:

Friedrich Meischer in 1869 isolated DNA from fish sperm and the pus of open wounds. Since it came from nuclei, Meischer named this new chemical, nuclein. Subsequently the name was changed to nucleic acid and lastly to deoxyribonucleic acid (DNA)..

During the 1920s, biochemist **P.A. Levene** analyzed the components of the DNA molecule. He found it contained four nitrogenous bases: cytosine, thymine, adenine, and guanine; deoxyribose sugar; and a phosphate group. He concluded that the basic unit (nucleotide) was composed of a base attached to a sugar and that the phosphate also attached to the sugar. He (unfortunately) also erroneously concluded that the proportions of bases were equal and that there was a tetranucleotide that was the repeating structure of the molecule. The nucleotide, however, remains as the fundemantal unit (monomer) of the nucleic acid polymer. There are four nucleotides: those with cytosine (C), those with guanine (G), those with adenine (A), and those with thymine (T).