

## DNA AS GENETIC MATERIAL AND NUCLEIC ACID METABOLISM

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### 1. Introduction

It is logical that some form of information is passed from generation to generation. This should carry the form and structure of each individual's characteristics from parents to offspring. This information would be stored in the genetic material. The genetic material will have a number of characteristics, which are necessary for it to be able to function effectively. These are:

- a) The storage of information
- b) A high degree of stability with respect to the information stored
- c) The ability to replicate the information without a high error level
- e) The ability to transfer the information into a form able to control the cell
- f) A limited ability to change to allow evolution to occur

From the beginning of the 20th Century, there were two major candidate biochemicals for the genetic material. These were proteins and nucleic acids. The abundance of proteins,

their diversity and their variability from organism to organism led to them being the major candidate for the first part of the century. The lack of understanding of the chemical structure of nucleic acid, particularly the proportions of its four constituent molecules, put nucleic acid into its second place. Only as microbiology and biochemistry advanced was it possible to answer clearly which biological molecule encoded the genetic information in living organisms

## 2. The structure of nucleic acids

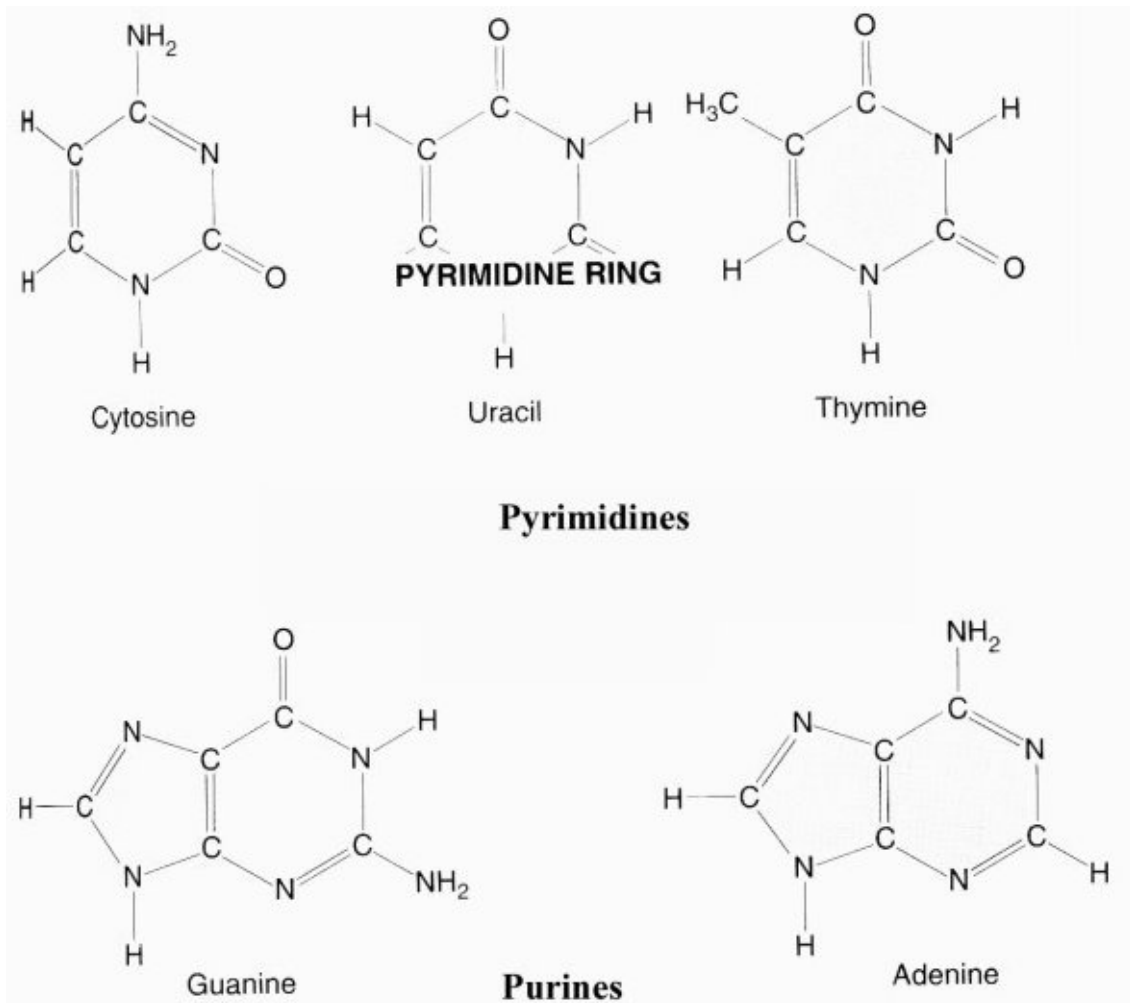


Figure1:

There are two chemically distinct forms of nucleic acid found in living organisms, these are ribonucleic acid (RNA) and deoxyribonucleic acid (DNA). They are made up of monomers of a different type polymerized into a chain. The building block of all nucleic acid is the nucleotide, which consists of a nitrogenous base, a pentose sugar and a phosphate group chemically linked. The nitrogenous bases can be divided into two type, the double ring structure of nine carbons called purines and the single ring structure of six carbons called pyrimidines. There are two purines, adenine and guanine abbreviated to A and G and three pyrimidines, cytosine, thymine and uracil, abbreviated to C, T and U. DNA contains A, C, G and T while RNA contains A, C, G and U. RNA also differs from

DNA in that it contains the pentose sugar ribose while RNA contains a different pentose sugar, deoxyribose which lacks a hydroxyl group at the 2' position compared to ribose. Figure 1 shows the structure of these chemicals individually while Figure 2 shows the structure of the complete nucleotides. Chemical analysis shows that in DNA, the ratio of G to C and A to T is always 1:1 while the ratio of G+C to A+T can vary dramatically. This so called Chargaff rule holds for the DNA of most organisms but not one happening in the does not hold for RNA.

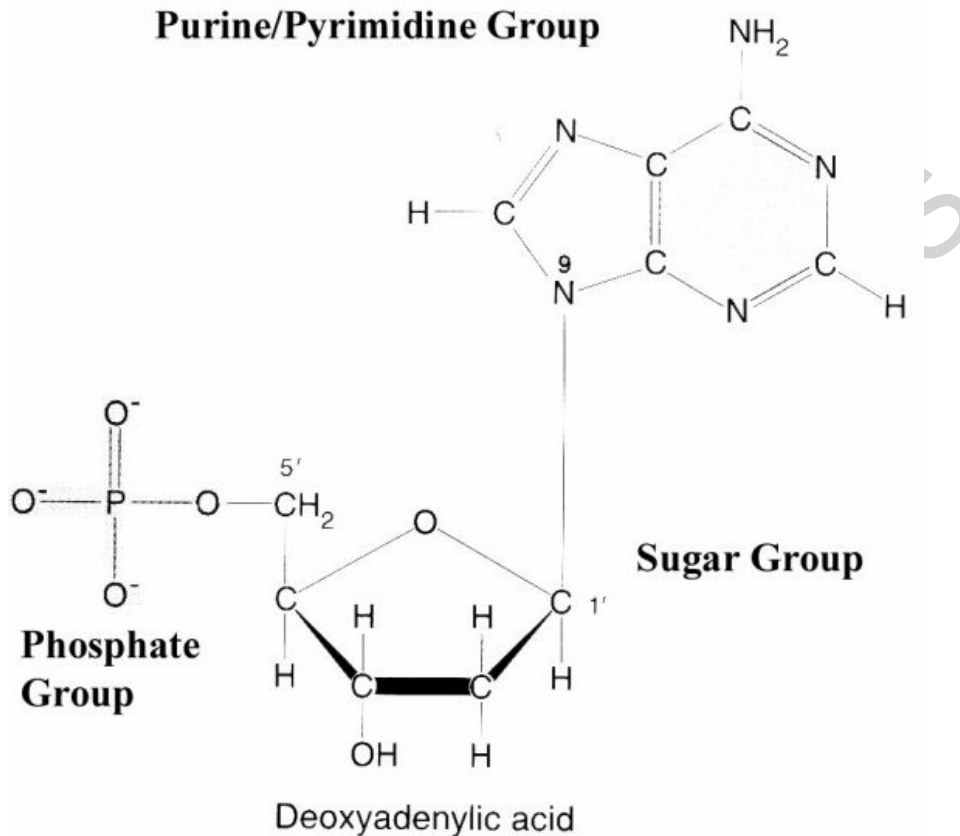


Figure 2:

## 2.1 Bacterial transformation and the genetic material

Griffith in 1927 performed a series of experiments on *Streptococcus pneumoniae*, a causative organism of pneumonia in some vertebrates including humans and mice. Some strains of this organism are virulent and cause the disease in mice while others are avirulent and do not cause the disease. The difference was due to the avirulent strains lacking a polysaccharide capsule. When injected into animal, the non-capsulated bacteria could be engulfed and destroyed by white blood cells while the capsulated bacteria were resistant to engulfment. It is possible to see the difference in capsulation when the strains are grown on solid media, the avirulent unencapsulated bacteria have a dull rough appearance while the virulent encapsulated bacteria have a smooth shiny appearance. Griffith used two strains in his experiment IIR (serotype II, rough, avirulent) and IIIS (serotype III, smooth, virulent).

Only living virulent bacterial cells of *S. pneumonia* can kill mice. Heat-killed virulent cells, live avirulent cells and heat-killed avirulent cells do not cause pneumonia in the mice. Griffith injected a mixture of heat-killed virulent cells and live avirulent cells into mice. These mice died of pneumonia and the bacteria isolated from them were smooth and virulent. Appropriate controls showed that only an interaction between the dead smooth virulent IIS and the live rough avirulent IIR cells resulting in live smooth virulent IIS cells could explain these results. Work by Dawson in 1931 showed that this so called transformation could occur in the test tube when the heat killed IIS was mixed with live IIR, resulting in live IIS on plates. Alloway showed in 1933 that a crude extract of IIS cells was sufficient to allow transformation. Although not clear to the above work, what was happening was a genetic transformation of the live IIR cells by the genetic material from the dead IIS cells to produce live IIS.

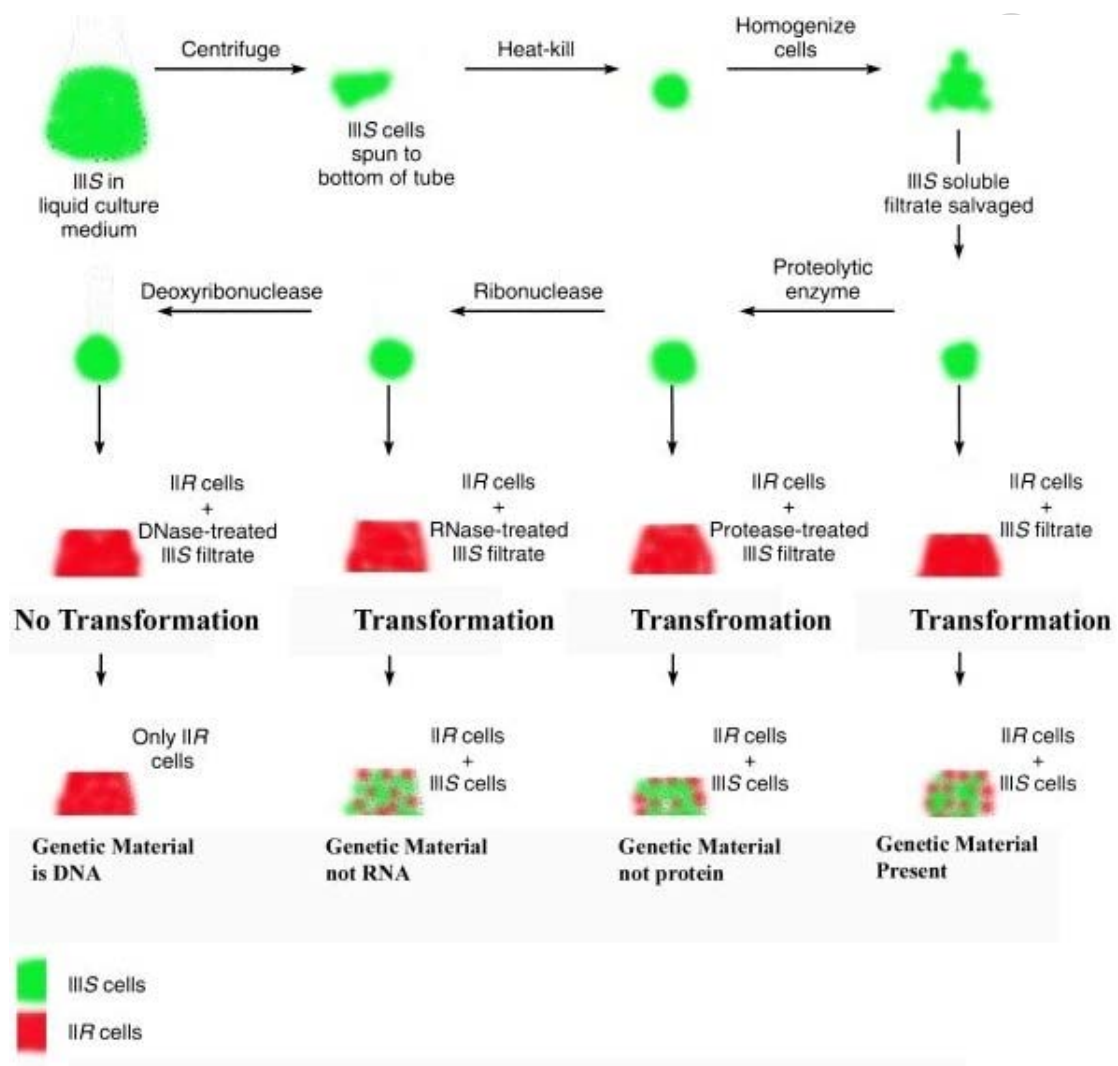


Figure 3:

Avery, MacLeod and McCarty in 1944 were the first to clearly place the genetic material as the molecule causing the transformation phenomena and to identify the molecule. To do this, they effectively fractionated the crude extract which could cause the

transformation event. To do this they used three enzymes, protease that destroys proteins, ribonuclease, which destroys RNA and deoxyribonuclease, which destroys DNA. Figure 3 outlines the experiment, which shows that destruction of RNA or protein did not destroy the transforming factor in the cell extract while destruction of the DNA did. Avery *et al* suggested that the DNA interacted with the cells and changed the heritable characteristics of the bacterial cell, that is, it was the genetic material.

## 2.2 Bacterial virus T2 and the genetic material

In 1952, Hershey and Chase published a series of experiments on how the bacterial virus or bacteriophage T2 reproduces in its host *Escherichia coli*. T2 consists of a protein coat surrounding a core of DNA about 1:1 protein to DNA, it reproduces by binding via a tail to the surface of *E. coli* and new bacteriophages are produced within the cell. DNA contains no sulphur atoms and proteins contains usually no phosphate atoms and Hershey and Chase used these facts to differentiate the two biomolecules. They added radioactive phosphorus P<sup>32</sup> or radioactive sulphur S<sup>35</sup> to reproducing T2 bacteriophage such that the T2 particles produced were either labelled in the DNA with P<sup>32</sup> or in the protein with S<sup>35</sup>. In two separate experiments, the two types of particle were allowed to reproduce for a short time on unlabelled bacterial cells, then the empty bacteriophage particles and infected bacteria were separated. It could be shown that the labelled DNA entered the bacterial cell while the labelled protein remained outside. More importantly, when the new generation of bacteriophage particles was produced, these were only labelled with P<sup>32</sup> proving that the DNA carried the genetic information from generation to generation.

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### **Biographical Sketch**

**Ralph Kirby** is Professor of Microbiology at Rhodes University, Grahamstown, South Africa. He has held this position for the last ten years. He graduated with his B.A. at Trinity College, Cambridge, UK, in 1972, and completed his Ph.D. at the University of East Anglia, UK, in 1976. Post-doctoral research followed at the University of Bristol, UK, then a lectureship and senior lectureship at the University of Cape Town, South Africa. His major interests are the molecular genetics of Actinomycetes, horizontal gene transfer, molecular population genetics, and the interaction between law and science. He is presently completing a LL.B.