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A brief review on the history of classic genetics

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Abstract. As we gain more knowledge about gene, DNA and inheritance, we began to understand that proper control of gene expression is the one of the most important aspects of life. This paper conducts a brief review on the history of classic genetics, helping people gain more knowledge about genes, DNA, and genetics.

Keywords: DNA; Inheritance; Genetics.

1. Introduction

Classical genetics is the branch of genetics based solely on visible results of reproductive acts. It is the oldest discipline in the field of genetics, going back to the experiments on Mendelian inheritance by Gregor Mendel who made it possible to identify the basic mechanisms of heredity [1]. Subsequently, these mechanisms have been studied and explained at the molecular level.

Classical genetics consists of the techniques and methodologies of genetics that were in use before the advent of molecular biology [2]. A key discovery of classical genetics in eukaryotes was genetic linkage. The observation that some genes do not segregate independently at meiosis broke the laws of Mendelian inheritance and provided science with a way to map characteristics to a location on the chromosomes [3]. Linkage maps are still used today, especially in breeding for plant improvement.

After the discovery of the genetic code and such tools of cloning as restriction enzymes, the avenues of investigation open to geneticists were greatly broadened. Some classical genetic ideas have been supplanted with the mechanistic understanding brought by molecular discoveries, but many remain intact and in use. Classical genetics is often contrasted with reverse genetics, and aspects of molecular biology are sometimes referred to as molecular genetics [4]. This paper aims to give a brief overview of the history of classic genetics.

2. History of classic genetics

The discovery in 1953 of the double helix, the twisted-ladder structure of DNA, by James Watson and Francis Crick marked a milestone in the history of science and gave rise to modern molecular biology, which is largely concerned with understanding how genes control the chemical processes within cells. In short order, their discovery yielded ground-breaking insights into the genetic code and protein synthesis. During the 1970s and 1980s, it helped to produce new and powerful scientific techniques, specifically recombinant DNA research, genetic engineering, rapid gene sequencing, and monoclonal antibodies, techniques on which today's multi-billion-dollar biotechnology industry is founded [5].

Researchers working on DNA in the early 1950s used the term "gene" to mean the smallest unit of genetic information, but they did not know what a gene actually looked like structurally and chemically, or how it was copied, with very few errors, generation after generation. What they do know, from Drosophila experiments conducted by Thomas H. Morgan in 1910s, that genes reside on chromosomes (Figure 1). Morgan proved that genes reside on chromosomes by crossing white-eye Drosophila to wildtype red-eye Drosophila and showed that the inheritance of eye color is sex-linked. This proves that such a gene must reside on sex chromosomes, thus genes must reside on chromosomes/DNA [6].

Figure 1. Fly Room at Columbia University with bunches of bananas featured prominently [7] [7].

Later in 1944, Avery and others showed that DNA was the "transforming principle", the carrier of hereditary information, in bacteria (Figure 2). To do so, they utilized two bacteria strains – the rough strain (R stain) that is nonvirulent to mouse, and the smooth strain (S strain) that is virulent to mouse. They then heat-killed the smooth strain (S strain), destroyed its protein, making it nonvirulent. Surprisingly they discovered that by mixing the nonvirulent R strain with this heat- killed S strain, the injected mouse was killed the nonvirulent R strain was transformed to virulent strain by the genetic material DNA, which is heat resistant. These results all pointed to DNA as the likely transforming principle. However, Avery was cautious in interpreting his results. He realized that it was still possible that some contaminating substance present in small amounts was the actual transforming principle.

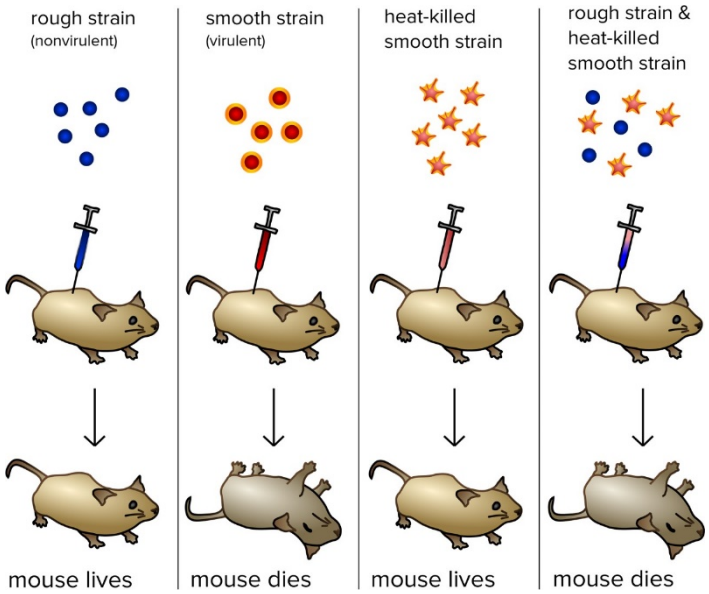

Figure 2. DNA as the "transforming principle" [8].

Because of this possibility, debate over DNA's role continued until 1952, when Alfred Hershey and Martha Chase used a different approach to conclusively identify DNA as the genetic material (Figure 3). Hershey and Chase studied phage, a virus that attacks bacteria. The phages they used were simple particles composed of protein and DNA, with the outer structures made of protein and the inner core consisting of DNA [9]. Hershey and Chase knew that the phages attached to the surface of a host bacterial cell and injected some substance (either DNA or protein) into the host. This substance gave "instructions" that caused the host bacteria to start making lots and lots of phages—in other words, it was the phage's genetic material.

To establish whether the phage injected DNA or protein into host bacteria, Hershey and Chase prepared two different batches of phage. In each batch, the phage were produced in the presence of a specific radioactive element, which was incorporated into the macromolecules (DNA and protein) that made up the phage.

One sample was produced in the presence of 35S, a radioactive isotope of sulfur. Sulfur is found in many proteins and is absent from DNA, so only phage proteins were radioactively labeled by this treatment. The other sample was produced in the presence of 32P, a radioactive isotope of phosphorous. Phosphorous is found in DNA and not in proteins, so only phage DNA (and not phage proteins) was radioactively labeled by this treatment.

After infecting those two differently labelled phages to bacteria, the bacteria culture was whirled in a blender, removing any remaining phage and phage parts from the outside of the bacterial cells. Finally, the cultures were centrifuged, or spun at high speeds, to separate the bacteria from the phage debris, which causes heavier material, such as bacteria, to move to the bottom of the tube and form a lump called a pellet [10]. Lighter material, such as phage and phage parts, remains near the top of the tube and forms a liquid layer called the supernatant.

When Hershey and Chase measured radioactivity in the pellet and supernatant from both of their experiments, they found that a large amount of 35S appeared in the pellet, whereas almost all of the 32P appeared in the supernatant. Based on this and similar experiments, Hershey and Chase concluded that DNA, not Protein, was injected into host cells and made up the genetic material of the phage.

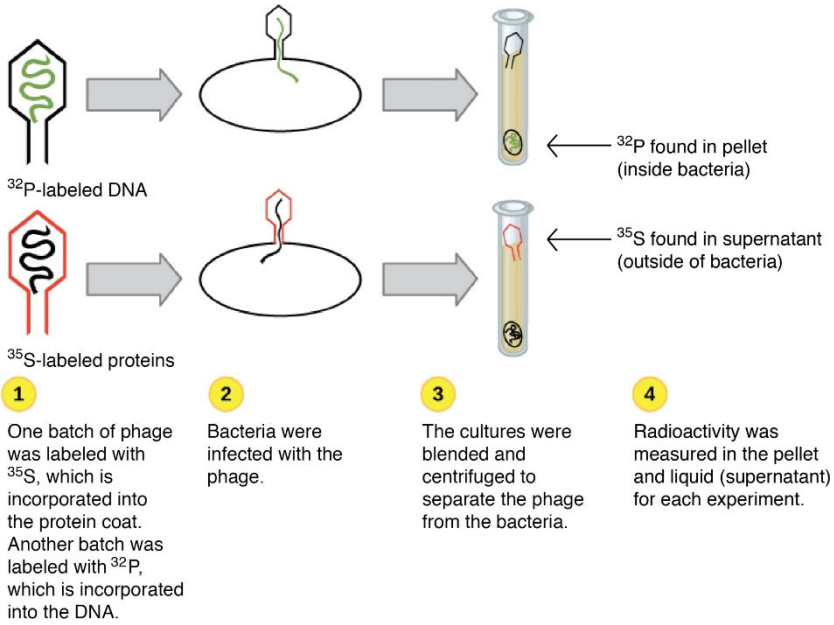

Figure 3. The Hershey-Chase experiments that proved DNA as the genetic material.

Later in 1953, Watson and Crick recognized that gaining a detailed knowledge of the three-dimensional configuration of the gene was the central problem in molecular biology. Without such knowledge, heredity and reproduction could not be understood. They inferred DNA structure from X-ray crystallography data (Figure 4). This unequivocally proves the double helix structure of DNA (Figure 5).

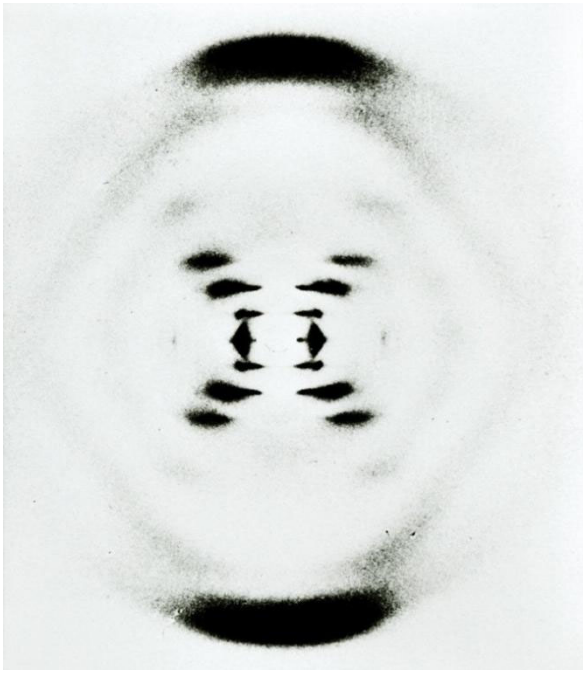

Figure 4. Watson and Crick inferred DNA double helix structure from this X-ray crystallography data of DNA.

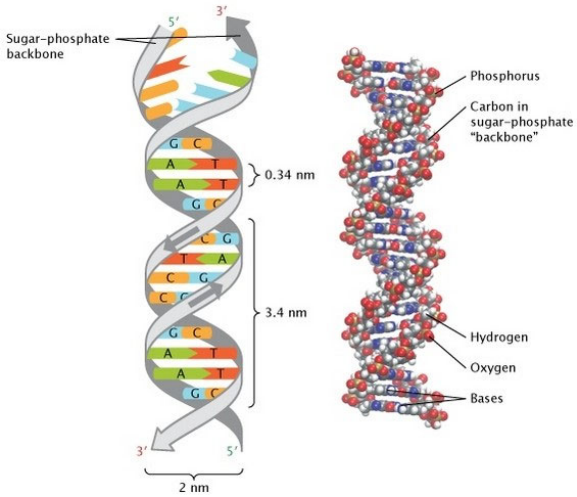

Figure 5. The double helix structure of DNA.

As we gain more knowledge about gene, DNA and inheritance, we began to understand that proper control of gene expression is the one of the most important aspects of life. In simple bacteria, genes are often regulated together as an operon, the most well-studied case is lac operon in E. coli, which is essential for lactose digestion in (Figure 6). E. coli bacteria generally prefer to digest glucose sugars instead of lactose. As glucose is a monosaccharide, it is easily broken down by the enzymes found in E. coli. In the event that glucose is not present in the growth medium, many E. coli turn to other food sources (such as lactose).

Under normal conditions (when glucose is plentiful), E. coli restrict the use of resources by suppressing the genes that produce enzymes to digest other sugars. Such control is achieved by the lac operon. lac operon has 3 genes – lacZ, lacY and lacA, and its production is controlled by cooperative working of 3 components – The lac Promotor is a DNA sequence; The lac Repressor is a Protein that binds to lac operator when glucose level is high. Its binding to the lac operator inhibits mRNA transcription of lacZ, lacY and lacA; The lac Activator is a Protein that binds to lac operator when lactose level is high. Its binding to the lac operator promotes mRNA transcription of lacZ, lacY and lacA [11].

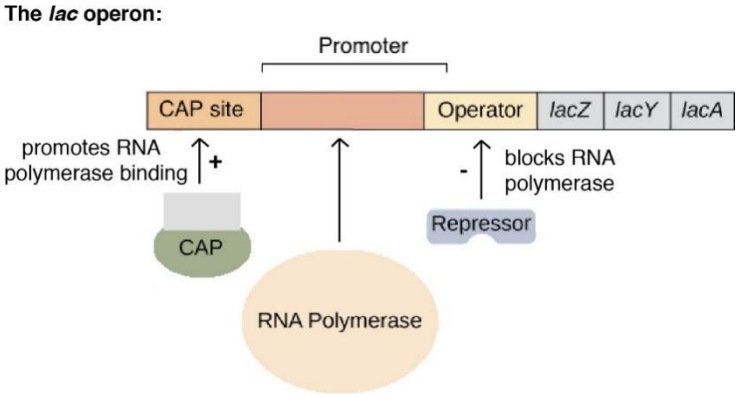

Figure 6. The lac operon in E. coli.

Such elegant and complex regulation of genes are the foundation of life, from single-cell organism like bacteria to complex form like us. A main difference between bacteria and us is nucleus – Prokaryote cells like E. coli have no nuclear membrane and its DNA is in cytoplasm, whereas Eukaryote cells have membrane-surrounded nucleus that separate DNA from cytoplasm (Figure 7). In Prokaryote cells, mRNA transcription and protein translation happen at the same time, whereas in Eukaryote cells, mRNA must be transported to cytoplasm before translation can happen [12].

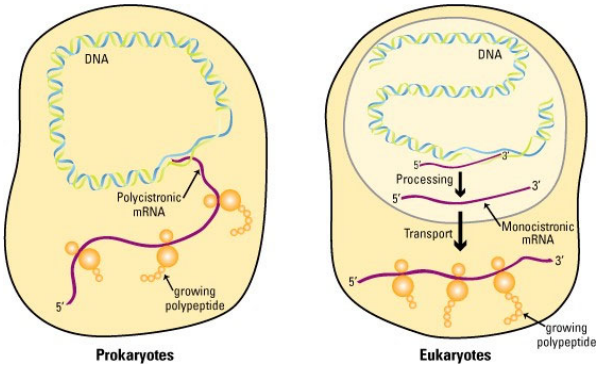

Figure 7. Prokaryote and Eukaryote cells have different structure.

Despite these differences, all life on earth share a common ancestor, and we can describe the relationship between all species using phylogeny (Figure 8).

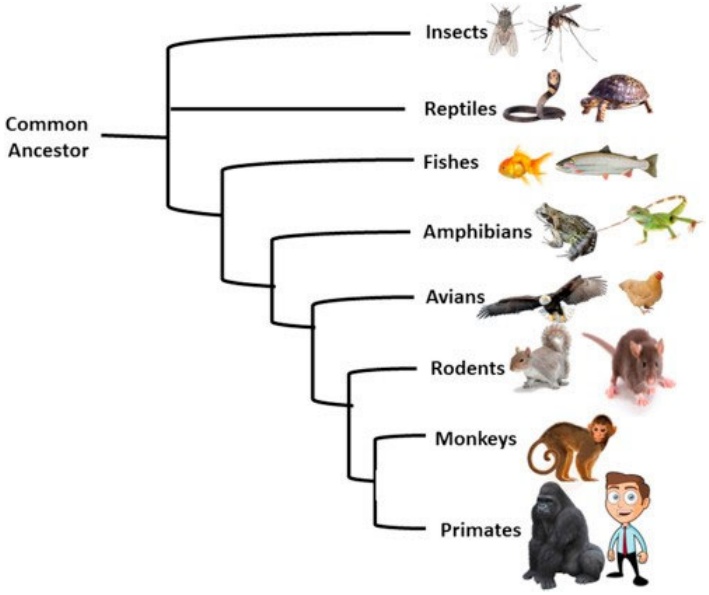

Figure 8. Phylogeny describes the relationship among all life.

3. Conclusion

Classical genetics is often referred to as the oldest form of genetics, and began with Gregor Mendel's experiments that formulated and defined a fundamental biological concept known as Mendelian inheritance. Mendelian inheritance is the process in which genes and traits are passed from a set of parents to their offspring. These inherited traits are passed down mechanistically with one gene from one parent and the second gene from another parent in sexually reproducing organisms. This creates the pair of genes in diploid organisms. This review helps people gain more knowledge about gene, DNA and inheritance, and is conducive to understand that proper control of gene expression is the one of the most important aspects of life.

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