Seventy years for DNA double helix: A brief historical approach, current developments, and future challenges

Setenta años para la doble hélice del ADN: una breve aproximación histórica, desarrollos actuales y desafíos futuros

To the Editor,

Dr. Saffie and collaborators[1] state that we face a historical moment, a true genetic revolution, due to advances in genetic sequencing techniques. Studying the genome more efficiently is increasingly possible, opening opportunities for gene therapy for diseases that historically have not had treatment[1]. Dr Ricardo Cruz-Coke, a former Associate Editor of this Journal, mentioned fifty years ago that Medicine's fundamental problems should be addressed with genetic criteria[2]. Genetics plays a central role in Biology at the molecular and population levels -and it is also prominent in Medicine[2]. However, modern Clinical Genetics, recent Genomics, and, in general, Medical Biotechnology arose only thanks to the deoxyribonucleic acid (DNA) structure was elucidated in 1953 by James Watson and Francis Crick[3]. This letter performs a brief historical approach to the discovery of DNA structure and comments on current developments and future challenges in the area when the famous double helix celebrates its Platinum Anniversary.

Progress in Cell Biology (formerly Cytology) during the early-20th century demonstrated that the Theory of Particulate Inheritance had a material basis in chromosomes[2]. Later, advances in Biochemistry demonstrated that the gene's chemical nature corresponded to DNA[2]. Nevertheless, there was initial resistance to accepting that the DNA and not the proteins carried the hereditary information. In the mid-20th century, Mendelism was accepted by the biomedical and clinical sciences[2]. However, it had yet to definitively cement its image in the most advanced biological research, such as the new science of Molecular Biology, supported by Biophysics[2]. In this context, the proposal of DNA structure came in 1953 from Watson and Crick[3] and other researchers such as Maurice Wilkins, Rosalind Franklin, and Raymond Gosling (Figure 1A). Using the composition of nitrogenous bases (purines and pyrimidines) determined by the chemist Erwin Chargaff as well as X-ray crystallography images of DNA taken by Franklin and Gosling, Watson and Crick proposed their model for DNA structure, an outstanding scientific contribution. DNA molecules comprise two poly-nucleotide antiparallel chains (or strands) wound one over the other, constituting a double helix, like a spiral staircase[3]. A nucleotide consists of deoxyribose (in the case of DNA) attached to a phosphate group and a nitrogen-containing base[3]. On the outside of the helix are the skeletons of the chains made up of phosphates and deoxyriboses, and the purine (adenine and guanine) and pyrimidine (cytosine and thymine) bases are inside[3]. Weak interactions (hydrogen bonds) are established between these bases, the sum of which gives the structure great firmness. According to Chargaff's rules, adenine pairs with thymine and cytosine with guanine (Figure 1B). Watson, Crick, and Wilkins received the Nobel Prize in 1962 for discovering the molecular structure of nucleic acids. Renowned crystallographer Rosalind Franklin did not receive this award because she died of ovarian cancer in 1958. Franklin has become a role model for women in science[4]. Independently of Watson and Crick, she would have understood how DNA structure could specify proteins[4]. Considering her critical role in this research, the fact that she did not receive proper recognition in her life continues to generate controversy today[4].

DNA structure discovery constitutes a paradigm shift in biology, opening new paths toward incredible medical advances. Solving the DNA structure revolutionized Molecular Biology, leading it to its Golden Age and originating the fields of Molecular Genetics[2] and Structural Biology. Multiple experimental findings confirmed the Watson and Crick model validity. As Dr Jaime Eyzaguirre Philippi mentioned[5], one of this model's essential attributes is its ability to predict a replication mechanism of genetic material[5]. Each DNA strand is complementary to the other strand because if the nitrogenous base sequence of one of them is known, that of the other is automatically determined[5]. Hence, a crucial concept arose from this complementarity, the template concept: A DNA strand acts as a template for complementary DNA strand synthesis[5].

In the late 1980s, a race to decipher the human genome started. The genome is an organism's complete set of DNA. Consequently, Genomics was born, a field focused on studying genes, their functions, and interactions in the genome. The discovery of the human Genome and the identification of hundreds of structural genes that encode for enzymes, proteins, hormones, and antigens have broadened the concept of the aetiology of classical diseases[6]. Undoubtedly, the Genomic Era began with the announcement of human genome sequencing in 2003. Its successful completion constitutes an outstanding scientific achievement of the early 21st century[7].

The vertiginous development of Genomics and Bioinformatics have conditioned an advance from phenotypic to genotypic or molecular medical vision, i.e., Personalized or Precision Medicine[7]; consistent with the advance of the Fifth Industrial Revolution, which

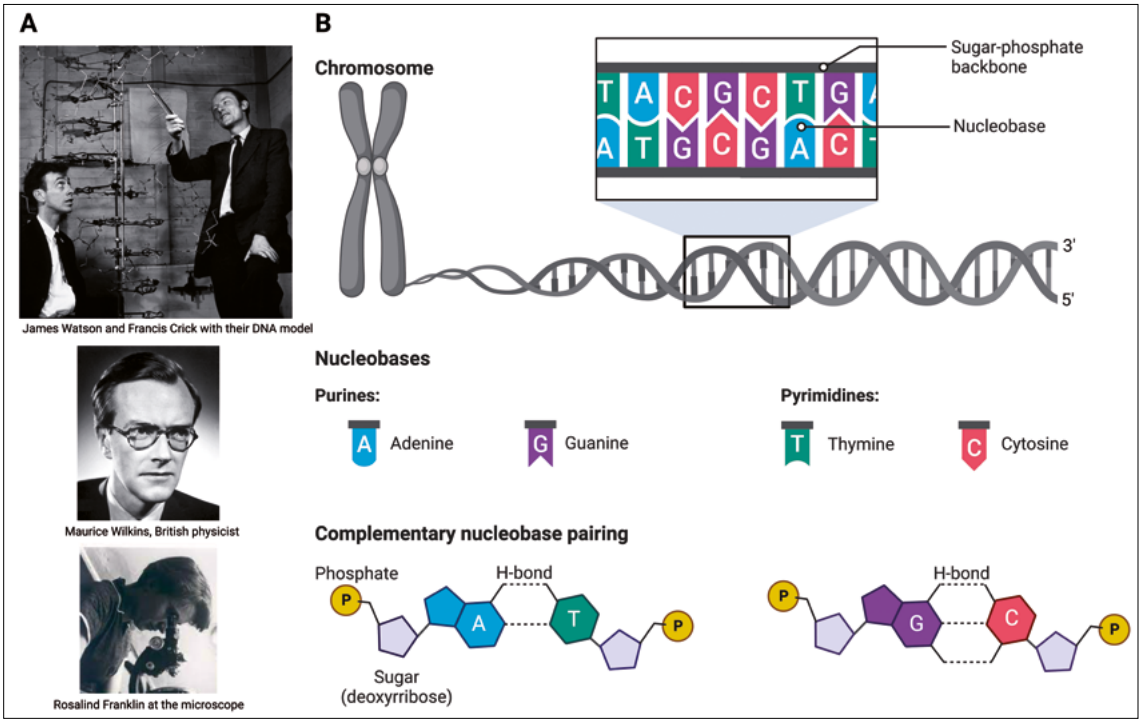

Figure 1. Main researchers (A) involved in DNA structure and (B) structural components. Source: CC and Wikimedia Commons licenses (educational use). *Created with BioRender.com*

includes mass personalization[8]. Current advances in genetic edition and the development of synthetic DNA open opportunities for new biomedical advances and raise interesting bioethical issues. Finally, we should always remember that these developments were only possible by elucidating DNA's structure seventy years ago.

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