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# Structure, Functions and Clinical Significance of DNA: A Review Article

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**ABSTRACT:** The deoxyribonucleic acid (DNA) carries hereditary codes which is translated by the cells to synthesize the ribonucleic acid (RNA) and polypeptides which can generate and perform vital function. The double helix structure is the most studied model of the DNA that was proposed by Watson and Crick. The capability of DNA to work as a genetic material can be stored and conducted during cell division to permit this information to be doubled and transmitted to the incoming generation. Any damage in the structure of DNA is an essential direct cause for the progression of cancer and other disorders. The factors for DNA damage can be classified as exogenous and endogenous factors. In this review article, we highlight the evidence-supported information about the structure, functions and clinical significance of DNA.

## 1. INTRODUCTION

The discovery of DNA dates back to 1869 when a Swiss biochemist named Friedrich Miescher was looking at leucocytes for their chemical composition source. He obtained these leucocytes from pus that came from clean surgical dressings. Although his interest was primiraly in all organelles and structures of the cell, he soon narrowed it down to the nucleus because upon treatment with acid, a precipitate appeared which he termed 'nuclein'. Most molecular bioscience students would have done some version of this experiment in labs where they isolate DNA from cells. Other researchers later characterized 'nuclein' further and it was renamed nucleic acid as studies revealed that this nucleic acid was made up of purine and pyrimidine bases, sugar and phosphate. Nucleic acids were further studied in the 1930s by a number of scientists, including the determination of four bases and the discovery that they contain deoxyribose— thus named deoxyribonucleic acid (DNA). The nitrogen-containing bases forming the backbone structure of DNA molecules are found as pairs: cytosine (C) with guanine (G) and an equal amount of adenosine (A) with thymine (T) (Minchin & Lodge, 2019).

DNA's elegant structure, from nucleotide to chromosome, is what makes it function as the carrier of genetic information. But this intricacy didn't come out of nowhere; Watson and Crick revealed in their 1953 paper two key aspects that make up this beautiful design: pairing nucleotide bases in a complementary way (adenine with thymine, cytosine with guanine) and the double helix (Watson & Crick, 1953).

## STRUCTURE

DNA structures are well-known, many geometrical parameters are considered as characteristics for them, these parameters include: Helical bend, groove widths, backbone and glycosidic torsion angles, sugar pucker, propeller twist, roll, displacement, inclination, and helical rise and twist (Saenger, 1984).

As shown in figure (1), Deoxyribonucleic acid is a polymerized molecule. It is formed by the repetition of monomeric units identified as nucleotides. A nucleotide consists of a 5-carbon sugar (deoxyribose), a nitrogenous base, and one or more phosphate groups; however, during the formation of DNA through these nucleotides that act as building blocks, three phosphate groups are introduced onto each other. Two phosphates are lost in this process; hence, in the end, the DNA strand has one phosphate group per nucleotide. (Lamprecht et al., 2015).

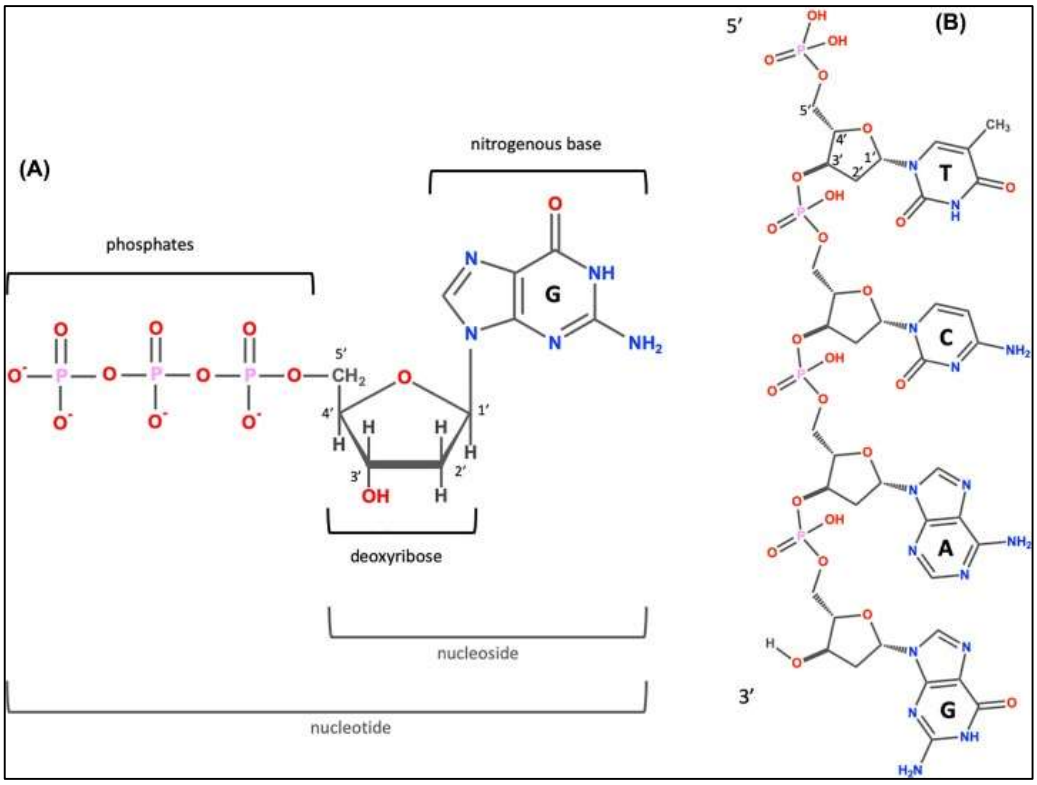


**Figure (1): The biochemical structure of DNA. (A): Nucleotide structure. (B): Part of DNA strand**

DNA is a polymer — consisting of monomeric units called nucleotides — where each nucleotide is composed of a 5-carbon sugar (deoxyribose), a nitrogenous base, and one or more phosphate groups. Specifically, the precursors for DNA synthesis have three phosphate groups; however, two phosphates are omitted during construction, resulting in only one phosphate group present per nucleotide strand (Travers & Muskhelishvili, 2015).

The numbering of carbon within the deoxyribose ring is from 1' to 5'. In each monomer, the phosphate is bonded to the 5' carbon of deoxyribose while the nitrogenous base is bonded to the 1' carbon— this connection is known as an N-glycosidic bond. The phosphate group exhibits acidity, hence nucleic acid. Along the DNA chain, a phosphate residue serves as a connector between the 3'-hydroxyl of one deoxyribose and the 5'-hydroxyl of the next— identified as a phosphodiester bond. DNA strands exhibit what can be termed as a 'sense of direction.' (Calverley & Walker, 2023).

The two strands that form a helix run in opposite directions; one runs from top to bottom in a 5′ to 3′ direction while the other runs in a 3′ to 5′ direction. The helix is right-handed-visualize it from above, and you'll see the coils turning clockwise as they recede away from your view. The chains interact through hydrogen bonds between base pairs: adenine always pairing with thymine, guanine always pairing with cytosine. The Watson-Crick structure thus rationalizes as well as elucidates the Chargaff data: it indicated that there is usually the same quantity of C and G, and of A and T. The uniformity of the double helix obtains because the distance between the 1' carbon of one deoxyribose to another on opposite strands is invariant irrespective of the base pair. Moreover, the 1' carbons of the deoxyribose opposing nucleotides do not align directly along the helical axis— this asymmetry results in unequal spacing of the sugar-phosphate backbones along the helical axis, giving rise to major and minor grooves (Pallan et al., 2007).

The helical symmetry in A-, B-, and Z-forms of double-stranded nucleic acids is a result of screw operators (see figure 2). In A-DNA, the fiber model is limited to 111 helical symmetry while in B-DNA it is limited to 101 symmetry; this implies that there are exactly 11 or 10 repeating units per right-handed turn of the helix. Hypothetical left-handed mirror duplexes of A- and B-DNA with 1110 or 109 symmetry are stereochemically impossible. The Z-DNA structure exhibits 65 symmetry due to its formation of six repeating units within a single left-handed helical turn. In all forms of canonical DNA double helices (A, B, and Z), the base pairs are WC at the center with strands running in an antiparallel fashion. The fiber models exhibit full regularity (Han et al., 2022).

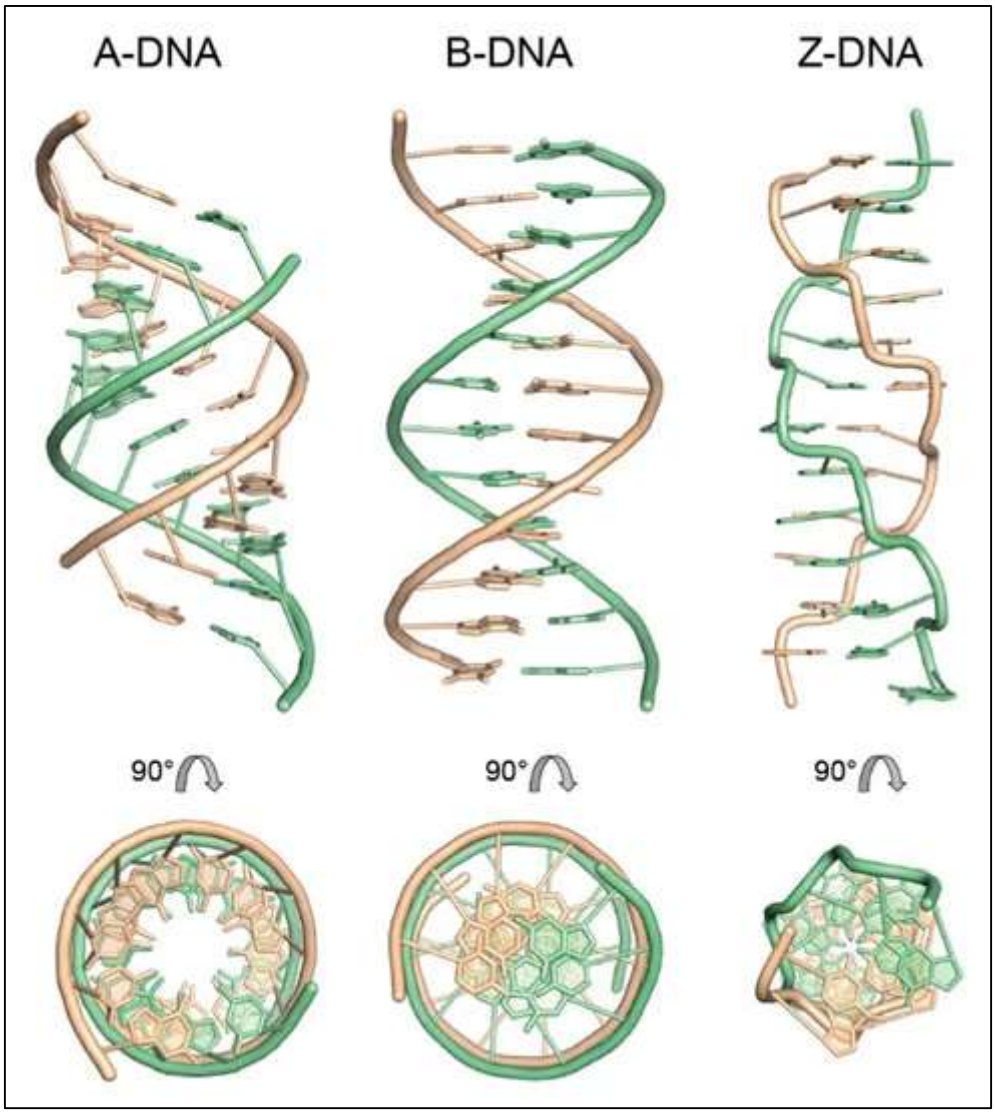


**Figure (2): The double-helical forms of DNA (A, B, Z) according to X-ray fiber diffraction analysis**

DNA typically favors the B-conformation, considered its biologically relevant state; however, it has the ability to shift to the A-form in specific situations. Transition to the A-form is promoted when the DNA is relatively exposed to decreased humidity (indicative of increased ionic strength) or in cases where the DNA sequence is rich in G/C content. Methods for controlling relative humidity have been a known aspect in X-ray fiber diffraction experiments for a while now, but they were recently revisited as part of a study on hydration forces in A-DNA and B-DNA fibers— unveiling valuable insights (Case et al., 2017).

DNA supercoiling doesn't happen by magic; it's the handiwork of DNA topoisomerases — enzymes that fall into the multitasking category as they play a major role in tweaking the topology of DNA within cells. How do they do it? By breaking and resealing single or double strands of DNA, thus introducing changes at a topological level. But wait, there's more than one way to achieve this remodeling outside the cellular confines; take for instance using intercalating molecules along with topoisomerases in vitro. Now let's talk about supercoiled DNA— when it's positively supercoiled, we see a left-handed superhelix; on the other hand (or should we say right?), negative supercoiling results in a right-handed superhelix twist. Although whether these terms really help us grasp the essence of superhelical structures is still up for debate, one interesting point to note before we wrap up is that these twisted coils are actually equivalent (in a topological sense) to toroidally wrapped helices like those found in nucleosomes. What does this mean? It means one form can seamlessly transition into another without needing any nicking-and-resealing drama or breaking covalent bonds along the way (Heinemann and Roske, 2020).

**FUNCTIONS**

DNA plays a crucial role in our bodies at the molecular level. It is responsible for governing numerous processes within our cells— ultimately defining how each individual functions as a human being. On a daily basis, the strands of DNA comprising our body's various cells are subjected to millions of diverse forms of harm and injurie. Some of this damage occurs as a byproduct of regular metabolic processes occurring within cells— aiming to generate energy and produce materials (Hakem, 2008).

At its core, the unique function of DNA is based on being able to store and pass genetic information between generations. DNA's structure plays a role here; the double helix is stabilised by a sugar-phosphate backbone which makes it less vulnerable to damage, and ensures that information is tightly packed along its length. However, it's also worth noting that hydrogen bonds hold the two strands together. These weak interactions mean that each strand can easily be accessed for use in biological processes. One interesting feature about DNA is its ability to replicate accurately: when it does so semi-conservatively each new molecule has one old strand (which acts as a template) and one newly synthesised strand with identical genetic information (Travers & Muskhelishvili, 2015).

The propagation of a living organism requires it to duplicate its genetic material. An initiation factor is responsible for recognizing an origin of replication on the double-stranded DNA molecule and subsequently recruiting a helicase enzyme. The role of the helicase enzyme is to unwind the double helix structure of DNA, thus exposing two strands acting as templates. The synthesis leads to two new strands of DNA: the leading and lagging strands. Ultimately, this intricate process results in two identical molecules of double-stranded DNA— ensuring successful duplication for future generations (Zhou & Costa, 2014).

Cancer and other diseases are majorly developed through DNA damage. The risk factors of this injury are twofold: exogenous and endogenous. Endogenous damage takes place inside the cell itself due to errors that occur during normal cellular processes. These include mismatched nucleotide insertion or instability of DNA because of depurination; free radicals formed as a result of oxidation-reduction reactions lead to deamination for both DNA and proteins. On the other hand, exogenous damage is brought about by factors external to the cell — induced damage. Common causes of this type of damage include UV radiation (from UVA and UVB light exposure) and ionizing radiations among others heat shock toxins drugs, which interfere with replication through various mechanisms such as base-pair mismatches or intercalation inhibition. UV also causes cytosine-thymine dimer formation by cross-linking after coming in contact with adjacent bases; more often than not, these are detrimental (Lewis and Dimri et al., 2023).

## CLINICAL SIGNIFICANCE

Mutations in nucleic acids play pivotal roles in pathophysiology. This involves numerous conditions from congenital to developmental diseases— even cancer. An important instance is sickle-cell anemia: a hereditary genetic disease that is predominantly found among individuals of African descent. The disease occurs due to a specific single point mutation where an A changes to a T in the gene encoding beta-globin; this leads to the sixth amino acid changing from glutamic acid to valine. When homozygous for this mutation, mutation in the beta-globin subunits will be found in the hemoglobin (referred to as HbS) that form crystals upon deoxygenation— resulting in erythrocyte deformation into sickle shapes leading to block capillaries and related complications (Ghannam et al., 2023).

At the core of our biological system, DNA repair acts as a silent hero— correcting the errors in our replicative machinery. Failure to address damages at the DNA level often paves the way for carcinogenesis: insidious development of cancer cells that lead to easy dissemination and propagation through mitotic division. On the flip side, understanding cancer development hinges on appreciating the intricate dance between genotoxic mechanisms and impact on repair processes— a waltz brought about by carcinogens introduced into our body's realm. This realm is extensively studied not only from its endogenous perspective but also in terms of exogenous damage like ionizing radiation that manifests as different shades of leukemia or melanomas; each unique based on varied UV or X-ray exposure histories (Trenner & Sartori, 2019).

DNA damage is a typical property of human sperms— often bonded with low rates of conception, hampered embryonic development plus the higher occurrence of miscarriages and various morbidities in offspring including childhood cancer. Anyhow, challenges arise in explanations as these associations are not universally reported among all datasets; such inconsistency underscores the complexity surrounding reproductive processes (including huge differences in sample sizes). Inadequate study designs are also at play due to differences in patient selection: inter-individual differences abound too, from the type of DNA damage being found to varying effectiveness levels of repair mechanisms within the oocyte. This article reviews the origin and types of DNA damage found in human sperm cells. It delves into the clinical value of data derived from such studies and pinpoints uncharted areas deserving more research attention— those that can stitch together the gap between a captivating biological occurrence and an evidence-based clinical orchestration for men with high levels of DNA-damaged sperm (Aitken et al., 2009).

The study showed that analysis of circulating tumor DNA (ctDNA) could exert a basic function in bettering the early stages of breast cancer treatment through non-invasive assessment of tumour burden. The bebining excretion of ctDNA 3 weeks after start of treatment has a predictive value for response to neoadjuvant chemotherapy (NAC) only in triple negative breast cancer (TNBC); whereas positivity is correlated with decreased distant recurrence free survival in both subtypes. There is a curious paradox where negativity after NAC actually correlates with positive outcomes even in cases of significant residual disease, identified through tumor mRNA profiling. This identification reveals an interesting association between ctDNA shedding and specific pathways: the cell cycle and immune-associated signaling. Such information can be useful in re-evaluating the treatment approach to enhance response as well as prognosis (Boe et al., 2021).

## CONCLUSION

Common geometric parameters used to characterize DNA structures include helical bend, groove widths, backbone and glycosidic torsion angles, sugar pucker, propeller twist, roll, displacement, inclination, and helical rise and twist. DNA is paramount in our molecular makeup— it governs a multitude of processes within our cells that define us as functioning human beings. DNA repair plays a critical role in rectifying errors made by our replicative machinery during the formation of new materials in our body systems.

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