



DNA Contains Genetic Information that is Inherited by Descendants

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Abstract

DNA is not a single molecule, but a pair of molecules that are interconnected by hydrogen bonds and organized so that their strands are complementary and antiparallel, from start to finish. Each strand of DNA consists of building blocks called nucleotides of which there are 4 types in DNA: adenine (A), cytosine (C), guanine (G) and thymine (T). These basic nucleic acid components can be polymerized in any order. Between the two chains, each base of one can be paired with the complementary base of the other chain so that adenine with two hydrogen bonds always joins with thymine and vice versa and cytosine always with guanine via three hydrogen bonds and vice versa. Thus we get possible combinations: A + T, T + A, C + G, G + C. In rare situations, mismatch occurs, eg when thymine converts to its enol form and cytosine to its imino form. The double-stranded structure of DNA provides a simple mechanism for DNA replication: DNA strands separate like zippers and thus open to a number of nucleotides in the environment. Enzymes create a new strand by looking for a complementary base in the environment and build a new strand of DNA. Of course, the base on the old chain determines which base will be on the new chain to preserve complementarity. Thus the cell completes replication with two copies of its DNA.

Keywords: DNA; Cells; Genetics; Human Body

Introduction

Deoxyribonucleic acid (DNA) contains the genes, or instructions, for cell growth and function [1]. It is found in all nucleated cells in the body. DNA strands are quite long, approximately 3 billion base pairs. These long strands are packaged into bundles, called chromosomes, inside the nucleus.

In addition, DNA is found in the mitochondria, organelles found in cells responsible for cellular energy production. Mitochondria are present in high numbers (100–1,000) in each cell. The mitochondrial genome is a relatively small, single, circular DNA chromosome of only about 16,500 base pairs. However, within each mitochondrion there are

multiple copies of its chromosome [2–10]. Therefore each cell potentially contains hundreds to thousands of copies of the mitochondrial chromosome.

Regardless of where the DNA is found in the cell, DNA has a double helix structure similar to a twisted ladder, with the legs of the ladder consisting of two antiparallel sugar phosphate backbones. The “rungs” of the ladder are composed of four different nucleotide bases (adenine, thymine, guanine, and cytosine) that hydrogen bond into set base pairs.

Encoded within the sequence of the three billion base pairs that make up the DNA of the human genome are the individual genes or instructions necessary for producing

and regulating the processes responsible for life. Since all humans are structurally and functionally similar (one head, two arms, one heart, etc.), the majority of their DNA is identical. However, there are areas in the DNA where genetic differences between individuals can be detected.

Technology

In the real world of the research and development laboratory, DNA technology is a diverse blend of molecular biology, genetics, chemistry, physics, mathematics, and high-tech biotechnology [2]. Producing proteins and manufacturing molecules are among the most elegant endeavors of the cell and of biological science in the lab; both are widely used in applied and experimental contexts now, which will continue in the future.

The science of recombinant DNA cloning allows scientists to use the natural biochemical processes of cells to do the work of copying DNA and producing specific proteins. The biochemistry behind DNA technology allows scientists to introduce new genes into cells. The cells then exhibit new biochemical activities as directed by the new gene that they carry. As the cells reproduce by cell division, they replicate the new gene along with their "original" chromosome DNA, producing millions of progeny cells containing millions of copies of the gene. In this way a gene is cloned and many identical copies are created.

The extremely powerful method of polymerase chain reaction (PCR) is routinely used to clone genes and other specific regions of DNA sequence in vitro (outside the cell), without copying the entire DNA genome. PCR harnesses the routine activity of heat-stable DNA polymerase enzymes that normally replicate DNA in special species that live in high-temperature environments. Some of the enzymes made by organisms growing in hot environments are thermally stable and retain enzyme activity even in the high temperatures required for PCR. The enzyme technologies used to manipulate and study DNA and RNA are often based on the ability to understand the processes normally performed by the enzymes in the cells, then repeat the processes outside the cells using purified enzyme proteins and appropriate substrates.

Chromosomal DNA must be replicated faithfully and propagated to daughter cells equally [3]. The mechanism of DNA replication is constrained by the characteristics of DNA polymerases, which synthesize chromosomal DNA; i.e., double-stranded DNA must be unwound to serve as a template and 3'-OH (RNA primer in cellular organisms) must be provided to DNA polymerases. Once these two conditions are fulfilled, DNA polymerase can start DNA synthesis everywhere. However, cells regulate this process strictly,

mainly at replication origins. DNA replication initiates from replication origins, to which the initiator protein binds. DNA helicase is loaded onto origins and unwinds double-stranded DNA for the syntheses of an RNA primer and subsequent DNA by primase and DNA polymerases. As DNA polymerases elongate the DNA chain in the 5' to 3' direction, both strands are synthesized in opposite directions from the initiation site. The synthesis of both DNA strands (leading and lagging) continues in a manner that is coupled with DNA helicase up to its termination. These fundamental mechanisms and regulation of cellular chromosomal DNA replication are outlined using prokaryotic and eukaryotic examples.

Characteristics

DNA is sometimes called the blueprint of life and has characteristics that are appropriate to its role [4]. Many, if not all, of these characteristics are important in Forensic Genetics, which is simply genetics in a legal context. These characteristics include its simplicity and yet complexity, both of which are incorporated within the polymeric chemical structure of the backbone molecule and the varied sequence of sidechain bases (the so-called letters of its information content), arranged in a double helix. The molecule is made from a relatively small number of building blocks yet contains a vast amount and range of information that can define the nature of the biological cell, and ultimately the multicellular organism, within which the DNA is located. The double helix structure is relatively stable in time yet is adaptable enough to "open up" to allow a living cell to use the contained information to go about its life functions (transcription) or to make copies of itself (replication). DNA is stable so as to enable transfer of the genetic information from generation to generation after replication (with cell division and mating where relevant), yet it can also change to varying extents. Some of the changes are important to only an individual organism and may be deleterious (e.g., mutation giving rise to a cancer), or are the basis for individual variation (e.g., mutation giving rise to a new variant, and the haploid segregation of chromosomes in gametes with the return of diploid pairing at fertilization to produce a new individual). Some changes affect a subpopulation (e.g., lineages) and even eventually an entire population (e.g., natural selection of mutations and new diploid combinations leading to evolutionary change).

The concept that DNA contains the information for biological life using a genetic code encoded within the sequence of bases along the double helix molecule means that if we as forensic scientists can "read" that code we can question and determine the source of a given sample of DNA. The general DNA structure and constituents are the same so that with the right analytical toolkits, we are able to answer that question. So, we could test not only whether the DNA is

from a human, horse, cannabis plant, or soil microbe, but in theory identify the individual human. Scientists are able to take advantage of the “adaptable stability” of DNA and mimic the process of replication so as to make multiple copies of a DNA sample, using the polymerase chain reaction. The amplified DNA is then processed and the data interpreted accordingly.

Structure

DNA contains the plans that are responsible for the construction of our cells, tissues, organs, and body [5]. DNA houses the information required to produce proteins. Proteins play a number of roles within cells as structural elements (keratin, actin, myosin, tubulin), hormones, antibodies, or enzymes. Less than 5% of our DNA contains the genes that code for the production of proteins. Enzymes are catalysts, chemicals that speed up the rate of a reaction but are not used up in the process. These proteins are necessary for the development and maintenance of cells that are then used to construct tissues. Tissues are groups of cells that function as a unit to form sheets or tubes (building elements). Tissues of different types can become physically and functionally related such that they give rise to organs, such as kidneys and livers. Thus, one can trace the pathway of life from the macromolecule known as DNA to the formation of cells, tissues, organs, and ultimately, to complete organisms.

To provide some perspective about the size of the DNA genome and where it is stored in the cell, imagine that you are able to travel within the cell. Cells are composed of nucleic acids [DNA and ribonucleic acid (RNA)], proteins, lipids, sugars, and a variety of other important molecules. Cells contain a large number of discrete membrane-bound structures, each with a unique and vital function. On this brief journey as you enter the outer cell membrane, you will encounter within the cytoplasm a large spherical nucleus, hundreds (and in some cases, thousands) of mitochondria, ribosomes, lysosomes, a Golgi body, interior membranes (endoplasmic reticulum) that provide channels within the cytoplasm and vacuoles, vesicles, and other structures related to cellular “feeding and drinking.” The intracellular structures of human cells (animal and plant cells are eukaryotic) differ from those of bacterial cells (prokaryotic) that are much more simply organized. In virtually every human cell there is a double membrane-enclosed and somewhat spherical structure called the nucleus. It floats in a liquid medium called the cytoplasm that has characteristics of both a solution and a gel. Most of the cell’s DNA is located in the nucleus and is known as genomic DNA. DNA within the nucleus is invisible to the naked eye as well as to the light microscope. It consists of 46 units. If the 46 molecules were linked end to end the resulting molecule would be 2 meters long, approximately 6 ft. However, it is so thin (20 Ångstrom

units) that one requires a transmission electron microscope to magnify its image to visualize it.

Development

DNA profiling as we know it today, was developed, thanks to two independent breakthroughs in molecular biology that occurred at the same time on different sides of the Atlantic [6]. In the United States, the polymerase chain reaction (PCR) was developed by Kary Mullis of Cetus Corporation. Almost simultaneously, the individual-specific banding patterns observed after restriction fragment-length polymorphism (RFLP) analysis of repeated DNA sequences were discovered by Professor Sir Alec Jeffreys at the University of Leicester. In its earliest incarnation, this technique termed as DNA fingerprinting by its creators was performed by restriction of 0.5–10 µg of extracted DNA using the restriction enzyme *HinFI*, followed by Southern blotting hybridization with probes termed 33.5, 33.6, and 33.15, designed to bind to multiple “minisatellites” present in the restricted DNA. This multilocus probing (MLP) technique would result in the binding of probes to multiple independent DNA fragments at the same time, giving rise to the traditional “bar code” pattern that is often visualized, discussing DNA profiling even today. Differences in the number of times the probe sequence is repeated in each DNA fragment form the basis of the individual patterns observed on the autoradiogram image.

The first report concerning the use of DNA profiling in a criminal investigation was published in 1987. This investigation used two unpublished SLPs to link semen stain samples collected from two rape and murder cases that had occurred 3 years apart in 1983 and 1986 in Leicestershire, United Kingdom. The probability of this match occurring by chance was calculated as 5.8×10^{-8} . This result not only linked the two crimes but also exonerated an innocent man implicated in the murders and led to the first mass screening project undertaken for DNA profiling in the world.

The potential of DNA analysis for forensic science had now been demonstrated; the technology now required statistical validation by analysis of population frequencies and application to casework samples before it could progress. Early evaluation studies on MLP 33.15 provided optimistic support for the use of DNA for the personal identification and the identification of male rapists from a mixed male/female sample. It does, however, also begin to uncover the limitations of this method. A mean success rate of only 62% for the DNA fingerprinting of donated vaginal swabs was observed and no typing was possible for blood or semen stains that had been stored for 4 years at room temperature, and difficulty in directly comparing related samples run on different gels was also cited as a potential problem. Similar studies and

European collaborations were undertaken on SLPs such as YNH24 and MS43a. Difficulties were again observed when interpreting gel images, with only 77.9% of 70 samples distributed between nine laboratories producing matching results when a 2.8% “window” for size differences between gel runs and laboratories was used. It was recognized that subtle differences between laboratory protocols were responsible for some of the observed discrepancies, leading to a requirement for the standardization of laboratory methodology and DNA profil interpretation.

Such standardizations could improve the reproducibility of DNA typing results for MLP and SLP (single locus probes) marker systems, but in order to be applicable to forensic investigation, DNA systems must be robust and must be applicable to samples of a less than pristine nature or that which consists of only a few cells. PCR was first applied to forensic DNA profiling for the investigation of the HLA-Q- α 1 gene, a polymorphic gene that encodes a human leukocyte antigen cell surface protein located in the major histocompatibility complex (MHC) class II region on chromosome 6.

Human Body

The human body is a universe of working parts and functional interactions [7]. We observe the physical manifestations of these interactions all the time, as we walk, talk, breathe, think, or eat. These gross or macroscopic functions of the human body, however, are driven by extremely complex interactions, occurring at the cellular and subcellular level.

Our bodies are made up of trillions of cells. Each cell has a prescribed function relative to its position in the body that is essential to healthy human life. The cells themselves are extremely complex and advanced pieces of biological machinery. A cell is comprised of a cytosol, which is bound by a permeable membrane, and contains a host of miniature organs (organelles) including the nucleus. The nucleus contains DNA – the material that prescribes the cell’s principal functional characteristics.

It may be useful to think of the cell as being like a factory. Membranes enclose the structure and separate different organelles, which can be thought of as departments with specialized functions. The nucleus is the central administration, containing in its DNA a library of information that determines cellular structure and processes. From it instructions are issued for proper regulation of the business of the cell. The mitochondria are the power generators. The cytosol can be thought of as the general work area, where protein machinery (enzymes) carries out the formation of new molecules from imported raw materials. There are

special molecular channels in the membranes between compartments and between the cell and its external surroundings. Like factories, cells tend to specialize in function. For example, many of the cells in higher organisms are largely devoted to the production and export of one or a few molecular products.

Despite the diverse functions of the different types of cells that constitute the human body, each nucleated cell contains an identical copy of a common DNA molecule from which genetic information is read in a linear fashion. Since the amount of information needed to specify the structure and function of a multicellular organism such as a human is immense, the DNA molecule is extremely long. In fact, if the DNA from a single human cell were stretched end to end it would extend approximately 2 m.

Genetics

Genetic research has far-reaching implications not just for how we think about child-rearing and schools but how we think about our own adult lives [8]. Genetics is the major systematic influence in our lives, increasingly so as we get older. Therefore, genetics is a big part of understanding who we are. Our experiences matter a lot – our relationships with partners, children and friends, our occupations and interests. These experiences make life worth living and give it meaning. Relationships can also change our behaviour, such as helping us to stop smoking or lose weight. They can affect our lifestyle by encouraging us to exercise, play sports and go to cultural events. But they don’t change who we are psychologically – our personality, our mental health and our cognitive abilities. Life experiences matter and can affect us profoundly, but they don’t make a difference in terms of who we are.

Cells

All living things are composed of cells, the smallest units of life [9]. One cell is about one tenth the diameter of a hair, and about three trillion cells are contained in the human body. Most body cells (the major exception being red blood cells) contain a smaller entity, called the nucleus, which is the organization center for the cell. Genetic information resides in the nucleus of the cell and is organized into physical structures called chromosomes. Chromosomes are generally transmitted as intact units from parent to child. Thus, markers residing close together on the same chromosome are inherited together; they exhibit genetic linkage. In contrast, markers on different chromosomes are generally inherited independently of one another. This principle is called random assortment. Markers that exhibit random assortment are not inherited together, or associated with each other in a given population, more often than might be expected by chance.

Traits that show random assortment are said to be in linkage equilibrium. Conversely, markers that show genetic linkage, such as those close together on the same chromosome, are said to be in linkage disequilibrium; in a population, they are associated together more often than chance would predict.

Human cells contain 23 pairs of chromosomes. Each person has two copies of each chromosome; one comes from Dad and one from Mom. Thus, you inherit half of Dad's genetic blueprint and half of Mom's, which together provide you with a full complement. Small variations in an individual's DNA allow for differentiation between people.

One pair of the 23 chromosomes contains the information that determines gender. These chromosomes are given letters, rather than numbers, and are designated X and Y; males have one X and one Y chromosome (XY), and females have two X chromosomes (XX). Female eggs can contain only X chromosomes, while male sperm can contribute either an X or a Y chromosome. Therefore, gender is determined by the paternal component. The information contained in the sex chromosomes is so different that they even look different visually. Gender can be determined by DNA testing, and is sometimes a useful piece of information in case investigation.

Blueprint of Life

DNA is sometimes referred to as the blueprint of life [9]. The information for the blueprint is encoded in the four chemical building blocks of DNA: Adenine (A), Thymine (T), Guanine (G), and Cytosine (C). These units, called bases, are strung together in a linear fashion, like beads on a string. The specific sequence of the bases determines all the genetic attributes of a person. The properties of the DNA molecule are directly related to its physical structure. DNA in nature takes the form of a double helix. Two ribbon-like entities are entwined around each other and are held together by crossbars, like rungs of a ladder. Each rung is composed of two bases that have strong affinities for each other; collectively, these forces hold the DNA molecule together. Each rung of two bases is called a base pair. Only specific pairings between the four bases will match up and stick together. A always pairs with T, and G with C. This obligatory pairing, called complementary base pairing, is exploited in all DNA typing systems. When the double helix is intact, the DNA is called double-stranded; when the two halves of the helix come apart, either in nature or in the test tube (in vitro), the DNA is called single-stranded.

In nature, complementary base pairing is responsible for the ability to accurately replicate the DNA molecule, with its genetic information, and pass it on to the next generation. The double helix is unzipped by special enzymes, and new building blocks (nucleotides) are brought in. Each nucleotide

contains one base attached to a piece of the backbone ribbon. Using each half of the original helix as a template, a second half is created, resulting in two molecules identical to the original. The order of bases in the new strands is specified by the existing strands. Each original base captures a complementary replacement to complete the base pair.

Short segments of complementary single-stranded DNA also show a specific affinity for each other in vitro, defined again by the specific base sequence. Under appropriate conditions, complementary DNA fragments will find each other and stick together. Technically, this is referred to as reannealing or hybridization. In the laboratory, it is crucial that the chemical conditions for hybridization be exact. These conditions, which are determined by scientific experimentation, are called stringency conditions. If the stringency is too high, no hybridization will occur; if the stringency is too low, reannealing will be less than exact and some DNA fragments might stick together even if they are not a perfect complementary match. If the sequence at a particular location in the genome is of interest, single-stranded fragments can be artificially synthesized to target that location. These single-stranded fragments of known sequence are variously called DNA probes or DNA primers, depending on their intended use.

DNA Profile

One of the most crucial stages in the development of a DNA profile is the ability of the scientist to recover cellular material from a substrate and to extract DNA from it in a manner that is suitable for further processing steps such as polymerase chain reaction (PCR) [10]. Forensic samples are, however, not always easy to deal with. Samples can be deposited in the most inconvenient of places, exposed to the harshest of environments, and mixed with many potential inhibitors of DNA profiling. Many of these factors are outside the control of the scientist.

Any method developed for forensic use must be validated according to the accreditation or other quality system in place in the laboratory. Each of the methods can include numerous, small, laboratory-specific variations, such as incubation times and temperatures; however, the basic steps are common to all procedures.

Most laboratories will maintain several different extraction methods as it is important to select the most appropriate extraction strategy that is best tailored to the biological sample type to increase the quality of DNA recovered. For example, recovery of DNA from bone requires a much more involved and aggressive demineralization chemistry to improve recovery success. Buccal (i.e., mouth) swabs for databases may be better suited for more efficient

automated protocols.

However, most extraction methods follow the basic approach of separating cells from other material, and analysis of cell membranes to free DNA followed by purification of the DNA itself.

Conclusion

DNA contains genetic information that is inherited by descendants. This information is determined by the order of the base pairs. The DNA strand contains genes, regions that regulate genes, and regions that have no function or have a function we do not yet know about. Genes can be understood as a kind of program of the organism. DNA, an inherited molecule, is a macromolecule consisting of two strands of molecules that are wrapped around each other in the form of a double helix. The chemical strand of DNA consists of a series of nucleotides, and each nucleotide consists of deoxyribose, phosphate, and nitrogen bases. Therefore, DNA is a polymer because it consists of certain subunits, ie nucleotides.

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