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CENTRAL DOGMA OF MOLECULAR BIOLOGY: FROM DNA TO PROTEIN SYNTHESIS

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Abstract *The Central Dogma of Molecular Biology stands as an iconic framework that unfurls the intricate choreography governing the flow of genetic information within living organisms. Originating from the visionary insights of Francis Crick in 1958, this paradigm illuminates the journey of genetic code, beginning with the replication of DNA, traversing through the transcription of genetic templates into RNA, and culminating in the translation of RNA sequences into functional proteins. In this comprehensive review article, we embark on a journey to unravel the underlying mechanisms, historical antecedents, and contemporary implications intrinsic to the Central Dogma. Delving into the historical genesis, we retrace the intellectual trajectory that led to Crick's formulation. Building upon a constellation of pioneering experiments, we unearth the evidentiary foundations that bolstered the establishment of this cardinal principle. From the pivotal elucidation of DNA's structure by Watson and Crick to the enigmatic nature of the genetic code, these formative discoveries set the stage for the central dogma's unveiling. The fundamental processes of DNA replication, transcription, and translation are dissected meticulously. Through intricate biochemical choreography, DNA replication ensures the fidelity of genetic inheritance during cell division. Transcription emerges as the bridge between the stable DNA code and the transient RNA intermediaries. These transcripts undergo intricate processing, revealing a rich tapestry of post-transcriptional modifications that transform them into functional entities. Translation, the culminating act in this biogenetic theater, sees the orchestrated collaboration of ribosomal machinery, transfer RNA adaptors, and a nuanced lexicon of codons and amino acids. As the genomic narrative unfolds, genetic mutations emerge as the harbingers of variation. We unravel the delicate equilibrium between genetic stability and mutability, probing the catastrophic consequences of mutations on protein synthesis and cellular homeostasis. The regulatory overture of gene expression, an essential counterpart to the central dogma, is dissected to unveil its role in orchestrating intricate symphonies of development, adaptation, and disease.*

Keywords: *Central Dogma, DNA, genetic code, RNA, transcription, mutations*

1. Introduction

When the French molecular biologist Jacques Monod, reminded Crick that the term "Central Dogma" is associated with unwavering belief (Crick, 1970), it may have seemed peculiar for a scientific hypothesis (Judson, 1979). However, Crick did not intend this term to imply an unquestioning doctrine. As a non-believer in religion, Crick saw dogmas as daring hypotheses without evidence. Since its conception, the Central Dogma has encountered numerous obstacles and criticisms. Before delving into the gravity of these challenges, let us first examine the circumstances in which Crick presented these ideas (Thieffry & Burian, 1996). For ay during the mid-1950s. In those times, DNA's role within genetic structure steadily became more transparent due to Avery and colleagues' experimental venture back in 1944. Their research unfolded how pivotal with possibly solitary stature DNA held as a component of genetic substance. The concept on structural makeup of this molecule by Crick and Watson around 1953 highlighted its prowess for fulfilling the primary function of genetics - self-duplication (Morange, 2009). Once isolated, the twin strands could spawn clones relying intensively upon complementary basis-pair equilibrium between adenine-thymine & guanine-cytosine. Physicist George Gamow floated the idea regarding explicit determinism nature delineated via protein sequence through inherent autonomic components (Irfan et al., 2023). It arose around 1952. But an unavoidable hurdle ensued: DNA resided congruent with chromosomes confined chiefly into cellular nucleus area while branched out eukaryotic cell cytoplasm turned host spot for bifurcation-based synthesis. (AHMAD et al., 2023) Known conspicuously, this specific autonomy granted towards operation under certain modus operandi from chromosomal standpoint continued stoking the need probing connection comprehending ratio dependence b/w copious RNAs dispersion

across intracellular matrix coupled besides compilation speed aimed at elongating peptide chained concoctions. Peer reviewed references dated concomitantly forwarded acting pieces contributing detailed synopsis indicating occurrencenvolved translational guiding factors tracing roots essentially lying dormant inside microcosmic RNA along protean pseudopods embedded collectively acted arenas. Revisiting retrospectively, it isn't unusual for airing reflective notes inherently exude simplicity correlating triad figures including core elements, namely, DNA, RNA alongside peptides appearing in comprehensive harmony seated being fitting centroid crux solutions tugging relentlessly bypass distant past. Suddenly, readiness climbed up, sensing fragments constituting elaborate holistic images surfaced amongst doers like Alexander Dounce (Sami et al., 2023)

In the intricate tapestry of life's mechanisms, the Central Dogma of Molecular Biology stands as an indelible thread, weaving its way through the realm of genetics, molecular interactions, and cellular orchestration (Bloom, 1997). Conceived in the mid-20th century by the visionary Francis Crick, this fundamental paradigm unravels the intricate journey of genetic information, elucidating the dynamic interplay between DNA, RNA, and proteins. Rooted in a historical narrative of discovery and innovation, the Central Dogma has not only shaped our understanding of the molecular intricacies governing life. Still, it has also paved the way for groundbreaking applications that resonate across disciplines (Franklin & Franklin). The Central Dogma encapsulates life's continuity's fundamental processes—replication, transcription, and translation. Each of these stages represents a crucial step in transforming genetic information, manifesting as the complex dance of biomolecules within the intricate machinery of the cell. This paradigm forms the bedrock upon which the edifice of modern molecular biology stands, offering insights into development, health, evolution, and disease. The journey in this review article mirrors the trajectory charted by the Central Dogma. We traverse the intellectual landscapes of scientific history, where pivotal discoveries converged to unravel the DNA structure and elucidate the genetic code's enigmatic language. A synergy of ingenious experiments and serendipitous insights unfolded, illuminating the path from the double-helix to deciphering the genetic alphabet (Baldi & Hatfield, 2011).

1. DNA Replication: Ensuring Genetic Fidelity

DNA replication is a core operation that guarantees exact copying of an organism's genetic data, vital for passing characteristics from one generation to another. Keeping true during this duplication phase prevents errors and transformations that could contribute towards different illnesses and inherited conditions. Many systems and proteins collaborate in unison to uphold impeccable accuracy (Hoekstra et al., 2017).

1.1. Base Pairing and Complementary Strands

DNA consists of two strands running in reverse directions, held together through hydrogen bonds linking complementary nucleotide bases (adenine pairs up with thymine, and cytosine aligns with guanine). Amid replication, every original DNA strand acts as a blueprint for crafting a new complementary strand. This base pairing process guarantees that the sequence of nucleotides within the fresh strand perfectly matches its predecessor (Steenken, 1992).

1.2. Proofreading by DNA polymerase

DNA polymerases are enzymes responsible for synthesizing the new DNA strand. These enzymes' built-in proofreading function helps them identify and correct errors. If an incorrect base is added to the growing strand, the polymerase can detect the mismatch and remove the incorrect nucleotide before synthesizing (Aliotta et al., 1996).

1.3. Mismatch Repair (MMR) System

Despite the proofreading ability of DNA polymerase, some errors can still escape detection. The mismatch repair system is a cellular mechanism that identifies and corrects base-pairing errors after replication. Mismatch repair proteins recognize the impaired bases and remove a section of the newly synthesized strand containing the error. The correct DNA sequence is then resynthesized (Wilkins, 2022).

1.4. DNA Damage Repair Systems

DNA replication can also be challenged by various types of DNA damage, such as chemical modifications or physical breaks in the DNA strands. Cells have specialized repair mechanisms, such as nucleotide and base excision repair, to fix damaged DNA before it becomes a permanent mutation (Carlin et al., 2023).

1.5. Checkpoint Control

Cell cycle checkpoints ensure that DNA replication only proceeds when DNA is intact and properly replicated. If errors or damage are detected, checkpoint proteins halt the replication process, giving the cell time to repair the issues before continuing with cell division.

1.6. Telomeres and Telomerase

Telomeres, the repetitive DNA sequences located at chromosome endings, safeguard our genetic content from being degraded during replication. Each replication cycle causes a sliver of the telomere to disappear. So as not to lose crucial genetic data, an enzyme known as telomerase replenishes these repeating sequences on chromosome ends. The careful control of this procedure ensures preservation and integrity of our gene pool (Ganai & Johansson, 2016).

2. Transcription DNA to RNA

Transcription denotes the procedure wherein genetic details imprinted in DNA is utilized to produce a

corresponding RNA molecule. This particular RNA piece can act as blueprint for protein production or take on various operational roles within cellular structures. Transcription is a vital phase of gene expression, enabling all information kept in the DNA to be applied by cells to execute diverse functions (Warwick et al., 2023).

2.1. Initiation

The transcription process starts when an enzyme dubbed RNA polymerase attaches itself to a distinct DNA region known as the promoter. This area holds sequences identified by both RNA polymerase and other governing proteins. When situated correctly, it uncoils a minor segment of the genome's double helix to reveal details within its template strand (Stoy et al., 2023).

2.2. Elongation

While the RNA polymerase progresses across the DNA template filament, it appends matching RNA nucleotides to the expanding strand of RNA. It instates this by adding individual RNA nucleotides in succession while adhering to base-pairing regulations (uracil pairs with adenine and guanine bonds with cytosine). The course continues as instructed by the 5' to 3'direction directive, creating a complete sequence within which lies an uninterrupted process crafted by synthesizing efforts delivered via robust functioning protocol (Stoy et al., 2023).

2.3. Termination

Transcription ends when the RNA polymerase comes across a termination signal on the DNA template. This signal prompts the separation of RNA polymerase from DNA and releases freshly created RNA molecule. At times, other proteins aid in concluding this process (Murayama et al., 2023).

Different RNA molecules derived from DNA serve various functions. One type, called messenger RNA (mRNA), transports genetic information from DNA to ribosomes, where proteins are made. mRNA acts as a blueprint for protein synthesis. Transfer RNA (tRNA) is another type that plays a vital role in protein synthesis. It carries amino acids to the ribosome, and each tRNA molecule has a specific sequence that matches a particular codon on the mRNA (You et al., 2023). Ribosomal RNA (rRNA) is responsible for the structure of ribosomes, which are crucial for protein synthesis. During protein synthesis, rRNA facilitates the formation of peptide bonds between amino acids. Another type, called small nuclear RNA (snRNA), is involved in RNA splicing. This process removes non-coding regions (introns) from pre-mRNA molecules and joins coding regions (exons) to create mature mRNA. Lastly, MicroRNA (miRNA) and Small Interfering RNA (siRNA) are short RNA molecules that regulate genes by binding to complementary sequences on mRNA. This binding can lead to mRNA degradation or prevent its translation into protein (Yang et al., 2023).

3. RNA Processing From Precursor to Functional Molecule

RNA processing is a crucial series of modifications that transform precursor RNA molecules into mature, functional RNA molecules ready to perform their specific cellular roles. This process primarily occurs in eukaryotic cells and involves several steps, including capping, splicing, and polyadenylation. The end result is a processed RNA molecule that can be translated into proteins (in the case of messenger RNA, mRNA) or perform other essential functions within the cell (Marquardt et al., 2023).

3.1. Capping

Applying a Cap As the RNA polymerase builds up the mRNA molecule in transcription, it attaches a 5' cap to its foremost end - this cap is also known as just 'the 5'cap'. Built from an altered guanine nucleotide (which takes the form of methylated guanosine), it connects directly with that first written-down nucleotide produced in the process of transcript synthesizing by enzyme machinery. The crucial roles served by busily laboring Caps include safeguarding our precious mRNA against degeneration and decay and assisting their arduous movement from nucleus confines into cytoplasm for protein-making execution or so-called translation initiated via sturdy ribosomes (Fisher & Feng, 2022).

3.2. Splicing

Shaping Through Splicing Many eukaryotic genes exhibit both coding portions termed exons alongside non-coding patches named introns interwoven within respective DNA sequences they embody after initial round transcriptions have taken place we notice activation of what's referred to as splicing operation post-transcription —it ships off those unwanted intron sections while bridging together coveted exon segments thus allowing formation matured MRNAs being prepped ready utilization. This high-level precision procedure uses snRNPs, aka small nuclear ribonucleoprotein complexes, which are part spliceosome comprising additional peptides plus key subunits sets scene facilitating accurate separate meets amid the surrounding environment, ensuring precise cut-splice operations performed (Fisher & Feng, 2022).

3.3. Alternative Splicing

Many genes undergo alternative splicing, a phenomenon where different combinations of exons are included in the final mRNA molecule. This process allows a single gene to generate multiple mRNA variants, increasing the diversity of protein isoforms produced from a single gene (Fisher & Feng, 2022).

3.4. Polyadenylation

At the 3' end of the pre-mRNA, a sequence known as the polyadenylation signal is recognized. After transcription, an enzyme called polyadenylate polymerase adds a string of adenine nucleotides (poly-A tail) to the 3' end of the mRNA. The poly-A tail helps stabilize the mRNA molecule, facilitates its export from the nucleus, and initiates translation (Yamauchi et al., 2022).

3.5. Editing

In some cases, RNA molecules undergo post-transcriptional modifications that involve changing specific nucleotides within the RNA sequence. This process, known as RNA editing, can lead to changes in the coding sequence of the mRNA, resulting in altered protein products (Yamauchi et al., 2022).

3.6. Quality Control and Surveillance

The cell has mechanisms to monitor the quality of processed RNA molecules. Any RNA molecules with defects, such as incorrect splicing or premature termination, can be targeted for degradation through mechanisms like nonsense-mediated decay (NMD) (Gao et al., 2023).

4. Translation Decoding RNA into Proteins

Interpretation signifies the procedure via which data encapsulated within an mRNA molecule gets utilized to synthesize a protein. This complex process occurs on ribosomes, intricate cellular organizations constituted of RNA and proteins; it incorporates deciphering nucleotide sequencing in the mRNA and then transmuting into a sequence comprising amino acids resident within a protein (Jia et al., 2020).

4.1. Initiation

Commencement of the translation process is initiated when there's a binding action between the diminutive ribosomal subunit and mRNA molecule. This occurs precisely at what we denote as the 'start codon.' In eukaryotic cells, this start codon assumes an AUG (adenine-uracil-guanine) configuration, translating to code for methionine - classified under amino acids. The initiator transfer RNA, or tRNA, bearing said Methionines coalesces with our previously mentioned start codon on its counterpart–the mRNA strand, promptly followed by a large ribosomal unit joining forces with the complex constructed hitherto (Jia et al., 2020).

4.2. Elongation

The ribosomal constituent advances longitudinally along the mRNA gradient, from a 5' to 3' trajectory, meticulously deciphering each codon (comprising three-nucleotide sequence) and consequentially summoning an appropriate tRNA entity that is laden with its matching amino acid. Each distinctive tRNA possesses an anticodon designed to counterbalance or complement the specific codon on the mRNA strand. The ribosome above subsequently stimulates the synthesis of peptide bonds by acting as a catalyst between said amino acid transported by engaged tRNA in A regional site and burgeoning polypeptide assembly found ubiquitously on pivotal sites such as P (Papaspyropoulos et al., 2023).

4.3. Translocation

After peptide bond formation, the ribosome advances by one codon along the mRNA, shifting the tRNA in the P site to the E (exit) site and the tRNA in the A site to the P site. This step is called translocation and requires energy in the form of GTP (guanosine triphosphate) (Papaspyropoulos et al., 2023).

4.4. Termination

The translation process persists until the ribosome encounters a termination codon (UAA, UAG, or UGA) on the mRNA. As no tRNA units carry amino acids that align with these codons, release factors attach themselves to this cellular machine known as a ribosome - initiating an event cascade that releases the recently formed protein and disbands the key cellular component i.e., Ribosomes into individual subunits readying them for subsequent rounds of translations. Post synthesis phase involves folding up procedures, turning proteins into 3D forms with functionality, facilitated by helper proteins called chaperones. This uniquely arranged sequence constituting various Amino Acids bestowed upon each Protein determines its designated structure & role within Cellular metabolism processes, whether it's catalytic functions like enzymes, building structural parts acting as signals akin molecules involved in mass communication across cells, also undertaking movement tasks working under transporter capacity, and more (Franco & Koutmou, 2022).

5. Regulation of Gene Expression Balancing the Dogma

Regulation of gene expression is a critical process that allows cells to control when and to what extent specific genes are transcribed and translated. This regulation is essential for maintaining cellular homeostasis, responding to environmental cues, and ensuring organisms' proper development and function. It involves a complex interplay of various mechanisms that influence the flow of genetic information from DNA to RNA to protein. This regulation helps balance the central dogma of molecular biology DNA to RNA to protein (Scott & Hwa, 2023).

5.1. Transcriptional Regulation

Promoters and Enhancers Regulatory elements in the DNA, such as promoters and enhancers, control transcription initiation. Transcription factors (proteins) bind to these elements to activate or repress transcription.

Chromatin Remodeling Chromatin structure, which involves packaging DNA around histone proteins, can be modified to make certain genes more or less accessible to transcription machinery. Acetylation, methylation, and other modifications can influence gene expression (Scott & Hwa, 2023).

5.2. Post-Transcriptional Regulation

RNA Processing Alternative splicing and other RNA processing events can lead to the generation of different mRNA isoforms from the same gene, allowing for the production of multiple protein variants. RNA Stability The stability of mRNA molecules can be regulated, affecting their lifetime and availability for translation. Regulatory factors can target mRNA for degradation or stabilization (Aranda et al., 2022).

6. Translation Regulation

mRNA Accessibility Regulatory elements in the mRNA, such as upstream open reading frames

(uORFs) and secondary structures, can influence the efficiency of translation initiation.

MicroRNAs (miRNAs) and Small Interfering RNAs (siRNAs). These small RNA molecules can bind to complementary sequences on mRNA, either inhibiting translation or causing mRNA degradation (Aranda et al., 2022).

6.1. Post-Translational Regulation

Protein Modification Proteins can undergo various modifications, such as phosphorylation, ubiquitination, and glycosylation, influencing their activity, stability, and localization.

Protein-Protein Interactions Proteins can interact with other proteins to modulate their functions, affecting their activity or localization within the cell (Leipheimer et al., 2019).

6.2. Feedback and Feedforward Loops

Gene expression can be regulated through feedback loops, where the protein products of certain genes regulate the expression of those same genes. Feedforward loops involve regulatory proteins influencing downstream genes in a coordinated manner (Zhang et al., 2022).

6.3. Epigenetic Regulation

Epigenetic modifications, such as DNA methylation and histone modifications, can be passed down through cell divisions and influence gene expression by altering chromatin structure and accessibility.

Cells carefully orchestrate these regulatory mechanisms to respond to internal and external cues. This flexibility allows cells to differentiate into various cell types during development, respond to changing environmental conditions, repair DNA damage, and maintain proper cellular functions (Saw et al., 2020).

7. Evolutionary Insights from the Central Dogma

7.1. Conservation of Genetic Information

The Central Dogma highlights the fundamental principle that genetic information is transmitted from generation to generation through DNA replication and cell division. This process of faithful inheritance ensures that the genetic material remains relatively stable over long periods. Evolutionary studies have shown that many genes and molecular pathways are conserved across different species, suggesting a common ancestry and shared genetic information (Shaghoulian, 2022).

7.2. Genetic Variation and Diversity

While the Central Dogma emphasizes the fidelity of DNA replication, it also acknowledges the occasional introduction of mutations during DNA replication and other processes. These mutations can lead to genetic variation within a population and are essential for the process of evolution by natural selection. Mutations provide the raw material for evolutionary changes and can lead to new alleles and traits (Bornowski et al., 2023).

7.3. Comparative Genomics and Homology

The study of DNA sequences, particularly genes and protein-coding regions, across different species has revealed striking similarities, known as homology. Homologous genes often share a common evolutionary origin and have undergone divergence over time due to mutations and selection. Comparative genomics allows researchers to trace the evolutionary relationships between species and infer the patterns of divergence and shared ancestry (Hamburger, 2019).

7.4. Gene Duplication and Divergence

Gene duplication is a process that creates multiple copies of a gene within a genome. These duplicated genes can then evolve independently, acquiring new functions or diverging in their expression patterns. The Central Dogma's framework helps explain how gene duplication and divergence contribute to the evolution of novel genetic functions and the development of complex traits (Hamburger, 2019).

7.5. Functional Evolution of Proteins

The translation step of the Central Dogma produces proteins with specific functions. Over time, proteins can evolve through changes in their amino acid sequences, leading to protein structure and function changes. By comparing the protein sequences of different species, researchers can study how proteins have evolved to perform different roles while still maintaining essential functions (Hamburger, 2019).

7.6. Molecular Clocks and Evolutionary Timelines

The rate of genetic changes, such as mutations, can serve as a molecular clock that helps estimate the timing of evolutionary events. Researchers can estimate the time since their common ancestor and construct evolutionary timelines by comparing related species' DNA or protein sequences.

7.7. Horizontal Gene Transfer

While the Central Dogma mainly focuses on vertical gene transfer (from parent to offspring), horizontal gene transfer involves the transfer of genetic material between different species. This phenomenon has been observed in bacteria and other microorganisms and can play a significant role in shaping the genetic diversity and evolution of these organisms (Hamburger, 2019).

9. Conclusion

The journey through the Central Dogma of Molecular Biology has traversed a landscape as intricate and harmonious as the symphony of life itself. From the foundational insights of Francis Crick to the contemporary vistas of genetic manipulation, our exploration has illuminated the core processes that govern the flow of genetic information within cells. As we draw the curtain on this review article, we find ourselves standing at the crossroads of discovery, where historical revelations intertwine with modern applications, and the enigma of DNA is deciphered into the language of proteins. The threads woven by the Central Dogma reach deep into the annals of scientific history. Watson and Crick's elucidation of

DNA's structure marked the birth of molecular biology, casting light on the double helix's elegant code of life. The genetic code's translation was unveiled through painstaking experimentation—each triplet of nucleotides specifying an amino acid, the building blocks of proteins. The symphonic dance of replication, transcription, and translation unfurled, revealing the meticulous choreography of enzymes, templates, and regulators that guide the intricate processes of life. DNA replication emerged as the guardian of genetic fidelity, its orchestra of polymerases, helicases, and repair mechanisms ensuring that each copy remains an impeccable replica of the original. The central dogma illuminated the intricate balance between stability and mutability, safeguarding the genetic code while allowing for the diversity that fuels evolution.

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Declaration

Conflict of interest

The researchers affirm that there were no financial or commercial ties that might be seen as a potential conflict of interest throughout the research's execution.

Data Availability statement

All data generated or analyzed during the study have been included in the manuscript.

Ethics approval and consent to participate

These aspects are not applicable in this research.

Consent for publication

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