زانکۆی سەلاحەدین - هەولێر
Salahaddin University-Erbil

Types of the RNA and their function

Research Project
Submitted to the Department of Biology in partial fulfillment of the requirements for the degree of B. A or BSc. in Biology

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May– 2021

- قال تعالى: (أَمَّنْ هُوَ قَٰنِتٌ ءَانَآءَ ٱلَّيْلِ سَاجِدًا وَقَآئِمًا يَحْذَرُ ٱلْءَاخِرَةَ وَيَرْجُواْ رَحْمَةَ رَبِّهِۦۗ قُلْ هَلْ يَسْتَوِى ٱلَّذِينَ يَعْلَمُونَ وَٱلَّذِينَ لَا يَعْلَمُونَۗ إِنَّمَا يَتَذَكَّرُ أُوْلُواْ ٱلْأَلْبَٰبِ).

صدق الله العظيم

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SUPERVISOR CERTIFICATE

This research project has been written under my supervision and has been submitted for the award of the degree of BSc. in General Science with my approval as a supervisor.

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DEDICATION

This work is dedicated to:

My merciful mother

Zryan Abd

My brothers

All whom I appreciate.

ACKNOWLEDGEMENTS

First of all, I would like to thank the merciful “Allah” help me successfully complete my study.

My deepest gratitude to my supervisor Prof. Dr. Zirak Faqe Ahmed for her supervision and choosing project, scientific guidance, and support during the period of the study

My deepest thanks to the deanery of the Education college head and all staff of the biology department for their kindness and support

I would like to express my thanks to the Ministry of Higher Education and Scientific Research and the presidency of Salahaddin University/Erbil.

Thank for all my friends who help me to complete my study and thanks to my family which help me complete my research.

Summary

RNA, like DNA, is a polymer consisting of nucleotides joined together by phosphodiester bonds. However, there are several important differences in the structures of DNA and RNA. Whereas DNA nucleotides contain deoxyribose sugars, RNA nucleotides have ribose sugars. With a free hydroxyl group on the 2_-carbon atom of the ribose sugar, RNA is degraded rapidly under alkaline conditions. The deoxyribose sugar of DNA lacks this free hydroxyl group; so DNA is a more stable molecule. Another important difference is that thymine, one of the two pyrimidines found in DNA, is replaced by uracil in RNA. A final difference in the structures of DNA and RNA is that RNA is usually single-stranded, consisting of a single polynucleotide strand, whereas DNA normally consists of two polynucleotide strands joined by hydrogen bonding between complementary bases. Some viruses contain double-stranded RNA genomes. Although RNA is usually single-stranded, short complementary regions within a nucleotide strand can pair and form secondary structures. These RNA secondary structures are often called hairpin-loops or stem-loop structures.

When two regions within a single RNA molecule pair up, the strands in those regions must be antiparallel, with pairing between cytosine and guanine and between adenine and uracil (although occasionally guanine pairs with uracil). The formation of secondary structures plays an important role in RNA function. Secondary structure is determined by the base sequence of the nucleotide strand; so different RNA molecules can assume different structures. Because their structure determines their function, RNA molecules have the potential for tremendous variation in function.

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INTRODUCTION

RNA, in one form or another, touches nearly everything in a cell. RNA carries out a broad range of functions, from translating genetic information into the molecular machines and structures of the cell to regulating the activity of genes during development, cellular differentiation, and changing environments. RNA is a unique polymer. Like DNA, it can bind with great specificity to either DNA or another RNA through complementary base pairing. It can also bind specific proteins or small molecules, and, remarkably, RNA can catalyze chemical reactions, including joining amino acids to make proteins. All the RNA in cells is themselves copies of DNA sequences contained in the genes of a cell's chromosomes. Genes that are copied—"transcribed"—into the instructions for making individual proteins are often referred to as "coding genes." The genes that produce RNAs used for other purposes are therefore called "noncoding RNA" genes (Xue et al., 2020).

Several key classes of RNA molecules help convert the information contained in the cell's DNA into functional gene products like proteins. Messenger RNAs (mRNAs) are copies of individual protein-coding genes and serve as an amplified read-out of each gene's nucleic acid sequence. Two key noncoding RNAs participate in the assembly of the proteins specified by mRNAs. Ribosomal RNA (rRNA) constitutes the core structural and enzymatic framework of the ribosome, the machine that synthesizes proteins according to the instructions contained in the sequence of an mRNA. Transfer RNAs (tRNAs) use complementary base pairing to decode the three-letter "words" in the mRNA, each corresponding to an amino acid to be sequentially incorporated into a growing protein chain (Carninci,2005).

Most RNA molecules, once transcribed from the chromosomal DNA, require structural or chemical modifications before they can function. In eukaryotic cells, mRNAs are assembled from longer RNA transcripts by the spliceosome, which consists of spliceosomal RNAs and protein partners. Spliceosomal RNAs help discard intervening sequences (introns) from pre-mRNA transcripts and splice together the mRNA segments (exons) to create what can be a complex assortment of distinct

protein-coding mRNAs from a single gene. Many noncoding RNAs also require post-transcriptional modifications. For instance, ribosomal RNAs receive numerous chemical modifications that are required for proper ribosome assembly and function. These modifications are introduced by protein enzymes in conjunction with specialized noncoding RNAs (called snoRNAs) that base pair with the rRNA and guide the modifying enzymes to precise locations on the rRNA. Some RNAs possess the intrinsic enzymatic activity and can directly catalyze RNA modification reactions. These catalytic RNAs include certain self-splicing RNA transcripts, ribozymes, and RNAse P, an RNA enzyme that trims the ends of tRNA precursors in essentially all cells (Djebali, 2012).

Regulation of the production of proteins from coding genes is the basis for much of cellular and organismal structure, differentiation, and physiology. Diverse classes of noncoding RNAs participate in gene regulation at many levels, affecting the production, stability, or translation of specific mRNA gene products (Djebali, 2012).

In prokaryotes (for example, bacteria), small antisense RNAs exert a variety of gene regulatory activities by base-pairing specifically to their target mRNAs. Also common in prokaryotes are riboswitches, non-coding RNA sequences that usually function as regulatory domains contained within longer mRNAs. Riboswitches regulate the activity of their host mRNAs by binding to small molecules such as nucleotides or amino acids, sensing the abundance of those small molecules and regulating the genes that make or use them accordingly (Core, 2008).

Eukaryotic cells contain thousands of small RNAs associated with various RNA interference (RNAi) pathways. For example, microRNAs (miRNAs) are regulatory RNAs approximately 22 nt long that are produced from longer transcripts that contain a certain kind of double-stranded "hairpin" structure. miRNAs associate with a protein of the Argonaute class, and base-pair specifically to mRNAs to inhibit their stability or translation. There are hundreds of miRNA genes in plants and animals, and each miRNA can regulate the activity of hundreds of protein-coding genes. Therefore,

miRNAs individually and collectively have a profound impact on the development and physiology of multicellular eukaryotes (Djebali, 2012).

Small interfering RNAs (siRNAs) are similar in length to microRNAs and are also associated with Argonaute proteins. Unlike miRNAs, which are produced from specific genetic loci that have evolved to regulate mRNAs, siRNAs can derive from essentially any transcribed region of the genome. siRNAs typically act directly upon the locus from which they are produced. So, siRNAs occur in cells where genes are under ongoing self-regulation by RNAi.

A major role for certain classes of small non-coding RNAs in the defense of the cell against viruses, transposons, and other nucleic acid sequences that pose a potential threat to cellular homeostasis or genome stability. The response of some cells against viral infection includes the production of siRNAs complementary to the virus. Many endogenous siRNAs in eukaryotic cells specify the silencing of transposons and repeat sequences that are already resident in the genome. Similarly, in animals, the Piwi-associated RNAs (piRNAs) promote genome integrity by silencing transposons and repeat sequences (Mayer, 2015).

Another class of regulatory RNA consists of diverse kinds of longer noncoding transcripts that generally function to regulate the expression of distant genetic loci, often by suppressing or promoting their transcription. For example, the rox RNAs of the fruit fly seem to facilitate the remodeling of chromosome structure to allow the male X chromosome to be transcribed at twice the rate as a single X chromosome in females, which have two X's. Similarly, the Xist RNA in mammals helps inactivate one of the two X chromosomes in females, allowing males and females to have equivalent levels of gene expression from the X chromosome. Xist is one example of a broader class of very versatile regulatory RNAs known as long intergenic noncoding RNAs (lincRNAs). lincRNAs can act as scaffolds for the assembly of complexes of transcriptional regulatory proteins and can facilitate the recruitment of defined combinations of protein regulators to specific genes (Xue et al., 2020).

LITERATURE REVIEW AND THEORETICAL BACKGROUND

Type RNA and function

Could be divided into two categories in accordance with their coding potential, that is, coding RNAs and non-coding RNAs.

Coding RNAs generally refer to mRNA that encodes protein to act as various components including enzymes, cell structures, and signal transductors.

Human genome analysis contributed to the first discovery of long Sequences of ncRNA such as tRNA and rRNA (Wright and Ea, 2011). In addition to this, other lncRNA sequences were also identified whose function is not found in protein translation machinery. When these long sequences of non-coding RNA were compared to ENCODE consortium data, it was found that several classes of ncRNA molecules are generated through pathways similar to that of protein-coding genes (Derrien et al., 2012; Harrow et al., 2012; Consortium et al., 2012). These findings in relation to previous studies sparked on the diversity of non-coding RNA, ncRNAs are classified into two major categories: structural non-coding RNAs and regulatory non-coding RNAs. Structural non-coding RNAs comprise of rRNAs and tRNAs. Regulatory non-coding RNAs are further divided into three classes, small, medium, and long non-coding RNAs (Ponting et al., 2009; Alvarez-Dominguez and Lodish, 2017). Further, miRNA, siRNA, piRNA, cisRNA, telsRNA were considered as short non-coding RNA with a size between 20–50 nucleotides, and snoRNA, prompts, tiRNA, snRNA, and many more are classified as medium non-coding RNA with a size between 50-200 nucleotides (Nagano and Fraser,2011; O'Day and Lal,2010) and a large class of RNA with maximum regulatory potency containing greater than 200 nucleotides are classified as long non-coding RNA (Derrien et al., 2012; Wang et al., 2014). With increasing studies on highly abundant and functionally important categories of lncRNAs (such as intronic, antisense, lincRNA, cisRNA, ceRNA, etc), we provide, with sufficient clarity, the classification of ncRNAs and list out all the existing lncRNAs (ma et al., 2013; Gulerova).

Coding RNA

(Messenger RNA) mRNA

Serves as an essential macromolecule in the central dogma for carrying genetic information from the nucleus to the cytoplasm, thereby expressing functional proteins as shown in figure (1) (Sharp, 2009). Aberrant alterations in the expression level of proteins lead to numerous congenital and acquired diseases like genetic disorders and cancers (Sahin, Kariko, & Tureci, 2014). Thus, it is critical to maintaining a normal level of mRNAs in the cytoplasm. Structurally, mRNA is a single-stranded RNA transcribed from a DNA template. The mature eukaryotic mRNA typically consists of a 5′-methylguanosine (m7G) cap, 5′- untranslated region (UTR), and coding region starting with AUG codon, 3′-UTR, and a polyadenylated a (poly (A) tail (Midoux & Pichon, 2015; Weissman, 2015; Figure 1). The Kozak sequence in the 5′-UTR is involved in the recognition by the ribosome to initiate the translation process. The 3′-UTR is another important component in regulating mRNA translation and stability, which may contain miRNA binding sites. Likewise, the poly-A) tail is also a critical component for mRNA translation and degradation. When the poly (A) tail is fewer than 12 adenosine residues, mRNA is degraded from the 5′ cap structure (Midoux & Pichon, 2015; Yamamoto, Kormann, Rosenecker, & Rudolph, 2009). Hence, the stability and translation efficiency of exogenous mRNA can be enhanced by a number of methods such as UTR manipulation, codon optimization, chemical modification, and elongation of poly(A) tail of mRNA (Grabbe et al., 2016; Loomis, Kirschman, Bhosle, Bellamkonda, & Santangelo, 2016; Presnyak et al., 2015; Yamamoto et al., 2009).

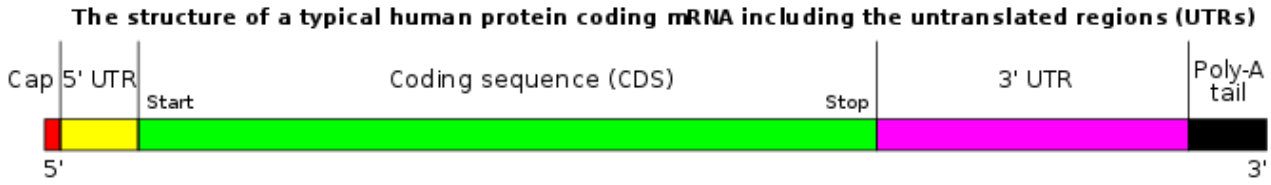

Fig 1. Structure of mRNA

Noncoding RNA

Transfer RNA:

Transferal RNA which functions as an amino acid carrier during protein synthesis, is heavily modified post-transcriptionally (Torres A.G and Batlle E,2014). It has been reported that there are 13 modifications, on average, in one human tRNA (Saikia M et al., 2010). These modifications can influence the structure, stability, and translation accuracy of tRNA (Novoa E.M &Pavon-Enternod M 2012; Schimmel P, 2018). As reported, a large subset of tRNA modification enzymes is linked to human diseases (fig.2) (Pan T, 2018).

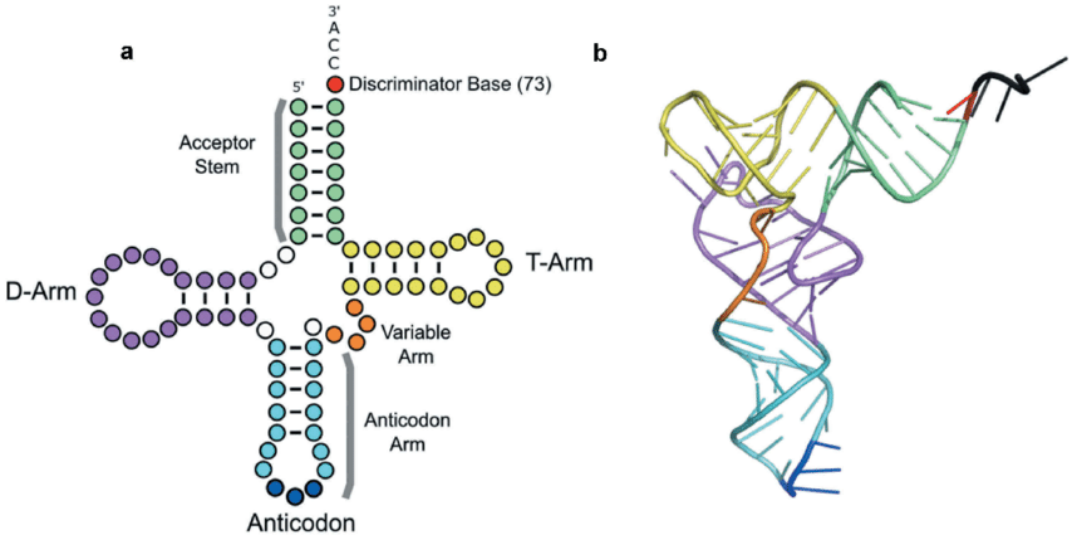

Fig 2. Structure of tRNA

Ribosomal RNA:

r*RNA*:

(rRNA) processing in eukaryotes is a complex, multi-step process that starts in the nucleolus, proceeds in the nucleoplasm, and culminates in the cytoplasm (Woolford J.L & Baserga S.J 2013; Tschochner H.& Hurt E 2003). The process is tightly regulated and involves the recruitment of small nucleolar RNAs (snoRNA) and multiple protein factors, including endo- and exonucleases, ATPases, helicases, and GTPases. The process begins with a pre-rRNA transcript that includes RNAs destined for both the small subunit (SSU; 18S) and large subunit (5.8S, LSU; 25S/28S in yeast/mammals, respectively) (Woolford J.L & Baserga S.J 2013; Tschochner H. & Hurt E 2003). These

elements are separated by long internally transcribed spacers (ITSs) that are processed during ribosome biogenesis (Woolford J.L & Baserga S.J 2013; Tschochner H. & Hurt E 2003).

MicroRNAs:

Are small non-coding RNAs of 19–25 nucleotides in length and are known to regulate several protein-coding genes both in plants and animals (fig.3). The first miRNA, lin-4 that controlled developmental timing in Caenorhabditis elegans was identified by two different groups in 1993 (Lee RC & Feinbaun RL 1993; Wightman B & Ruvakun G. 1993). Later, let-7 miRNAs were found to control the timing of fate specification of neuronal and hypodermal cells during larval development (Slack FJ & Basson M 2000; Grosshans H& Johnson 2005). Subsequently, numerous miRNAs have been implicated in a variety of cellular processes including differentiation, apoptosis, cell proliferation, embryonic development, stem cell renewal, stress response, and metabolism (Krap X &Ambros2005; Lu S & Sun 2005). Their profound impact on the regulation of numerous cellular processes clearly suggests that any aberration in the miRNA biogenesis pathway or its regulation contributes to several human diseases such as cancer (Lynam-Lennon N & Maher SG 2009; Li C & Vagin 2009), Cardiovascular diseases (Latronico MV and Catalucci D., 2007), schizophrenia (Latronico MV and Catalucci D., 2007), psoriasis (Sonkoly E et al., 2007), diabetes (Williams MD and Mitchell.,2012), chronic hepatitis (Murakami Y et al.,2006), AIDS (Hariharan M et al.,2005), and obesity (Weiler J and Hunziker.,2006).

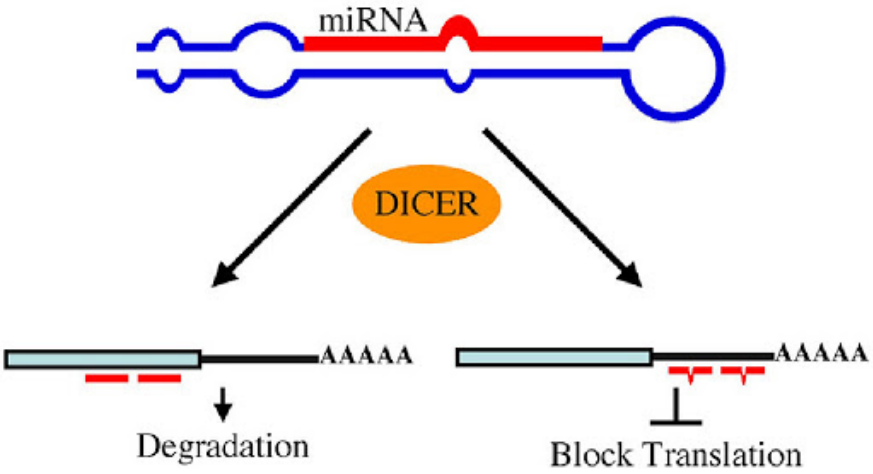

Fig.3 MiRNA structure

Small interfering RNAs:

siRNA:

The therapeutic potential of sequence-specific gene knockdown by small interfering RNAs (siRNAs) was demonstrated over 20 years ago (Fire A. & Xu S.1998; McCaffrey A.P&Meuse L.2002). However, the lack of effective and nontoxic delivery systems has limited their clinical progress. Ineffective delivery is compounded by specific siRNA properties, including high molecular weight, anionic charge, hydrophilicity, and potential for degradation by nucleases; these properties limit the ability of siRNAs to cross negatively charged plasma membranes and survive intracellularly without degradation in lysosome for prolonged periods. Facilitating siRNA delivery and promoting endosomal and/or lysosomal escape is essential for effective gene silencing (Kanasty R and Dorkin J., 2013). Liposomal formulations overcome some of these challenges and remain the most widely used strategy for siRNA delivery (Zhao Y and Huang L.,2014); ease of formulation and the tunability of critical parameters such as size, charge, siRNA loading, and circulation time make liposomes an attractive choice (Landen Jr.C.N &Chavez-Reyes A.2005; Torchilin V.P2005).

Piwi-interacting RNAs:

piRNAs:

Are 21–30 nucleotide (nt) small RNAs that bind to members of the Piwi subfamily of Argonaute proteins. Conserved across animals, their ancestral role appears to be to defend the genome against transposable elements (TEs). piRNAs hybridize to TE-derived RNAs, instigating post-transcriptional and transcriptional silencing of TEs (Siomi et al., 2011). In many organisms, piRNAs are essential for fertility, and germ cell development is defective in their absence (Weick and Miska, 2014). Fertility defects in mutants lacking piRNAs can occur in the absence of defective TE silencing (Gou et al., 2014, Simon et al., 2014, Vourekas et al., 2012); thus, piRNAs are likely to have further, poorly understood, functions in germline development (Fig4).

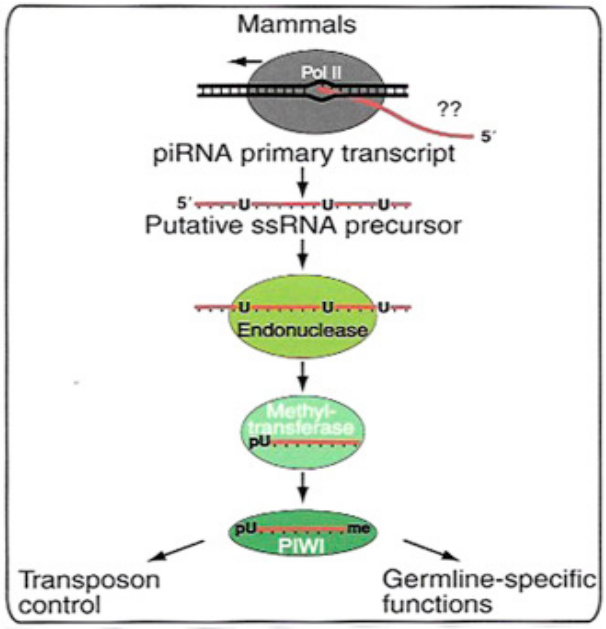

Fig 4.Structure of PIWI RNA

Single-cell RNA:

ScRNA:

High-throughput single-cell RNA sequencing (scRNA- seq) techniques have developed rapidly in recent years, making it feasible to generate transcriptional profiles from thousands of cells in parallel (Macosko EZ&Basu 2015; Jaitin DA&Kenigsberg E 2014). This technology has deepened our understanding of the cell types within tissues, their interactions, and cellular states. It is also a cornerstone of the Human Cell Atlas Project (HCA), a large collaborative initiative that aims to identify every cell type in the human body. Human samples present particular logistical challenges: the clinic may be distant from the processing lab and tissue can become available at short notice and/or at inconvenient times. These scenarios necessitate a fast, simple method of preserving samples that require minimal processing at the clinic.

To address the logistical difficulties and rapid transcriptional changes/stress responses observed upon tissue dissociation or storage (Ferreira PG et al., 2018), a range of cell freezing or fixation methods have been developed. (Guillaumet-adkins A. et al., 2017). Demonstrate that although viability is reduced, the transcriptional profiles from cultured cells or minced mouse tissue biopsies cryopreserved with DMSO are not significantly altered. However, some cell types are more vulnerable to freezing than

others, for example, in human endometrium biopsies; stromal cells survive freezing better.

Circular RNA:

(circRNA) was discovered in RNA viruses as viroids in the mid-70s, initially hypothesized to be an endogenous RNA splicing error (Hsu MT and Coca-Prados M., 1979). Thanks to advancements in computational analysis and RNA sequencing techniques in the same decade, these misunderstood circular structures have finally been recognized correctly and deeply both in structure and functionality (Ozaslak F and Milos PM., 2011). At its core, circRNA is a single-stranded RNA, but it differs from the far better known linear RNA in that it continuously closed in on itself by covalently joining its 5′and 3′ends (Holdt LM et al., 2018), thus presenting some fascinating properties which are not fully explored: protein complex scaffolding, parental gene modulation, RNA-protein interaction, and microRNA (miRNA) sponge, just to name a few (Husen TB, 2013; Xu X, 2016). They are now considered to provide an essential regulatory functions for plants and animals alike (Danan M et al., 2012).

An increasing number of study groups have shown and verified to an extent the level of effectiveness and efficacy displayed in circular RNAs that are typically required in viable medical treatments and other biotechnological applications. For instance, cases of traditional biomarkers being vastly outperformed by proposed circRNA substitutes are being reported often. Backed up by growing support and evidence about the promising capabilities of circRNAs, more investigation and interest ought to be brought out as such, not merely from a basic comprehensive biological understanding of its structures and mechanisms, but also on a systematic level of their interactions with surrounding molecules and environments. Applicably speaking, circRNAs are on par in terms of their potential and viability to target cancer and other malignant diseases with other novel treatments such as personalized medicine and stem cell therapies.

Small nucleolar RNAs

snoRNA:

Small nucleolar RNAs (snoRNAs) are a large conserved group of abundant small non-coding RNAs predominantly serving as guides for the chemical modification of ribosomal RNA (rRNA) (Matera et al., 2007)) (Fig.5). Over the past three years, however, snoRNAs have attracted attention not only for their fundamental role in ribosome biogenesis but also because of their extensive processing and their likely involvement in other cellular regulatory roles. And while some snoRNAs may display only non-traditional functions, evidence is also accumulating of a subset of snoRNAs showing duality in their function. Two main classes of snoRNAs have been defined, the box C/D snoRNAs and the box H/ACA snoRNAs that differ in terms of sequence and structural elements, binding partners, and nature of the chemical modification catalyzed. Both types of snoRNAs bind specific conserved protein partners, forming complexes referred to as snoRNPs (small nucleolar ribonucleoprotein complexes). Box C/D and H/ACA snoRNAs are highly conserved throughout evolution and are present in all eukaryotic organisms examined thus far. They have also been identified in some archaea where they are known as small RNAs (sRNAs) (P.P.Dennis & Omer, 2005; A.D.Omer &T.M.Lowe, 2000). In addition, core snoRNP proteins are highly conserved in eukaryotes and have homologs in archaea, indicating that traditional snoRNP functions are ancient and fundamental (A.D.Omer &Ziesche, 2003; S.L Reichow&T.Hamma, 2007). Box C/D snoRNAs are molecules of approximately 60e200 nucleotides in length characterized by the presence of highly conserved boxes referred to as C (canonical motif RUGAUGA where R is a purine) and D (canonical motif CUGA). Box C/D snoRNPs carry out the 20 -O-ribose methylation of specific rRNA residues (T.Kiss, 2001).

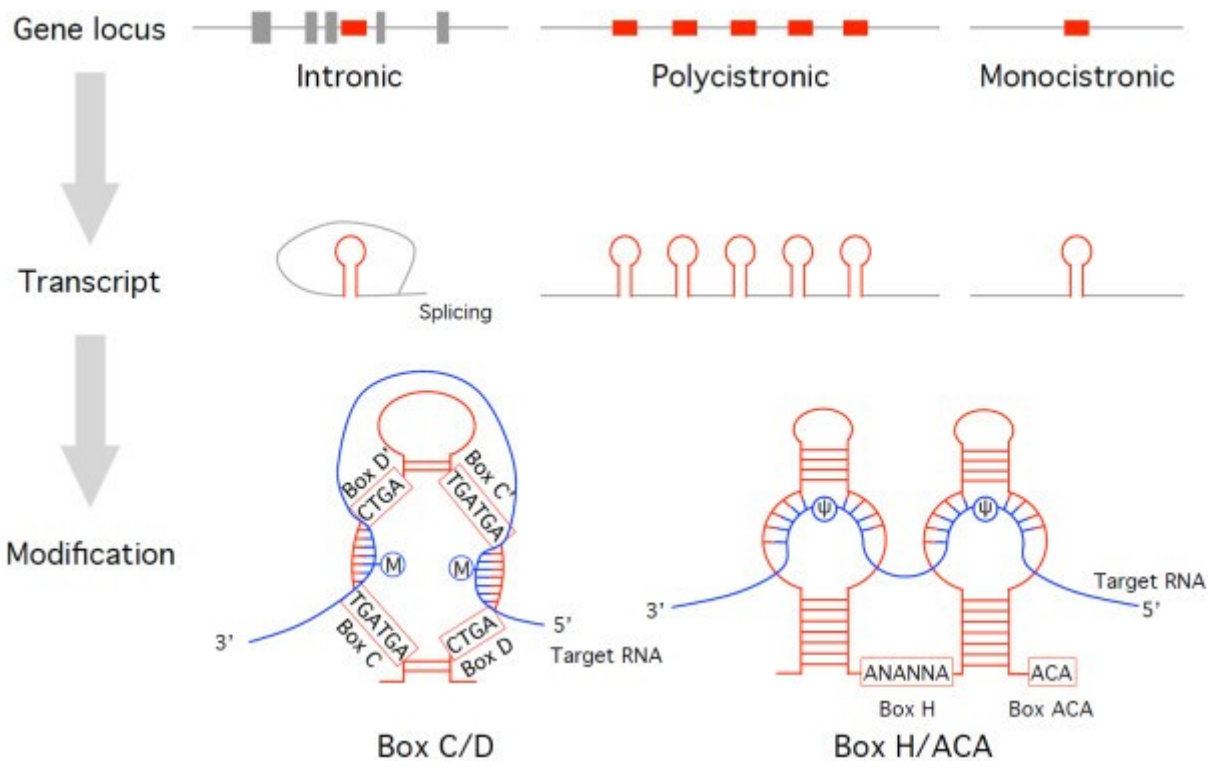

Fig.5 structure of snoRNA

Scaffolds:

The lncRNAs can serve as adaptors to bind more than 2 protein partners, thus are involved in structural roles. The telomerase RNA TERC (TERRA), an example of an RNA scaffold, is responsible for telomerase function (Tsai MC et al., 2010).

Apart from the aforementioned functions, lncRNAs have been reported to be functional in some substructures of the mouse brain (Mercer TR et al., 2008), and have some role associated with transcriptional factors involved in conferring pluripotency to cells (Dinger ME et al.,2008). Long intergenic non-coding RNAs (lincRNAs) are lncRNAspresent in the intergenic regions and have an important role in the maintenance of a pluripotent state of cells. A study on mice embryonic stem cells revealed that knockdown of lincRNA gene effects on gene regulation (Rinn JL, 2012).

Guides:

The lncRNAs are required for the proper localization of specific proteins including ribonucleoprotein complexes. Home obox antisense intergenic RNA (HOTAIR) is an example of a guide lncRNA to localize polycomb repressor complex2 (PRC2) in developmental and cancer-related gene expression.

It is associated with tumor invasiveness and metastasis in gastrointestinal, liver, breast, and pancreatic cancers (Cupta RA et all., 2010).

CRISPR: An Adaptive Immune System

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat) sequences were initially discovered in the E. coli genome in 1987, but their function as a safeguard against bacteriophages was not elucidated until 2007. Scientists hypothesized that prokaryotes used CRISPR as part of an adaptive immune system - utilizing various CRISPR-associated (Cas) genes to not only store a record of invading phages but also to destroy the phages upon re-exposure (Bondy-Denomy et al.,2015).

More specifically, specialized Cas proteins snip foreign DNA into small fragments approximately 20 bp in length and paste them into contiguous stretches of DNA known as CRISPR arrays. Separate Cas proteins then express and process the CRISPR loci to generate CRISPR RNAs (crRNAs). Through sequence homology, these crRNAs guide a Cas nuclease to the specified exogenous genetic material, which must also contain a species-specific sequence known as a protospacer adjacent motif (PAM). The CRISPR complex binds to the foreign DNA and cleaves it to destroy the invader (Fig. 6) (Cong et al., 2013).

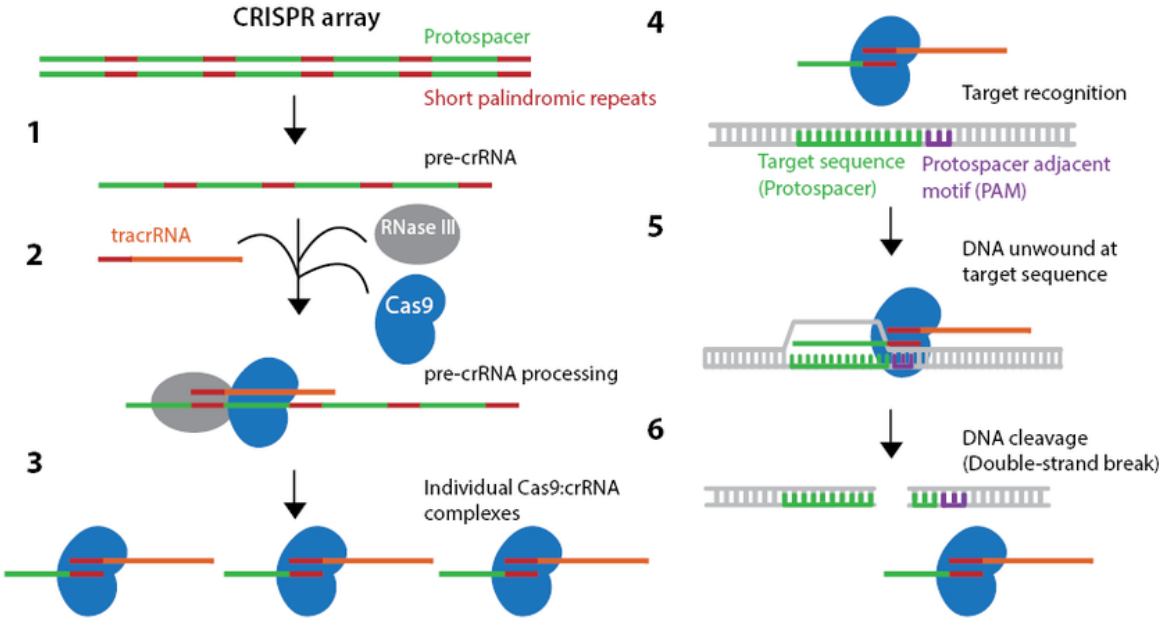

Fig 6**.** An overview of the endogenous Type II bacterial CRISPR system. Within the bacterial genome, a CRISPR array contains many unique protospacer sequences that have homology to foreign DNA. Protospacers are separated by short palindromic repeat sequences. **(1)** The CRISPR array is transcribed to make the pre-CRISPR RNA (pre-crRNA). **(2)** The pre-crRNA is processed into individual crRNAs by a special trans-activating crRNA (tracrRNA) with homology to the short palindromic repeat. The tracrRNA helps recruit RNAse III and Cas9 enzymes, which together separate the individual crRNAs. **(3)** The tracrRNA and Cas9 nuclease form a complex with each individual, unique crRNA. **(4)** Each crRNA:tracrRNA: Cas9 complex seeks out the DNA sequence complementary to the crRNA. In Type II CRISPR systems, a potential target sequence is only valid if it contains a special Protospacer Adjacent Motif (PAM) directly after where the crRNA would bind. **(5)** After the complex binds, Cas9 separates the double-stranded DNA target and cleaves both strands near the PAM. **(6)** The crRNA:tracrRNA: Cas9 complex unbinds after the double-strand break (Cong et al., 2013).

CONCLUSIONS

The central dogma of molecular biology suggests that DNA maintains the information to encode all of our proteins and that three different types of RNA rather passively convert this code into polypeptides. Specifically, messenger RNA (mRNA) carries the protein blueprint from a cell's DNA to its ribosomes, which are the "machines" that drive protein synthesis. Transfer RNA (tRNA) then carries the appropriate amino acids into the ribosome for inclusion in the new protein. Meanwhile, the ribosomes themselves consist largely of ribosomal RNA (rRNA) molecules.

However, in the half-century since the structure of DNA was first elaborated, scientists have learned that RNA does much more than simply play a role in protein synthesis. For example, many types of RNA have been found to be catalytic--that is, they carry out biochemical reactions just like enzymes do. Furthermore, many other varieties of RNA have been found to have complex regulatory roles in cells.

Thus, RNA molecules play numerous roles in both normal cellular processes and disease states. Generally, those RNA molecules that do not take the form of mRNA are referred to as noncoding, because they do not encode proteins. The involvement of noncoding mRNAs in many regulatory processes, their abundance, and their diversity of functions has led to the hypothesis that an "RNA world" may have preceded the evolution of DNA and proteins.

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