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Non- Coding RNA and Cell Regulation

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Abstract**—***The term non-coding RNA (ncRNA) is widely used to refer to RNA that fails to encode a protein; nevertheless, this does not mean that such RNAs lack information or function. Recent evidence suggests that most of the genomes of mammals and other complex organisms are transcribed into ncRNAs, several of which are alternatively spliced and/or managed into smaller products. Large ncRNAs, like ribosomal RNAs (rRNAs), which are involved in the synthesis of proteins, and small ncRNAs, like small nucleolus RNAs (snoRNAs) for RNA modifications, small nuclear RNAs (snRNAs) for RNA splicing, and transfer-RNAs (tRNAs) for transporting amino acids, have been extensively investigated in the past fifty years since the beginnings of molecular biology. These ncRNAs may be considered 'constitutive' because they are abundant and ubiquitously expressed in all cell types and play critical roles in the organism. In conclusion, a growing number of particular non-coding RNAs (ncRNA) are important modulators of numerous biological processes, such as chromatin remodeling, epigenetic changes, apoptosis, control of the cell cycle, and gene expression. Furthermore, the reason for the irregular relationship between an organism's complexity and this class might additionally encompass the telomere complex-associated guide RNA, which is essential for the end formation as well as preservation of chromosomes in normal proliferating.*

Keywords**—** *nc RNA, modification of RNA, protein synthesis, RNA molecules*.

I. INTRODUCTION

The majority of RNA molecules were once thought to be information carriers from the translation machinery to the gene. Ribosomal RNA (rRNA) and transfer RNA (tRNA), which are both directly engaged in translation, are the most notable exceptions to this rule. Nevertheless, subsequently the late 1990s, it was acknowledged that a variety of RNA molecules that do not code for proteins can be found in animals, ranging from bacteria to mammals, and these molecules have an impact on a wide range of processes, such as DNA transcription, RNA-processing and alteration, bacterial pathogenicity, phage progress, and chromosome structure, and plasmid replication, among others [1&2&49]. These findings imply that the conventional understanding of how organisms' genetic regulatory systems are structured is far from comprehensive. Furthermore, studies on non-protein-coding RNA will contribute new insights into the genetic architecture of biological difficulty. On the other hand, non-protein-coding RNAs are disorganized, which may make research more difficult to do. Non-coding RNAs (ncRNAs) have been used more commonly than short RNAs (sRNAs) in eukaryotes [3&4]. Specific ncRNA categories, such as RNase P RNAs, tmRNAs, and SRP RNAs, are the sole focus of specific databases, while other categories of ncRNA have been gathered by others, like the Rfam Database, the Non-coding RNA -Database, and Small RNA- Database [5]. Nonetheless, several ncRNA members or classes are absent from even the latter type of databases. The fact that several classification systems for non-coding RNAs are being utilized and that there haven't been many attempts to combine them is another issue with all of the present databases. Certain non-coding RNA groups (ncRNAs) in these classification systems are named based on their cellular localizations (snRNAs, snoRNAs, or snRNAs), while other groups are named based on their functions (guide RNAs, package RNAs, transfer-messenger RNAs, or pRNAs), whereas others are just identified by their sedimentation- coefficients (6S RNA, 5.3S RNA, etc.). Additionally, because of this absence of incorporation, a single category of ncRNA commonly seems under many terms or multiple categories [6, 7, 8, and 9].

Types of ncRNAs

Non-coding RNAs (ncRNAs) are divided into two categories: "small" RNAs and RNAs longer than 200 nucleotides [10]. Tiny ncRNAs comprise a variety of unique RNAs, such as piwi RNAs (piRNAs), small- nucleolar RNAs (snoRNAs), and micro RNAs (miRNAs) [10]. Unquestionably, defining lncRNA only by length is arbitrary. LncRNAs are defined by Amaral et al. as ncRNAs [11]. Those subtypes are working as primary or spliced transcripts, regardless of the several tiny ncRNA subtypes that are currently known to exist. This is an attempt, based mainly on biological grounds, to separate long noncoding RNAs (lncRNAs) from short noncoding RNAs [11]. As a result, certain lncRNAs do not cross the artificial barrier in length (such as BC1 and snaR, which are less than or near 200 nt yet mentioned in lncRNAdb) [11].

Non-coding RNA functions

Many of these RNAs may be non-functional because they have little coding ability, however, a growing number of particular non-coding RNAs (ncRNA) are important modulators of numerous biological processes, such as chromatin remodeling, epigenetic changes, apoptosis, control of the cell cycle, and gene expression [19**,** 13 & 20]. Furthermore, the reason for the erratic relationship between an organism's complexity [20].

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The increasing amount of functional noncoding RNA (ncRNA) in complex organisms could contribute to changes in cellular DNA composition and the number of protein-coding genes [21&22], ncRNAs are essential for both functional and regulatory aspects of the cell's gene expression. Ribozymes are one of the ncRNAs' most important roles [23]. ncRNAs regulate an astounding array of biological activities, comprising essential organization, cell variation, development, post-transcriptional regulator, epigenetic changes, transcriptional interference, telomere repairs, imprinting, and regulation of translation (Figure 1) [24]. Long, fully complementary, double-stranded RNAs are the source of small interfering RNAs (siRNAs), which act as an additional layer of gene control and a defense mechanism for cells against external and dangerous nucleic acids like transposable elements and viral RNA. Long, single-stranded transcripts are digested into small hairpin structures by miRNAs. A model organism for siRNA synthesis in *C. elegance*, which generates siRNAs by using RNA-dependent -RNA polymerases (RDRPs) to transcribe single-stranded RNAs into double-stranded RNA precursors [25, 26 & 27].

TABLE 1: Types of non-coding RNA, their properties, and functions.

no	Name	Characteristics	Functions	References
1	Small interfering RNAs (siRNAs)	21–22 nt length RNAs that are created when complementary dsRNA duplexes are cleaved by dicer.	Gene regulation, transposon control, and viral defense	[12&13]
2	MicroRNAs (miRNAs)	Produced by dicer cleavage of faulty RNA hairpins, which are around 22 nt long and encoded in either long primary transcripts or short introns.	Post-transcriptional gene regulation	[14]
3	MicroRNA-offset RNAs (moRNAs)	RNAs, around 20 nucleotides long, that originate from areas close to pre-miRNAs	Gene regulation	[15]
4	SnoRNAs, or small nucleolar RNAs	Regulation of pseudouridylation and rRNA methylation	Proof of the regulatory roles of genes	[16]
5	PIWI-interacting RNAs (piRNAs)	Small RNA ~24–30 nt, restricted to the germline and germline bordering somatic cells	Associated with PIWI-clade Argonaut proteins, regulate transposon mobility and chromatin state	[17]
6	HOTAIR(HOX antisense intergenic RNA)(long-non-coding)	Transcribed from the HOXC locus, 2.2 kb	Suppresses gene expression at the HOX D locus epigenetically	[18]

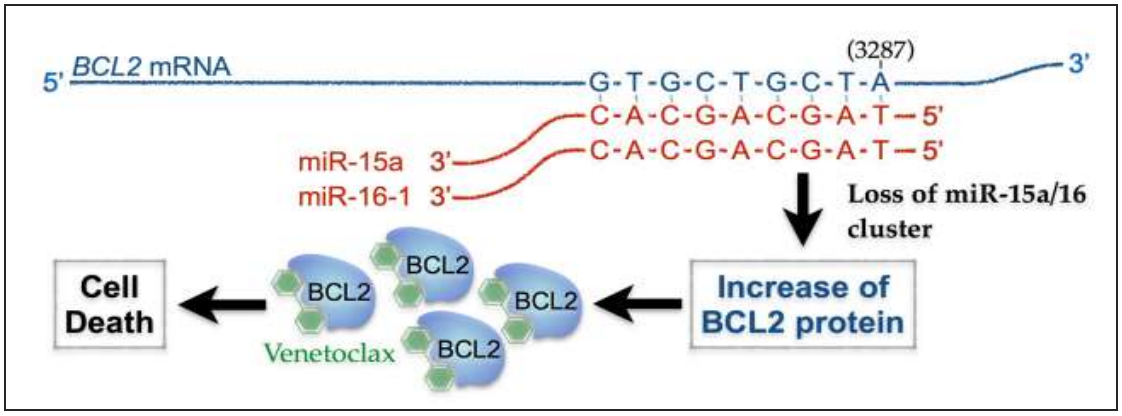

Figure 1. The effect of micro RNAs on cell death from gene expression for BCL2 gene [27].

1: Transcriptional interference: ncRNA-mediated regulation of gene expression:

Translation of ncRNA transcripts originating from an upstream promoter may induce chromatin remodeling or hinder the recruitment of RNA polymerase II, thus impacting the downstream gene's expression either positively or negatively [28]. For instance, the lnc transcript produced by the human dihydrofolate reductase (DHFR) locus represses the manifestation of the protein-coding gene by forming upstream of the primary DHFR promoter [29&30].

2: RNAs without codons in telomeres:

Functional nucleoprotein complexes known as telomeres shield the endpoint of chromosomes since deterioration and the onset of DNA-damaging activities that would have an effect if they were known as breaks of DNA double-stranded. Genetic stability, senescence, and aging are all maintained[31]. Because of their heterochromatin state, telomeres have long been thought of as transcriptionally silent DNA-protein complexes. The lncRNA known as telomere repeat-containing RNA (TERRA), or TelRNAs, are created via transcription in many organisms, including plants, yeast, *Danio rerio, Homo sapiens, and Mus musculus* [32]. A recent study has shown that telomeres are the source of TelRNAs [32&33]. By controlling the length of the telomere the function of telomerase, and the change of heterochromatin at the final positions of chromosomes, the TERRA molecules maintain telomere homeostasis [33]. Variations in the regulation of these molecules cause the instability of chromosomes and accelerate the aging of the cells [34].

3: Epigenetic modifications:

Previous research has demonstrated that subsets of non-coding RNAs (ncRNAs) are essential for preserving

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chromosomes in their active or inactive states by attracting proteins from the trithorax group (TrxG) and polycomb group (PcG) to the target area. More than a thousand mammalian genes are bound by PcG proteins, which inhibit their expression [35,36&37].

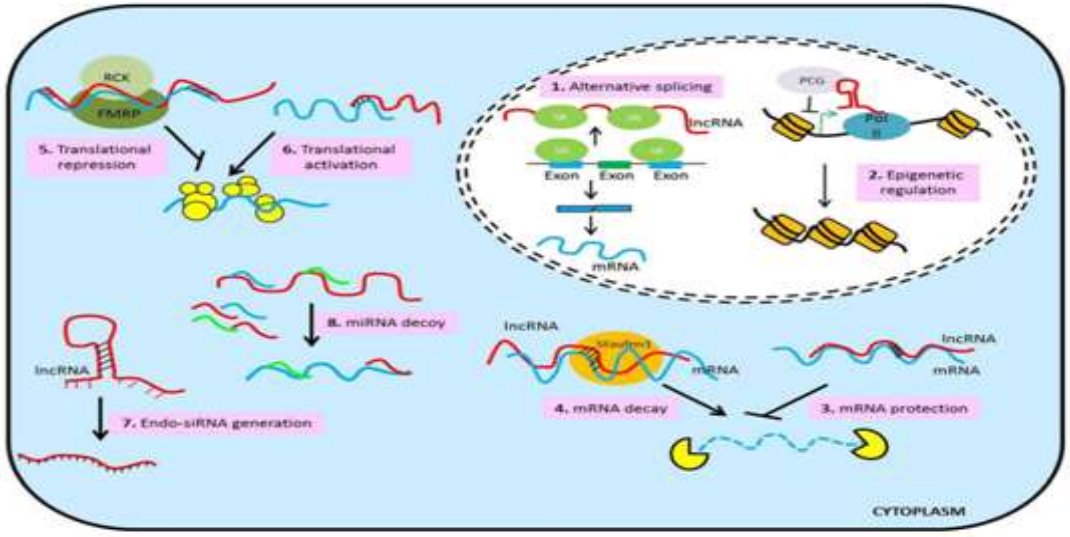

Figure 2. Non-coding RNAs' biological responsibilities are schematically represented, highlighting their contributions to alternative splicing, translational repression, activation, mRNA turnover, and the production of siRNA [37].

4: ncRNA-mediated post-transcriptional modification:

Certain isoforms of the non-coding RNA SRA serve as co-activators of steroid receptor transcription[38&39]. It has been discovered that ncRNAs control the subcellular location of proteins which affects the target gene in those proteins. The nuclear factor of activated T cells (NFAT) is a transcription factor that initiates transcription, it first localizes to the cytoplasm and then is brought back into the nucleus by signals that depend on calcium. [40]. Tiny interspersed ncRNA binds to RNA polymerase II during heat shock to stop other mRNA, including actin, from being transcriptionally transcribed [41].

5: ncRNAs' translational regulation of other proteins

Several studies have shown that RNA transcripts derived from pseudogenes can co-synthesize with spliced mRNA. Dicer cleaves the double-stranded RNA that is produced by this process to form endogenous siRNA or endo-siRNA. Consequently, the protein-coding gene is further downregulated by using coding mRNA to produce endo-siRNA, which can direct the RNA-induced silencing complex (RISC) to cleave further mRNA transcript [42].

6: ncRNA-mediated control of structural organizations:

Mammalian cell nuclei paraspeckles have recently been identified as ribonucleoproteins located in the interchromatin gap. These proteins create paraspeckles and preserve their integrity when they interact with the lncRNA nuclear-enriched autosomal transcript 1 (NEAT1). Enriched in pre-mRNA splicing factor are highly dynamic sub-nuclear areas called interchromatin granule clusters, or nuclear speckles, which are thought to number in the 20–30 range. It has been proposed that splicing factors are drawn to transcriptionally active areas from speckles [43].

7: Disease condition associated with ncRNAs:

Splicing factor activity is influenced by the accumulation of RNA repeats. CGG repeats in the fragile X mental retardation gene-1 cause changes in alternative splicing by drawing a group of splicing regulators into nuclear inclusions, which is another example of a gain of RNA function. The term "fragile X-associated tremor ataxia syndrome" describes this illness [44].

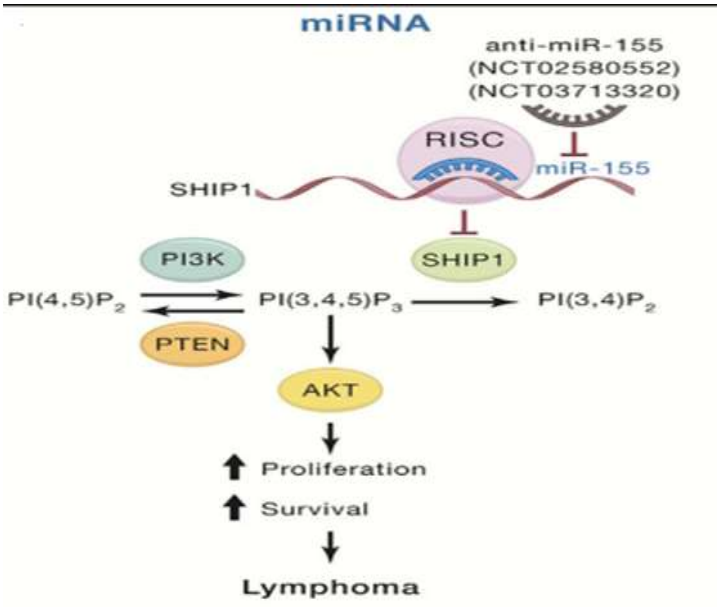

Figure 3. miRNA: miR-155 targets and inhibits the production of SHIP1, a hematopoietic cell-specific phosphatase that converts [PI (3,4,5) P3] to phosphatidylinositol-3,4-bisphosphate [48].

Many studies have indicated that miRNAs could express as oncogenes, stimulating abnormal cell proliferation and serving the growth of cancers. These miRNAs have two

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possible modes of action: either they reduce the action of tumor suppressors or indirectly relax the genetic constraints on oncogene activation. For example, miR-155 can encourage irregular production of B cells, which can set off a sequence of events that initiate the enhancement of leukemia and lymphoma as in figure (3) [45 &48].

Because these oncogenic miRNAs are essential to the tumors' survival, they display the phenomena known as oncogene addiction or oncomiR addiction [46]. These are therefore significant prospective targets for anti-cancer treatment. Targeting oncomiRs that are specifically overexpressed in a patient's tumors has recently been shown to be possible, paving the path for customized miRNA therapy [47&48].

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