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LncRNAs: A new trend in molecular biology of diseases; A review

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Review Article

Abstract

BACKGROUND: Non-coding ribonucleotide sequences, including short and long-term ribonucleic acid (RNA) molecules, are a major part of the gene expression products, which have recently been identified on a large genomic scale. The long non-coding RNAs (lncRNAs) have a length of greater than 200 nucleotides. Only a small fraction of the function of lncRNA molecules is known to date.

METHODS: PubMed, Scopus, Embase, and Google Scholar were searched from January 2000 to May 2018. Based on the study inclusion and exclusion criteria and specific keywords, 92 original, relevant, experimental studies with moderate bias were selected. LncRNAs were evaluated as a new trend in molecular biology of diseases.

RESULTS: Our analysis showed that the presently available evidence confirmed that lncRNAs can be a tool for the diagnosis and prognosis of many diseases and alternative therapies.

CONCLUSION: LncRNAs are an emerging field of investigation as they are suggested to regulate key biological processes, including cellular proliferation and differentiation, and their aberrant expression is associated with many diseases. An improved understanding of the role of lncRNAs in disease would provide valuable information about key biological-promoting pathways and might be highly useful for diagnostic, prognostic, and alternative therapies assessments. This knowledge might also lead to advancement in the management of disease through the development of novel, personalized lncRNAs-based therapies.

KEYWORDS: Long Non-Coding RNA, Autoimmune Disease, Neurodegenerative Diseases, Cardiovascular Diseases, Immune System Diseases

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Introduction

The 20000 gene encodes a protein in the human genome, accounting for less than 2% of the entire human genome sequence.[1] It is very important that 90% of the genomes be actively transcribed, but they do not have the potential to encode protein.[2] Each of these sequences organizes cell structures, regulates gene expression patterns, and ultimately determines cell identity and function.[3] This non-coding transcript can be divided into the two categories of short non-coding ribonucleic acids (snRNAs) such as microRNA, and long non-coding RNAs (lncRNAs). More than 80% of transcripts are in the lncRNA cells.[4] These RNAs are very similar to mRNAs regarding processing and presence of polyadenylation signals.[5]

LncRNAs have a length of more than 100 to 200 nucleotides, and their transcription is accomplished by RNA polymerase II.[6-8]

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Research on the lncRNA promoter showed that the transcription of this class is regulated by the protein-coding RNA transcription factors. It is also hypothesized that the transcription of lncRNAs complies with the same rules in coding-RNA transcription, and the processing involves the capping, polyadenylation, and alternative splicing.[9]

LncRNAs have recently been identified on a massive genomic scale, and only a small part of their function is known. By analyzing the human genome, it is estimated that there are about 23,000 lncRNAs that is greater than the number of mRNAs, and this is comparable to protein-encoding RNAs.[10] LncRNAs sequences have encompassed about 90% of the human genome and spread throughout the genome.[11] Studies have shown that lncRNAs act as a mediator between DNA and proteins, and play an important role in cellular function.[2]

Currently, lncRNAs have emerged as fundamental approaches to biology. Several common features among lncRNAs, which support their independence and biological significance, include the following[12]:1) Genes encoding lncRNAs a) have epigenetic symptoms compatible with a transcriptional gene (H3K4me3 in the promoter gene, H3K36me3 all over the gene length), b) are transcribed through the RNA polymerase II enzyme, c) are under the regulation of well-defined transcription factors, and d) are expressed in abundance and a special texture. 2) Transcripts for lncRNAs a) often undergo polyadenylation, and b) are undergoing processing through their conventional processing location motifs. Moreover, studies have shown that the inappropriate expression of lncRNAs can cause various disorders and diseases, and lncRNAs are directly linked to several human diseases such as various cancers,[13] neurodegenerative disease, autoimmune disease, and inflammatory disease.[14] In this review article, we aimed to investigate the biology of lncRNAs and their role in human diseases.

Materials and Methods

PubMed, Scopus, Embase, and Google Scholar were searched from January 2000 to May 2018. Based on the inclusion and exclusion criteria and specific keywords, such as long non-coding RNA, autoimmune disease, neurodegenerative disease, cardiovascular disease, and immunological disease, 92 original, relevant experimental studies, which were written in English with moderate bias, were selected. LncRNAs were evaluated as a new trend in molecular biology of diseases.

Types of LncRNAs: The types of lncRNAs in terms of transcription and genetic location are classified into the 5 categories of sense, antisense, intronic, intergenic, and bidirectional. In the sense category, the transcription of lncRNAs takes place in a single-gene expression of exons. In the antisense category, the transcription of lncRNAs is performed from the opposite field exons in a gene. In the intronic category, the intron of a transcriptional gene is carried out. The intergenic lncRNAs are independent and are located between two other genes. The bidirectional lncRNA has a common promoter with another gene, but is transcribed in the opposite direction.[15] Based on this specific classification, the study of lncRNA subunits can help identify potential functional relationships between lncRNAs and the related protein-associated genes.

The biological evolution of lncRNAs: The lncRNA sequences, in contrast to their rapid biological evolution, display obvious and weak indications of natural selection.[16] Contrary to protein-coding genes, which are the result of all or part of the doubling of a sequence and diversity, many lncRNAs exhibit a low degree of evolutionary pressure and have different evolution with the coding genes.[17] There are different sources for the appearance of lncRNAs.[17,18] Chromosome rearrangements can produce lncRNAs from sequences that were not previously transcribed. The collapse of the protein-coding gene framework can create lncRNAs that include some early coding

sequences.[16] The non-coding RNAs retrotransposition during the duplicate process can produce a reverse transcriptional gene or a false pseudogene. Local sequential repeat sequences may also create a new lncRNAs.This phenomenon is seen in the '5' X-inactive specific transcript (Xist). The insertion of a moving element can also produce lncRNAs such as a cytoplasmic RNA of 200 nucleotides (brain cytoplasmic 200-nucleotide or BC200). Unlike mRNA and many non-coding RNA classes, mammalian lncRNAs lack the known orthogonal species in non-mammalian species. The only exception, in this case, is that the RNA contains telomeric repeats (Terra) maintained between human and yeast.[19] Only about 12% of lncRNAs of mice and humans are preserved in other species.[20]

Biology of lncRNAs: Like other non-coding RNA genes, lncRNA genes lack specific structural indices. The lncRNA genes are usually shorter than protein-coding genes and have fewer exons than they have.[21-23]

Transcription regulation and chromatin alteration patterns of lncRNA genes are similar to those of encoding proteins. The processing signal of the lncRNA molecules, although sometimes performed at a lower processing efficiency, is similar to that of the transcription codons of protein-coding genes.[23,24] Repetitive elements have also been reported in lncRNAs, which assist in the interaction with their family members in other RNAs and play an essential role in the lncRNA performance mechanism.[25] The main part of the lncRNA molecules are polyadenylate, but sometimes their 3′ end is seen in another form. In humans, there are about 80 lncRNAs with circular isoforms.[26] A little of lncRNAs, due to the formation of a three-spiral structure at the end of the 3', and some of others by snoRNA molecules at both 5' and 3' ends are stable.[27,28]

LncRNAs have an openreading frame (ORF) without coding the protein, but when lncRNAs come along with the ribosome in the cytoplasm, other ORFs of these molecules may play the role of mRNA metabolism.[29] Frame reading open upstream of lncRNA genes plays an important role in regulating the expression and stability of lncRNA molecules.[30,31] The lncRNAs can be translated in a way that the transcribed lncRNAs from the downstream are protected from the ribosomal scan and can freely perform their function in the cytoplasm without interfering with the ribosomes. LncRNAs may also direct agents to the ribosomal or modulate the stability of lncRNAs by affecting the pathways of RNA degradation.[32] LncRNAs are preferably in the nucleus, can also be seen in the cytoplasm, and are expressed in specific cells and at low levels. LncRNAs can express the gene through alternative splicing, transcription, and post-transcription.[33] The transcription of lncRNAs takes place between the encoding genes and often from the opposite DNA strand.[34]

The shape and second form of lncRNAs: The formation of a secondary structure is of particular importance for lncRNAs.[35] The rate of formation of the secondary structure coincides with the expression level of lncRNAs, in such a way that more organized, more stable lncRNAs, and therefore, lower expressions are observed. Higher C/G content is also associated with greater organization, higher stability, and lower expression of lncRNAs.[36] The prediction of secondary stem-ring structures is useful in identifying lncRNA function. Mfold software, which is widely used, is designed to predict the secondary structure of RNA.[37] For this purpose, newer programs, such as CompaRNA, have been developed.[38,39] Studies have uncovered the many functions of lncRNAs and their strategic roles in the advancement and development of intracellular pathways. The pattern suggested by these studies indicates that the performance characteristics of lncRNAs may be due to their unique structure in bringing together specific regulatory components, including specific

proteins and tissue-specific RNAs, and the subsequent interactions with these DNAs.[40]

The mechanisms of lncRNAs function: Various research methods have been developed to uncover the functional and molecular mechanisms of lncRNAs. The most efficient approaches to discovering the function of lncRNAs include high-performance lncRNA expression analysis, obtained data validation, and lncRNA-protein interactions evaluation. All of these approaches are possible with special laboratory processes.[41]

Studies on the role of lncRNAs in the regulation of the gene expression pattern indicate the complexity of their control mechanism; these molecules are involved in different levels of gene expression regulation, including regulation at the transcriptional level and after transcription. Regulation at the transcription level involves the role of lncRNAs in the epigenetic inactivation of some genes. However, regulatory levels after transcription, which are affected by the action of lncRNAs, include[42] mRNA degradation protection, pre-mRNAs processing, translation suppression, acceleration of mRNA degradation, mRNA translation activation, and collaboration with microRNAs. The protection of mRNA from degradation by miRNAs in antisense lncRNAs is achieved through these lncRNAs forming a hybrid with the mRNA molecule. Pre-mRNAs processing involves the competing of some lncRNAs with mRNA in binding to the process regulator proteins, and thus, affecting the mRNA values of the mature cell in the cell. Translation suppression is achieved through the imperfect interference of lncRNAs with the mRNA and invoking of the translation inhibitors. 4) The degradation of specific mRNAs is accelerated through the cooperation of some lncRNAs with other mRNA degrading proteins. The mRNA translation activation has been observed in some antisense lncRNAs; these lncRNAs are part of their structure that perfectly complements the end of the '5 mRNA molecule. They attach to the mRNA, stabilize it, and help call the ribosomes to the mRNA. The result of such an approach is increase in translation. Moreover, some of the lincRNAs act in the same direction (in collaboration with) or reverse to the activity of the microRNA molecules, and thus, play a prominent role in activating or inhibiting the expression of the gene.[43]

A theory was proposed by Wang and Chang, which showed different modes of gene expression regulation by lncRNAs. According to this theory, lncRNAs are influenced by gene expression through four mechanisms, which are described in the following section. This division was also proposed by Perin et al.[44] Typically, many of the lncRNAs can be performed by a set of these processes. These mechanisms include splicing, decoy, guide, and scaffold. In splicing, some of the lncRNAs are used to stimulate a cell through a method, such as cellular stress and temperature change, along with growth factors, in order to activate a gene. In decoy, a number of lncRNAs bind to transcription factors preventing the binding of these factors to the gene, and thus, prevent the transcription and inhibit the gene. In the guide mechanism, lncRNAs have the ability to bind to ribonucleoprotein and cause changes in chromatin, and thus, lead to epigenetic changes. In the scaffold mechanism, lncRNAs aggregate the protein complex and bind to the target gene, causing changes in the chromatin structure and transcription to the inhibitor or activation.

LncRNA–DNA interactions: Approximately, all the lncRNAs mentioned so far act by regulating the transcription of target genomic locus in cis- (nearby genes) or trans- (distant genes) acting manner through binding to the target DNA by identification of specific chromatin structures or as an RNA–DNA heteroduplex or RNA–DNA DNA triplex. Therefore, RNA molecules can interact with

single-stranded DNA by Watson-Crick base pairs (duplex) or can interact with double-stranded DNA by inserting into the major groove of the double helix DNA structure with sequence specificity (triplex).[45] Previously, it has been reported that lncRNAs can form a stable duplex with promoter sequences[46] or can form a triplex structure at ribosomal RNA promoters in fibroblasts.[47] Local chromatin changes can result from the transcription of lncRNAs that are not induced by the non-coding transcript.[48-50] In a study, the mechanisms of local gene regulation by twelve lncRNAs were evaluated five of which regulate the expression of their neighboring genes in a cis-acting manner. Surprisingly, none of the five cis-regulators required the lncRNAs transcripts themselves, but this procedure depended on lncRNAs transcription processes such as lncRNA promoters enhancer activity, transcription, or splicing of the lncRNA.[50]

LncRNA–RNA interactions: Numerous classes of lncRNAs act by RNA–RNA interactions. For example, the Epstein-Barr virus (EBV) non-coding RNAs (EBER2) form base pairs with nascent transcripts of the locus from the latent EBV genome and recruit the PAX5 transcription factor to the terminal repeats. Recruitment of PAX5 transcription factor regulates the expression of nearby genes to the TRs, and thereby, regulates the lytic replication cycle of EBV.[51] A major mechanism of gene expression modulation in circRNAs is RNA binding. Until now, studies have indicated two functional consequences of RNA–RNA binding via circRNAs. The first is a reduction in the availability of partner RNA transcripts through direct base pairing, in particularly, with microRNAs. The second consequence is a reduction in alternative RNA transcription by competition for transcriptional machinery components. As 'sponges' for microRNA, circular RNAs can efficiently 'titrate' microRNA from its functional target genes. For example, the ciRS-7 includes 70 sites for miR-7 binding which controls mid-brain development through 'titrating' of miR-7 transcripts.[26,52] CiRS-7 is fully resistant to target destabilization mediated by miR-7, so it intensely suppresses the miR-7 function, which leads to an increased number of miR-7's targets. Similarly, the Sry circRNAs, a circRNA in testis, act as a sponge for miR-138.[52] Generally, the lack of 5′ phosphate and 3′ OH ends in circRNAs results in more stability than that of linear RNAs and this proposes that long non-coding RNAs can temporally modulate the gene expression via base-pairing interactions and modification of their secondary structures.

Controlling the destruction of mRNA molecules: The frequency of mRNA has a direct correlation with protein output, and factors affecting this frequency play their role through the effect of the transcriptional mRNA and its degradation rate. The mRNA can be decomposed through various processes during transcription or after the completion of transcription. One of these processes is the STAU1-mediated decay of the STAU1 agent by mRNA, which results in the decomposition of active mRNAs. The formation of the open pair between the Alu elements in lncRNAs and the Alu elements in the UTR'3 of the STAU1 target mRNA molecule causes the formation of STAU1 binding sites. This event is associated with the activation of the STAU1 agent and its attachment to the mRNA. This finding uncovers a new approach to invoking proteins to mRNA, and to decompressing mRNA through them.[53]

Controlling of gene expression: LncRNAs are commonly expressed at low levels, retain little consensus among species, and often display specific tissue/specific expression patterns of the cell.[21,32]

LncRNAs have different effects on gene expression. One of the first functions identified in lncRNAs is the variation in gene expression by alteration of the chromatin structure. In humans, a large number of lncRNAs have been

identified with different roles in gene expression. Human lncRNAs participate in a range of biological processes, including epigenetics, alternative splicing, and RNA destruction and translation.[17] Furthermore, the role of lncRNAs has been shown to disable chromosome X and genetic imprinting as well as growth and differentiation.[54]

Studies have shown that lncRNAs are also involved in protein translation. For example, an antisense lncRNAs for quinine-carboxy-terminal hydrolyzate (UCHL1-AS) mRNA can enhance mRNA stability and increase UCHL1 protein synthesis. This activity is dependent on the presence of a SINEB2 containing replication.[55] Beta-secretase-1 antisense (BACE1-AS) is a natural antisense transcript for BACE1 mRNA (Beta positioning enzyme in amyloid precursor protein), which is associated with mRNA stability and increased BACE1 protein levels.[56]

Epigenetic functions: The epigenetic concept was first introduced by Waddington Conrad in 1942 as a theme for expanding evolutionary and developmental programs and processes related to an undifferentiated egg, including complete cleansing and re-projection at a point in the cellular cycle. Although this perception remains valid, the term "epigenetic", in its current application, includes inherited gene expression changes that do not result from genetic code key differences. Epigenetics is defined as stable and inherited changes in the chromatin structure and is different from the phenomenon of mutation that occurs at the DNA sequence level. Epigenetic events, by changing and modifying the pattern of euchromatin to heterochromatin, and vice versa, regulate the expression of multiple genes. The most important of these events may include the methylation of some of the cytosine openings in the CpG dinucleotides (particularly near the promoter of some genes), as well as the reactions of methylation, acetylation, and other changes on histones.[57] Many lncRNAs have diverse epigenetic activities. Some lncRNAs can interact with chromatin-altering enzymes and cause changes in the transcriptional activity of some of the genes, or some other extinction.[58]

Xist, including the best-known lncRNAs, is responsible for initiating and extending the inactivation of chromosome X in somatic cells in women.[59] It is thought to be necessary to silence hundreds of genes based on chromosome X.Xist, which has a small repeat region called RepA, and is transcribed from both chromosomes X.[60] Tsix is another antisense of the RepA sequence, and it attaches to this sequence in the Xist transcript of one of the chromosomes X. This prevents the Xist from binding to its chromosome X, which is associated with active chromosome X activation. In the next step, another Xist transcript containing RepA is free, with polycomb repressive complex 2 set to a chromatin-modifying complex in the X-inactivation center of the other chromosome X, causing it to be deactivated.[60] Moreover, Tsix apply their regulatory function to a portion of the chromatin adjacent to their coding gene. This type of regulation is called the cis type. Another epigenetic event, in which the expression of the gene is responsible for lncRNAs, is a genomic role.[61] The expression of the implanted genes depends on their parent origin, and the differential expression level between the two involved alleles can vary from gene to gene. Because of the role played by genes in the development of mammals, their expression should be carefully regulated.[62] In a study by Rinn et al., another lncRNA called HOTAIR was discovered that regulates the expression of human HOX genes trans.[63] Subsequent studies showed that HOTAIR regulates the expression of the gene in the form of trans in conjunction with chromatin-modifying sets, including PRC2, LSD1, and COREST/REST.[63-65] HOTAIR serves as a guide as well as a framework for guiding

these collections to their intrinsic target genes. COREST/LSD1 sets up lysine 4 from histone H3, and PRC2 performs methylation of lysine 27 from histone H3. These events are associated with the inactivation of the HOTAIR target genes.[65] HOTAIR was one of the first lncRNAs to be known to play a critical role in the epigenetic regulation of cancer.[66] 34a-miR is a kind of microRNA that can decrease the HOTAIR stability; this process plays a role in the development of prostate cancer.[67] It can be emphasized that many of the role-bearing sites have an expression, and code the lncRNAs that play a major role in regulating the adjacent protein-encoding genes in the form of cis.[68] ANRIL is also a lncRNA identified in 2013, and its coding site is located on the 9p21 chromosomal bar. This site is considered as a hotspot for multidisciplinary diseases and is associated with cardiovascular disease (CVD), cancers, diabetes, glaucoma, and endometriosis. It has been determined that ANRIL regulates the expression of its adjacent gene, B/CDKN2A, using epigenetic mechanisms and via polycambotic proteins as cis, and therefore, plays a significant role in controlling the proliferation and aging of the cell.[69] Other roles of lncRNAs in post-transcription expression control include regulating the intermittent processing, maintaining the state of pluripotency, and controlling the flow of molecules between the nucleus and the cytoplasm discussed below.

Role in the alternating processing mechanism: Since a single mRNA may be constructed of several proteins with non-tangled functions, intermittent processing of pre-mRNA increases the complexity of the proteome in the cells. For the first time in connection with metastasis, a lncRNAs plays a critical role in the pre-mRNA intermittent processing. MALAT1 is in the nucleus speckle, which involves several proteins involved in the intermittent processing of mRNAs. It seems that MALAT1 provides a molecular scaffold for the function of these proteins. MALAT1 also regulates the phosphorylation of SR proteins. SR proteins are serine/threonine-rich proteins involved in the regulation and selection of processing sites in pre-mRNAs. MALAT1 can regulate the level of the SR proteins by regulating the phosphorylation of SR proteins, thereby influencing the processing of many pre-mRNAs.[70] This lncRNA target is a microRNA-Ago2-RISC complex, and the extinction of Ago2 expression results in the formation of constant levels of MALAT1 in the cell. An increase in the expression of 9-miR is also associated with a decrease in the level of this lncRNA in the cell.[71]

The role of lncRNAs in diseases

Cancer: A lncRNA was identified in lncRNA-ATB in 2014, which was activated via the TGF-β messenger pathway and adjusted several stages of the hepatocellular carcinoma metastasis process through two independent mechanisms. In the first mechanism, this transcript acts as a ceRNA, and by arresting members of the miR200 family, it reduces their access to their transcripts. This event induces the expression of another lncRNA called 2Zeb1, which increases its values by decreasing E-cadherin, followed by a change from epithelial to mesenchymal state and increased metastasis. In the second mechanism, lncRNA-ATB binds to IL-11 mRNA and increases its stability. Increase in the levels of IL-11 by lncRNA-ATB activates the STAT3 molecule. This is associated with an increase in the intrinsic tendency of cells to survive and their success in the formation of a colony in new tissue. The expression of lncRNA-ATB is a valid predictor of the incidence or non-recurrence of disease and estimates of the overall survival rate in patients with hepatocellular carcinoma.[72]

LncRNA-EPS is one of the types of lncRNAs that are effectively expressed at the time of the

final differentiation of the types of blood cells. Silencing this lncRNA prevents the differentiation of blood cells and induces apoptosis in them. At the same time, its aberrant expression is associated with inhibition of apoptosis in blood cells. LincRNA-EPS is capable of suppressing the expression of a pro-apoptotic gene called Pycard, and thus, the inhibition of apoptosis.[73,74] High levels of Pycard inhibit the proliferation of blood cells and induce apoptosis or differentiation in these cells.[75]

DiGeorge syndrome: DiGeorge syndrome is a heterogeneous disorder characterized by evolutionary deformity, cognitive and behavioral disorders, and an increased risk of psychiatric disorders. This syndrome is caused by the removal of the chromosomal region 22q11.2. This region encodes a REST regulated lncRNA called DGCR4, which indicates the potential role of this lncRNA in regulating neural evolution and the phenotype of the disorder.[76]

Cardiovascular Disease: Antisense non-coding RNA in the INK4 locus is indicated as a risk factor for CVD.[77,78] Myocardial infarction associated transcript (MIAT) is related to MI.[79] As yet, the studies of circulating lncRNAs serving as cardiac biomarkers make less progress due to the instabilities of lncRNAs in body fluids as usually expected. Long intergenic non-coding RNA predicts cardiac remodeling (LIPCAR), is well known as a mitochondrial lncRNAs, is related with cardiac remodeling and chronic heart failure, and is suggested to be a potential cardiac biomarker.[80]

Multiple sclerosis: Multiple sclerosis (MS) is a complex autoimmune disease, and recent immunological studies have demonstrated abnormal activity of cluster of differentiation 8 ($CD8^+$) T cells in the pathology of MS.[81] Because lncRNAs are involved in the differentiation and activity of CD8-T cells, they may be important in MS development and progression. LncRNAs derived from the promoter of the T cell chain of α are responsible for regulating the use of downstream genes, and thus, the production of various T cell receptors.[82] In recent studies, researchers have found that the locus associated with the α interleukin-2 receptor is code-labeled with some lncRNAs, one of which, called M21981, greatly increases with T cell activity. It is important to note that this locus is associated with MS talent.[83] Tmevpg1 is another lncRNA that may interfere with MS. This lncRNA is transcribed in human and mouse immune cells from a cluster of cytokine genes that includes interferon γ[84]. Tmevpg1 is believed to be involved in controlling TME infection sustainability.[84] TME infection is used as a laboratory model for MS because it is characterized by chronic inflammatory demyelination associated with apoptotic oligodendrocytes and axonal degeneration.[85] These observations suggest that lncRNAs can be responsible for regulating CNS immune responses.

The role of lncRNAs as diagnostic and prognostic factors: The discovery that lncRNAs are key regulators of diseases, including cancer and its progression, have been associated with prospects for the use of these molecules as diagnostic and therapeutic targets. The expression of many lncRNAs such as ANRIL, HOTAIR, and MALAT-1 is limited to specific tissue and a specific disease, and can be used as prognostic markers. The number of lncRNAs used as biochemical markers for diagnosis and prognosis is increasing, and some have been approved for clinical use.[86] One of the main advantages of lncRNAs is their high stability and their presence in body fluids, especially when exposed to nanoparticles such as exosomes and apoptotic body.[87] Therefore, they can be measured by blood, urine, or saliva sampling, and then, using the Real-Time polymerase chain reaction (PCR) method.[86-88] Some lncRNAs can act as a diagnostic agent or as a prognostic factor. For example, a lncRNA called the prostate cancer

antigen 3 (PCA3) is associated with prostate cancer to a large extent, and is commonly used to determine the risk of prostate cancer from urine specimens and avoid unnecessary prostate biopsy.[89] All lncRNAs, with a determining role in diagnosis and prognosis, affect the cell cycle processes that create a specific phenotype, such as proliferation, invasion, and survival.[90-92]

Conclusion

LncRNAs are non-coding transcripts of protein that interact with other molecules through their molecular structure and have vital roles in controlling different types of cellular processes, such as growth, division, and cell differentiation. Furthermore, lncRNAs have a role in different human diseases and their dysregulation cause viral disease. Therefore, lncRNAs have a potential application as a biomarker for screening, diagnosis, prognosis, treatment response prediction, and treatment evaluation. By increasing the trend in studying lncRNAs, gradually a deeper understanding of these molecules is achieved.

Conflict of Interests

Authors have no conflict of interests.

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