



Potential of Large Non-coding RNA (lncRNA) in Plants and Human Specially Neurogenerative and Cancer Diseases

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Abstract

The discovery of DNA by Watson and Crick led to the idea of Central Dogma, stating that the genetic information stored in DNA is transcribed to mRNA to produce protein. The idea is that the gene or DNA is directly responsible for the coding of proteins in the organism. But that constitutes only 1% of DNA and the remaining 99% are non-coding. Coding RNA (mRNA) encodes protein while non-coding RNAs have no protein-coding capacity. With the development of Next Generation Sequencing Technology large number of non-coding RNAs have been discovered. Again, Transcriptome analysis in mammals and many organisms showed that there is large number of long transcripts having no protein coding capacity are known as Long Non-coding RNAs or lncRNAs. The function of lncRNAs that regulate mainly gene expression has been discussed. The role of lncRNA in Abiotic and Biotic stresses of plants has been shown. Then the role of lncRNAs in human diseases like neurodegenerative disease and cancer has been discussed with their therapeutic and diagnostic uses.

Keywords: Long non-coding RNA (lncRNA), Plant lncRNA, Human lncRNA, Neurodegenerative diseases, Cancer biology, Gene regulation and Epigenetics

Introduction

With the discovery of the structure of DNA by Watson and Crick in 1953, there comes the discovery of the Central Dogma which states that genetic information stored in DNA is transcribed to messenger RNA (mRNA), followed by the formation of protein. Further research has found the discovery of non-coding RNAs in the period 1950 to 1980s, the non-coding tRNA and rRNA in 1960, followed by early regulatory non-coding RNA (ncRNA) in 1980. The publication of Human Genomes in 2001, high-throughput sequencing and the ENCODE project have significantly boosted this research, leading to the characterisation of many ncRNAs. In this way, several ncRNAs have been known, such as micro RNAs (miRNAs), small interfering RNAs (siRNAs), small nuclear RNAs (snRNAs), small nucleolar RNAs (snoRNAs), small Cajal body-specific RNA (scaRNA), piwi-interacting interacting RNA (piRNA) and Long non-coding RNAs (lncRNAs).

This scaRNA is a class of small non-coding RNA located in the Cajal body (membrane-less nuclear organelles found in eukaryotic cells), crucial for small nuclear riboprotein (snRNP) biogenesis. Their functions are to guide the modification of spliceosomal RNAs (U1, U2, U4, U5 and U12) for the proper functioning of the spliceosome during RNA processing.

The piwi-interacting RNAs are small non-coding RNAs of generally 25-33 nucleotides long found in animal cells to form RNA-protein complexes with PIWI-like proteins to silence transposable elements from moving within the genome. PIWI proteins are a family of Argonaute proteins that interact with piRNA to regulate gene expression.

Different types of non-coding RNAs found in different organisms have a great potential in understanding the complexity of the organism and the regulatory functions of these RNAs in many cellular processes, particularly in gene regulation. With the advancement of transcriptome analysis in mammals large number of long transcripts have been known which have no protein-coding capacity and so it is called Long or Large non-coding RNAs (lncRNAs), the potential of which will be discussed below.

Large/Long Non-coding RNA (lncRNA) and its Function

With the advancement of transcriptome analysis in many organisms, it has been noted that the genomes of mammals and other organisms have produced thousands of long transcripts without any protein-coding capacity. These are called long non-coding RNAs (lncRNAs). It has been noted that about 70% of the mammalian genome is actively transcribed, but only 1-2% of it are protein-coding genes [1].

Large non-coding RNAs (lncRNAs) are generally of more than 200 nucleotides long without any protein-coding capacity but it has been noted that they have functions in gene regulation and disease development. With respect to protein-coding genes, lncRNAs can be intergenic, can be intergenic, antisense or intronic. They are also derived from pseudogenes. About 10,000 pseudogenes were found in the mouse and about 15,000 were identified in the human genome [2, 3].

Pseudogenes are non-functional copies of genes that have lost their protein-coding capacity due to mutations during evolution.

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They are derived from functional genes and are located near their parent genes. Pseudogenes have similarities with functional genes and they can produce non-coding RNAs on occasion. The mammalian pseudogene *Lethe* is known as large non-coding RNA (lncRNA) that plays a role in regulating the inflammatory stimuli and can be used as anti-inflammatory therapeutic suggesting the regulatory functions within the genome. But not all pseudogenes are functional but some have regulatory functions. The pseudogene *Lethe* can inhibit the ability of RelA protein (p65), encoded from *RELA* gene, by binding to NF- κ B promoters leading to RelA deficiency which can cause chronic muco-cutaneous lesions and susceptibility to TNF-induced apoptosis.

lncRNAs can originate from various genomic processes like duplication of protein-coding genes, existing non-coding genes and through retrotransposition, tandem duplications and the insertion of transposable elements. lncRNAs may also originate from nuclear RNA polymerases through transcription and post transcriptional modifications. Five RNA polymerases, such as POL I, POL II, POL III and plant specific POL IV and POL V are transcribing diverse types of lncRNAs involving RNA-directed methylation as well as regulating transposable elements in plants [4].

On the basis of genomic localisation, lncRNAs are classified into three types such as i) Long intergenic non-coding RNAs without any overlapping with other gene; ii) Intronic Large non-coding RNAs which is localised within the intron of a gene; and iii) antisense lncRNA which is transcribed from the opposite DNA strand of the protein coding gene.

Again some of the lncRNAs of mammals are derived from RNA polymerase II, for this reason those lncRNAs are similar to mRNA [1]. There is another functional lncRNA known as *Xist* that helps in the inactivation of one of the X chromosomes of mammals. Dr. Maite Huarte, a molecular biologist at the University of Navarra in Pamplona, Spain, established the functional importance of lncRNA in cellular pathways and the regulatory functions in gene expression and also in different diseases of human, including cancer.

It has been known that Transposable elements (TE) is responsible for providing new transcripts but they have another function of bringing functional elements into lncRNA. During the study of Genomic evolution, it has been noted that 45% to 65% of the genome originated from the parasite genome through the insertion of transposable elements. It has been observed that most of the lncRNAs contain at least one TE and human Endogenous Retrovirus (ERV). The function of *Xist* (X chromosome inactivation) and dosage compensation in mammals, is due to the presence of lncRNA. The sequence study of the *Xist* region showed that there are several repeat domains, like i) Rep-A originated through insertion of ERVB5; ii) Rep-C and Rep-F from ERVB 4; and iii) insertion of transposon. Another interesting finding is that the number of lncRNA has increased during animal evolution, leading to the idea that there is a role of lncRNA in forming complexity in higher organisms [1].

Function of lncRNA

Large ncRNAs have a diverse function in cellular processes like cell proliferation, differentiation, stress responses and apoptosis. They also have a role in many human diseases, particularly in cancer which can be used as a biomarker in diagnosis and therapeutic targets. It has been found that RNAs are involved in many functions of genome organisation, cell structure and gene regulation through RNA-RNA, RNA-DNA and

RNA-protein interactions. Of these lncRNAs are mostly involved in the regulation of chromatin structure, scaffolding by bringing together multiple proteins or protein complexes to form functional units.

Some lncRNAs act as decoys by binding to microRNAs or specific proteins to prevent from performing their normal functions. They are also doing epigenetic regulation by modulating histone and DNA modifications to influence gene transcription. lncRNAs can also help in Cis-regulation by affecting the expression of neighbouring genes on the same chromosome and in Trans-regulation on genes located on different chromosomes [1, 3].

Transcriptional Regulatory Functions

Some mammalian lncRNAs function as transcriptional regulators both at the cis- and trans-level gene expression and chromatin organisation with the interactions of chromatin. These functions may act from two sites either from enhancer regions or from promoter-like lncRNA loci. lncRNAs regulate enhancers or enhancer RNAs by acting as guides for chromatin remodelers, functioning as scaffolds for protein complexes influencing enhancer-promoter functions to regulate gene expression and enhancer activity [5]

Cis-regulation

When the gene expression is controlled by regulatory elements present in surrounding areas, then it is called Cis-action. These regulatory elements are lncRNAs here. Its mechanism is done through chromatin remodelling. The example of lncRNA doing Cis-action is Cold-Induced Long Antisense Intragenic RNA (COOLAIR), Flowering Locus C (FLC), which regulates flowering due to vernalization. COOLAIR transcribing from the antisense strand of the FLC locus binds and recruits Polycomb Repressive Complex 2 (PRC2) to the FLC locus to control flowering during vernalization. Further, lncRNA 16397 of Tomato induces transcription of Glutaredoxin SGRX22 and SGRX21 genes to reduce ROS accumulation and cell membrane injury [6].

Trans-regulation

The trans-regulation or action of lncRNA controls the expression of genes by binding the target gene with a specific protein. As for example, lncRNA ELENA1 of *Arabidopsis* interacts with the subunit of MED19A protein as a mediator complex to regulate gene expression by bridging transcription factors and RNA polymerase II. MED19A is involved in the abscisic acid (ABA) pathway for stress tolerance and immunity to plants.

RNA-seq and Ch1RP-seq methods showed that Flowering Associated Intergenic lncRNA [FLAIL] binds Circadian (CIR1) and Lactase 8 (LAC8) genes connected to flowering for regulating flowering in *Arabidopsis* through trans-action [6].

About 10,000 intergenic long non-coding RNAs (lncRNAs) have been studied in mammals which have a role in a variety of biological processes. These are generally located in the nucleus. On the basis of genomic origins of lncRNA, they can be classified into five groups such as

- i) Stand-alone lncRNAs are intergenic. The stand-alone lncRNA is transcribed from a distinct, independent region without any overlap with any protein coding gene. These RNAs are sometimes called long intergenic non-coding RNAs (lincRNA) without any protein coding capacity but is regulating gene expression at various levels.
- ii) Antisense transcripts found in the opposite strand of protein coding gene

iii) Pseudogenes with loss of coding ability
iv) Long intronic non-coding RNAs which originate from within the introns of other genes having a regulatory function by interacting with chromatin-remodelling complexes.

v) Divergent transcripts of lncRNA are transcribed in the opposite direction from the promoters of active protein -coding genes, producing a large proportion of the lncRNA repertoire in mammalian genomes. They have also a function of regulating the expression of their neighbouring protein coding genes.

In some cases, lncRNAs was found to inhibit DNA methylation of an enhancer to control the expression of adjacent genes on the sister chromosomes. Genome binding profile studies of several lncRNAs have shown that a single type of lncRNA can control gene expression after associating with many genome loci on different chromosomes [7].

Some intergenic RNAs are functioning as transcriptional regulators i.e. regulating gene expression either at the site of synthesis or distally across many chromosomes. These RNAs also regulate chromatin organisation by interacting with the chromatin. It has been observed that small number of eRNAs (Enhancer RNA) and elncRNAs have been found to function at their site of synthesis to regulate the expression of neighbouring protein-coding genes on the same chromosome [5].

lncRNAs in Abiotic and Biotic Stresses in Plants

Abiotic stresses are from drought, salinity and cold stresses while biotic stresses are from pathogens. Further studies have noted that non-coding RNAs (ncRNAs) are regulatory molecules in biotic and abiotic stresses. In addition to ncRNAs, lncRNAs have also regulatory functions in stresses in plants. lncRNAs are performing their functions both as cis-acting and trans-acting in the plant genome. Several stress-induced lncRNAs have been found in other plants like *Medicago*, *Zea mays* and *Arabidopsis* which played a major role in drought and salt stress conditions [8,9].

lncRNAs in High temperature or Drought Stress (Abiotic)

Global warming causing heat waves in most of the countries, have reduced the productivity of crops by affecting growth and development. Heat stresses cause damage to plant cells by disturbing membrane integrity, protein denaturation, changes in the synthesis of metabolites, activity of enzymes, heat shock proteins (HSP) and heat shock transcription factor [10]. It has been noted that lncRNAs confer heat tolerance by regulating molecular pathways, mainly BR signalling pathway. The BR pathway is the fully elucidated receptor kinase signalling pathway in plants. The Brassinosteroid is a class of steroid hormones in plants that regulate plant development through the receptor kinase signal transduction pathway. This hormone, Brassinosteroid (BR) was first discovered from the pollen extract of Brassica plants (*Brassica napus*) in 1979 and found to promote cell elongation and later it was found in pollen, seeds and fruits of other plants. BR signalling pathways have been studied in detail with the help of genetic, proteomic and genomic approaches [10].

In Wheat, heat stress affects cell division at the meiotic stage affecting the maturation of pollen leading to the loss of productivity. lncRNA may help in developing heat tolerant crop plants by manipulating the overexpression of lncRNA by RNAi and CRISPR technology showing the potential of lncRNA by targeting genes critical to heat stress response for bringing plant resilience under heat or drought stress. Research has been carried out to find out the importance of lncRNAs in several plants like Rice, Maize, Wheat, Cotton, Tomato, Poplar and

others. With response to drought stress in plants differentially expressed long non-coding RNAs (DEGs) are identified in plants through high-throughput sequencing and bioinformatics. Different DEGs in response to drought stress are found in association with drought tolerance in Cotton as GhDNA1 (transcribed by Pol II) targeting AAAG DNA motif double strands with the help of core binding site of Dof TFs to regulate drought-responsive genes. Yang et al 2023 thereby showed that lncRNAs can induce or suppress the expression of drought -responsive genes in bringing Drought tolerance (Fig.1 A).

lncRNAs in Cold stress (Abiotic)

Plant growth and development is also affected under low temperature stress conditions. lncRNAs can regulate gene expression and also influence many physiological processes to enhance cold tolerance by activating or repressing target genes in pathways like oxidative stress, osmotic adjustment and energy metabolism. lncRNAs are doing this by forming regulatory modules with transcription factors, miRNAs through cis-acting regulation. There is one COLD-INDUCED lncRNA 1 (CIL1) that acts as a positive regulator of the plant response to cold stress in *Arabidopsis*. Genome-wide transcriptome analysis showed that there were 256 downregulated genes and 34 upregulated genes in *clt1* mutants under cold stress, involving signal transduction pathway.

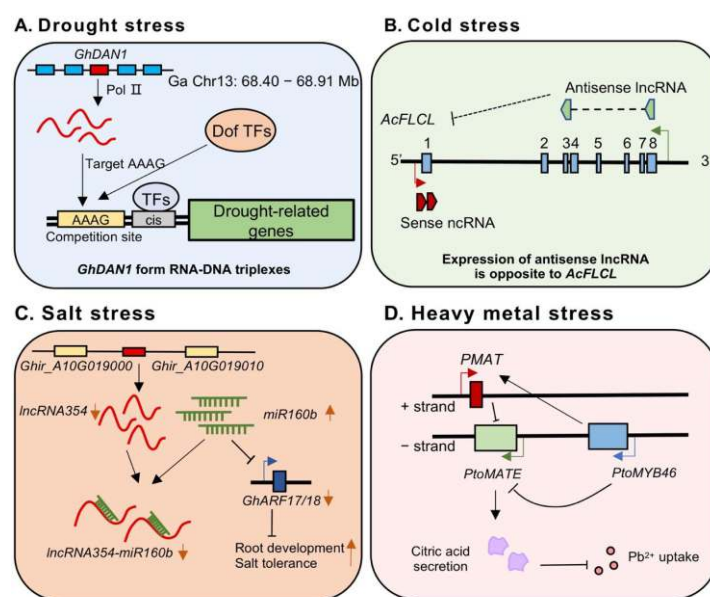


Fig.1 (A—D). Showing Role of lncRNAs in Various Abiotic Stresses. Taken from [4].

ROS homeostasis and glucose metabolism in regulating the cold stress [13]. An antisense non-coding transcript, COOLAIR, was expressed in cold stress which reduces the expression of gene FLC. The FLC is the FLOWERING LOCUS gene that has responds to cold stress, affecting inhibition of flowering, prolonging the period of vernalization. A gene homologous to FLC was identified in Kiwi fruit is AcFLCL which is a MADS-box transcription factor that plays a key role in cold stress. The Kiwi fruit antisense lncRNA showed the opposite expression of AcFLCL under cold stress, bringing cold tolerance (Fig.1.B).

lncRNAs in Heavy Metal Toxicity (Abiotic)

In case of metal toxicity to plants, the uptake of several heavy metals like lead, Copper, Arsenic and Mercury is associated with lncRNAs. It has been identified that 226 lncRNAs were associated with lead uptake, aluminium uptake in *Medicago truncatula* plants was associated with 515 differentially

expressed lncRNAs out of 3284. It has been found that lncRNAs are not directly involved in the uptake of metals but they indirectly regulate the process of protein-coding genes responsible for the uptake of plants. The actual uptake is carried out by specific membrane proteins, like ALMT (Aluminium-activated Malate Transporters) and MATE (Multidrug and Toxic compound Extrusion) family transporters. This process was observed during Aluminium uptake. lncRNAs can also regulate tolerance to heavy metals in plants by influencing gene expression that activates downstream Aluminium resistance processes.

Again in Poplar plants, one long non-coding RNAs (lncRNAs) were found known as PMAT which is called Lead -induced multidrug and toxic compound extrusion antisense lncRNA which helps to regulate the tolerance of plant to Lead contamination. The overexpression of PtoMYB46 promotes Lead (Pb) uptake, tolerance and plant growth and lncRNA is a regulator of metal stress responses in plants [4].

The interaction of lncRNA and PMAT with PtoMYB46 inhibits the expression of PtoMATE under Lead stress leading to reduce lead uptake in plants. Actually PMAT is not a gene but it is a gene product (transporter protein) encoded by the gene SLA29A4. While ptoMATE is gene found in plant Poplar. It has been noted that lncRNA -PMAT help to regulate the ptoMATE gene for giving lead tolerance to lead contamination. The lead uptake is regulated by the secretion of Citric acid (Fig.1.D)

lncRNAs in Salinity or Salt Stress (Abiotic)

It has been noted that salinity affects the production of Rice crops in 33% of the arable lands of the world. Rice is the main crop in most of the countries of the world. Rice is very sensitive to salinity or salt stress affecting growth and development of plants and most sensitive to salt stress is the seedling stage. It is necessary to find out the salt-tolerant varieties to maintain Rice production or to achieve global food security.

In addition to Rice, several salt stress-responsive lncRNAs were found in other plants like *Medicago*, Maize and *Arabidopsis*. About 3714 lncRNAs have been noted in Rice under stress conditions. Of them 1010 were differentially expressed in stress conditions. Differentially expressed genes show that the activity level of genes is significantly different in one condition or some genes are expressed more in some conditions like stress. The study of Differentially Expressed (DE) lncRNAs may help to understand the biological changes occurring in a cell under special conditions. In this case some lncRNAs are active and others are silent or inactive. Differentially expressed lncRNAs were identified in salt tolerant varieties FL478 compared to salt-sensitive varieties IR29. A Deep Neural Network (DNN) was used to predict the change in the expression of different genes under stress conditions [8]. Four DE-lncRNAs were identified in salt-tolerant variety FL478 where 2 are up-regulated and 2 are down-regulated while in IR29 salt sensitive varieties DE-lncRNAs, 6 up-regulated and 3 down-regulated were noted under salt stress.

In another studies, salt stress-responsive lncRNAs were noted in *Arabidopsis*, Sweet Sorghum, Barley, Cotton, Alfalfa, Soybean, Chickpea and others [12]. Yang and others also noted differentially expressed 154 and 137 lncRNAs in less salt-tolerant cultivated M82 genotype of Tomato. The lncRNA 354 in Cotton found between the gene Ghir_A10G019000 and Ghir_A10G019010 shows reduced expression under salt stress through binding to miR160b [12].

Thus the accumulation of more and more miR160b RNA inhibits the expression of GHARF17/18 to increase salt tolerance as well as promotes root development (Fig. 1.C).

Another lncRNA TRABA, suppresses the expression of salt-sensitive gene (GhBGLU24-A) for increasing the salt tolerance in certain varieties of Cotton. There are different lncRNAs which are involved in responding to salt stress conditions targeting various genes and pathways related to plant growth and development. The important role of lncRNAs in stress conditions acts through endogenous RNAs (ceRNA) to decoy mature miRNAs. MiRNAs are a type of endogenous non-coding small RNAs (20-24 nucleotides long) which mediate the translational inhibition or degradation of target mRNAs at the transcriptional and post-transcriptional level. It has been observed that lncRNA973 regulated the expression of a number of genes through trans- action to increase the tolerance of plants to salt stress [11,12].

It has been noted that salt-responsive lncRNAs were identified in FL 478 varieties (salt tolerant) of Rice compared to its susceptible parent (IR29) using the RNA-seq method. These salt-responsive lncRNAs were differentially expressed lncRNAs (DE-lncRNAs) that has been identified through transcriptome analysis. DE-lncRNAs were identified in FL478 and a total of nine DE-lncRNAs were identified in IR29 varieties. Of the total identified DE-lncRNAs, two and seven were expressed in FL478 and IR29 respectively which are playing critical role in response to salt stresses in Rice. DE-lncRNAs were identified in FL478 and a total of nine DE-lncRNAs were identified in IR29 varieties. Of the total identified DE-lncRNAs, two and seven were expressed in FL478 and IR29 respectively which are playing critical role in response to salt stresses in Rice plants [8]. lncRNAs are achieving controls through epigenetic processes like DNA methylation , histone modification serving as miRNA decoys by regulating RBA splicing and control responses to stresses through some plant hormones like Absciscic acid. Modern technology like High-Throughput Sequencing and Bioinformatics have improved the identification and understanding the functional mechanism of lncRNAs in stress responses.

Besides this, a large number of lncRNAs were found in response to extra micro – and macro nutrients like Boron, Phosphorus and Nitrogen and some toxic chemicals like Cadmium, Aluminium, Gibberellin and others. Some lncRNAs were differentially expressed in two different Poplars and about 1183 lncRNAs were differentially expressed in response to salt stress [6].

Some lncRNAs were differentially expressed in two different Poplars and about 1183 lncRNAs were differentially expressed in response to salt stress [6].

Again it has been noted that some lncRNAs can respond to more than one abiotic stresses such as , Drought-Induced lncRNA (DRIR) is found as a regulator in two stress conditions in *Arabidopsis* like drought and salt. Further polyadenylated and non-polyadenylated lncRNAs were also found to be active under Absciscic Acid (ABA), drought and cold stress in *Arabidopsis* which has been identified by high-depth ssRNA seq method [6].

lncRNAs in Biotic Stresses

Biotic stress in plants is caused by living organisms like fungi, bacteria, viruses, nematodes, insects and weeds. These are also called phytopathogens causing agricultural losses due to depletion of nutrients, reducing growth and crop yield. In powdery mildew infection of Wheat, 48 responsive lncRNAs were identified, which is known as TapmlnRNA.

The disease is caused by the fungus *Blumeria graminis f.sp.tritici*. Some lncRNAs act as precursors for miRNAs by regulating gene expression. When wheat is infected by powdery mildew, the expression of certain lncRNAs and their corresponding miRNAs plays a regulatory role in the defence system of the plant [9].

Again, the role of lncRNAs in the infection of Black Streaked Dwarf Virus and Stripe Virus was noted in Rice, where 21 lncRNAs were up-regulated in response to both viruses with about 1000 co-regulated transcripts. They are found to control infection through transcriptional regulation, plant hormone signal transduction, phenylpropanoid synthesis and plant pathogen interaction [13].

The infection of *Phytophthora infestans* in Tomato plant causes Leaf Curling Disease leading to the loss of yield. Research has been carried out on infected Tomato to find out the regulatory effect of lncRNAs. It has been identified one lncRNA40787 in the infected potato plant by *P. infestans*. This lncRNA40787 works like Competitive endogenous RNA (ceRNA) which is a type of molecule involved in gene regulation. Ce RNAs are RNA transcripts that compete with the same miRNAs to regulate each other. It has been found that lncRNA40787 was predicted as a ceRNAs of miR394 as this lncRNA has an endogenous target mimic (eTM) structure of miR394. Thus lncRNA40787 regulates Leaf Curling Responsiveness by activating genes found in IAA biosynthesis components [12, 13].

It has also been found that the overexpression of lncRNA40787 can reduce the expression of miR394 to such a level that inhibits the cleavage effect of miR394 on the IAA biosynthetic gene LCR, leading to enhanced resistance to *P. infestans* in Tomato [9].

Tomato lncRNAs are enhancing resistance to viruses by controlling viral replication and transcription. It has been noted that lncRNA (SILNR1) in Tomato can mediate Viral DNA replication and transcription in hosts to suppress Tomato Yellow Leaf Curl Virus (TYLCV) infection with the help of viral small-interfering RNA (vsRNA) from TYLCV IR sequence [7].

TYLCV IR sequence is a non-coding intergenic variable region in the TYLCV genome that contains regulatory elements like a promoter and replication region. This is a specific 25nucleotide segment within the IR sequence which is the source of vsRNAs. These vsRNAs can target and silence host-specific lncRNAs in susceptible plants, which is linked to disease symptoms. The vsRNA is a Virus Small RNAs which are short non-coding RNA molecules that can originate from a virus or formed after response of host to virus. They play an important role in antiviral defence like siRNAs or miRNAs. They can target and silence viral RNA, inhibiting viral replication. Here TVCLV IR sequence acts like vsRNAs to bring resistance to viral diseases.

lncRNAs in Human Diseases

It has been noted that many lncRNAs are associated with human diseases. Some lncRNAs are located in the nucleus and some are found in the cytoplasm. In the nucleus, lncRNAs are found in different sub-compartments of the nucleus, such as i) in the nucleolus known as PAPAS, nuclear matrix (XIST), nuclear speckles (MALAT1) and nuclear para-speckles (NEAT1). Nuclear speckles are also known as interchromatin granules that store pre-mRNA splicing factors and other proteins involved in gene expression. These speckles are not membrane bound and their size and shape can change on the basis of needs of the cell. These are also implicated in human diseases like cancer and neurological disorders. Paraspeckles are unique subnuclear structures composed of specific proteins and RNAs [14].

XIST is responsible for the inactivation of X chromosome in females. The function of lncRNA PAPAS is to inhibit Ribosomal RNA synthesis (rRNA) by recruiting epigenetic modifiers like Suva4-20h2 and CHD4/NuRD to ribosomal DNA promoters to cause chromatin compaction and block transcription.

The function of lncRNA Metastasis Associated Lung Adenocarcinoma transcript 1 (MALAT1) is in gene regulation and cellular processes. It plays an important role in the development and progression of various diseases especially cancer. The function of lncRNA NEAT1 is mainly in cancer by promoting proliferation, migration and invasion while inhibiting Apoptosis and it is involved in immune responses and chemotherapy resistance through various molecular interactions.

Some lncRNAs are going to the cytoplasm for certain specific functions but exportation to the cytoplasm requires some activation, 5'-capped, spliced and polyadenylated. Cytoplasmic lncRNAs are forming ribonucleoprotein complexes by binding mRNAs and proteins or binding with a specific protein. As for example, lncMyoD plays an important role in the (lncMyoD) the development of skeletal muscle by regulating the balance between proliferation and differentiation.

i) Neurodegenerative diseases

These lncRNAs are involved in neurodegenerative diseases like Alzheimer's, Parkinson's and Amyotrophic Lateral Sclerosis (ALS) as they have role in regulating gene expression and cellular processes. Their dysfunction may cause diseases by affecting epigenetic regulation, mRNA stability and cellular responses. ALS is a fatal motor neuron disease that causes nerve cells in the brain and spinal cord to degenerate, affecting the ability to move, speak and breathe.

Alzheimer's Disease is now very common neurological disease occurring to many aged persons in the world. It generally occurs due to the overexpression of β Amyloid protein in the brain forming Senile plaque, affecting the activity of brain, particularly the memory, etc. It has been noted that one secretase enzyme, known as Beta-site Amyloid precursor protein Cleaving Enzyme 1 (BACE 1), splices Amyloid precursor protein (APP) in the production and aggregation of β Amyloid protein in the brain. It has been found that antisense lncRNA BACE1AS of BACE1 plays an important role in the development of Alzheimer's Disease. This antisense lncRNA (BACE1-AS) forms a complex with mRNA to increase the stability of β Amyloid, preventing its degradation [15]. It has been observed that 40% of lncRNAs in humans are expressed in the brain, which is equivalent to 4000- 20,000 lncRNA genes. These lncRNAs have regulatory functions in different stages of neurogenesis and synaptic plasticity. So any dysfunction of these lncRNAs may cause different diseases of neurodegenerative [14]. Primate-specific Cytoplasmic RNA in brain BRC200 is synthesised in the cell body and is transported to the dendrites to regulate the synthesis of proteins needed for synaptic plasticity. Synaptic plasticity is the ability of synapses, i.e, the connections between neurons leading to increase or decrease the activity. It allows the brain to physically change and adapt by altering the strength of communications between the neurons or neural connections. Another function of synaptic plasticity is a mechanism for learning and memory by forming new neural networks in the brain.

It has been noted that cytoplasmic antisense lncRNAs (BC1) are expressed in the brain to regulate mRNA or protein translation by inhibiting translation-initiation factors to disrupt protein translation or delivery of mRNA at the synapse leading to

neurodegeneration [14, 16].

Another lncRNA UCHL1-AS has been found to be responsible for Parkinson's Disease. UCHL1 is a gene producing enzyme that is linked to Parkinson's Disease and is playing a key role in the ubiquitin-proteasome system for clearing damaged proteins. Antisense transcript of lncRNAs BC 1 (UCHL1-AS) may control sense gene expression leading to loss of UCHL1 activity to cause Parkinson's Disease. Actually antisense transcription makes a regulatory networks to control the activity of protein-coding genes. A large number of lncRNAs have some role in the development of early diagnosis and treatment of Parkinson's disease by thorough study of the expression of lncRNA. Some lncRNAs like UCHL1, MAPT-AS 1, and Mirt 2 play a protective role and others like HOTAIR, MALAT 1, NEAT 1 and SNHG 1 may aggravate the disease progression [17].

lncRNAs also have a role in the regulation of psychiatric diseases like depression, autism, schizophrenia, bipolar disorder. lncRNADISC2 acts as an antisense transcript for the DISC1 gene in psychiatric disorders. The interaction and dysregulation of DISC1 and lncRNADISC2 are responsible for mental illnesses, particularly schizophrenia and bipolar disorder. It has been noted that lncRNADISC1 and lncRNADISC2 are significantly altered in patients with bipolar disorder. The expression levels of these transcripts may be used as a biomarkers for bipolar disorder. This dysfunction in patients with psychiatric disorders may be corrected by modulating the expression of these lncRNA molecules [9, 15].

ii) Cancer

Cancer is a group of diseases with about 100 types and is the most common cause of death in the world. It is characterised first by uncontrolled proliferation of cells, secondly cells have the ability to spread in other tissues (metastasis) and thirdly lose the ability of cells to die normally (apoptosis). The development of lncRNA and other noncoding RNAs has opened a new vistas in understanding the development of cancer and in the treatment of cancer. Genetic alterations in genes encoding non-coding RNAs have been found to initiate cancer although few studies have been done in this line. It has been noted that the deletion of 13q14.3 in Chronic Lymphocytic Leukaemia (CLL) removes the miR-1516 tumour suppressors. Again, the amplification of lncRNAs FAL1 and PVT1 is found in cancer cells. Single -nucleotide polymorphisms (SNPs) in the genes of lncRNAs H19, ANRIL and CCAT2 are also associated with the development of cancer. Besides genetic mechanisms, the up and downregulation in the expression of non-coding RNA is helping in cancer development through some cellular processes like epigenetic, transcriptional and post-transcriptional methods [18].

It has also been found that many of the gene mutations in cancer are present in the regions which do not encode proteins. These regions are transcribed into lncRNAs that have been observed from the study of growing number of transcriptomes of cancer cells applying the next-generation sequencing. The observations showed that there are several lncRNAs whose aberrant expression is responsible for different cancer types [18]. It has also been studied to understand how the biogenesis of lncRNA is different from mRNAs. It has also been found that lncRNAs are linked with specific localisations and their interactions with DNA, RNA and Proteins leading to modulate chromatin function as well as the function of membraneless nuclear bodies to alter the stability of mRNAs and interfering signaling pathways to affect gene expression.

This causes many diseases in human like neurological disorder, immune responses and cancer [19].

lncRNAs have played some role in the development of cancer and its progression. Various types of lncRNAs are involved in different types of cancer with different expression levels in the cancerous tissues. In cell transformation from normal cell to cancerous cells, six properties have been noted such as, such as, i) signaling of self-sustained growth; ii) loss of properties of growth inhibition; iii) loss of normal process of Apoptosis; iv) so uncontrolled proliferation; v) development of new blood vessels in the cancerous tissues, called Angiogenesis and vi) Metastasis i.e., the spread of cancer from one organ or one part of the body to other parts of the body or organs [19]. The most important function of lncRNAs is to regulate many cellular processes in humans. Some of the processes are mentioned below.

Growth Signalling

lncRNAs regulate growth signalling through various mechanisms, like i) acting as scaffolds to assemble protein complexes by binding together multiple proteins, ii) modulating the activity of signalling proteins like kinases and receptors, and iii) competing with other molecules for binding to miRNA. lncRNAs can act as competing endogenous RNAs (ceRNAs) for binding to miRNAs to increase the expression of target mRNAs. lncRNAs can interact with receptors and some signalling proteins for facilitating or inhibiting signalling cascades.

Signaling to growth takes place generally through some receptors present on the exterior of the cell with the help of signalling pathways. lncRNAs can promote self-sufficiency in growth in cells using signal receptors. As lncRNAs bind to nuclear receptors so there is no need for exterior cell receptors to receive growth signals. Nuclear receptors are proteins that act as ligand-activated transcription factors inside cells for regulating growth and development. lncRNAs are showing regulatory function by activating or repressing genes through cis- or trans- regulation. Sometimes their roles are found through chromatin modifications, cytosol regulating mRNA translation or acting as miRNA decoys [20].

The SRA1 (Steroid Receptor Activator) gene produces both long noncoding RNA (lncRNA) and a protein SRAP, which acts as co-receptors like oestrogen receptor to induce hormone-dependent breast cancer by increasing the activity of steroid receptors. The expression of SRA1 may be used as a biomarker in diagnosing and monitoring the progress of breast cancer. The importance of the steroid signalling pathway in the progression of breast cancer is leading to the use of endocrine therapy with the drug Tamoxifen [26]. However, lncRNA PVT1 (Plasmacytoma Variant Translocation 1) does not affect the receptor but regulates receptor abundance to induce the proliferation of cancerous cells [21, 22].

Growth Inhibition

This cellular process, Growth inhibition, is done by influencing CDKs (Cyclin Dependent Kinase) or by regulating the expression of tumour suppressor genes. Transcriptions and translations are also influenced by lncRNA molecules by inhibiting the activity of miRNA to promote the formation of tumour protein [19]. lncRNAs act as scaffolds for proteins to interact with miRNA to change the expression of genes that control growth and proliferation. lncRNA285194 inhibits cancer cell growth by suppressing the activity of miRNA (miRNA-211) and also targeting the p53 gene.

Again, lncRNA 21q22.11 suppresses gastric cancer through inhibition of the MEK/ERK signalling pathway. lnc285194 is also called LSAMP antisense RNA3 contains 4 exons with less than 2kb in length (Gene Id285194) functions as a tumour suppressor. But the actual mechanism is still not known. It has been noted that lncRNA 285194 inhibits tumour cell growth through negative regulation of miR-211, showing that some endogenous RNA regulatory network is present. Again, lncRNA285194 may also promote tumour cell growth with the help of RNAi [23].

Apoptosis

It is a natural programmed process for the self-destruction of cells to eliminate unwanted or damaged cells without damaging surrounding tissues, and also to maintain the stability of the internal environment. It is a defence against cancer as it regulates uncontrolled cell growth in cancer cells. This process is driven by an enzyme called Caspases.

lncRNAs can inhibit apoptosis to continue unregulated cell proliferation in cancer cells. So lncRNAs are regulating Apoptosis or Programmed Cell Death including autophagy, Necroptosis and Ferroptosis. lncRNAs can influence the apoptosis pathway by affecting membrane surface receptors or acting as molecular sponges to bind and sequester miRNAs or some protein complexes for controlling the expression of apoptosis genes. lncRNA MALAT1 can inhibit breast cancer metastasis. But the overexpression of MALAT1 can promote tumour progression, migration and invasion and epithelial mesenchymal transition of small cell lung cancer by inhibiting miR-150-5p. Again, lncRNA UICLM is promoting cell proliferation and reducing apoptosis, and lncRNA UICLM is regulating the expression of zinc finger E-box binding homeobox 2 (ZEB2) to promote liver metastasis and colorectal cancer [24]. The relationship between lncRNA and Apoptosis has great implications in clinical research. Autophagy can promote cell survival or may cause cell death in some conditions.

lncRNAs in Telomerase

Telomeres are conserved repetitive sequences located at the end of chromosome. Telomeres of human cells are 10 to 15 kb in length with tandem repeats of TTAGGG. In the normal condition, the shortening of telomeres takes place as the cells are dividing. Hence, there is a control in cell division. But in the case of cancer, there is an uncontrolled cell division and cell proliferation due to continuous elongation of telomeres. The shortening of telomeres is done by the production of lncRNA molecules called TERRA (Telomeric Repeat containing RNA) which binds to telomerase and can inhibit telomerase activity in normal cells and prevent telomere elongation. There is another lncRNA called TERC, which acts as a template for the telomerase enzyme to lengthen telomeres.

In cancer cells, TERRA expression is repressed allowing telomerase to function for maintaining telomere length, which is essential for cell division to maintain cell immortality. Another lncRNA, TERC, is found to be overexpressed in cancer cells to promote cell migration and cell survival. The inhibition of TERC showed cell cycle arrest, inhibition of cell migration and cell immortality. Thus, TERC or TERRA may be used as therapeutic targets in cancer therapy. It has been found that TERC targeting therapies showed very positive results in cancer cells after clinical trials even in advanced stages [25].

Therapeutic and Diagnostic Uses of lncRNAs

With the study of the function of lncRNAs in different diseases, there comes an idea that lncRNAs may have some role in the diagnosis of disease as biomarkers as well as have some therapeutic value. The therapeutic use of lncRNAs may be done by manipulating them as targets in different diseases like Cancer, Neurological disease and others. One way is to inactivate oncogenic lncRNAs with the use of anti-sense oligonucleotides or RNA interference (RNAi). In other ways, antisense oligonucleotides can be used to neutralize inhibitory lncRNAs and by increasing the activity of tumour suppressor genes. It can also be done by interacting lncRNAs with the epigenome using antisense oligonucleotides, RNAi and CRISPR technology. It has been noted that many of the mutations found in cancer is not due to protein coding genes but due to some Long non-coding RNAs (lncRNA). Many lncRNAs are highly expressed in specific tissue and cell types with diversity of functions in cancer cells. So, lncRNAs can be a potential target for cancer treatments through inhibition of the progress of tumours. The amplification of somatic copy number in cancer leads to the gain of oncogenic transcription factor MYC 1581. This regulation of MYC has been carried out by several lncRNAs such as PVT1, PCAT1, CCAT1 and CCAT 2. Thus, lncRNA is helping to regulate MYC expressions indirectly [26]. It has been found that certain lncRNAs in blood samples are correlated with the occurrence of diseases and so they can be used as a biomarker and also have some therapeutic application. It is known that p53 is the tumour suppressor gene that helps to stop progression of cancer cells. There is one lncRNA called MEG3 that activates p52 to give anticancer effect showing the therapeutic use of lncRNA. Again, DNA damage caused generally by some exogenous factors giving the dangerous signals to normal cells that may lead to cancer. In that case, the transcription of lncRNA-damage induced non coding (DINO) activates p53 to control the progress of cancer cells. Immune escape has been noted as the important cause of cancer as macrophages and regulatory T cells have achieved some capacity to avoid threats of killer T cells leading to loss of immunity in cancer cells. The function of immune cells can be activated by some lncRNAs [27].

After modulating the activity of lncRNA some clinical trials have been made by Abivax (a clinical stage biotechnology company) in patients of Ulcerative colitis and Rheumatic arthritis by developing a small molecule that helps in splicing of lncRNA 0599-205. It produces miR124 as this lncRNA activates three miR loci in the genome. MiR 124 has been found to reduce pro-inflammatory cytokines as well as regulate innate and adaptive immunity [14].

Another cancer HNSCC (Head and Neck squamous Cell Carcinoma), is now very common throughout the world. It occurs in the lip, tongue, mouth, nasal cavity, paranasal sinuses, pharynx and larynx. It is known that Human papilloma virus (double-stranded DNA virus) is one of the causal agent of this type of cancer. Various types of treatments are going on like chemotherapy, radiation therapy, targeted therapy, immune therapy and surgical removal. Still it is not 100% successful. As the aberrant expression of lncRNAs is related with pathophysiological functions to stimulate tumorigenesis, so there must be a scope of using lncRNAs in therapeutic applications in various types of cancer including HNSCC. It has been found that the inhibition of lncRNA can alter the regulatory network of cancer cells, leading to the study of the mechanism and function of lncRNAs in detail to use it as a therapeutic target [28].

The therapeutic use of lncRNAs can be done through modulation of lncRNA expression by several mechanisms, like small interfering RNAs (siRNA), Antisense oligonucleotides, CRISPR-Cas9 and small molecule inhibitors in animal models. Further development is needed for clinical trials in humans [29]. It has also been noted that lncRNAs are also associated with Cardio vascular disease. Their roles have been observed in causing hypertension, atherosclerosis, atrial fibrillation, myocardial infarction and heart failure. Thus, lncRNAs may also have some potential value in therapeutic applications. It has also been reported that an intergenic lncRNA MIAT is responsible for the progression of several cardio vascular diseases. This lncRNA is located on chromosome 22 of the human cell. Recently, RNA-based therapies including antisense oligonucleotides, siRNAs and CRISPR based technologies have been tested in humans through clinical trials [30]. Further research is needed using lncRNAs as therapeutic targets.

Conclusions

The central dogma showed that protein- coding mRNA is produced from DNA which produces protein. According to central dogma other RNAs have no function except Transfer RNA and Ribosomal RNA, so these may be called junk RNA. But it has been noted that other non-coding RNAs exist and perform diverse functions, particularly regulatory functions. Different types of non-coding RNAs found in different organisms perform regulatory functions in many cellular processes leading to a great potential value in understanding their roles under stress conditions and may cause many diseases due to some dysfunction of lncRNAs. Thus this lncRNAs can be used in diagnostic purposes as well as in therapeutic applications.

References

1. Marin-Bejar, Oskar and Maite Huarte. 2015. Long non-coding RNAs: from identification to functions and mechanisms. *Advances in Genomics and Genetics* 5: 257-274.
2. Marchese, F.P, Ivan Raimondi and Maite Huarte 2017. The multidimensional mechanisms of long non-coding RNA function. *Genome Biol.* 18:206. Doi:10.1186/s13059-017-1348-2
3. Mattick, John S., Paulo P.Amaral, Piero Carninci, Susan Carpenter, Howard Y.Chang, Ling-Ling, Chen, Runsheng Chen et al 2023. Long Non-coding RNAs: definitions, functions, challenges and recommendations. *Nature Reviews Mol. Cell Biol.* 24:430-447. <https://doi.org/10.1038/s41580-022-00566-8>.
4. Yang Hong, Yuting Cui, Yanrong Feng, Yong Hu, Li Liu and Liu Duan. 2023. Long Non-Coding RNAs of Plants in response to Abiotic stress And Their regulating Roles in Promoting Environmental Adaptation. *Cells* 12: 729. <https://doi.org/10.3390/cells12050729>.
5. Vance, Keith W and Chris P. Ponting .2014. Transcriptional regulatory functions of nuclear long non-coding RNAs. *Trends in Genet.* 30(8): 348-355. <http://creativecommons.org/licenses/by/3.0>. <http://dx.doi.org/10.1016/j.tig.2014.06.001>
6. Bao, Xiyue, Xiaofeng, Dai, Jieyin Chen and Ran Li. 2025. Plant Long Non-Coding RNAs: Multilevel Regulators of Development, Stress Adaptation, and Crop improvement. *Agronomy* 15:1950. <https://doi.org/10.3390/agronomy15081950>.
7. Chen.Yung-Chia Ariel and Alexai A. Aravin.2015. Non-coding RNAs in transcriptional regulation. *Curr.Mol.Bio. Rep.* 1: 10-18. Doi.10.1007/s40610-015-0002-6.
8. Mansuri, raheleh Mirdar, Amir-Hossein Azizi, Amir-Hossein Sadri and Zahra-Sadat Shobbar.2022. Long non-coding RNAs as the regulatory hubs in Rice response to salt stress. *Scientific Reports* 12: 21896. <https://doi.org/10.1038/s41598-022-26133-x>.
9. Li Qian, Heng Shen, Shoujuan Yuan, Xigang Dai and Changxian Yang. 2023. miRNAs and lncRNAs in tomato: Roles in biotic and abiotic stress responses. *Frontiers in Plant Science* 13.1094459. doi: 10.3389/fpls.2022.1094459.
10. Zhu, Ja-Ying, Juthamas Sae-Seaw and Zhi-Yong Wanh. 2013. Brassinosteroid signalling. *Development* 140(8): 1615-1620. Doi: 10.1242/dev.060590.
11. Zhang, Xiaopei, Jian Shen, Qingjiang Xu, Jie Dong, Lirong Song, Wei Wang and Fafu Shen . 2021. Long non-coding RNA lncRNA354 function as a competing endogenous RNA of miR160b to regulate ARF genes in response to salt stress in upland cotton. *Plant Cell and Environment* 44(10) :3302-3321. <https://doi.org/10.1111/pce.14133>
12. Lakhani Komal G.,Rasmieh, Hamid and Gopal V. Marviya. 2025. Perspective Chapter : Long Non-Coding RNAs in Plants-Unlocking Hidden Regulators for Stress Tolerance and Crop resilience. Published in May 2025. Intech Open. Doi: <http://dx.doi.org/10.5772/intechopen.1008955>
13. Jin Xin, Zemin Wang, Xuan Li, Qianyl Al , Darren Chern Wong Feiyan Zhang et al. 2023. Current perspectives of lncRNAs in abiotic and biotic stress tolerance in plants. *Front. Plant Sci.* 14. 1334620
14. Tsagakis, Ioannis, Katerina Douka, Isabel Birds and Julie L. Aspden 2020. Long non-coding RNAs in development and disease conservation to mechanisms. *J. Pathol.* 250: 480-495. Doi:10.1002/path.5405
15. Li, Wenchao, Yang Yang Wang, Lifei Xiao, Jiangwei Ding, Lei Wang , Feng Wang and Tao Sun. 2023. Mysterious Long non coding RNAs and their relationships to human disease. *Frontiers in Molecular Biosciences.* 9:950408. doi: 10.3389/fmolb.2022.950408.
16. Lee,Younghoon, Hee-Seung Lee, Meebyein, Kim and Heegwon Shin. 2020. Brain Cytoplasmic RNAs in Neurons: From Biosynthesis to Function. *Biomolecules.*17:313. Doi:10.3390/biom10020313.
17. Qiankun, LV, Ziyu Wang, Zhen, Zhong and Wei Huang. 2020. Role of long Noncoding RNAs in Parkinson's Disease Putative Biomarkers and Therapeutic Targets. *Parkinsons Dis. Jun.* 12: 5374307. Doi:10.1155/2020/5374307.
18. Slack, Frank J. and Arul M. Chinnaiyan. 2019. The Role of Non-coding RNAs in Oncology. *Cell* 179, November 14. <https://doi.org/10.1016/j.cell.2019.10.017>.
19. Statello, Luisa , Chun-Jie Guo , Ling-Ling Chen and Maite Huarte. 2021. Gene regulation by long non-coding RNAs and its biological functions . *Nature Reviews Molecular Cell Biology* 22: 96-98.
20. Cathcart Paul, Walter Lucchesi , Silvia Ottaviani, Alex De Georgia, Justin Stebbing and Laendro Castellana. 2015. Non-coding RNAs and the control of signalling via nuclear receptor regulation in health and disease. *Best Practice & Research Clinical Endocrinology & Metabolism.* 29(4) : 529-543. <https://doi.org/10.1016/j.beem.2015.07.003>
21. Leygue, Etienne .2007. Steroid receptor RNA activator (SRA 1) : Unusual bifaceted gene products with suspected relevance to breast Cancer. *Nucl. Receipt Signal* Aug.3;5e006. Doi.10.1621/ncs.05006.
22. George, Tina P, Suja Subramanian and M. H. Supriya.2024. A brief review of non-coding RNA. *Egyptian J. of Medical Human Genetics* 25: 98. <https://doi.org/10.1186/s43042-024-00553-y>
23. Liu, Qian, Jianguo Huang, Nanjiang Zhou, Ziqiang Zhang, Ali Zhang, Zhaohui, Lu et al.2013. LncRNA loc 285194 is a p53-regulated tumo-Suppressor. *Nucleic Acid research* 41,issue9 : 4976-4987. Doi.org/10.1093/nar/gkt182.

24. Jiang Na, Xiaoyu Zhang, Xuejun Gu , Xiaozhuang Li and Lei Shang. 2021. Progress in understanding the role of lncRNA in programmed cell death. *Cell Death Discovery* 7, Article number 30. Doi.org/10.1038/s41420-021-1.
25. Gala, Kavita and Ekta Khattar. 2021. Long Non-coding RNAs at work on telomeres : Functions and Implications in cancer therapy. *Cancer Letters* Vol.502,1 April: 120-132. <https://doi.org/10.1016/j.canlet.2020.12.036>
26. Gayatri, Arun, Sarah D. Diermeier and David L. Spector. 2018. Therapeutic Targeting of Long Non-Coding RNAs in Cancer. *Trends Mol. Biol.* 24(3): 457-277. Doi:10.1016/i.i.moimed.2018.01.001
27. Jiang, Ming-Chun, Jiao-Jiao Ni, Wen-Yu Cui, Bo-ya Wang and Wei Zhuo. 2019. Emerging roles of lncRNA in cancer and therapeutic opportunities. *Ann. J. Cancer Res.* 9(7):1354-1366.
28. Tran, Ellen T, Ruchi A. Patel, Amogh Chariyamane and Ratna B. Ray. 2025. Long Non-coding RNAs as therapeutic targets in head and neck squamous cell carcinoma and clinical application. *FEBS Open Bio.* : 1419-1435. Published by John Wiley and Sons Ltd. On behalf of Federation of Biochemical Societies. doi:10.1002/2211-5463.70042.
29. Tamblin-Hopper, Phoebe, Endre Kiss-Toth, Ian Sudbery, David Young and J. Mark Wilkinson. 2024. . *J. Transl. Genetics and Genomics* 8:225-243. DOI: 10.20517/jtgg.2024.12.
30. Quinones, Noella Bellon, Ruggero Belluoma , Rio P. Juni and Reinier A. Boon. 2025. Long Non-coding RNA Based Therapy for Cardio Vascular Disease. *J. of Cardiovascular Translational Research* Published Online 3 September. <https://doi.org/10.1007/s12265-025-10686-z>