

A review: p53 relationship with long non coding RNAs (lncRNAs)

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REVIEW

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ABSTRACT: The p53 a tumor suppressor gene has been mapped to chromosome that is able to inhibits cellular proliferation and induce apoptosis in response to DNA damage. Under stress, p53 levels rise in the cell and leads to cell cycle arrest in G1 phase. Long noncoding RNAs(lncRNAs) are relatively abundant component of mammalian transcriptome. There are many Long noncoding RNA which are regulated by p53. In this review we have discussed some of the lncRNAs which are related to p53 such as MALAT1, NEAT1, LOC285194, LOC401317, PANDA, lincRNA-p21, LincRNA-ROR, lincRNA H19, MEG3 and PURPL. It is very difficult to discriminate between lncRNAs and mRNA. But there are some criteria which can be used to discriminate between protein coding genes and lncRNAs such as, lncRNA genes are shorter and have fewer numbers of exons. Exon in lncRNAs are shorter than protein coding genes. Protein coding genes have protein coding domains as demonstrated by pfam.

KEYWORDS: p53, lncRNAs, apoptosis, DNA damage

INTRODUCTION

The p53, a gene that codes for a protein which acts as transcriptional factor involves in cell cycle regulation. It is very important for cells in multicellular organisms to suppress cancer. p53 has been described as "the guardian of the genome", due to its role in preventing genome mutation [1]. The name is due to its molecular mass: it is in the 53 kDa fraction of cell proteins. In normal condition p53 is present at lower level in the cell. After stress, p53 level rises in the cell and leads to transcription of many other genes, leading to inhibition of G1/S-Cdk and S-Cdk complex arresting cell in G1 phase.

lncRNAs contain 200-100,000 nucleotides. lncRNAs exhibit an mRNA-like structure with a poly (A) tail in certain cases. lncRNA have been classified based on their location with respect to protein coding genes such as; i) Intergenic lncRNAs (lincRNA): Located between two protein-coding genes; ii) intronic lncRNAs: Transcribed from the introns of protein-coding genes; iii) overlapping lncRNAs: Contain a coding gene within an intron on the same strand; iv) antisense lncRNAs: Transcribed from the opposite of the protein-coding strand; v) processed lncRNAs: Do not contain an open reading frame (ORF) [2]. lncRNAs are a relatively abundant component of the mammalian transcriptome and have been implicated in several cellular functions, such as regulation of gene transcription by recruitment of chromatin-modifying enzymes.

It is very difficult to separate coding and non-coding transcript. However to differentiate between lncRNAs and protein coding genes, there are some criteria.. For instance, lncRNA genes are shorter than protein coding genes with less number of exons [3-5]. Exons in the lncRNAs are longer than protein coding genes [4, 6]. Most of lincRNAs have many introns in their sequences but some lincRNAs are found with single exon e.g. Malat1 and Neat1 [7]. Splicing of lincRNAs occurs inefficiently as compared to protein coding genes [8]. Mostly lincRNAs are linear but some circular isoform has been observed [9]. Many lincRNA has been found to be stabilized by triple helical structure at their 3'end [10, 11]. lncRNAs can have snoRNAs at both ends [12]. It has been found that lincRNAs are more tolerable than other portion of the genome for retrotransposon insertion.

On the other hand, Protein coding genes have known protein domains as shown in the pfam database. Protein coding region has sequence similarity to protein sequences which are found in the protein sequence alignment data bases. Expression of lncRNA is more variable than mRNA in many tissues [3-5]. The median lncRNAs level is only about a tenth than median mRNA level [3-6, 13-16].

It has been described previously in the literature that many lncRNAs are under the control of p53. These p53 associated lncRNAs may act as better biomarkers for early diagnosis and prognosis of different type of tumors. p53 regulated lncRNA have been broadly classified in to 2 groups. Group 1 are those lncRNAs serving as p53 regulators such as MALAT1, maternally expressed gene 3 (MEG3), p53-eRNAs, and Wrap53. Group1 lincRNA regulate the mRNA stability of p53 and have impact on the transcription of p53 target genes. Group 2 lincRNAs act as p53 effector for e.g. lncRNA-p21, PANDA, H19, and loc285184. lincROR is a unique that it not only suppress the DNA damage induced by p53 but also form auto regulatory loop with p53 [17]. In this review, some lncRNA are discussed which are under the control of p53 such as lincRNA-p21, LincRNA-ROR, lincRNA H19, MEG3 and PURPL, MALAT1, NEATI, LOC285194, LOC401317, PANDA.

MALAT1

MALAT1 metastasis-associated lung adenocarcinoma transcript-1 is intergenic long non coding RNA. MALAT1 size is 7kb in human having single exon. Because of depletion of MALAT1, cell cycle arrest occurs in human. Its depletion also leads to activation of p53 and its target genes [18]. It has been shown that MALAT1 lincRNA is not essential for life and development in mice [19-21]. Abundant MALAT1 isoform is non polyadenylated. It has triple helical structure at its 3' end [10, 11]. It is localized to speckles, a suborganelle inside the nucleus.

NEATI

NEAT1 is a intergenic long noncoding RNA, which is responsible for inactivation of p53 [22]. NEAT1 is found at the upstream of MALAT1 lincRNA. It is expressed in mouse and human tissues [7]. NEAT1 has 2 isoforms. 3.7 kb Men α which ends with a proposed polyadenylation site, and 22.7 kb Men β (beta). NEAT1 is localized to paraspeckles inside the nucleus. NEAT1 isoform, Men β is essential for the formation of para speckles [23]. Depletion of NEAT1 by RNAi leads to disintegration of paraspeckles [24]. Both type of NEAT1 isoform have triple helical structure at their 3' end.

LOC285194

LncRNA Loc 285194 is transcriptionally regulated by p53. Loc285194 is a lincRNA which is down regulated in many cancer types especially, osteo sarcoma in humans. Increased expression of loc285194 in vivo and in vitro leads to suppression of tumor. Loc285194 acts as tumor suppressor by inhibiting the normal function of mir-211. It has been shown previously that loc285194 act as transcription target of p53 [25].

lincRNA-p21

lincRNA-p21 is intergenic long noncoding RNA. Its size is unknown. It is directly regulated by p53. lincRNA-p21 promoter has p53 binding domain. It was further observed that lincRNA-p21 function overlap with that of p53. It was observed that lincRNA-P21 involves in p53 dependent apoptosis but not in the cell cycle arrest [26].

LOC401317

LncRNA LOC401317 is induced by p53. Over expression of lincRNA LOC401317 leads to inhibition of nasopharyngeal carcinoma cell line HNE2 cells in humans, in vivo and in vitro. It inhibits cell cycle progress by increasing p21 expression. LOC401317 leads to decreases cyclin D1 and cyclin E1 expression. It promotes apoptosis through the induction of poly(ADP-ribose) polymerase and caspase-3 cleavage. Collectively, these results suggest that LOC401317 is directly regulated by p53 and exerts antitumor effects in HNE2 nasopharyngeal carcinoma cells [27].

PANDA

PANDA (P21 associated ncRNA DNA damage activated) is 1.5 kb long and contains single exon. PANDA surrounds the transcription start site of CDKN1A. It is located ~5 kb upstream of the CDKN1A (p21) transcription start site. In human's fibroblast, it is induced by doxorubicin treatment along with CDKN1A gene. CDKN1A gene cannot directly activate the PANDA. P53 binds to CDKN1A and leads to activation of PANDA. It has been shown that PANDA cannot be activated in DNA damage without p53 [28].

LincRNA-ROR

LincRNA-ROR (lincRNA-Regulator of Reprogramming) gene with a sequence length of 2.6 kb located on chromosome 18 (hg19 chr18:54,721,802-54,739,350), consisting of four exons. It has been shown that knockdown of lincRNA-ROR leads to increase in apoptosis and activation of p53 pathway [29]. However, lincRNA-ROR has little effect on the p53 in the unstressed cells. The lincRNA-ROR form an autoregulatory loop with p53. The expression of p53 is positively regulate the expression of lincRNA- ROR. P53 interacts with p53 response element in the promoter of lincRNA-ROR. High expression of lincRNA-ROR has been observed in embryonic stem cell and iPSCs. The expression of LincRNA-ROR has been found to be regulated by transcriptional factors such as Oct4, Sox2 and Nanog [30].

lncRNA H19

lncRNA H19 size is 2.3 kb (The imprinted oncofetal long non-coding RNA) is specifically expressed in the embryos. At birth it is repressed inside the human body. But it is highly expressed in the tumors. It is expressed at all stages of human cancers. In all type of human tumors its expression is up regulated. In tumors upregulation of lncRNA H19 leads to genomic instability and hypoxia. lncRNA H19 response in tumors correlate with the functioning of tumor suppressor gene p53. The p53 suppress the promoter activity of lncRNA H19 gene [31, 32].

MEG3

The sequence length of MEG3 is 1.6kb. MEG3 is located on chromosome 14q32. MEG3 activates p53. Normally, in the cell, the level of p53 is very low due to its degradation by ubiquitin-proteasome pathway. The ubiquitin of p53 is mediated by MDM2 and E3 ubiquitin ligase. MEG3 downregulates MDM2 leading to activation of p53 [33].

PURPL

PURPL is long noncoding RNA which controls the level of p53 in the cell. Targeted depletion of PURPL in colorectal cancer cells leads to increase in the level of p53. MYBBP1A is a protein which interact and stabilize p53. PURPL interact with MYBBP1A and prevents its binding with p53 [34].

CONCLUSIONS AND FUTURE PROSPECT

There are many lncRNAs which are regulated by p53. It is need of hour to look for lncRNAs which are regulated by p53 directly. Those lncRNAs which are regulated by mutant p53 can act as biomarkers for early diagnosis and prognosis of tumors.

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Competing interests

The author declares that they have no conflict of interest.

REFERENCES

1. Strachan, T. and A.P. Read, Human molecular genetics. 2nd ed. 1999, New York: Wiley. xxiii, 576 p.
2. Zhang, R., et al., LncRNAs and cancer. *Oncol Lett*, 2016. 12(2): p. 1233-1239.
3. Cabili, M.N., et al., Integrative annotation of human large intergenic noncoding RNAs reveals global properties and specific subclasses. *Genes Dev*, 2011. 25(18): p. 1915-27.
4. Derrien, T., et al., The GENCODE v7 catalog of human long noncoding RNAs: analysis of their gene structure, evolution, and expression. *Genome Res*, 2012. 22(9): p. 1775-89.
5. Pauli, A., et al., Systematic identification of long noncoding RNAs expressed during zebrafish embryogenesis. *Genome Res*, 2012. 22(3): p. 577-91.
6. Ravasi, T., et al., Experimental validation of the regulated expression of large numbers of non-coding RNAs from the mouse genome. *Genome Res*, 2006. 16(1): p. 11-9.
7. Hutchinson, J.N., et al., A screen for nuclear transcripts identifies two linked noncoding RNAs associated with SC35 splicing domains. *BMC Genomics*, 2007. 8: p. 39.
8. Tilgner, H., et al., Deep sequencing of subcellular RNA fractions shows splicing to be predominantly co-transcriptional in the human genome but inefficient for lncRNAs. *Genome Res*, 2012. 22(9): p. 1616-25.
9. Memczak, S., et al., Circular RNAs are a large class of animal RNAs with regulatory potency. *Nature*, 2013. 495(7441): p. 333-8.
10. Brown, J.A., et al., Formation of triple-helical structures by the 3'-end sequences of MALAT1 and MENbeta noncoding RNAs. *Proc Natl Acad Sci U S A*, 2012. 109(47): p. 19202-7.
11. Wilusz, J.E., et al., A triple helix stabilizes the 3' ends of long noncoding RNAs that lack poly(A) tails. *Genes Dev*, 2012. 26(21): p. 2392-407.
12. Yin, Q.F., et al., Long noncoding RNAs with snoRNA ends. *Mol Cell*, 2012. 48(2): p. 219-30.
13. Guttman, M., et al., Chromatin signature reveals over a thousand highly conserved large non-coding RNAs in mammals. *Nature*, 2009. 458(7235): p. 223-7.
14. Guttman, M., et al., Ab initio reconstruction of cell type-specific transcriptomes in mouse reveals the conserved multi-exonic structure of lincRNAs. *Nat Biotechnol*, 2010. 28(5): p. 503-10.
15. Ulitsky, I., et al., Extensive alternative polyadenylation during zebrafish development. *Genome Res*, 2012. 22(10): p. 2054-66.
16. Sigova, A.A., et al., Divergent transcription of long noncoding RNA/mRNA gene pairs in embryonic stem cells. *Proc Natl Acad Sci U S A*, 2013. 110(8): p. 2876-81.
17. Ali, A., A.S. Shah, and A. Ahmad, Gain-of-function of mutant p53: mutant p53 enhances cancer progression by inhibiting KLF17 expression in invasive breast carcinoma cells. *Cancer Lett*, 2014. 354(1): p. 87-96.
18. Tripathi, V., et al., Long noncoding RNA MALAT1 controls cell cycle progression by regulating the expression of oncogenic transcription factor B-MYB. *PLoS Genet*, 2013. 9(3): p. e1003368.
19. Eissmann, M., et al., Loss of the abundant nuclear non-coding RNA MALAT1 is compatible with life and development. *RNA Biol*, 2012. 9(8): p. 1076-87.
20. Nakagawa, S., et al., Malat1 is not an essential component of nuclear speckles in mice. *RNA*, 2012. 18(8): p. 1487-99.
21. Zhang, B., et al., The lncRNA Malat1 is dispensable for mouse development but its transcription plays a cis-regulatory role in the adult. *Cell Rep*, 2012. 2(1): p. 111-23.
22. Adriaens, C., et al., p53 induces formation of NEAT1 lncRNA-containing paraspeckles that modulate replication stress response and chemosensitivity. *Nat Med*, 2016. 22(8): p. 861-8.
23. Sasaki, Y.T., et al., MENepsilon/beta noncoding RNAs are essential for structural integrity of nuclear paraspeckles. *Proc Natl Acad Sci U S A*, 2009. 106(8): p. 2525-30.
24. Clemson, C.M., et al., An architectural role for a nuclear noncoding RNA: NEAT1 RNA is essential for the structure of paraspeckles. *Mol Cell*, 2009. 33(6): p. 717-26.
25. Liu, Q., et al., LncRNA loc285194 is a p53-regulated tumor suppressor. *Nucleic Acids Res*, 2013. 41(9): p. 4976-87.
26. Huarte, M., et al., A large intergenic noncoding RNA induced by p53 mediates global gene repression in the p53 response. *Cell*, 2010. 142(3): p. 409-19.

27. Gong, Z., et al., LOC401317, a p53-regulated long non-coding RNA, inhibits cell proliferation and induces apoptosis in the nasopharyngeal carcinoma cell line HNE2. *PLoS One*, 2014. 9(11): p. e110674.
28. Wang, K.C. and H.Y. Chang, Molecular mechanisms of long noncoding RNAs. *Mol Cell*, 2011. 43(6): p. 904-14.
29. Loewer, S., et al., Large intergenic non-coding RNA-RoR modulates reprogramming of human induced pluripotent stem cells. *Nat Genet*, 2010. 42(12): p. 1113-7.
30. Zhang, A., et al., The human long non-coding RNA-RoR is a p53 repressor in response to DNA damage. *Cell Res*, 2013. 23(3): p. 340-50.
31. Dugimont, T., et al., The H19 TATA-less promoter is efficiently repressed by wild-type tumor suppressor gene product p53. *Oncogene*, 1998. 16(18): p. 2395-401.
32. Lee, D.F., et al., Modeling familial cancer with induced pluripotent stem cells. *Cell*, 2015. 161(2): p. 240-54.
33. Zhou, Y., X. Zhang, and A. Klibanski, MEG3 noncoding RNA: a tumor suppressor. *J Mol Endocrinol*, 2012. 48(3): p. R45-53.
34. Li, X.L., et al., Long Noncoding RNA PURPL Suppresses Basal p53 Levels and Promotes Tumorigenicity in Colorectal Cancer. *Cell Rep*, 2017. 20(10): p. 2408-2423.

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