

Long non-coding rnas; new perspective for autoimmune disease

Abstract

Long non coding RNAs (lncRNAs) are subpopulation of transcriptome that has crucial activity in cells and also molecular pathways.¹ Autoimmune diseases as immune system dysregulation have been proposed to be regulated by lncRNAs.² LncRNAs can be used as a potential prognostic and diagnostic tool in autoimmune disease, as their expression have been widely shown in particular cells and tissues in a specific time.³

Keywords: autoimmune disease, lncRNAs, TH17, immune system, TNF α , immune cells, autoimmune disorders

Volume 3 Issue 3 - 2016

Fattah Sotoodehnejadnematalahi,¹
Mohammad Hossein Khani,¹ Farshid Yeganeh
Hossein Khani²

¹Department of Biology, School of Basic Science, Science and Research Branch, Islamic Azad University, Iran

²Department of Immunology, Shahid Beheshti University of Medical Sciences, Iran

Correspondence: Fattah Sotoodehnejadnematalahi,
Department of Biology, School of Basic Science, Science and Research Branch, Islamic Azad University, Tehran, Iran,
Email Fattah212@gmail.com

Received: May 05, 2016 | **Published:** June 01, 2016

Introduction

Non coding RNAs refer to RNAs that Lack the potential to code protein.⁴ There are different categories in separation of transcriptome, the common categories separate RNAs based on size.⁵ Long non-coding RNAs (lncRNAs) are the class of transcriptome, with size larger than 200 nucleotides.⁶ The functions of these RNAs are less understood than the other part of transcriptome.⁷ There are documents that show the important role of lncRNAs in different cellular aspects such as development, epigenetic marking, chromatin remodeling and regulation of gene expression and in immune system.⁸ In the beginning of this century ncRNA of the transcriptome was considered as junk RNA that have no function at all and maybe they are transcription noise, but this concept became extinct with new information founded about this part of transcriptome.⁹ LncRNAs play important role in regulation of innate and adaptive immune responses and immune cell development.¹⁰ Recent studies have also shown the different expression of lncRNAs in autoimmune diseases.¹¹

lncRNAs and immune system

There are a different lncRNAs that has particular activity in the cell and tissue of immune system.¹² LncRNAs represent newly regulatory molecules that influence variety of function from innate to activation of adaptive immune system.¹³ It is known that the development of immune cells from hematopoietic stem cell and activation of immune cell afterward, such as cell proliferation, needs particular and key lncRNAs which participate in this manner of differentiation.¹⁰ For example THRIL lncRNA regulate the TNF α expression.¹⁴ THRIL can form a RNA-protein interaction with hnRNPL and then this complex can regulate transcription of TNF α by binding to its promoter. This is a straight action of an lncRNA on expression of a key molecule in immune system.¹⁴ Some lncRNAs suggested to be involved in differentiation of immune cells.¹⁵ One of them is lnc-DC that controls the differentiation of dendritic cells by binding to STAT3 transcription factor. Knock down of lnc-DC can cause inhibition of dendritic cells differentiation in human monocyte in vitro.¹⁶ Natural killer cells are immune cells that have roles in innate immune system.¹⁷ KIR antisense lncRNA have been suggested to have a role in silencing

the KIR gene. Killing feature of NK cells is related to KIR gene.¹⁸ In addition, development of B cells from Ancestral cell to the active B cells like memory or plasma cells shows different expression of noncoding RNAs specially lncRNAs.¹⁹

Study of individual cells isolated from tissues has indicated the specific pattern of lncRNA expression in different cells.²⁰ So this suggests that lncRNAs have cell and tissue specificity of expression which make them notable candidate to be used as new class of biomarkers for various diseases.²¹

lncRNAs and autoimmune diseases

Autoimmune diseases are well known as disorders with dysregulation of immune system responses.²² There are solid evidences about different expression of lncRNAs in patient with autoimmune disorders.²³ Some lncRNAs has been shown to be up regulated and/or down regulated in autoimmune disease.²⁴ Several investigations aiming to introduce new biomarkers have indicated strong correlation between autoimmune disease and context of lncRNA changes.²⁵ For example, the ethology of Crohn's disease which is a chronic inflammatory disorder has not yet fully understood. It has been found that DQ786243 lncRNA can be over expressed in these patients. It has been also suggested that this lncRNA might be responsible for the severity of Crohn's disease in patients.²⁶ Rheumatoid arthritis is a well-known example of autoimmune disease. It has been shown that TNF- α and Il-6 can induce lincRNAs (a subgroup of lncRNAs) in CD14⁺ of these patients. The interesting fact is the specificity of correlating between lincRNAs and each cytokine. This study suggests that such lincRNA might affect the pathogenesis of rheumatoid arthritis.^{27,28} Other study has also investigated the role of lncRNA in systemic lupus erythematosus (SLE). HIVEP2 is an lncRNA which is shown to be over expressed more than fifty times in SLE patients.²⁹ There is a lack of information about lncRNAs which are involved in multiple sclerosis (MS). Recent data suggests the association of lncRNAs and T helper 17 (TH17) lymphocytes which are well-known cells to be involved in multiple sclerosis.³⁰ Rmrp is an lncRNA found in TH17 cells showed different level of expression and indicated to cause various gene expression in this cells which might lead to

multiple sclerosis progression [30]. In addition, it has been shown that the lncRNA SAS-ZFAT plays role in autoimmune thyroid disease. SAS-ZFAT is antisense ZFAT gene. This lncRNA may have important role in susceptibility of autoimmune thyroid disease.¹¹

Study the role of lncRNAs is a growing field in disease and immune system regulation that brings hope to understand complex diseases such as autoimmune disorders. So it can be a respectable shot for targeting the immune system disorders in addition to be powerful tool for diagnosis and prognosis due to lncRNAs specificity to a type of cell or tissue.³¹

Acknowledgments

None.

Conflicts of Interest

None.

References

- Schmitz SU, Grote P, Herrmann BG. Mechanisms of long noncoding RNA function in development and disease. *Cell Mol Life Sci*. 2016;1–19.
- Li J, Xuan Z, Liu C. Long non-coding RNAs and complex human diseases. *Int J Mol Sci*. 2003;14(9):18790–18808.
- Zhou M, Zhao H, Wang Z, et al. Identification and validation of potential prognostic lncRNA biomarkers for predicting survival in patients with multiple myeloma. *J Exp Clin Cancer Res*. 2005;34(1): 1.
- Kung JT, Colognori D, Lee JT. Long noncoding RNAs: past, present, and future. *Genetics*. 2013;193(3):651–669.
- Quinn JJ, Chang HY. Unique features of long non-coding RNA biogenesis and function. *Nat Rev Genet*. 2013;17(1): 47–62.
- Cao J. The functional role of long non-coding RNAs and epigenetics. *Biol Proced Online*. 2014;16(1):1.
- Monya B. Long noncoding RNAs: the search for function. *Nature methods*. 2011;8(5):379–383.
- Sun M, Kraus WL. From discovery to function: the expanding roles of long noncoding RNAs in physiology and disease. *Endocrine reviews*. 2014;36(1):25–64.
- Palazzo AF, Lee ES. Non-coding RNA: what is functional and what is junk? *Front Genet*. 2015;6:2.
- Aune TM, Spurlock CF. Long non-coding RNAs in innate and adaptive immunity. *Virus research*. 2015;212:146–160.
- Wu GC, Pan HF, Leng RX, et al. Emerging role of long noncoding RNAs in autoimmune diseases. *Autoimmunity reviews*. 2015;14(9):798–805.
- Heward JA, Lindsay MA. Long non-coding RNAs in the regulation of the immune response. *Trends in immunology*. 2004;35(9):408–419.
- Zhang Y, Cao X. Long noncoding RNAs in innate immunity. *Cellular & molecular immunology*. 2005;13(2):138–147.
- Li Z, Chao TC, Chang KY, et al. The long noncoding RNA THRIL regulates TNF α expression through its interaction with hnRNPL. *Proc Natl Acad Sci U S A*. 2004;111(3):1002–1007.
- Gene H, Tan XD. Functional diversity of long non-coding RNAs in immune regulation. *Genes & Diseases*. 2016;3(1):72–81.
- Wang P, Xue Y, Han Y, et al. The STAT3-binding long noncoding RNA lnc-DC controls human dendritic cell differentiation. *Science*. 2014;344(6181):310–313.
- Vivier E, Tomasello E, Baratin M, et al. Functions of natural killer cells. *Nature immunology*. 2008;9(5):503–510.
- Wright PW, Huehn A, Cichocki F, et al. Identification of a KIR antisense lncRNA expressed by progenitor cells. *Genes & immunity*. 2013;14(7):427–433.
- Petri A, Dybkær K, Bøgsted M, et al. Long Noncoding RNA Expression during Human B-Cell Development. *PLoS one*. 2005;10(9):e0138236.
- Liu SJ, Nowakowski TJ, Pollen AA, et al. Single-cell analysis of long non-coding RNAs in the developing human neocortex. *Genome Biol*. 2006;17(1):67.
- Shi T, Gao G, Cao Y. Long Noncoding RNAs as Novel Biomarkers Have a Promising Future in Cancer Diagnostics. *Disease Markers*. 2006;2016:10.
- Cho JH, Feldman M. Heterogeneity of autoimmune diseases: pathophysiologic insights from genetics and implications for new therapies. *Nature medicine*. 2015;21(7):730–738.
- Scaria V. Joining the long shots: emerging evidence on the role of long noncoding RNAs in rheumatoid arthritis. *Int J Rheum Dis*. 2014;17(8):831–833.
- Hrdlickova B, Kumar V, Kanduri K, et al. Expression profiles of long non-coding RNAs located in autoimmune disease-associated regions reveal immune cell-type specificity. *Genome med*. 2014;6(10):1-14.
- Stachurska A, Zorro MM, van der Sijde MR, et al. Small and long regulatory RNAs in the immune system and immune diseases. *Front Immunol*. 2004;5:513.
- Qiao YQ, Huang ML, Xu AT, et al. LncRNA DQ786243 affects Treg related CREB and Foxp3 expression in Crohn's disease. *J Biomed Sci*. 2004;20(1):87.
- Park JY, Pillinger MH. Interleukin-6 in the pathogenesis of rheumatoid arthritis. *Bull NYU Hosp Jt Dis*. 2007;65(Suppl 1):S4–S10.
- Müller N, Döring F, Klapper M, et al. Interleukin-6 and Tumour Necrosis Factor- α differentially regulate lincRNA transcripts in cells of the innate immune system *in vivo* in human subjects with rheumatoid arthritis. *Cytokine*. 2014;68(1):65–68.
- Shi L, Zhang Z, Yu AM, et al. The SLE transcriptome exhibits evidence of chronic endotoxin exposure and has widespread dysregulation of non-coding and coding RNAs. *PLoS one*. 2004;9(5):e93846.
- Huang W, Thomas B, Flynn RA, et al. DDX5 and its associated lncRNA Rmrp modulate TH17 cell effector functions. *Nature*. 2015;528(7583):517–522.
- Lin X, Lo HC, Wong DT, et al. Noncoding RNAs in human saliva as potential disease biomarkers. *Front Genet*. 2015;6:175.