Exploration of Immunology

Open Exploration

Open Access Mini Review

Long-chain noncoding RNA *NEAT1* and autoimmune diseases

Cheng Bao[1†], Li-Li Tian[2†], Xiao-Liu Li[2], Min Xu[2], Hong-Wei Chen[1,3*]

[1]Department of Rheumatology and Immunology, Joint Institute of Nanjing Drum Tower Hospital for Life and Health, College of Life Science, Nanjing Normal University, Nanjing 210023, Jiangsu, China

[2]Department of Rheumatology and Immunology, Nanjing Drum Tower Hospital, Clinical College of Nanjing University of Chinese Medicine, Nanjing 210008, Jiangsu, China

[3]Department of Rheumatology and Immunology, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing 210008, Jiangsu, China

[†]These authors contributed equally to this work.

***Correspondence:** Hong-Wei Chen, Department of Rheumatology and Immunology, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, No. 321 Zhongshan Road, Nanjing 210008, Jiangsu, China. chenhw@nju.edu.cn

Academic Editor: Sofia Kossida, The International ImMunoGeneTics Information System, France

Received: July 17, 2024 **Accepted:** September 23, 2024 **Published:** October 18, 2024

Cite this article: Bao C, Tian LL, Li XL, Xu M, Chen HW. Long-chain noncoding RNA *NEAT1* and autoimmune diseases. Explor Immunol. 2024;4:616–23. https://doi.org/10.37349/ei.2024.00162

Abstract

Autoimmune diseases result from the immune system's response to autoantigen components, leading to damage to one's own tissues and organs. The correlation between long noncoding RNAs (lncRNAs) and autoimmune diseases remains inconclusive. However, recent studies have revealed that the lncRNA nuclear paraspeckle assembly transcript 1 (*NEAT1*) plays a vital role in the development of various autoimmune diseases. Here, this review briefly summarizes the progress in understanding *NEAT1* expression variations and related mechanisms in different autoimmune diseases, and discusses its potential use for future therapeutic applications.

Keywords

Nuclear paraspeckle assembly transcript 1, autoimmune disease, systemic lupus erythematosus

Introduction

When the human body is exposed to various factors, such as viral infection, aberrant secretion of immune factors, and genetic predispositions, a reduction in the immune system's tolerance toward its own antigenic components occurs [1]. Consequently, this triggers a pathological autoimmune response characterized by the production of numerous autoantibodies and immune complexes, resulting in tissue damage and organ dysfunction. This condition is referred to as an autoimmune disease. On the basis of the extent of organ and tissue involvement, these diseases can be classified into either organ-specific or systemic autoimmune diseases, such as autoimmune hepatitis and primary biliary cholangitis, or systemic autoimmune diseases, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and scleroderma. In 1999, autoimmune diseases were classified by the World Health Organization as the third leading cause of mortality, following cardiovascular diseases and cancers. Moreover, they were also included in China's

medium- and long-term science and technology programs as one of the top ten major diseases. Globally, the overall incidence rate of autoimmune diseases is approximately 0.09% [2], and the prevalence ranges from 7.6% to 9.4% [3]. The incidence and prevalence of this disease vary significantly depending on the specific type of autoimmune disease. Nevertheless, there has been a general upward trend in their occurrence over recent decades.

Long noncoding RNAs (lncRNAs) are functional RNA molecules that lack protein translation ability. Initially, it was thought that lncRNAs do not have a biological function. However, with in-depth studies in the last decade, lncRNAs have been found to be functionally diverse and highly specific in controlling immune cell differentiation, and function. Among them, nuclear paraspeckle assembly transcript 1 (*NEAT1*), a widely known lncRNA, has been shown to be involved in viral infection [4], neurodegenerative diseases [5], autoimmune diseases [6], inflammatory diseases, cancers [7] and many other diseases. Hence, we address the current understanding of the relationship between *NEAT1* and autoimmune diseases in this review.

Overview of *NEAT1*

NEAT1 serves as the central component of membraneless subcellular organelles known as paraspeckles. Paraspeckles are composed of the lncRNA *NEAT1* and a variety of RNA-binding proteins located in the interchromosomal region of mammalian cells. *NEAT1*, as the main component, is essential for the formation of paraspeckles. It plays a supporting role in the nucleus and regulates gene expression [8]. These dynamic ribonucleoprotein complexes (RNPs) in paraspeckles play crucial roles in regulating transcription by sequestering specific proteins and RNA molecules, thereby influencing RNA processing. Additionally, *NEAT1* functions as a molecular sponge for various microRNAs, impacting downstream RNA function [9, 10]. As discovered in 2007, the lncRNA *NEAT1* is transcribed by Pol II from the MENI site on human chromosome 11q13 and is essential for the structural formation, and stability of paraspeckles [11]. Unlike many other lncRNAs that have limited expression and tissue specificity, *NEAT1* is abundantly expressed and can be upregulated to promote paraspeckle formation during certain developmental stages, and during cellular stress [12].

There are two transcript isoforms of *NEAT1*, NEAT1_1 (3.7 kb) and NEAT1_2 (23 kb), in humans, with the former being completely contained within the latter. *NEAT1* contains three RNA domains, A, B, and C, which are involved in stabilization, isomer conversion, and paraspeckle assembly [13]. Both NEAT1_1 and NEAT1_2 are encoded by a single exon. While NEAT1_2 is confined to the nucleus, NEAT1_1 has been detected in both the cytoplasm and nucleus of acute myeloid leukemia (AML) cells [14]. NEAT1_1 is expressed in most human tissues, whereas NEAT1_2 expression is tissue-specific. Although the biological function of *NEAT1* is attributed mainly to NEAT1_2, which is located in the nucleus and participates in the formation of paraspeckles, and the regulation of gene expression, NEAT1_1 exists predominantly in the cytoplasm of cells, affecting posttranscriptional regulation [15]. *NEAT1* is regulated by a variety of transcription factors, such as p53, HIF1α, ERα, Oct4, and ATF2, under different conditions [8, 16–18]. The two transcripts share the same 5' end. Moreover, NEAT1_1 possesses a classical polyadenosine signal (PAS) at its 3' end, whereas NEAT1_2 lacks a typical poly(A) tail but features a characteristic triple helix structure at its 3' end. Notably, the middle domain element of NEAT1_2 can recruit 54 kD nuclear RNA- and DNA-binding protein (p54nrb), which is also known as non-POU-domain-containing octamer-binding protein (NONO), to initiate the formation of paraspeckles [8]. These transcripts exhibit significant differences in biogenesis and processing, subnuclear localization, and gene expression.

Research progress on the role of *NEAT1* in autoimmune diseases

NEAT1 and SLE

SLE is a chronic autoimmune disease characterized by multisystem damage that can affect the skin, serous membranes, joints, kidneys, central nervous system, etc. The pathological manifestation involves the deposition of autoantibodies and immune complexes [19], the exact cause of which remains incompletely

understood. Studies have revealed significantly elevated expression of *NEAT1* in the peripheral blood mononuclear cells (PBMCs) of patients with SLE compared with healthy individuals. *NEAT1* is upregulated in monocytes, one of the major components of the innate immune system, and its expression is stimulated by lipopolysaccharide (LPS) via the p38-mediated pathway, which promotes the activation of mitogen-activated protein kinases (MAPK) and increases the expression of the cytokines IL-6 and CXCL10. Additionally, the downregulation of *NEAT1* inhibits the expression of chemokines and cytokines such as IL-6 and CXCL10, resulting in a positive correlation between them [20]. As a competitive endogenous RNA, *NEAT1* can serve as a sponge to bind with miR-365a-3p, effectively promoting the expression and secretion of IL-6 in monocyte-derived dendritic cells (moDCs) [21]. In addition, the expression of *NEAT1* in the PBMCs of SLE patients is significantly increased, which disrupts the balance of Th1 and Th2 cells, increases the proportion of Th2 cells, promotes the secretion of IL-4, and ultimately enhances the body's immune response [22]. However, excessive production of chemokines and cytokines may play a role in SLE pathogenesis.

Furthermore, Dong et al. [23] reported a correlation between the pathogenesis of SLE and the activation of interferon (IFN)-I signaling in B cells. Moreover, *NEAT1* was overexpressed in granulocyte-myeloid-derived suppressor cells (G-MDSCs) from MRL/lpr mice. G-MDSCs with elevated *NEAT1* expression were found to secrete B-cell activating factor (BAFF), subsequently inhibiting the expression of suppressor of cytokine signaling-3 (*SOCS-3*). This dysregulation ultimately leads to abnormal activation of the IFN-I signaling pathway in B cells and consequently contributes to the development of SLE. More directly, in their pristane-induced lupus mouse model, the lack of *NEAT1* alleviated lupus symptoms, reducing urinal protein levels, spleen size, the serum level of anti-dsDNA antibody, kidney infiltration by immune cells, and IgG and IgM deposition in the glomerulus.

NEAT1 and RA

RA is another chronic systemic autoimmune disease primarily characterized by progressive joint erosion and destruction, with the main pathological changes being synovial inflammation, cartilage matrix damage, and marginal bone invasion [24]. Studies indicate that the lncRNA *NEAT1* is significantly upregulated not only in the PBMCs of patients with RA [25] but also in the synovial tissues of patients with RA and in fibroblast-like synoviocytes (FLSs) [26]. miR-23a, a member of the miR-23a-27a-24-2 cluster, is capable of regulating cellular motility, cellular activation, and immune cell infiltration [27]. Moreover, the lncRNA *NEAT1* can inhibit the expression of miR-23a [28]. Murine double minute-2 (*MDM2*) is the downstream target gene of miR-23a, and its ubiquitination can decrease the expression of sirtuin 6 (*SIRT6*) during the onset of RA [29]. Previously, Kawahara et al. [30] reported that *SIRT6* can inhibit the activation of the nuclear factor κB (NF-κB) signaling pathway by reducing the acetylation level of histone 3 lysine 9 (*H3K9*) in downstream target genes of NF-κB. Similarly, *SIRT6* plays a crucial role in the regulation of FLS, which is a pivotal regulator of RA and a major contributor to synovial hyperplasia [31].

In addition, the differentiation of $CD4^+$ T cells into Th17 cells is an important factor affecting the occurrence and development of RA. Liu et al. [32] reported that the lncRNA *NEAT1* was significantly downregulated in activated $CD4^+$ T lymphocytes but was moderately upregulated during the differentiation of $CD4^+$ T cells to Th17 cells *in vitro*. In contrast, Shui et al. [33] reported that the knockdown of *NEAT1* reduced the protein level of *STAT3*, a key transcription factor for Th17 cell differentiation, which in turn inhibited the differentiation of $CD4^+$ T cells into Th17 cells and blocked the development of RA.

NEAT1 and psoriasis

Psoriasis is an immune-mediated, chronic inflammatory skin disease characterized by recurrent squamous erythema or plaques that can be localized or widespread. The etiology of psoriasis is multifactorial and involves both environmental and genetic factors. Furthermore, keratinocytes exhibit abnormal hyperproliferation and differentiation in response to nonspecific stimuli such as microbial infection, chemical stimulation, and trauma, leading to the development of this disease [34].

Recent studies have demonstrated significant upregulation of the lncRNA *NEAT1* in 3 mm deep psoriatic lesion tissue samples, which is positively correlated with the expression levels of inflammatory factors, including IL-6, IL-8, TNF-α, IL-17, and IL-22 [35]. Conversely, the lncRNA *NEAT1* is expressed at low levels in the skin tissues of patients with psoriasis. Wang et al. [36] reported that upregulation of NEAT1 resulted in the targeted mediation of downstream miR-3194-5p to increase Galectin-7 expression, which subsequently inhibited the activity of psoriasis HaCat cells and exhibited therapeutic effects. In a mouse model of psoriasis, high expression of *NEAT1* and *STAT3* was observed in skin lesion tissue from the model group, whereas miR-485-5p was expressed at low levels due to complementary binding sites with *NEAT1* [37]. Notably, *STAT3* plays crucial roles in various pathophysiological processes associated with psoriasis, including Th17 cell differentiation, epidermal cell hyperproliferation, and abnormal differentiation, abnormal dermal vascular hyperplasia, and inflammatory cell infiltration [38].

NEAT1 and multiple sclerosis

Chronic autoimmune disease of the central nervous system, known as multiple sclerosis (MS), is mediated primarily by $CD4^+$ T cells and characterized by spatial and temporal multiplicity. It predominantly affects young and middle-aged individuals, with a higher prevalence among women. The primary clinical manifestations are inflammatory demyelination and neuronal degeneration [39].

Dysregulation of Th17 and Treg populations is pivotal in the pathogenesis of MS. Furthermore, *FOXP3* exerts a regulatory effect on Treg cell stability, and its reduced expression hampers Treg cell differentiation, thereby disrupting immune cell balance and homeostasis. A study demonstrated significant upregulation of *NEAT1* expression in PBMCs from MS patients, concomitant with decreased *FOXP3* expression. RNA sequencing (RNA-seq) analysis also revealed greater *NEAT1* expression in effector Th17 cells than in primary Th17 cells [40]. Th1/Th2 imbalances are commonly observed in individuals with autoimmune diseases such as psoriasis and RA. In the context of MS, both Th1-related TNF-α and Th17-related IL-17 are positively correlated with *NEAT1* levels, greatly increasing susceptibility to MS [41].

Conclusions

In recent years, the investigation of lncRNAs in autoimmune diseases has garnered increasing attention. Concurrently, numerous studies have substantiated the highly specific role of lncRNAs in regulating immune cell differentiation and function. Dysregulation of the lncRNA *NEAT1*, whether through overexpression or underexpression, is implicated in the pathogenesis and progression of various autoimmune diseases (Table 1). Therefore, further elucidating its regulatory mechanisms is crucial for uncovering the underlying mechanisms of autoimmune diseases. Targeting the lncRNA *NEAT1* as a therapeutic approach for autoimmune diseases represents not only a practical and reliable novel endeavor but also a promising direction.

Table 1. Role of *NEAT1* in different autoimmune diseases

Disease type	Effects of *NEAT1*	Reference
Systemic lupus erythematosus	Upregulation of the activation of MAPK signaling pathway in TLR4-mediated inflammatory process;	Zhang et al. [20]
	Upregulation of chemokines and cytokines;	Xiang et al. [21]
	Abnormal activation of IFN-I signaling.	Dong et al. [23]
Rheumatoid arthritis (RA)	Regulating glutamine metabolism and FLSs-RA dysfunction in FLSs of RA;	Wang et al. [26]
	Influencing FLSs physiological function by inhibiting miR-23a expression;	Wade et al. [27] and Zhao et al. [28]
	Regulating the NF-κB signaling pathway;	Kawahara et al. [30]
	Influence of $CD4^+$ T cells differentiation into Th17 cells;	Liu et al. [32] and Shui et al. [33]
	RA aggravation via p300/CBP/IL-18 axis.	Guo et al. [6]

Table 1. Role of *NEAT1* in different autoimmune diseases (*continued*)

Disease type	Effects of *NEAT1*	Reference
Psoriasis	Upregulation of inflammatory factors;	Jin et al. [35]
	Controlling the proliferation and differentiation of epidermal cells by interacting with miRNA.	Wang et al. [36] and Tang et al. [37]
Multiple sclerosis	Regulating the imbalance of Th1/Th2;	Karimi et al. [40]
	Upregulation of TNF-α and IL-17.	Li et al. [41]

NEAT1: nuclear paraspeckle assembly transcript 1; MAPK: mitogen-activated protein kinases; FLSs: fibroblast-like synoviocytes; NF-κB: nuclear factor κB

Abbreviations

G-MDSCs: granulocyte-myeloid-derived suppressor cells

IFN: interferon

lncRNAs: long noncoding RNAs

MS: multiple sclerosis

NEAT1: nuclear paraspeckle assembly transcript 1

NF-κB: nuclear factor κB

PBMCs: peripheral blood mononuclear cells

RA: rheumatoid arthritis

SIRT6: sirtuin 6

SLE: systemic lupus erythematosus

Declarations

Author contributions

CB, LLT, XLL, and MX wrote the manuscript. HWC designed the review and was responsible for the final proofreading. All the authors read and approved the final manuscript.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

This work was supported by the National Natural Science Foundation of China No. [82271843]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

1. Miller FW. The increasing prevalence of autoimmunity and autoimmune diseases: an urgent call to action for improved understanding, diagnosis, treatment, and prevention. Curr Opin Immunol. 2023; 80:102266. [DOI] [PubMed] [PMC]
2. Cooper GS, Stroehla BC. The epidemiology of autoimmune diseases. Autoimmun Rev. 2003;2:119–25. [DOI] [PubMed]
3. Cooper GS, Bynum MLK, Somers EC. Recent insights in the epidemiology of autoimmune diseases: improved prevalence estimates and understanding of clustering of diseases. J Autoimmun. 2009;33: 197–207. [DOI] [PubMed] [PMC]
4. Wang Z, Fan P, Zhao Y, Zhang S, Lu J, Xie W, et al. NEAT1 modulates herpes simplex virus-1 replication by regulating viral gene transcription. Cell Mol Life Sci. 2017;74:1117–31. [DOI] [PubMed] [PMC]
5. An H, Williams NG, Shelkovnikova TA. NEAT1 and paraspeckles in neurodegenerative diseases: A missing lnc found? Noncoding RNA Res. 2018;3:243–52. [DOI] [PubMed] [PMC]
6. Guo T, Xing Y, Chen Z, Zhu H, Yang L, Xiao Y, et al. Long Non-Coding RNA NEAT1 Knockdown Alleviates Rheumatoid Arthritis by Reducing IL-18 through p300/CBP Repression. Inflammation. 2022;45: 100–15. [DOI] [PubMed]
7. Park MK, Zhang L, Min KW, Cho JH, Yeh CC, Moon H, et al. *NEAT1* is essential for metabolic changes that promote breast cancer growth and metastasis. Cell Metab. 2021;33:2380–97.e9. [DOI] [PubMed] [PMC]
8. Wang Y, Hu S, Wang MR, Yao RW, Wu D, Yang L, et al. Genome-wide screening of NEAT1 regulators reveals cross-regulation between paraspeckles and mitochondria. Nat Cell Biol. 2018;20:1145–58. [DOI] [PubMed]
9. Knutsen E, Harris AL, Perander M. Expression and functions of long non-coding RNA *NEAT1* and isoforms in breast cancer. Br J Cancer. 2022;126:551–61. [DOI] [PubMed] [PMC]
10. Pan Y, Wang T, Zhao Z, Wei W, Yang X, Wang X, et al. Novel Insights into the Emerging Role of Neat1 and Its Effects Downstream in the Regulation of Inflammation. J Inflamm Res. 2022;15:557–71. [DOI] [PubMed] [PMC]
11. Ghafouri-Fard S, Taheri M. *Nuclear Enriched Abundant Transcript 1* (*NEAT1*): A long non-coding RNA with diverse functions in tumorigenesis. Biomed Pharmacother. 2019;111:51–9. [DOI] [PubMed]
12. Fox AH, Nakagawa S, Hirose T, Bond CS. Paraspeckles: Where Long Noncoding RNA Meets Phase Separation. Trends Biochem Sci. 2018;43:124–35. [DOI] [PubMed]
13. Hirose T, Yamazaki T, Nakagawa S. Molecular anatomy of the architectural NEAT1 noncoding RNA: The domains, interactors, and biogenesis pathway required to build phase-separated nuclear paraspeckles. Wiley Interdiscip Rev RNA. 2019;10:e1545. [DOI] [PubMed]
14. Yan H, Wang Z, Sun Y, Hu L, Bu P. Cytoplasmic NEAT1 Suppresses AML Stem Cell Self-Renewal and Leukemogenesis through Inactivation of Wnt Signaling. Adv Sci (Weinh). 2021;8:e2100914. [DOI] [PubMed] [PMC]
15. Zhang Y, Luo M, Cui X, O'Connell D, Yang Y. Long noncoding RNA NEAT1 promotes ferroptosis by modulating the miR-362-3p/MIOX axis as a ceRNA. Cell Death Differ. 2022;29:1850–63. [DOI] [PubMed] [PMC]
16. Chakravarty D, Sboner A, Nair SS, Giannopoulou E, Li R, Hennig S, et al. The oestrogen receptor alpha-regulated lncRNA NEAT1 is a critical modulator of prostate cancer. Nat Commun. 2014;5:5383. [DOI] [PubMed] [PMC]
17. Choudhry H, Mole DR. Hypoxic regulation of the noncoding genome and NEAT1. Brief Funct Genomics. 2016;15:174–85. [DOI] [PubMed] [PMC]

18. Jen J, Tang YA, Lu YH, Lin CC, Lai WW, Wang YC. Oct4 transcriptionally regulates the expression of long non-coding RNAs *NEAT1* and *MALAT1* to promote lung cancer progression. Mol Cancer. 2017;16:104. [DOI] [PubMed] [PMC]
19. Yu H, Nagafuchi Y, Fujio K. Clinical and Immunological Biomarkers for Systemic Lupus Erythematosus. Biomolecules. 2021;11:928. [DOI] [PubMed] [PMC]
20. Zhang F, Wu L, Qian J, Qu B, Xia S, La T, et al. Identification of the long noncoding RNA NEAT1 as a novel inflammatory regulator acting through MAPK pathway in human lupus. J Autoimmun. 2016;75:96–104. [DOI] [PubMed]
21. Xiang M, Wang Y, Chen Q, Wang J, Gao Z, Liang J, et al. LncRNA *NEAT1* promotes IL-6 secretion in monocyte-derived dendritic cells via sponging *miR-365a-3p* in systemic lupus erythematosus. Epigenetics. 2023;18:2226492. [DOI] [PubMed] [PMC]
22. Jiang Y, Zhao Y, Mo X. Expression of lncRNA NEAT1 in peripheral blood mononuclear cells of patients with systemic lupus erythematosus and its correlation with Th1/Th2 balance. Int J Clin Exp Pathol. 2021;14:646–52. [PubMed] [PMC]
23. Dong G, Yang Y, Li X, Yao X, Zhu Y, Zhang H, et al. Granulocytic myeloid-derived suppressor cells contribute to IFN-I signaling activation of B cells and disease progression through the lncRNA NEAT1-BAFF axis in systemic lupus erythematosus. Biochim Biophys Acta Mol Basis Dis. 2020;1866:165554. [DOI] [PubMed]
24. Cush JJ. Rheumatoid Arthritis: Early Diagnosis and Treatment. Med Clin North Am. 2021;105:355–65. [DOI] [PubMed]
25. Song J, Kim D, Han J, Kim Y, Lee M, Jin EJ. PBMC and exosome-derived Hotair is a critical regulator and potent marker for rheumatoid arthritis. Clin Exp Med. 2015;15:121–6. [DOI] [PubMed]
26. Wang Y, Hou L, Yuan X, Xu N, Zhao S, Yang L, et al. LncRNA NEAT1 Targets Fibroblast-Like Synoviocytes in Rheumatoid Arthritis via the miR-410-3p/YY1 Axis. Front Immunol. 2020;11:1975. [DOI] [PubMed] [PMC]
27. Wade SM, Trenkmann M, McGarry T, Canavan M, Marzaioli V, Wade SC, et al. Altered expression of microRNA-23a in psoriatic arthritis modulates synovial fibroblast pro-inflammatory mechanisms via phosphodiesterase 4B. J Autoimmun. 2019;96:86–93. [DOI] [PubMed]
28. Zhao C, Wang S, Zhao Y, Du F, Wang W, Lv P, et al. Long noncoding RNA NEAT1 modulates cell proliferation and apoptosis by regulating miR-23a-3p/SMC1A in acute myeloid leukemia. J Cell Physiol. 2019;234:6161–72. [DOI] [PubMed]
29. Thirumurthi U, Shen J, Xia W, LaBaff AM, Wei Y, Li CW, et al. MDM2-mediated degradation of SIRT6 phosphorylated by AKT1 promotes tumorigenesis and trastuzumab resistance in breast cancer. Sci Signal. 2014;7:ra71. [DOI] [PubMed] [PMC]
30. Kawahara TL, Michishita E, Adler AS, Damian M, Berber E, Lin M, et al. SIRT6 links histone H3 lysine 9 deacetylation to NF-kappaB-dependent gene expression and organismal life span. Cell. 2009;136:62–74. [DOI] [PubMed] [PMC]
31. Engler A, Niederer F, Klein K, Gay RE, Kyburz D, Camici GG, et al. SIRT6 regulates the cigarette smoke-induced signalling in rheumatoid arthritis synovial fibroblasts. J Mol Med (Berl). 2014;92:757–67. [DOI] [PubMed]
32. Liu H, Hu PW, Couturier J, Lewis DE, Rice AP. HIV-1 replication in $CD4^+$ T cells exploits the down-regulation of antiviral NEAT1 long non-coding RNAs following T cell activation. Virology. 2018;522:193–98. [DOI] [PubMed] [PMC]
33. Shui X, Chen S, Lin J, Kong J, Zhou C, Wu J. Knockdown of lncRNA NEAT1 inhibits Th17/$CD4^+$ T cell differentiation through reducing the STAT3 protein level. J Cell Physiol. 2019;234:22477–84. [DOI] [PubMed]
34. Deng Y, Chang C, Lu Q. The Inflammatory Response in Psoriasis: a Comprehensive Review. Clin Rev Allergy Immunol. 2016;50:377–89. [DOI] [PubMed]

35. Jin Z, Li CH, Cheng Y, Su H, Fu T. The Expression of lncRNA NEAT1 and its Correlations with Disease Activity and Inflammatory Factors Level in Psoriasis Patients. J Fujian Med Univ. 2020;54:8–12. Chinese.
36. Wang D, Cheng S, Zou G, Ding X. Paeoniflorin inhibits proliferation and migration of psoriatic keratinocytes via the lncRNA NEAT1/miR-3194-5p/Galectin-7 axis. Anticancer Drugs. 2022;33: e423–33. [DOI] [PubMed]
37. Tang ZM, Jing MQ, Lu L, Shan X, Zhang CX, Zhang XY, et al. Effect of Xidi Liangxue recipe on the proliferation and apoptosis of HaCaT cells through the lncRNA NEAT1/miR-485-5p/STAT3 regulatory network. Chin J Dermatol. 2023;56:642–50. Chinese. [DOI]
38. Chen YW, Su T, Su ZL. Association between psoriasis and STAT3. Chin J Dermatol. 2019;52:502–5. Chinese. [DOI]
39. Hemmer B, Kerschensteiner M, Korn T. Role of the innate and adaptive immune responses in the course of multiple sclerosis. Lancet Neurol. 2015;14:406–19. [DOI] [PubMed]
40. Karimi E, Azari H, Tahmasebi A, Nikpoor AR, Negahi AA, Sanadgol N, et al. LncRNA-miRNA network analysis across the Th17 cell line reveals biomarker potency of lncRNA NEAT1 and KCNQ1OT1 in multiple sclerosis. J Cell Mol Med. 2022;26:2351–62. [DOI] [PubMed] [PMC]
41. Li X, Ye S, Lu Y. *Long non-coding RNA NEAT1* overexpression associates with increased exacerbation risk, severity, and inflammation, as well as decreased lung function through the interaction with *microRNA-124* in asthma. J Clin Lab Anal. 2020;34:e23023. [DOI] [PubMed] [PMC]