Heliyon 10 (2024) e27307

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Review article

The role of ncRNAs in depression

Xinchi Luan [a,b,1], Han Xing [a,b,1], Feifei Guo [a,1], Weiyi Liu [a,b], Yang Jiao [a,b], Zhenyu Liu [a,b], Xuezhe Wang [a,b], Shengli Gao [c,*]

[a] Department of Physiology and Pathophysiology, School of Basic Medicine, Qingdao University, Qingdao, Shandong, China
[b] Department of Clinical Medicine, Qingdao Medical College, Qingdao University, Qingdao, Shandong, China
[c] Biomedical Center, Qingdao Medical College, Qingdao University, Qingdao, Shandong, China

ARTICLE INFO

Keywords:
NcRNAs
Depression
MicroRNA
Biomarker
Mechanism

ABSTRACT

Depressive disorders have a significant impact on public health, and depression have an unsatisfactory recurrence rate and are challenging to treat. Non-coding RNAs (ncRNAs) are RNAs that do not code protein, which have been shown to be crucial for transcriptional regulation. NcRNAs are important to the onset, progress and treatment of depression because they regulate various physiological functions. This makes them distinctively useful as biomarkers for diagnosing and tracking responses to therapy among individuals with depression. It is important to seek out and summarize the research findings on the impact of ncRNAs on depression since significant advancements have been made in this area recently. Hence, we methodically outlined the findings of published researches on ncRNAs and depression, focusing on microRNAs. Above all, this review aims to improve our understanding of ncRNAs and provide new insights of the diagnosis and treatment of depression.

1. Introduction

Depression (known as major depressive disorder or MDD), one of the most widespread and painful disorders affecting people's personal and public health, has been deemed to have an unsatisfactory recurrence rate and to be challenging to treat [1,2]. It not only places a heavy financial burden on families and affected individuals but also has a detrimental effect on their quality of life [3,4]. However, the mechanisms behind depression's development remain poorly understood, and the precise diagnostic markers of depression are difficult to determine, so many patients are still not helped by the available medications [5,6]. Recently, more and more studies on non-coding RNAs (ncRNAs) have been conducted in the context of depression, suggesting their great potential in the pathogenesis, diagnostic detection and clinical treatment of depression [7].

NcRNA refers to non-coding RNA molecules transcribed from the genome, which do not encode proteins. In general, ncRNAs can be categorized into two groups: housekeeping ncRNAs and regulatory ncRNAs. The housekeeping ncRNAs, ranging from 50 to 500 nucleotides (nt) in size, are ubiquitously expressed across all cell types and play an indispensable role in maintaining cellular viability. Examples of such essential ncRNAs include ribosomal RNA (rRNA) and transfer RNA (tRNA). On the other hand, regulatory ncRNAs can be further classified into small non-coding RNAs (sncRNAs) and long non-coding RNAs (lncRNAs), depending on whether their lengths exceed 200 nt. Among them, sncRNA comprises microRNAs (miRNAs), small interfering RNAs (siRNAs), and other similar

* Corresponding author.
E-mail address: witft@163.com (S. Gao).
[1] These authors contributed equally.

https://doi.org/10.1016/j.heliyon.2024.e27307
Received 29 June 2023; Received in revised form 27 February 2024; Accepted 27 February 2024
Available online 6 March 2024

molecules. However, certain ncRNAs with variable lengths, such as circular RNAs (circRNAs), may fall into both categories [8].

Recently, an increasing number of studies have revealed a strong correlation between non-coding RNAs and depression. Specifically, certain circRNAs function as miRNA sponges to shield them from pathogenic factors. Moreover, several ncRNAs are promising diagnostic targets for the treatment of depression [8].

The ncRNAs we focus on are miRNA, siRNA, lncRNA and circRNA, which are crucial for transcriptional regulation [9]. NcRNAs have become a very hot area in biomedical research, and high-throughput genome technology has been expanding quickly. There have been numerous clinical uses and studies of the mechanisms of ncRNAs. Specifically, they serve as biomarkers for diagnosing depression and anxiety and tracking therapeutic responses to these conditions [10]. A lot of recent research has proved the relationship between ncRNAs and depression [11,12]. For instance, siRNA can be an effective experimental tool to study depression [13]. MiRNA can be thought of as a peripheral indicator of diagnosis and therapeutic response [14–16].

Additionally, the available types of databases and tools are expanding. Native and denaturing NcRNA purification technologies are becoming more common and advanced, collecting or combining basic annotations and functional information from ncRNA transcripts [17,18]. The development of common computational methods for the detection of ncRNAs and common statistical tools for their analysis is also progressing [19]. These developing technologies have brought us countless conveniences.

A potential association between the dysregulation of ncRNAs and the onset and progression of depression has recently been noted. Additionally, ncRNAs have a variety of effects and have been extensively studied, with promising experimental advances. It is necessary to systematically organise the existing results on ncRNAs because their significant potential in the research on depression has been highlighted.

This review will summarize the role of various ncRNAs in depression and the potential of ncRNAs to act as biomarkers in different tissue sources. In addition, the specific mechanism of certain miRNAs in the onset and treatment of depression will be discussed. We hope that this review will shed light on the clinical application of ncRNAs in the treatment and diagnosis of depression.

2. MiRNA

2.1. Role of MiRNA in depression

MiRNA is a type of small ncRNA that has a size range of 19–25 nucleotides and is abundant in eukaryotes. Each miRNA can target hundreds of mRNAs, and post-transcriptional regulation of gene expression typically takes place at this level [20]. Base-pairing to target mRNAs, which primarily takes place in the mRNA 3′-untranslated region (3′-UTR), allows miRNAs to control the production of proteins [21]. Numerous published studies have demonstrated the role of miRNA at the onset, during the progression and in the treatment of depression.

At the onset of depression, increasing some miRNAs can make a difference. For example, the up-regulation of miR-323a can bring on depression by causing the down-regulation of erb-b2 receptor tyrosine kinase 4 (ERBB4), and the up-regulation of miR-139-5p

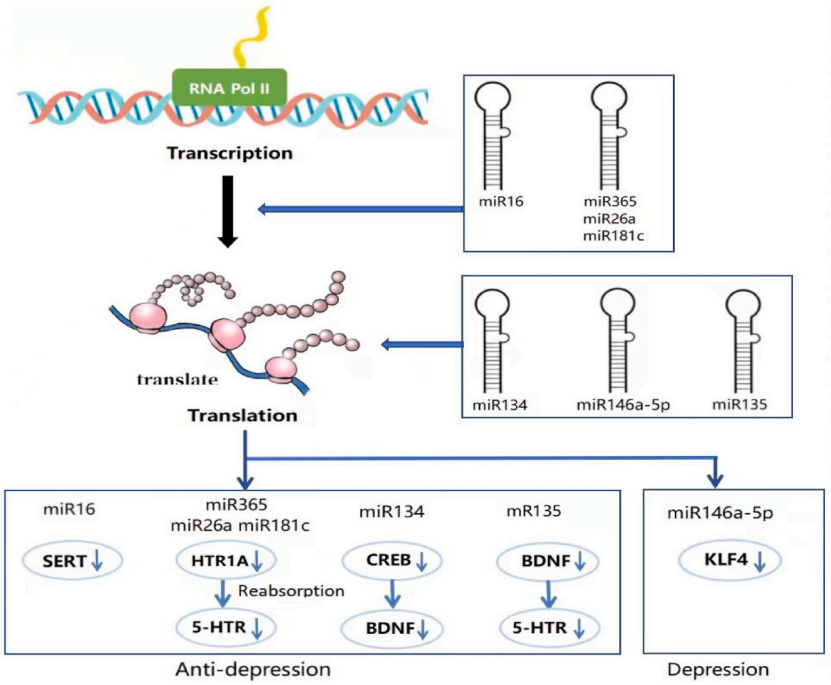

Fig. 1. The potential mechanism by which ncRNAs modulate the expression of specific genes, thereby impacting depression.

decreases hippocampal neurogenesis and contributes to depression [22,23]. Decreasing some miRNAs can also make a difference; for example, the down-regulation of miR-26a-3p in dentate gyrus regions coupled with the activation of the chromosome ten (PTEN)/-phosphatidylinositol-3 kinase (PI3K)/protein kinase (AKT) signalling pathway can cause depression [24]. For the treatment of depression, depressive symptoms can be alleviated by the NOD-like receptor3 (NLRP3) cascade, which is controlled by the miRNA-27a/Spleen tyrosine kinase (SYK)/nuclear factor-κB (NF-κB) axis [25]. MiRNA-199a-5p targets WNT2 to alleviate depression in hippocampus neurons by activating cAMP response element-binding protein (CREB)/Brain-derived neurotrophic factor (BDNF) signalling [26]. And the up-regulation of miR-211-5p within the DG area via suppression of the dosage of the serine threonine kinase (Dyrk1A)/signal transducer and activator of transcription 3 (STAT3) signalling pathway can relieve depression-like behaviors [27]. Although the precise mechanism underlying the influence of miRNAs on depression remains unknown, direct evidence of altered miRNA expression in depressed individuals is highly significant for advancing pathophysiological research on depression [28,29].

The possible mechanism by which ncRNAs regulate the expression of specific genes, thereby influencing depression, is illustrated in Fig. 1.

2.2. The mechanism of MiRNAs in influencing depression

2.2.1. MiRNAs and neurotransmitter serotonin

In numerous relevant studies, a comparatively well-established claim is that miRNAs target alterations in the level and metabolism of serotonin (5-HT) to influence the occurrence of depression. In addition, changes in the associated expression levels of serotonin autoreceptors (HTR1A) and serotonin transporters (SERTs) may accompany this process. Studies by Orna Issler found that miRNA135a targets SERT and HTR1A. High expression of miRNA135a affects global 5-HT levels and metabolic changes in the brain, with decreased 5-HT concentrations and increased metabolism in multiple brain nuclei of mir-135aOE (overexpressing) mice. This blocked the occurrence of depression in response to social defeat induction in mice and brought about a reduction in 5-HT [30].

It was also found in this study that the levels of mir135a in the midbrain raphe nuclei (RN) were significantly decreased in depressed patients, and conversely, the expression levels of mir-135a were up-regulated in adult mice after antidepressant treatment. In transgenic experiments, knocking out the mir-135 gene in the RN of adult mice led to increased depression-like behaviour and impaired response to antidepressants. Interestingly, the RN, which is the main source of 5-HT, contains serotonergic neurons whose primary function is to produce the neuronal transmitter 5-HT, and in many studies, it was also found that miRNAs can target acting on the RN and produce corresponding depression or antidepressant-related effects. For example, it was demonstrated in a study by Lo lacono L et al. [31]. The expression levels of mir-34a in the RN of mice with chronic unpredictable mild stress (CUMS) were significantly up-regulated, which alters the serotoninergic neuronal signal and leads to the development of depression [31]. This suggests that the recruitment of some miRNAs in the RN is a possible condition affecting the function of the 5-HT system and induces/inducing depressive behaviour.

Stimulation of HTR1A inhibits the discharge of 5-hydroxytryptaminergic neurons and the release of 5-HT. It should be pointed out that in the experiment of Xie on social failure in mice, the overexpression of miR-26a-2 in 5-HT neurons inhibited the depression and anxiety behaviour caused by social failure in mice [32]. In contrast, the overexpression of HTR1A eliminates this function. The function of SERT is to ensure the reuptake of 5-HT, which is a plasma membrane transporter. It terminates the effect of 5-HT by recycling it from the synaptic space to the presynaptic neurons in a sodium-dependent manner. The pharmacological target of antidepressant fluoxetine (SSRI) is SERT, which is a selective 5-HT reuptake inhibitor. SERT is a target of miR-361-3p, which can affect 5-HT in this way [33].

In Baudry's study, it was observed that the level of miR-16 of serotonergic neurons in the RN of mice chronically treated with SSRI increased, thereby reducing SERT expression further. Interestingly, this is also similar to the antidepressant effect observed after miR-16 was injected into the RN of mice [34].

In this experiment, a luciferase reporter gene assay was used to confirm the regulatory effect of miR-16 on SERT gene expression. In addition, the same approach was used in Orna Issler's experiment, which confirmed the same targeting effect of mir-135 on the 5-HT transporter SLC6A4 (serotonin transporter protein) gene [30]. Besides, the level of miR-16 in the blood and RN of suicide victims is significantly lower than that in controls. This also corroborates the relationship between a reduction in mir-16 expression levels and depressive behaviour.

This illustrates that SSRI possibly alters the expression of miR-16 to regulate SERT. It is speculated that the rise of miR-16 inhibits the expression of SERT, leading to a block in the reuptake process of 5-HT, which maintains a high level of 5-HT in the brain to achieve the function of antidepression. Interestingly, regarding Baudry's experiments, it should be added that under conditions of exposure to fluoxetine, the RN was able to release the neurotrophic factor s100β acting on noradrenergic cells of the locus coeruleus, promoting the expression of serotonergic functions in noradrenergic neurons.

The various experiments amply demonstrate the influence of miRNA on depression. Overall, part of miRNAs' antidepressant efficacy is achieved through 5-HT. It must be emphasised that the key to influencing the pathway is to directly promote the expression and release of 5-HT or to indirectly reduce the expression and activity of 5-HT transporter and 5-HT, promoting the accumulation of 5-HT in the synaptic cleft and the efficient transmission of 5-HT as a neurotransmitter between synapses.

The above experiments have demonstrated a possible mechanism of action for miRNAs to influence depression and illustrated the existing link between a subset of miRNAs and 5-HT that will lay the foundation for further unravelling the onset of, susceptibility to and treatment for depression.

Fig. 2 illustrates the potential mechanism by which miRNAs exert their influence on depression via 5-HT.

2.2.2. MiRNAs and Wnt2/CREB/BDNF signalling

2.2.2.1. Wnt 2. The Wnt signalling pathway is a complex network of protein actions whose abnormities may contribute to the development of numerous psychiatric or psychological disorders. The proper expression of Wnt receptors and proteins is beneficial for preventing the disturbance of nervous system function and for promoting the maintenance of synaptic plasticity and the normal development of the brain and other organs. It is generally agreed that Wnt2/CREB/BDNF signalling is critical for the development of treatments for depression or antidepressants. Interestingly, the inhibition of these pathways has been proven to lead to the occurrence of depressive behaviour, while their activation is closely related to a reduction in depressive performance and an improvement in the antidepressant response of the nervous system.

Liu et al. showed that mirna-199a-5p targets Wnt2 signalling and affects the CREB/BDNF signalling pathway [26], which regulates the synaptic structure and function and is involved in the development of depression. Notably, the expression of mir-199a-5p in the hippocampus of mice in the depression group was significantly higher than that in the normal control group, and mir-199a-5p was able to promote the apoptosis of hippocampal neurons and inhibit cell proliferation. Lian et al. showed a similar effect of mirna-221, which negatively regulates Wnt2/CREB/BDNF signalling [35]. In their experiments, the presence of the mirna-221 inhibitor promoted the expression of CREB and BDNF protein; however, the knockdown of Wnt2 reversed the effect. This illustrates the connection of the Wnt2/CREB/BDNF axis. In addition, the overexpression of mirna-221 has even been able to reverse the therapeutic effect of fluoxetine on depression. In the research by Lopez et al., miRNAs 146a, B-5, 425-3p and 24-3p were shown to be the biomarkers for depression response via target prediction analysis, and they regulate the expression of more than 30 genes associated with the mitogen-activated protein kinases (MAPK) and Wnt signalling pathways, which have been proven to be very closely linked to antidepressant performance. Roy B et al. [36,37]. Found that miR-128-3p acts on target genes located in the amygdala via Wnt signalling, whose up-regulation resulted in the occurrence of depressive-like behaviours. MiRNAs with similar functions that influence the development of depression by regulating Wnt signalling also include miR-155 and mir-383 [38,39]. Although the specific mechanism of the Wnt2 signalling pathway is not clear, the experiments above have preliminarily demonstrated the crucial role of the signalling pathway in the treatment of depression.

2.2.2.2. CREB. CREB, whose function is to regulate the transcription process of genes, acts by receiving the regulation of Wnt signalling and directing the expression and normal function of downstream genes in the Wnt2/CREB/BDNF axis, which are closely linked to the expression of BDNF and the stability of synaptic plasticity. It has been reported that the up-regulation of miR-134 reduces the expression of CREB, which also represses the transcription and expression of BDNF. However, the up-regulation of silent information regulator sirtuin 1 (SIRT1) can improve this process by repressing the expression of miR-134 [40]. The study by Shen J et al. showed that resveratrol may be a preventive treatment for cognitive deficits in CUMS rats by activating the SIRT1/mir-134 pathway, which increases the expression of CREB/BDNF protein in the hippocampus [41]. It has been reported that miR-182 similarly suppressed the CREB/BDNF signalling pathway in the hippocampus of mice with depression-like behaviour [42]. The aforementioned studies have demonstrated that the down-regulation of CREB exerts inhibitory effects on the transcription and expression of BDNF, thereby eliciting depressive symptoms. Additionally, miRNA modulates depression through this regulatory mechanism.

2.2.2.3. BDNF. BDNF is highly expressed in the hippocampal region of the brain and deeply involved in the processes of regulation

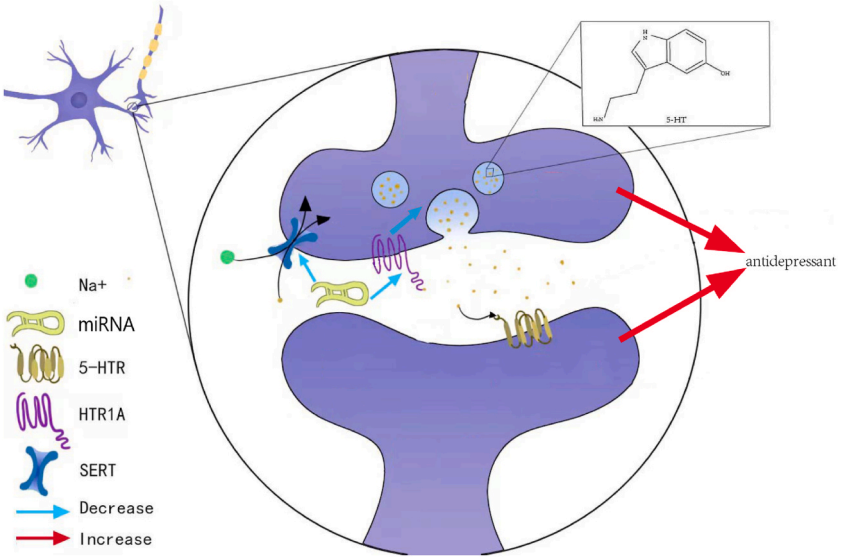

Fig. 2. The potentially plausible mechanism of action for miRNAs exerting influence on depression via 5-HT.

and development of the nervous system, and it is closely linked to synaptic plasticity. Studies have found that BDNF can act as a sensor to regulate neuronal activity and thereby participate in antidepressant processes [43]. Wang G et al.'s study found that BDNF is the downstream target of miR-134 and is negatively regulated by miR-134 [44]. Their research found that overexpressed miR-134 inhibited the expression and activity of BDNF. Interestingly, ginsenoside Rb1 exerted intensified effects on BDNF signalling via mir-134, achieving the goal of treating CUMS mice. In addition, numerous studies have shown that a large number of miRNAs target and regulate BDNF. For instance, mir-503-3p and mir191a-5p play a positive function for BDNF, favouring its expression [45]. The study by Fu X et al. showed that miR-132-3p and miR-206 target BDNF and reduce its expression [46]. In addition, it was reported that the expression levels of mir-30e, mir-181b, miR-34a, mir-346 and miR-7 were significantly higher in patients with psychiatric disorders than in healthy controls and decreased after antidepressant treatment [47]. A large number of studies have demonstrated the powerful targeting effects and regulatory functions of miRNAs acting on BDNF.

MiRNAs may also affect the expression of BDNF indirectly through some pathways. For instance, low expression of Methyl CpG binding protein 2 (MECP2) inhibits the formation and development of synapses, producing disruption to synaptic function [48]. Su M et al. showed that the reduced expression of MeCP2 inhibits the normal expression of BDNF and, conversely, that the expression of mir-132 is negatively correlated with it [49]. Altogether, the above studies illustrate the regulatory capability of miRNAs acting on BDNF and the pivotal role that they play in the process of synaptic plasticity and antidepressant treatment.

Overall, the Wnt2/CREB/BDNF signalling pathway, as a key signalling axis in the nervous system, is critically involved in neuronal activity and synaptic function and is closely associated with the occurrence of depressive disorders. Different miRNAs can have an impact on each part of this pathway, which in turn affects the function of the overall pathway, modulating nervous system activity. Wnt signalling activates CREB and promotes the expression of BDNF indirectly, and in the process, miRNAs can target upstream pathways and ultimately affect the activity of BDNF or directly target BDNF and thereby modulate the signalling pathway, which in turn is involved in the development of depression and other psychiatric disorders.

Fig. 3 illustrates the potential involvement of miRNAs in the Wnt2-CREB-BDNF signaling pathway, which may contribute to antidepression.

2.2.3. MiRNAs and proinflammatory cytokine

According to numerous relevant studies, the presence of some miRNAs can affect the synthesis and release of pro-inflammatory cytokines, promoting the occurrence of inflammatory reactions in the brain nervous system and damage in normal nerve tissues, which produces negative effects that aggravate the neuronal damage. This leads to lower tolerance to depression or other mental stimuli and more sensitivity and vulnerability to adverse mental stimulation, which undoubtedly exacerbates the occurrence of depression.

Lou et al. found that miR-124 targeted transcription activator STAT3, which was found to be involved in the activation of microglia and the inflammatory reaction of the nervous system [50,51]. According to the Lou D's experiment, miR-124 targets STAT3 to regulate the activation of microglia, which release proinflammatory cytokines, including Monocyte chemoattractant protein-1 (MCP-1), Interleukin 6 (IL-6) and Necrosis Factor alpha (TNF-α). It has been reported that miR-9-5p can promote M1 polarisation of microglia and then lead to the excessive release of pro-inflammatory cytokines. At the same time, the overexpression of miR-9-5p activates the STAT3 pathway, exacerbating the nerve injury and depressive symptoms of CUMS mice [52]. Li et al. found that secretions containing

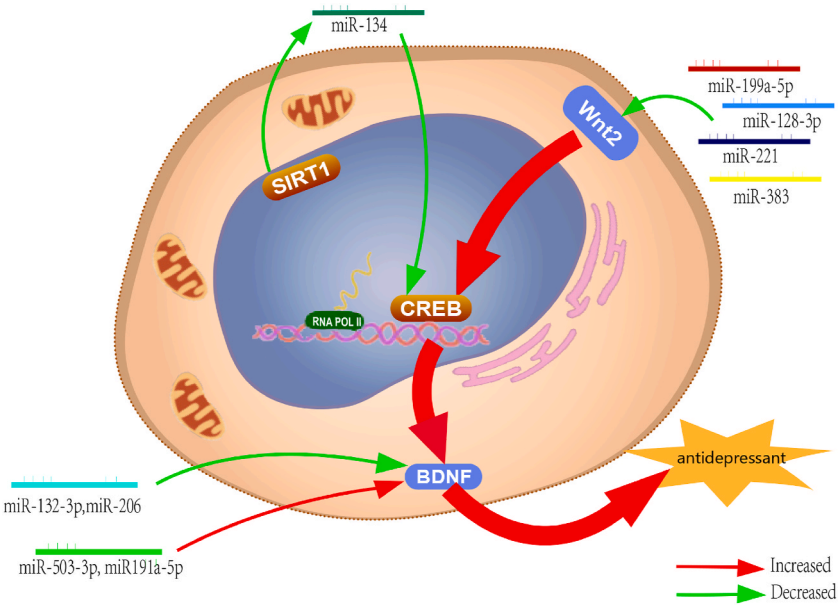

Fig. 3. The potential mechanism underlying the involvement of miRNAs in the Wnt2-CREB-BDNF antidepressant action.

miR-207 transferred from Natural killer cells (NK cells) to brain neurons can alleviate the depressive symptoms of mice [53]. It has been speculated that miR-207 targets Toll-like receptor 4 (TLR4) interactors rich in leucine repeats (Tril) to reduce its expression and inhibit the NF-κB signal, which reduces the release of pro-inflammatory cytokines to relieve the stress symptoms of mice.

In addition, numerous studies have reported similar mechanisms. This proves the rationality and feasibility of the idea that miRNA indirectly regulates the synthesis and release of pro-inflammatory cytokines in the brain in various ways and additionally leads to the aggravation of depressive symptoms. It also provides new ideas and methods for antidepressant treatment.

Collectively, the factors affecting the occurrence of depression by miRNAs include 5-HT, the Wnt/CREB/BDNF signalling axis and proinflammatory cytokines, and miRNAs are directly or indirectly involved in the process of the mechanism and finally affect the occurrence of depressive symptoms, which provides reliable ideas and methods for depression treatment. As a summary, Table 1 will conclude the depressant change of the miRNAs and their targets in depression.

2.3. MiRNAs' potential to serve as biomarkers in clinical practice

2.3.1. MiRNAs in the central nervous system

Numerous miRNAs have been shown to have aberrant expression and altered function in brain tissues, which may be connected to degenerative changes in the central nervous system (CNS) in depressed patients [54]. There is ample evidence that miRNAs serve as biomarkers for depression. Some down-regulation miRNAs can predict depression; for instance, Lou et al. demonstrated that depression can be predicted by the down-regulation of miR-124 in the hippocampus [50]. Azevedo et al. found that depression can be predicted by the down-regulation of miR-34a in the anterior cingulate cortex [55]. Torres-Berrío et al. claimed that depression can be predicted by the down-regulation of the miR-218 in the prefrontal cortex (BA44) [56].

Furthermore, more and more evidence has demonstrated the importance of miRNAs as post-diagnostic biomarkers for depression that can evaluate the effect of antidepressants. For example, by measuring and comparing the levels of miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p in the ventrolateral prefrontal cortex (vPFC) of depressed people who died by suicide and psychiatrically healthy controls, Lopez et al. demonstrated the potential of miRNAs as postdiagnostic biomarkers. This difference was significant and provides strong evidence for the therapeutic effect of escitalopram (selective 5-HT reuptake inhibitor), accompanied by the biochemical examination of the peripheral samples from antidepressant treatment responders [36]. Patrcio et al. found two pre-miRNAs, namely miR-409 and miR-411, to be considerably elevated across the whole hippocampus DG of CMS-exposed rats, in comparison to control rats. Additionally, by using antidepressants from four distinct classes (fluoxetine, imipramine, tianeptine and agomelatine) on a long-term basis, their levels recovered [57,58].

Even though the content of miRNAs varies significantly in the CNS, due to difficulty in sampling, it has little clinical application and can only be used in basic animal experiments. Therefore, the significant content changes of miRNAs in peripheral fluids have great advantages as clinical biomarkers.

2.3.2. MiRNAs in peripheral biofluids

MiRNAs have been found in biological fluids, including whole blood, plasma and serum; cerebrospinal fluid (CSF); urine; saliva; breast milk; seminal plasma; and tears, in addition to tissue in the CNS, and are also called circulating miRNAs (cimiRNAs) [59]. Since cimiRNAs are actively produced as messengers and play a crucial role in regulating developmental and differentiation processes, they have been suggested as possible biomarkers for disorders of the CNS [60,61].

Table 1
The depressant change of the miRNAs and their targets in depression.

MicroRNAs	Depressant change	Targets in depression	References
miR135a	Decrease	SERT, HTR1A	[30]
miR34a	Increase	5-HT neuron	[31]
miR-139-5p	Increase	Hippocampal neurons	[23]
miR-26a-2	Decrease	HTR1A	[32]
miR-361-3p	Increase	SERT	[33]
miR-16	Decrease	SERT	[34]
miR-199a-5p	Increase	Wnt	[26]
miR-221	Increase	Wnt	[35]
miR-128-3p	Increase	Wnt	[37]
miR-383	Increase	Wnt	[39]
miR-155		Wnt/β-catenin signaling pathway	[38]
miR-146a, B-5, 425-3p, 24-3p		MAPK and Wnt signal	[36]
miR-134		CREB, BDNF	[40,41,43]
miR-182	Increase	CREB	[42]
mir-503-3p, mir191a-5p	Increase	BDNF	[45]
miR-132-3p,miR-206	Decrease	BDNF	[46]
miR-132	Increase	MeCP2, BDNF	[48,49]
miR-124	Increase	STAT3, pro-inflammatory cytokines	[50]
miR-9-5p	Increase	STAT3, pro-inflammatory cytokines	[52]
miR-207	Decrease	TLR4 interactor, pro-inflammatory cytokines	[53]
mir-30e, mir-181b, mir-34a, mir-346, mir-7	Increase		[47]

2.3.2.1. MiRNAs in CSF. CSF fills the ventricles, subarachnoid space and central canal of the spinal cord [61]. The choroid plexus located in the ventricle produces CSF, which is extracellular fluid, much like lymph and plasma [62–64]. According to a meta-regression analysis, the identification of miRNA expression in CSF significantly increases diagnostic accuracy [65]. As a result, lumbar puncture is frequently carried out to find CSF when disorders of the CNS manifest themselves, helping with diagnosis [66–70]. It is thought that miRNAs in CSF are vital biomarkers. Some increasing miRNAs can act as biomarkers for depression; for example, Shao et al. claimed that despite reflecting raphe miR-16 levels and consequently influencing raphe SERT expression, CSF miR-16 is engaged in the pathophysiology of depression [71]. Lian et al. and Wan et al. both found that an increase in miR-221 in CSF promotes depression [35,72]. Some decreasing miRNAs can also act as biomarkers for depression; for example, Song et al. reported that patients with serious depression had lower levels of CSF miR-16 and that silencing it in rats caused depressive-like behaviours via the 5-HT transmitter system [73]. Also, Wan et al. discovered that, as a postdiagnostic biomarker for depression, down-regulating miR-451a in the CSF can cause depressive-like behaviours and may provide a theoretical justification for the action of ketamine [72]. Therefore, the extraction and detection of miRNA in CSF is undoubtedly one of the convenient and accurate methods for detection, deserving widespread promotion.

2.3.2.2. MiRNAs in peripheral blood. MiRNA levels in peripheral blood (including whole blood, plasma and serum) have been reported on numerous occasions, and their concentrations might serve as biomarkers for a variety of diseases, including depression. Firstly, miRNA in whole blood plays a vital role in depression. MiR-144-3p in whole blood inhibition reduces depressive symptoms in mice, and miRNA expression levels tend to return to normal after either repeated imipramine treatment or a single dose of ketamine [74]. MiR-425-3p in whole blood can induce depression in humans through its up-regulation [75]. According to Maffioletti et al., up-regulation of miR-24-3p in whole blood causes depression [75]. Secondly, miRNA in plasma also makes a big difference. Plasma from adolescents exhibiting significant depressive symptoms demonstrates dysregulated levels of the VEGF protein, miR-101-3p, and miR–5p [76]. Jia Hu and colleagues found that post-stroke depression was more prevalent in patients with higher plasma levels of miR-22. These findings suggest that miR-22 acts as a biomarker in post-stroke depression and cerebral microvascular dysfunction [77]. What's more, the miRNA in serum can also influence depression. Gheysarzadeh et al. claimed that miR-135a's down-regulation in serum can predict depression, and miR-16's down-regulation in serum can cause depression by targeting the serotonergic transmitter system (SERT), BDNF (neurogenesis) and B cell lymphoma-2 (Bcl-2) (neuron survival and apoptosis) genes [34,78]. Also, miR-1202's down-regulation in serum can cause depression by targeting the glutamate receptor, metabotropic 4 (GRM4) gene and controlling glutamate [36,78]. According to Feng et al.'s research, miR-124's content in plasma tends to return to normal following an 8-week course of citalopram therapy, giving it an advantage as a biomarker for detecting various signs of depression after therapy [79]. Interestingly, in response to stress, mitochondrial DNA (mtDNA) and miRNAs are released from the cytoplasm. Moreover, the association between miRNAs and the efficacy of antidepressant therapy has been established, making them potential post-diagnostic biomarkers [80]. An increasing number of miRNAs have been detected in peripheral blood, and as biomarkers have become a popular topic, pointing towards a simpler and non-invasive method for diagnosing depression.

2.3.2.3. MiRNAs in other biofluids. In addition to blood and CSF, miRNAs have been found to act as biomarkers in many other biofluids, such as saliva and urine [81]. Exosomes, which are extracellular vesicles (EVs) of endocytic origin, contain the majority of

Table 2
The expression of promising microRNA biomarkers in different position.

miRNA	Position	Role	References
miR-124	hippocampus	the CNS tissue can act as biomarkers of the diagnosis of the depression.	[50]
miR-34a	anterior cingulate cortex		[55]
miR-218	Prefrontal cortex (BA44)		[56]
miR-146a-5p miR-146b-5p miR-24-3p miR-425-3p	vPFC	as post-diagnostic biomarkers of depression, which can evaluate the effect of antidepressants	[36]
miR-409 and miR-411	hippocampus DG	post-diagnostic biomarkers	[57,58]
miR-16	CSF	silencing it in rats causes depressive-like behaviors via the 5-HT transmitter system.	[71]
miR-221	CSF	post-diagnostic biomarkers	[35,72]
miR-451a	CSF	post-diagnostic biomarkers	[72]
MiR-144-3p	whole-blood	miR-144-3p was identified as a new target for the diagnosis of depression and antidepressant therapy	[74]
MiR-425-3p	whole-blood	the up-regulation of miR-24-3p in whole-blood causes depression.	[75]
miR-22	plasma	miR-22 may act as a biomarker in post-stroke depression and cerebral microvascular dysfunction.	[77]
miR-135a	serum	miR-135a′s down-regulation in serum can predict depression	[78]
miR-16	serum	miR-16 down-regulation in serum can predict depression	[34]
miR-1202	serum	miR-1202 down-regulation in serum can predict depression	[36,78]
miR-124	serum	as a biomarker for detecting various signs of depression	[79]

miRNAs that treat depression in other biofluids. Cells release these vesicles, which are present in biofluids and typically contain miRNAs, which are crucial for several physiological processes. Disease situations cause changed miRNA expression in exosomes, making the miRNA cargo an interesting research prospect. EVs are naturally lipophilic and may pass across the blood–brain barrier with ease. Exosomes are a recommended method for the treatment or early detection of illnesses of the CNS such as depression because of this particular feature. It has been claimed that miRNAs in exosomes play a role in depression, but further research is needed [82–84]. Urine, saliva and blood are examples of biological fluids from which exosomes can be easily extracted [85]. Additionally, because exosome contents are shielded by a membrane, they are not easily broken down by the biological fluids or enzymes in our bodies [86]. That the direct content and structural changes of miRNA in other biofluids may also affect depression has been reported recently [87–89]. In general, these benefits make miRNAs in EVs crucial targets for depression diagnostic biomarkers.

In conclusion, miRNAs can be detected in almost every part of the body, giving them a distinct advantage as diagnostic biomarkers for depression. Relevant studies have revealed their practicability and feasibility, which can be used clinically in the future (Table 2).

3. LncRNA

3.1. The role of lncRNAs in depression

LncRNAs comprise a class of RNA with a length of 200–100,000 nucleotides [90]. They exert their functions by directly binding to DNA, RNA and proteins [91]. LncRNAs have received much attention recently, and the RNA produced by the related genes has received the majority of the attention when discussing lncRNAs' modes of action [92]. The association of aberrant lncRNAs sequence and spatial conformation, dysregulated expression levels, and disrupted protein interactions has been extensively documented as a pivotal determinant in various severe human health conditions, encompassing depression and degenerative neurological disorders. Consequently, the investigation of lncRNAs merits profound exploration.

3.2. The mechanism of lncRNAs in influencing depression

At the onset of depression, lncRNA XR_351665 increases DNA methyltransferase1 (DNMT1) by sponging miR-152-3p, which leads to chronic depression In postpartum depression, lncRNA Gm14205 activates the NLRP3 inflammasome by blocking the oxytocin receptor [93,94]. MiRNA-320-3p/CRHR1 (G protein-coupled receptors) axis-mediated induction of neuronal vitality in rats' brains to aggravate depression is regulated by lncRNA NEAT1 [95]. For the treatment of depression, the lncRNA MIR155HG controls the miR-155/BDNF axis to reduce depressive-like behaviours in mice [96]. By controlling the MiRNA-26a/EGR1 (Early growth response factor 1) axis, lncRNA GAS5 down-regulation reduces hippocampus neuronal damage in mice with depressive-like behaviors [97]. In conclusion, lncRNAs generally contribute to depression by altering other ncRNAs.

3.3. LncRNAs' potential to serve as biomarkers

Large and varied concentrations of lncRNAs, which are involved in the control of crucial CNS biological processes, have been discovered in the brain [98]. In addition, because of their ubiquitous expression, tissue-specific expression patterns and high detection efficiency, lncRNAs have the potential to be used as diagnostic biomarkers in psychiatric illnesses [99,100]. Issler et al. found that, as a diagnostic biomarker, LINC00473 up-regulation in adult mouse medial prefrontal cortex (mPFC) neurons only benefits females, and it may be a biomarker for females who struggle with depression [101,102]. Wang et al. reported that potential diagnostic biomarkers for perinatal depression have the place of lncRNAs NONHSAG004550 and NONHSAT125420 [103]. Ye et al. discovered that the peripheral blood leukocytes of depressive patients had significantly higher levels of LINC01108 expression and significantly lower levels of LINC00998 expression when compared to those of healthy participants [104].

It has been confirmed that the lnc-PLA2G12A-1/PLA2G12A transcript/prostaglandin axis, as a post-diagnostic biomarker, can be modified by mood stabilisers and targeted by non-steroidal anti-inflammatory medications such as celecoxib, which have been utilised as adjunct treatments for bipolar disorder [105,106]. Ni et al. discovered that, after imipramine treatment, the expression level of lncRNA TCONS 00019174 in the hippocampus of CUMS mice can be regained and that TCONS 00019174 may stimulate the Wnt/b-catenin pathway to exhibit antidepressant-like effects [107]. Roy et al. demonstrated that fluoxetine significantly reduces the expression of learned helplessness-mediated 52 up-regulated and 29 down-regulated lncRNAs [108]. These studies demonstrate the potential of lncRNAs as biomarkers, both in the brain and other tissues, highlighting their significance in clinical applications.

4. CircRNA

4.1. Role of circRNA in depression

CircRNA is a family of long, ncRNA molecules that have no poly A tail and form a covalently closed continuous loop [109]. CircRNA has a high level of stability within cells and is not readily destroyed by RNA enzymes as a result of its circular structure, which enables it to fulfil cellular functions over an extended period of time [110,111]. The impact of circRNA content variations and their associated response on depression has been acknowledged by researchers, suggesting a potential focus for future investigations in this area.

4.2. The mechanism of CircRNA for influencing depression

From the onset, the circRNA ANKS1B affects depression by acting as a miRNA sequester for miR-146a-5p and influencing the post-transcriptional regulation of Kruppel-like factor 4 (KLF4) expression, fatty acid amide hydrolase messenger RNA N6-methyladenosine alteration in circRNA STAG1-regulated astrocyte dysfunction and depressive-like behaviors [112,113].

For the treatment of depression, The transcription factor TATA-box binding protein associated factor 1 (TAF1) can bind mechanistically to circDYM, which causes the expression of its downstream target genes to reduce, thereby suppressing depression [114]. By reducing the quantity or density of astrocytes and their activity, circHIPK2 induces depression [115]. By targeting miR-9, circDYM reduces depressive-like behaviour by modulating microglial activation via Heat shock proteins 90 (Hsp90) ubiquitination [116]. And through the miR-497a-5p/glucocorticoid receptor (NR3C1) axis, circDYM reduces depressive-like behaviour in CUMS mice and prevents damage to hippocampus neurons [117].

CircRNA functions as a miRNA sponge in cells and has a lot of miRNA binding sites. When studying the pathophysiological mechanisms of depression, circRNAs have an advantage because they can alleviate the inhibition of miRNA on its target genes, increase the expression level of genes and produce the corresponding biological effects through the competitive endogenous RNA (ceRNA) mechanism [118].

4.3. CircRNAs' potential to serve as biomarkers in clinical practice

CircRNAs, which are extensively expressed in a wide range of biological cells, are covalently closed RNA molecules created by the reverse splicing of mRNA and lack 5′ caps and 3' tails [119,120]. Their unique structure makes it difficult for RNA enzymes to break it down [121–123]. Additionally, they have been found in peripheral blood and other tissues, making them simple to sample, and they have a significant benefit as diagnostic biomarkers because of the things discussed before [124–126].

In their 2016 paper, Cui et al., who were the first to uncover circRNA biomarkers for depression, stated that hsa_circRNA_103636 in peripheral blood mononuclear cells could be employed as novel non-invasive biomarkers for depression [127]. Song et al. revealed greatly reduced expression of circDYM in depressed patients' plasma [128]. According to Huang et al., circSTAG1 expression was considerably reduced in the hippocampal tissues and peripheral blood of CUMS mice as well as in the peripheral blood of depressed patients [113]. Zhang et al. demonstrated that circRNAs in the blood of depression patients contained an abnormality. Hsa_circ_0002473, hsa_circ_0079651, hsa_circ_0137187, hsa_circ_0006010 and hsa_circ_0113010 have all been tentatively shown to be significantly expressed in depressive patients and can be utilised as diagnostic markers for depression [129]. According to research by Shi et al., whole-blood circFKBP8 and circMBNL1 are both promising biomarkers for the diagnosis of depression [130].

As a post-diagnostic biomarker, Mao et al. demonstrated that after ketamine injection, five circRNAs were expressed abnormally in the rat hippocampus, with rno circRNA 014900 greatly increased and rno_circRNA_005442 significantly decreased [131]. Greer et al. found that after repetitive transcranial magnetic stimulation treatment for 4 weeks, the level of circFKBP8 increases, leading to less depressive-like activity [132]. Zhang et al. discovered that administering the total saponins from the leaves of *Panax notoginseng* greatly elevated mmu_circ_0001223 expression and predicted that these saponins had an antidepressant effect [133]. Additionally, Shi et al. discovered circFKBP8's significant promise as a biomarker after therapy with antidepressants [130]. In summary, numerous studies have demonstrated the significant potential of circRNAs as a biomarker in clinical treatment.

5. SiRNA

siRNAs are double-stranded, 21–25 nucleotide RNAs that can be either endogenous or exogenous [13,134]. Endogenous siRNAs are created by one's cells, while exogenous siRNAs are typically used as a tool of RNA interference (RNAi), with the procedure beginning with the cleavage of long double-stranded RNA into siRNA by the Dicer enzyme. After that, siRNA and argonaute protein combine to cause the matching mRNA to be cleaved [135]. Research on siRNA has produced a wide assortment of results. Few studies have focused on endogenous siRNA, while the majority of reviews have concentrated on the experimental technique of inducing depression through exogenous siRNA. For instance, siRNA-mediated nuclear factor-erythroid 2-related factor 2 (Nrf2) and SIRT1 knockdown in depression were used to study how melatonin induces depression via Nrf2 and the SIRT1 pathway [135]. When glutamate aspartate transporter (GLAST) and glutamate transporter 1 (GLT-1) expression in infralimbic cortex of mice was reduced by siRNA, the effects of local glutamatergic neurotransmission, which is typically regarded as a sign of depression, were examined [136]. Forkhead box protein O1 (FoxO1)-specific siRNA was used to determine whether FoxO1 was involved in the effect of baicalin on TLR4 expression to detect early depression [137]. In summary, with its many other smart applications, siRNA has emerged as a crucial tool for the genetic research of depression.

6. Interconnections between ncRNAs in depression

6.1. Association of lncRNAs with miRNAs in depression

In recent years, it has been discovered that problems in lncRNA structure and function are closely related to several neurodegenerative illnesses, including depression. There is mounting proof that lncRNAs can affect other ncRNAs to cause depression in various ways [94,138,139]. In earlier research, it was discovered that one way lncRNA mediates depression is by influencing miRNA through competitive inhibition. The binding sites of miR-124 can be occupied by BDNF-AS (a specific kind of lncRNA) in a competitive

manner. In addition, elevated miR-124 levels have been shown to induce depression and related neurobehavioral defects [140]. It has also been confirmed that lncRNA T-UCstem1 can control progenitor proliferation and neurogenesis by mediating with miR-9-3p and miR-9-5p in the forebrain neurogenic lineage that develops the interneurons of the adult olfactory bulb [141]. Further, the proliferation of olfactory bulb neurons and their synaptic connections is directly associated with depressive-like behaviour [142]. This indicates that lncRNAs may contribute to the development of depression by causing olfactory dysfunction. Zhang et al. showed that MIR 155 HG has potential binding sites with Mir-155. In 293T cells overexpressing MIR155HG, miR-155 expression was down-regulated. As a sponge, MIR 155 HG has been shown to lessen the inhibitory impact of miR-155 on BDNF production and enhance depressive-like behaviour [96]. The lncRNA XR_351665 upregulates1 by acting as a miR-152-3p sponge, thereby contributing to the development of depression induced by chronic pain [93]. Consequently, it is highly plausible that lncRNAs exert an impact on depression through their interaction with miRNAs.

6.2. Association of circRNAs with miRNAs in depression

It has been hypothesised that circRNAs bind to miRNAs as a chelator and further influence the expression of several factors that influence depression, such as mRNA stability, resulting in depressive-like behaviour [143,144]. The former study demonstrated that microglia transfer a microglia-enriched microRNA, miR-146a-5p, by secreting exosomes to improve neurogenesis and depression-like behaviour. circANKS 1B, a special circular RNA, binds specifically to miR-146a-5p derived from microglia cells as miRNA 'sequesters' and modulates the translational expression of KLF 4, which inhibits neurogenesis and the spontaneous firing of excitatory neurons in the hippocampal DG [112]. There is now another theory that circRNAs may influence depression-like symptoms by controlling microglia activation. Zhang et al. showed that circDYM promotes target-HECT domain E3 ubiquitin protein ligase 1 (HECTD1) expression by acting on the 3′-UTR of HECTD 1 and as a microRNA-9 (miR-9) sponge [116]. This causes an increase in HSP90 ubiquitination, which in turn causes a reduction in the activation state of microglia. The binding of circRNAs with miRNAs modulates their genetic characteristics and stability, thereby contributing to the development of depression.

6.3. Association of CircRNAs with lncRNAs in epression

The majority of studies have claimed that both lncRNAs and circRNAs can bind to miRNAs as chelators or sponges and influence

Table 3
The biological processes of the ncRNAs.

NcRNA	Role in depression	Biological processes	Reference
miR-323a	etiology	Its up-regulation cause the downregulation of ERBB4	[22]
miR-26a-3p	etiology	Its down-regulation coupled with activation of the PTEN/PI3K/Akt signaling pathway can cause the depression	[24]
miR-139-5p	etiology	Its up-regulation decrease hippocampal neurogenesis and will contribute to depression	[23]
miRNA-27a	treatment	miRNA-27a/SYK/NF-κB axis can control the NLRP3 cascade to alleviate depression	[25]
miRNA-199a-5p	treatment	targets WNT2 to alleviate depression in hippocampus neurons by activating CREB/BDNF signaling	[26]
miR-211-5p	treatment	Its up-regulation relieve depression-like behaviors via suppression of the Dyrk1A/STAT3 signaling pathway	[27]
SiRNA	as a tool for experiment	siRNA-mediated Nrf2 and SIRT1 knockdown in depression was used to study how melatonin induces the depression via Nrf2 and SIRT1 pathway	[174]
		When GLAST and GLT-1 expression in mouse IL was reduced by siRNA, the effects of local glutamatergic neurotransmission were examined, which is typically regarded as a sign of depression	[136]
		FoxO1-specific siRNA was used to determine whether FoxO1 was involved in the effect of baicalin on TLR4 expression to detect early depression.	[137]
LncRNA XR_351665	etiology	increases DNMT1 by sponging miR-152-3p, which leads to chronic depression	[93]
LncRNA Gm14205	etiology	activates the NLRP3 inflammasome by blocking the oxytocin receptor	[94]
lncRNA NEAT1	etiology	Regulate the microRNA-320-3p/CRHR1 axis-mediated induction of neuronal vitality in rats' brain to aggravate depression	[95]
lncRNA MIR155HG	treatment	controls the miR-155/BDNF axis to reduce depressive-like behaviors	[96]
lncRNA GAS5	treatment	Its down-regulation reduces hippocampus neuronal damage in mice with depressive-like behaviors by the control of the MicroRNA-26a/EGR1 axis	[97]
circRNA ANKS1B	etiology	act as a miRNA sequester for miR-146a-5p and influencing post-transcriptional regulation of KLF4 expression	[112]
circRNA STAG1	etiology	Fatty acid amide hydrolase messenger RNA N6-methyladenosine alteration in circRNA STAG1-regulated astrocyte dysfunction and depressive-like behaviors	[113]
CircDYM	treatment	Bind mechanistically to the transcription factor TAF1, which causes the expression of its downstream target genes to reduce, so suppressing depression	[114]
		CircDYM reduce depressive-like behavior by modulating microglial activation via HSP90 ubiquitination by targeting on miR-9	[116]
		reduce depressive-like behavior in CUMS mice and prevents damage to hippocampus neurons through the miR-497a-5p/NR3C1 axis	[117]
CircHIPK2	treatment	reduce the quantity or density of astrocytes and their activity to induce depression	[115]

how those miRNAs affect depression [139,143,145–147].

Due to the presence of microRNA response elements, they can communicate with one another by competing specifically for common miRNAs, cooperate in the reduction of mRNA degradation or inhibition by miRNAs and control the transcriptional expression of genes in vivo. Zhou et al. showed that ceRNAs (circRNA-miRNA-mRNA and lncRNA-miRNA-mRNA) are differentially expressed in patients with depression and normal people, and they can be used as biomarkers for depression [148,149]. Xi Wang et al. found that by inhibiting miR-344-5p, CircSYNDIG1 reduced the aberrant behaviors induced by stress in mice [150]. By regulating the miR-497a-5p/HECTD1 axis, Circ-Bnc2 mitigates neuroinflammation in LPS-stimulated microglial cells to prevent neuronal cell death, thereby impacting depression [151]. With more and more studies on the transcription factor (TF)-mRNA regulatory network, there is also the view that lncRNAs and circRNAs affect depression-like behaviours by mediating genes or transcription factors [152]. However, the exact process is still unclear.

6.4. Association of siRNAs with other ncRNAs in depression

The significance of siRNAs in the development and treatment of depression is now being understood from a growing number of studies, and their interactions with other ncRNAs have also gained attention as a potential therapy or mechanism for depression [137,153,154]. The former studies demonstrated that siRNAs and miRNAs each can selectively target the corresponding mRNA segment to degrade certain mRNA and control the related gene network [155]. Although an appropriate mix of the two has been shown to have some impact on depression associated with metastatic breast cancer, further research is required to determine the precise mechanism and the interaction between the two ncRNAs. Currently, siRNAs are often employed as an experimental technique to silence gene expression by directing the siRNA carrier to the correct gene or mRNA [155,156]. However, more research is needed right now to fully understand how existing siRNAs cause depression by interacting with other ncRNAs.

In conclusion, both lncRNAs and circRNAs are thought to operate on miRNAs to alter depression-like behaviours through a competitive interaction. More investigation is required on how siRNAs affect depression through other ncRNAs.

7. The biological processes of ncRNAs in depression

NcRNAs can make a difference in the onset and treatment of depression in various ways. They act as an essential clinical potential target. Mechanisms of ncRNAs, with miRNA as an example, influencing depression should be subsequently discussed, and the biological processes of these above ncRNAs are summarised in Table 3.

8. NcRNAs' potential in the clinical treatment of depression

In the clinical management of depression, including severe depression, several drugs play a part. Escitalopram, an antidepressant, could affect the expression of more than 30 kinds of miRNA, which were detected in human blood after the drug was absorbed by the body [157]. Paroxetine is used to treat depression and is effective for treating patients with anxiety who also have depression. When compared to normal individuals, depression patients had reduced serum levels of miR-451a and higher levels of miR-34a-5p and miR-221-3p. MiR-451a expression rose significantly among depression patients taking paroxetine, but miR-34a-5p and miR-221-3p expression decreased significantly [158]. Citalopram is a selective 5-HT reuptake inhibitor with antidepressant effects. MiR-335 was significantly reduced in blood samples from depression patients; moreover, it could directly target GRM4 and promote GRM4 overexpression. Citalopram treatment could upregulate the expression of miR-335 and inhibit the expression of GRM4, which has an antidepressant effect [159]. In addition, several natural products, such as Ginsenoside Rg1, Gypenosides and Saikosaponin d, have been shown to play a role in the treatment of depression by regulating ncRNA. Recently, Chao Chen et al. discovered that MiR-1281 contributes to depression disorder and the antidepressant effects of Kai-Xin-San (a Chinese medicine formulation). This finding also suggests that Chinese medicine influences the application of ncRNAs in depression treatment [160].

For decades, researchers have been actively studying postmortem brain tissue from depressed patients and different animal models of depression, but its pathogenesis is still not fully understood. Most studies of patients with depression have been conducted using peripheral blood, and postmortem brain tissue has mainly been used in studies of small cohorts and brain tissue homogenates, which restricts the study of pathological mechanisms, particularly epigenetic regulatory mechanisms such as ncRNAs. Due to the genetic and environmental factors that influence depression risk, its pathological mechanisms are complicated. The differences and impacts of ncRNAs may be influenced by these genetic and environmental variables, according to studies on their role in the epigenetic regulation of depression. This makes it difficult to begin using ncRNAs to diagnose and cure depression. However, a large number of basic and clinical studies are currently underway, highlighting the pivotal role that ncRNAs will play in both the diagnosis and treatment of depression.

9. The role of MicroRNAs in other psychiatric disorders

There is increasing evidence that ncRNAs play a crucial role in the occurrence and development of mental disorders, which not only include the depression we mentioned earlier, but also contain schizophrenia, Alzheimer's disease (AD), posttraumatic stress disorder (PTSD), Autism Spectrum Disorder (ASD), etc [161].

B. Miller et al. suggested that the imbalance of miR-132 can seriously affect the development process of the nervous system and the normal functioning of the brain, which exacerbates the development of schizophrenia [162]. In addition, significant abnormalities in

the expression of miR-22-3p, miR-92a-3p, and miR-137 were detected in peripheral blood of patients with schizophrenia, which might be used as a biomarker for clinical application [163]. J Wong et al. found a significant upregulation of miR-17 in the prefrontal cortex of patients with schizophrenia [164]. These provide new evidence for exploring the relationship between schizophrenia and miRNA.

An increasing number of studies have demonstrated a strong correlation between miRNAs and AD. According to reports, the expression of miR-107 has significantly decreased in AD patients and it is speculated that miR-107 may exacerbate the further development of AD by regulating amyloid precursor protein lyase [165]. It is suggested that miR-144 may promote the generation of amyloid β (Aβ) by negatively regulating ADAM10, which exacerbates the development of symptoms [166]. Similar studies have also demonstrated a negative correlation between the expression of miR-27a-3p, miR-137, and miR-181c and the development of symptoms in AD [167,168].

Additionally, patients with ASD or Schizophrenia have significantly increased expression of miR-218, which could affect the morphology and function of cortical neurons by regulating Satb2 [169]. Similarly, the expression of miR-23a in the peripheral blood of ASD patients was significantly upregulated [170], and a higher concentration of miR-106a was found in autistic children [171].

A large number of differences between normal individuals and PTSD patients in miRNAs expression were also found through high-throughput analysis of PBMCs, especially significant downregulation of miR-125a and 181c [172] and overexpression of miR-132 in the hippocampus [173], which proved a connection between PTSD and ncRNAs.

Overall, a considerable amount of evidence indicates the association between miRNA and various psychiatric diseases, which shows its enormous potential application for health.

In addition, numerous miRNAs are involved in the occurrence of related mental illnesses, as shown in Table 4.

10. Discussion

In this review, we highlighted the importance of ncRNAs as biomarkers for diagnosing depression and as effective experimental tools for studying depression and tracking responses to its treatment. The potential link between the abnormal regulation of ncRNAs and the onset and development of depression has recently been noted, but because the specific mechanism of ncRNAs has not been clearly defined, they have not been widely used in clinical practice. Therefore, based on previous research results, we systematically summarised the role of various ncRNAs in depression and their potential as biomarkers and drug targets in different tissue sources. We also discussed the specific mechanisms of some ncRNAs in the pathogenesis and treatment of depression. Finally, we speculate that ncRNAs can regulate post-transcriptional gene expression by interfering with the stability and translation of RNA molecules. They may also be involved in other epigenetic mechanisms.

Funding

This study was supported by the ShanDong Undergraduate Training Programs for Innovation and Entrepreneurship (S202311065054).

Table 4
The role of MicroRNAs in other psychiatric disorders.

MicroRNAs	Pathogenic change	mental disease	References
miR-132	Increase	Schizophrenia	[162]
miR-181b	Increase	Schizophrenia	[175]
miR-132-3p,miR-212, miR-544,miR-34a, miR-7 and miR-154-3p	Decrease	Schizophrenia	[176]
miR-17	Increase	Schizophrenia	[164]
miR-22-3p, miR-92a-3p and miR-137	Increase	Schizophrenia	[163]
miR-30a-5p	Decrease	Schizophrenia	[177]
miR-107	Decrease	AD	[165,178]
miR-29c	Decrease	AD	[179]
miR-188-3p	Decrease	AD	[180]
miR-339-5p	Decrease	AD	[181]
miR-144	Increase	AD	[166]
miR-27a-3p	Decrease	AD	[167]
miR-137 and miR-181c	Decrease	AD	[168]
miR-33	Increase	AD	[182]
miR-125a and 181c	Decrease	PTSD	[172]
miR-92a	Increase	PTSD	[183]
miR-132	Increase	PTSD	[173]
miR-222	Increase	PTSD	[184]
miR-182	Decrease	PTSD	[185]
miR-218	Increase	ASD	[169]
miR-23a	Increase	ASD	[170]
miR-106a	Increase	ASD	[171]
miR-19a-3p,miR-361-5p,miR-3613-3p,miR-150-5p,miR-126-3p and miR-499a-5p	Decrease	ASD	[186]

Data availability statement

Data included in article/supp. material/referenced in the article.

Declaration

Review and/or approval by an ethics committee was not needed for this study because this review does not involve clinical and basic experiments.

CRediT authorship contribution statement

Xinchi Luan: Writing – original draft. **Han Xing:** Writing – original draft. **Feifei Guo:** Writing – review & editing. **Weiyi Liu:** Writing – original draft. **Yang Jiao:** Writing – review & editing. **Zhenyu Liu:** Writing – review & editing. **Xuezhe Wang:** Writing – original draft. **Shengli Gao:** Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The author is deeply grateful to my parents Fazong Luan and Linna Liu for their support and many enlightening discussions, without whom I would not have been able to complete this review.

References

[1] R.H. McAllister-Williams, C. Arango, P. Blier, K. Demyttenaere, P. Falkai, P. Gorwood, M. Hopwood, A. Javed, S. Kasper, G.S. Malhi, et al., Reconceptualising treatment-resistant depression as difficult-to-treat depression, Lancet Psychiatr. 8 (1) (2021) 14–15.
[2] S.M. Monroe, K.L. Harkness, Major depression and its recurrences: life course Matters, Annu. Rev. Clin. Psychol. 18 (2022) 329–357.
[3] F.L. Lynch, G.N. Clarke, Estimating the economic burden of depression in children and adolescents, Am. J. Prev. Med. 31 (6 Suppl 1) (2006) S143–S151.
[4] B. Sanne, A.A. Dahl, G.S. Tell, [Depression–socioeconomic perspectives], Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke 121 (5) (2001) 590–595.
[5] J. Dean, M. Keshavan, The neurobiology of depression: an integrated view, Asian J. Psychiat. 27 (2017) 101–111.
[6] S. Marwaha, E. Palmer, T. Suppes, E. Cons, A.H. Young, R. Upthegrove, Novel and emerging treatments for major depression, Lancet (London, England) 401 (10371) (2023) 141–153.
[7] S. Penner-Goeke, E.B. Binder, Epigenetics and depression, Dialogues Clin. Neurosci. 21 (4) (2019) 397–405.
[8] M. Matsui, D.R. Corey, Non-coding RNAs as drug targets, Nat. Rev. Drug Discov. 16 (3) (2017) 167–179.
[9] S. Panni, R.C. Lovering, P. Porras, S. Orchard, Non-coding RNA regulatory networks, Biochimica et Biophysica Acta Gene Regulatory Mech. 1863 (6) (2020) 194417.
[10] Y.Y. Xu, Q.H. Xia, Q.R. Xia, X.L. Zhang, J. Liang, MicroRNA-based biomarkers in the diagnosis and monitoring of therapeutic response in patients with depression, Neuropsychiatric Dis. Treat. 15 (2019) 3583–3597.
[11] S. Ochi, Y. Dwivedi, Dissecting early life stress-induced adolescent depression through epigenomic approach, Mol. Psychiatr. 28 (1) (2023) 141–153.
[12] B. Roy, Y. Dwivedi, An insight into the sprawling microverse of microRNAs in depression pathophysiology and treatment response, Neurosci. Biobehav. Rev. 146 (2023) 105040.
[13] M.M. Zhang, R. Bahal, T.P. Rasmussen, J.E. Manautou, X.B. Zhong, The growth of siRNA-based therapeutics: updated clinical studies, Biochem. Pharmacol. 189 (2021) 114432.
[14] J.P. Lopez, A. Kos, G. Turecki, Major depression and its treatment: microRNAs as peripheral biomarkers of diagnosis and treatment response, Curr. Opin. Psychiatr. 31 (1) (2018) 7–16.
[15] Z. Li, S. Liu, X. Li, W. Zhao, J. Li, Y. Xu, Circular RNA in schizophrenia and depression, Front. Psychiatr. 11 (2020) 392.
[16] F. Bella, S. Campo, Long non-coding RNAs and their involvement in bipolar disorders, Gene 796–797 (2021) 145803.
[17] F. Kanwal, C. Lu, A review on native and denaturing purification methods for non-coding RNA (ncRNA), J. Chromatogr., B: Anal. Technol. Biomed. Life Sci. 1120 (2019) 71–79.
[18] S. Ning, X. Li, Non-coding RNA resources, Adv. Exp. Med. Biol. 1094 (2018) 1–7.
[19] Q. He, Y. Liu, W. Sun, Statistical analysis of non-coding RNA data, Cancer Lett. 417 (2018) 161–167.
[20] T.X. Lu, M.E. Rothenberg, MicroRNA, J. Allergy Clin. Immunol. 141 (4) (2018) 1202–1207.
[21] M.R. Fabian, N. Sonenberg, W. Filipowicz, Regulation of mRNA translation and stability by microRNAs, Annu. Rev. Biochem. 79 (2010) 351–379.
[22] L.M. Fiori, A. Kos, R. Lin, J.F. Théroux, J.P. Lopez, C. Kühne, C. Eggert, M. Holzapfel, R.E. Huettl, N. Mechawar, et al., miR-323a regulates ERBB4 and is involved in depression, Mol. Psychiatr. 26 (8) (2021) 4191–4204.
[23] Z.X. Wei, G.J. Xie, X. Mao, X.P. Zou, Y.J. Liao, Q.S. Liu, H. Wang, Y. Cheng, Exosomes from patients with major depression cause depressive-like behaviors in mice with involvement of miR-139-5p-regulated neurogenesis, Neuropsychopharmacol.: Off. Pub. Am. College Neuropsychopharmacol. 45 (6) (2020) 1050–1058.
[24] Y. Li, C. Fan, L. Wang, T. Lan, R. Gao, W. Wang, S.Y. Yu, MicroRNA-26a-3p rescues depression-like behaviors in male rats via preventing hippocampal neuronal anomalies, J. Clin. Invest. 131 (16) (2021).
[25] Y. Li, W. Song, Y. Tong, X. Zhang, J. Zhao, X. Gao, J. Yong, H. Wang, Isoliquiritin ameliorates depression by suppressing NLRP3-mediated pyroptosis via miRNA-27a/SYK/NF-κB axis, J. Neuroinflammation 18 (1) (2021) 1.
[26] Z. Liu, J. Yang, Q. Fang, H. Shao, D. Yang, J. Sun, L. Gao, MiRNA-199a-5p targets WNT2 to regulate depression through the CREB/BDNF signaling in hippocampal neuron, Brain Behav. 11 (8) (2021) e02107.
[27] Y. Li, C. Fan, R. Gao, T. Lan, W. Wang, S.Y. Yu, Hippocampal miR-211-5p regulates neurogenesis and depression-like behaviors in the rat, Neuropharmacology 194 (2021) 108618.
[28] S. Mouillet-Richard, A. Baudry, J.M. Launay, O. Kellermann, MicroRNAs and depression, Neurobiol. Dis. 46 (2) (2012) 272–278.

[29] W. Li, X. Li, Y. Li, Y. Chen, L. Zhu, R. Guo, Diagnostic value of MicroRNAs for depression: a systematic review and meta-analysis, J. Psychiatr. Res. 157 (2023) 132–140.
[30] O. Issler, S. Haramati, E.D. Paul, H. Maeno, I. Navon, R. Zwang, S. Gil, H.S. Mayberg, B.W. Dunlop, A. Menke, et al., MicroRNA 135 is essential for chronic stress resiliency, antidepressant efficacy, and intact serotonergic activity, Neuron 83 (2) (2014) 344–360.
[31] L. Lo Iacono, D. Ielpo, A. Accoto, M. Di Segni, L. Babicola, S.L. D'Addario, F. Ferlazzo, T. Pascucci, R. Ventura, D. Andolina, MicroRNA-34a regulates the depression-like behavior in mice by modulating the expression of target genes in the dorsal raphè, Mol. Neurobiol. 57 (2) (2020) 823–836.
[32] L. Xie, J. Chen, Y.M. Ding, X.W. Gui, L.X. Wu, S. Tian, W. Wu, MicroRNA-26a-2 maintains stress resiliency and antidepressant efficacy by targeting the serotonergic autoreceptor HTR1A, Biochem. Biophys. Res. Commun. 511 (2) (2019) 440–446.
[33] Y. Zhang, Y. Chen, G. Chen, Y. Zhou, H. Yao, H. Tan, Upregulation of miR-361-3p suppresses serotonin-induced proliferation in human pulmonary artery smooth muscle cells by targeting SERT, Cell. Mol. Biol. Lett. 25 (2020) 45.
[34] A. Baudry, S. Mouillet-Richard, B. Schneider, J.M. Launay, O. Kellermann, miR-16 targets the serotonin transporter: a new facet for adaptive responses to antidepressants, Science 329 (5998) (2010) 1537–1541.
[35] N. Lian, Q. Niu, Y. Lei, X. Li, Y. Li, X. Song, MiR-221 is involved in depression by regulating Wnt2/CREB/BDNF axis in hippocampal neurons, Cell Cycle 17 (24) (2018) 2745–2755.
[36] J.P. Lopez, L.M. Fiori, C. Cruceanu, R. Lin, B. Labonte, H.M. Cates, E.A. Heller, V. Vialou, S.M. Ku, C. Gerald, et al., MicroRNAs 146a/b-5 and 425-3p and 24-3p are markers of antidepressant response and regulate MAPK/Wnt-system genes, Nat. Commun. 8 (2017) 15497.
[37] B. Roy, M. Dunbar, J. Agrawal, L. Allen, Y. Dwivedi, Amygdala-based altered miRNome and epigenetic contribution of miR-128-3p in conferring susceptibility to depression-like behavior via Wnt signaling, Int. J. Neuropsychopharmacol. 23 (3) (2020) 165–177.
[38] J. Dai, J.Y. Pan, N. Liao, J. Shi, Q. Zeng, L. Huang, L.P. Chen, Influence of miR-155 on behaviors of depression mice through regulating Wnt/β-catenin signaling pathway, Eur. Rev. Med. Pharmacol. Sci. 24 (3) (2020) 1398–1407.
[39] S. Liu, Q. Liu, Y. Ju, L. Liu, Downregulation of miR-383 reduces depression-like behavior through targeting Wnt family member 2 (Wnt2) in rats, Sci. Rep. 11 (1) (2021) 9223.
[40] J. Gao, W.Y. Wang, Y.W. Mao, J. Gräff, J.S. Guan, L. Pan, G. Mak, D. Kim, S.C. Su, L.H. Tsai, A novel pathway regulates memory and plasticity via SIRT1 and miR-134, Nature 466 (7310) (2010) 1105–1109.
[41] J. Shen, L. Xu, C. Qu, H. Sun, J. Zhang, Resveratrol prevents cognitive deficits induced by chronic unpredictable mild stress: sirt1/miR-134 signalling pathway regulates CREB/BDNF expression in hippocampus in vivo and in vitro, Behav. Brain Res. 349 (2018) 1–7.
[42] Y. Tang, J. Yang, C. Ye, X. Xu, M. Cai, Y. Zhang, H. Lu, F. Mo, H. Li, H. Shen, miR-182 mediated the inhibitory effects of NF-κB on the GPR39/CREB/BDNF pathway in the hippocampus of mice with depressive-like behaviors, Behav. Brain Res. 418 (2022) 113647.
[43] C. Björkholm, L.M. Monteggia, Bdnf - a key transducer of antidepressant effects, Neuropharmacology 102 (2016) 72–79.
[44] G. Wang, T. An, C. Lei, X. Zhu, L. Yang, L. Zhang, R. Zhang, Antidepressant-like effect of ginsenoside Rb1 on potentiating synaptic plasticity via the miR-134-mediated BDNF signaling pathway in a mouse model of chronic stress-induced depression, J. Ginseng. Res. 46 (3) (2022) 376–386.
[45] J.R. Lytle, T.A. Yario, J.A. Steitz, Target mRNAs are repressed as efficiently by microRNA-binding sites in the 5' UTR as in the 3' UTR, Proc. Natl. Acad. Sci. U. S. A. 104 (23) (2007) 9667–9672.
[46] X. Fu, Y. Liu, A. Baranova, F. Zhang, Deregulatory miRNA-BDNF network inferred from dynamic expression changes in schizophrenia, Brain Sci. 12 (2) (2022).
[47] X.Y. Sun, J. Zhang, W. Niu, W. Guo, H.T. Song, H.Y. Li, H.M. Fan, L. Zhao, A.F. Zhong, Y.H. Dai, et al., A preliminary analysis of microRNA as potential clinical biomarker for schizophrenia, Am. J. Med. Genet. B Neuropsychiatr. Genet. 168b (3) (2015) 170–178.
[48] T. Fukuda, M. Itoh, T. Ichikawa, K. Washiyama, Y. Goto, Delayed maturation of neuronal architecture and synaptogenesis in cerebral cortex of Mecp2-deficient mice, J. Neuropathol. Exp. Neurol. 64 (6) (2005) 537–544.
[49] M. Su, J. Hong, Y. Zhao, S. Liu, X. Xue, MeCP2 controls hippocampal brain-derived neurotrophic factor expression via homeostatic interactions with microRNA-132 in rats with depression, Mol. Med. Rep. 12 (4) (2015) 5399–5406.
[50] D. Lou, J. Wang, X. Wang, miR-124 ameliorates depressive-like behavior by targeting STAT3 to regulate microglial activation, Mol. Cell. Probes 48 (2019) 101470.
[51] S.A. Bhat, R. Goel, R. Shukla, K. Hanif, Angiotensin receptor blockade modulates NFκB and STAT3 signaling and inhibits glial activation and neuroinflammation better than angiotensin-converting enzyme inhibition, Mol. Neurobiol. 53 (10) (2016) 6950–6967.
[52] X. Xian, L.L. Cai, Y. Li, R.C. Wang, Y.H. Xu, Y.J. Chen, Y.H. Xie, X.L. Zhu, Y.F. Li, Neuron secrete exosomes containing miR-9-5p to promote polarization of M1 microglia in depression, J. Nanobiotechnol. 20 (1) (2022) 122.
[53] D. Li, Y. Wang, X. Jin, D. Hu, C. Xia, H. Xu, J. Hu, NK cell-derived exosomes carry miR-207 and alleviate depression-like symptoms in mice, J. Neuroinflammation 17 (1) (2020) 126.
[54] Y. Dwivedi, B. Roy, G. Lugli, H. Rizavi, H. Zhang, N.R. Smalheiser, Chronic corticosterone-mediated dysregulation of microRNA network in prefrontal cortex of rats: relevance to depression pathophysiology, Transl. Psychiatry 5 (11) (2015) e682.
[55] J.A. Azevedo, B.S. Carter, F. Meng, D.L. Turner, M. Dai, A.F. Schatzberg, J.D. Barchas, E.G. Jones, W.E. Bunney, R.M. Myers, et al., The microRNA network is altered in anterior cingulate cortex of patients with unipolar and bipolar depression, J. Psychiatr. Res. 82 (2016) 58–67.
[56] A. Torres-Berrío, J.P. Lopez, R.C. Bagot, D. Nouel, G. Dal Bo, S. Cuesta, L. Zhu, C. Manitt, C. Eng, H.M. Cooper, et al., DCC confers susceptibility to depression-like behaviors in humans and mice and is regulated by miR-218, Biol. Psychiatr. 81 (4) (2017) 306–315.
[57] P. Patrício, A. Mateus-Pinheiro, N.D. Alves, M. Morais, A.J. Rodrigues, J.M. Bessa, N. Sousa, L. Pinto, miR-409 and miR-411 modulation in the adult brain of a rat model of depression and after fluoxetine treatment, Front. Behav. Neurosci. 14 (2020) 136.
[58] P. Patrício, A. Mateus-Pinheiro, M. Irmler, N.D. Alves, A.R. Machado-Santos, M. Morais, J.S. Correia, M. Korostynski, M. Piechota, R. Stoffel, et al., Differential and converging molecular mechanisms of antidepressants' action in the hippocampal dentate gyrus, Neuropsychopharmacol.: Off. Pub. Am. College Neuropsychopharmacol. 40 (2) (2015) 338–349.
[59] F. Bao, A.L. Slusher, M. Whitehurst, C.J. Huang, Circulating microRNAs are upregulated following acute aerobic exercise in obese individuals, Physiol. Behav. 197 (2018) 15–21.
[60] M.M.J. van den Berg, J. Krauskopf, J.G. Ramaekers, J.C.S. Kleinjans, J. Prickaerts, J.J. Briedé, Circulating microRNAs as potential biomarkers for psychiatric and neurodegenerative disorders, Prog. Neurobiol. 185 (2020) 101732.
[61] W.M. Pardridge, CSF, blood-brain barrier, and brain drug delivery, Expet Opin. Drug Deliv. 13 (7) (2016) 963–975.
[62] A. Kopková, J. Šána, M. Večeřa, P. Fadrus, R. Lipina, M. Smrčka, M. Lojová, O. Slabý, MicroRNAs in cerebrospinal fluid as biomarkers in brain tumor patients, Klin. Onkol. : casopis Ceske a Slovenske onkologicke spolecnosti 32 (3) (2019) 181–186.
[63] T. Shalaby, M.A. Grotzer, Tumor-associated CSF MicroRNAs for the prediction and evaluation of CNS malignancies, Int. J. Mol. Sci. 16 (12) (2015) 29103–29119.
[64] K. Wakamatsu, Y. Chiba, R. Murakami, Y. Miyai, K. Matsumoto, M. Kamada, W. Nonaka, N. Uemura, K. Yanase, M. Ueno, Metabolites and biomarker compounds of neurodegenerative diseases in cerebrospinal fluid, Metabolites 12 (4) (2022).
[65] Q. Zhou, J. Liu, J. Quan, W. Liu, H. Tan, W. Li, MicroRNAs as potential biomarkers for the diagnosis of glioma: a systematic review and meta-analysis, Cancer Sci. 109 (9) (2018) 2651–2659.
[66] K. Blennow, H. Zetterberg, Biomarkers for Alzheimer's disease: current status and prospects for the future, J. Intern. Med. 284 (6) (2018) 643–663.
[67] P. Hermann, B. Appleby, J.P. Brandel, B. Caughey, S. Collins, M.D. Geschwind, A. Green, S. Haïk, G.G. Kovacs, A. Ladogana, et al., Biomarkers and diagnostic guidelines for sporadic Creutzfeldt-Jakob disease, Lancet Neurol. 20 (3) (2021) 235–246.
[68] B. Olsson, R. Lautner, U. Andreasson, A. Öhrfelt, E. Portelius, M. Bjerke, M. Hölttä, C. Rosén, C. Olsson, G. Strobel, et al., CSF and blood biomarkers for the diagnosis of Alzheimer's disease: a systematic review and meta-analysis, Lancet Neurol. 15 (7) (2016) 673–684.
[69] L. Parnetti, L. Gaetani, P. Eusebi, S. Paciotti, O. Hansson, O. El-Agnaf, B. Mollenhauer, K. Blennow, P. Calabresi, CSF and blood biomarkers for Parkinson's disease, Lancet Neurol. 18 (6) (2019) 573–586.

[70] K. Satoh, CSF biomarkers for prion diseases, Neurochem. Int. 155 (2022) 105306.
[71] Q.Y. Shao, F. You, Y.H. Zhang, L.L. Hu, W.J. Liu, Y. Liu, J. Li, S.D. Wang, M.F. Song, CSF miR-16 expression and its association with miR-16 and serotonin transporter in the raphe of a rat model of depression, J. Affect. Disord. 238 (2018) 609–614.
[72] Y. Wan, Y. Liu, X. Wang, J. Wu, K. Liu, J. Zhou, L. Liu, C. Zhang, Identification of differential microRNAs in cerebrospinal fluid and serum of patients with major depressive disorder, PLoS One 10 (3) (2015) e0121975.
[73] M.F. Song, J.Z. Dong, Y.W. Wang, J. He, X. Ju, L. Zhang, Y.H. Zhang, J.F. Shi, Y.Y. Lv, CSF miR-16 is decreased in major depression patients and its neutralization in rats induces depression-like behaviors via a serotonin transmitter system, J. Affect. Disord. 178 (2015) 25–31.
[74] Y.Y. van der Zee, L.M.T. Eijssen, P. Mews, A. Ramakrishnan, K. Alvarez, C.K. Lardner, H.M. Cates, D.M. Walker, A. Torres-Berrío, C.J. Browne, et al., Blood miR-144-3p: a novel diagnostic and therapeutic tool for depression, Mol. Psychiatr. 27 (11) (2022) 4536–4549.
[75] E. Maffioletti, A. Cattaneo, G. Rosso, G. Maina, C. Maj, M. Gennarelli, D. Tardito, L. Bocchio-Chiavetto, Peripheral whole blood microRNA alterations in major depression and bipolar disorder, J. Affect. Disord. 200 (2016) 250–258.
[76] M. Krivosova, J. Adamcakova, E. Kaadt, B.H. Mumm, D. Dvorska, D. Brany, Z. Dankova, M. Dohal, M. Samec, N. Ferencova, et al., The VEGF protein levels, miR-101-3p, and miR-122-5p are dysregulated in plasma from adolescents with major depression, J. Affect. Disord. 334 (2023) 60–68.
[77] J. Hu, W. Zhou, Z. Zhou, Q. Yang, J. Xu, W. Dong, miR-22 and cerebral microbleeds in brainstem and deep area are associated with depression one month after ischemic stroke, Braz. J. Med. Biol. Res. 53 (5) (2020) e9162.
[78] A. Gheysarzadeh, N. Sadeghifard, L. Afraidooni, F. Pooyan, M.R. Mofid, H. Valadbeigi, H. Bakhtiari, S. Keikhavani, Serum-based microRNA biomarkers for major depression: MiR-16, miR-135a, and miR-1202, J. Res. Med. Sci. 23 (2018) 69.
[79] Y. Fang, Q. Qiu, S. Zhang, L. Sun, G. Li, S. Xiao, X. Li, Changes in miRNA-132 and miR-124 levels in non-treated and citalopram-treated patients with depression, J. Affect. Disord. 227 (2018) 745–751.
[80] H. Ogata, K. Higasa, Y. Kageyama, H. Tahara, A. Shimamoto, Y. Takekita, Y. Koshikawa, S. Nonen, T. Kato, T. Kinoshita, et al., Relationship between circulating mitochondrial DNA and microRNA in patients with major depression, J. Affect. Disord. 339 (2023) 538–546.
[81] S. Bhatt, J. Kanoujia, A.K. Dhar, S. Arumugam, A.K.A. Silva, N. Mishra, Exosomes: a novel therapeutic paradigm for the treatment of depression, Curr. Drug Targets 22 (2) (2021) 183–191.
[82] C.C. Chen, L. Liu, F. Ma, C.W. Wong, X.E. Guo, J.V. Chacko, H.P. Farhoodi, S.X. Zhang, J. Zimak, A. Ségaliny, et al., Elucidation of exosome migration across the blood-brain barrier model in vitro, Cell. Mol. Bioeng. 9 (4) (2016) 509–529.
[83] M.C. Cufaro, D. Pieragostino, P. Lanuti, C. Rossi, I. Cicalini, L. Federici, V. De Laurenzi, P. Del Boccio, Extracellular vesicles and their potential use in monitoring cancer progression and therapy: the contribution of proteomics, J. Oncol. 2019 (2019) 1639854.
[84] Z.Y. Yao, W.B. Chen, S.S. Shao, S.Z. Ma, C.B. Yang, M.Z. Li, J.J. Zhao, L. Gao, Role of exosome-associated microRNA in diagnostic and therapeutic applications to metabolic disorders, J. Zhejiang Univ. - Sci. B 19 (3) (2018) 183–198.
[85] L. Jiang, H. Dong, H. Cao, X. Ji, S. Luan, J. Liu, Exosomes in pathogenesis, diagnosis, and treatment of Alzheimer's disease, Med. Sci. Mon. Int. Med. J. Exp. Clin. Res. 25 (2019) 3329–3335.
[86] K.M. Kanninen, N. Bister, J. Koistinaho, T. Malm, Exosomes as new diagnostic tools in CNS diseases, Biochim. Biophys. Acta 1862 (3) (2016) 403–410.
[87] D.Q. Beversdorf, K. Sohl, D. Levitskiy, P. Tennant, R.P. Goin-Kochel, R.C. Shaffer, A. Confair, F.A. Middleton, S.D. Hicks, Saliva RNA biomarkers of gastrointestinal dysfunction in children with autism and neurodevelopmental disorders: potential implications for precision medicine, Front. Psychiatr. 12 (2021) 824933.
[88] T. Kircher, M. Wöhr, I. Nenadic, R. Schwarting, G. Schratt, J. Alferink, C. Culmsee, H. Garn, T. Hahn, B. Müller-Myhsok, et al., Neurobiology of the major psychoses: a translational perspective on brain structure and function-the FOR2107 consortium, Eur. Arch. Psychiatr. Clin. Neurosci. 269 (8) (2019) 949–962.
[89] A. Masotti, A. Baldassarre, M.P. Guzzo, C. Iannuccelli, C. Barbato, M. Di Franco, Circulating microRNA profiles as liquid biopsies for the characterization and diagnosis of fibromyalgia syndrome, Mol. Neurobiol. 54 (9) (2017) 7129–7136.
[90] M.C. Bridges, A.C. Daulagala, A. Kourtidis, LNCcation: lncRNA localization and function, J. Cell Biol. 220 (2) (2021).
[91] Z. Yang, S. Jiang, J. Shang, Y. Jiang, Y. Dai, B. Xu, Y. Yu, Z. Liang, Y. Yang, LncRNA: shedding light on mechanisms and opportunities in fibrosis and aging, Ageing Res. Rev. 52 (2019) 17–31.
[92] T. Ali, P. Grote, Beyond the RNA-dependent function of LncRNA genes, Elife 9 (2020).
[93] X. Ding, Y. Lin, B. Yan, X. Jiao, Q. Liu, H. Miao, Y. Wu, C. Zhou, LncRNA XR_351665 contributes to chronic pain-induced depression by upregulating DNMT1 via sponging miR-152-3p, J. Pain 24 (3) (2023) 449–462.
[94] J. Zhu, J. Tang, LncRNA Gm14205 induces astrocytic NLRP3 inflammasome activation via inhibiting oxytocin receptor in postpartum depression, Biosci. Rep. 40 (8) (2020).
[95] Y. Huang, Y. Jin, S. Yao, G. Nan, Y. Mao, LncRNA NEAT1 Inhibits Neuronal Apoptosis and Induces Neuronal Viability of Depressed Rats via microRNA-320-3p/CRHR1 Axis, 2022. *Neurochemical research*.
[96] Z. Huan, Z. Mei, H. Na, M. Xinxin, W. Yaping, L. Ling, W. Lei, Z. Kejin, L. Yanan, lncRNA MIR155HG alleviates depression-like behaviors in mice by regulating the miR-155/BDNF Axis, Neurochem. Res. 46 (4) (2021) 935–944.
[97] Y. Wu, W. Rong, Q. Jiang, R. Wang, H. Huang, Downregulation of lncRNA GAS5 alleviates hippocampal neuronal damage in mice with depression-like behaviors via modulation of MicroRNA-26a/EGR1 Axis, J. Stroke Cerebrovasc. Dis. : Off. J. Nat. Stroke Assoc. 30 (3) (2021) 105550.
[98] X. Huang, Y.L. Luo, Y.S. Mao, J.L. Ji, The link between long noncoding RNAs and depression, Prog. Neuro-Psychopharmacol. Biol. Psychiatry 73 (2017) 73–78.
[99] T. Derrien, R. Johnson, G. Bussotti, A. Tanzer, S. Djebali, H. Tilgner, G. Guernec, D. Martin, A. Merkel, D.G. Knowles, et al., The GENCODE v7 catalog of human long noncoding RNAs: analysis of their gene structure, evolution, and expression, Genome Res. 22 (9) (2012) 1775–1789.
[100] H. Ling, K. Vincent, M. Pichler, R. Fodde, I. Berindan-Neagoe, F.J. Slack, G.A. Calin, Junk DNA and the long non-coding RNA twist in cancer genetics, Oncogene 34 (39) (2015) 5003–5011.
[101] O. Issler, Y.Y. van der Zee, A. Ramakrishnan, J. Wang, C. Tan, Y.E. Loh, I. Purushothaman, D.M. Walker, Z.S. Lorsch, P.J. Hamilton, et al., Sex-specific role for the long non-coding RNA LINC00473 in depression, Neuron 106 (6) (2020) 912–926.e915.
[102] Y. Zhou, P.E. Lutz, Y.C. Wang, J. Ragoussis, G. Turecki, Global long non-coding RNA expression in the rostral anterior cingulate cortex of depressed suicides, Transl. Psychiatry 8 (1) (2018) 224.
[103] L. Wang, M. Zhang, H. Zhu, L. Sun, B. Yu, X. Cui, Combined identification of lncRNA NONHSAG004550 and NONHSAT125420 as a potential diagnostic biomarker of perinatal depression, J. Clin. Lab. Anal. 35 (8) (2021) e23890.
[104] N. Ye, S. Rao, T. Du, H. Hu, Z. Liu, Y. Shen, Q. Xu, Intergenic variants may predispose to major depression disorder through regulation of long non-coding RNA expression, Gene 601 (2017) 21–26.
[105] S.I. Rapoport, Lithium and the other mood stabilizers effective in bipolar disorder target the rat brain arachidonic acid cascade, ACS Chem. Neurosci. 5 (6) (2014) 459–467.
[106] D.V. Bavaresco, T. Colonetti, A.J. Grande, F. Colom, S.S. Valvassori, J. Quevedo, M.I. da Rosa, Efficacy of celecoxib adjunct treatment on bipolar disorder: systematic review and meta-analysis, CNS Neurol. Disord. - Drug Targets 18 (1) (2019) 19–28.
[107] X. Ni, Y. Liao, L. Li, X. Zhang, Z. Wu, Therapeutic role of long non-coding RNA TCONS_00019174 in depressive disorders is dependent on Wnt/β-catenin signaling pathway, J. Integr. Neurosci. 17 (2) (2018) 125–132.
[108] B. Roy, Q. Wang, Y. Dwivedi, Long noncoding RNA-associated transcriptomic changes in resiliency or susceptibility to depression and response to antidepressant treatment, Int. J. Neuropsychopharmacol. 21 (5) (2018) 461–472.
[109] H.D. Zhang, L.H. Jiang, D.W. Sun, J.C. Hou, Z.L. Ji, CircRNA: a novel type of biomarker for cancer, Breast Cancer 25 (1) (2018) 1–7.
[110] J. Salzman, C. Gawad, P.L. Wang, N. Lacayo, P.O. Brown, Circular RNAs are the predominant transcript isoform from hundreds of human genes in diverse cell types, PLoS One 7 (2) (2012) e30733.
[111] H.A. Vincent, M.P. Deutscher, Substrate recognition and catalysis by the exoribonuclease RNase R, J. Biol. Chem. 281 (40) (2006) 29769–29775.

[112] C. Fan, Y. Li, T. Lan, W. Wang, Y. Long, S.Y. Yu, Microglia secrete miR-146a-5p-containing exosomes to regulate neurogenesis in depression, Mol. Ther.: J. Am. Soc. Gene Therapy 30 (3) (2022) 1300–1314.
[113] R. Huang, Y. Zhang, Y. Bai, B. Han, M. Ju, B. Chen, L. Yang, Y. Wang, H. Zhang, H. Zhang, et al., N(6)-Methyladenosine modification of fatty acid amide hydrolase messenger RNA in circular RNA STAG1-regulated astrocyte dysfunction and depressive-like behaviors, Biol. Psychiatr. 88 (5) (2020) 392–404.
[114] X. Yu, Y. Bai, B. Han, M. Ju, T. Tang, L. Shen, M. Li, L. Yang, Z. Zhang, G. Hu, et al., Extracellular vesicle-mediated delivery of circDYM alleviates CUS-induced depressive-like behaviours, J. Extracell. Vesicles 11 (1) (2022) e12185.
[115] Y. Zhang, R. Huang, M. Cheng, L. Wang, J. Chao, J. Li, P. Zheng, P. Xie, Z. Zhang, H. Yao, Gut microbiota from NLRP3-deficient mice ameliorates depressive-like behaviors by regulating astrocyte dysfunction via circHIPK2, Microbiome 7 (1) (2019) 116.
[116] Y. Zhang, L. Du, Y. Bai, B. Han, C. He, L. Gong, R. Huang, L. Shen, J. Chao, P. Liu, et al., CircDYM ameliorates depressive-like behavior by targeting miR-9 to regulate microglial activation via HSP90 ubiquitination, Mol. Psychiatr. 25 (6) (2020) 1175–1190.
[117] X. Li, X. Sun, J. Xie, H. Wan, CircDYM ameliorates CUMS mice depressive-like behavior and inhibits hippocampal neurons injury via miR-497a-5p/NR3C1 axis, Brain Res. 1787 (2022) 147911.
[118] J. Wang, Z. Yang, C. Chen, Y. Xu, H. Wang, B. Liu, W. Zhang, Y. Jiang, Comprehensive circRNA expression profile and construction of circRNAs-related ceRNA network in a mouse model of autism, Front. Genet. 11 (2020) 623584.
[119] H. Meng, R. Niu, C. Huang, J. Li, Circular RNA as a novel biomarker and therapeutic target for HCC, Cells 11 (12) (2022).
[120] Y. Shi, X. Jia, J. Xu, The new function of circRNA: translation, Clin. Transl. Oncol. 22 (12) (2020) 2162–2169.
[121] J. Li, D. Sun, W. Pu, J. Wang, Y. Peng, Circular RNAs in cancer: biogenesis, function, and clinical significance, Trends Cancer 6 (4) (2020) 319–336.
[122] S. Özdemir, H. Arslan, circRNA-based biomarker candidates for acute cypermethrin and chlorpyrifos toxication in the brain of Zebrafish (Danio rerio), Chemosphere 298 (2022) 134330.
[123] Z. Zhang, T. Yang, J. Xiao, Circular RNAs: promising biomarkers for human diseases, EBioMedicine 34 (2018) 267–274.
[124] L. Caba, L. Florea, C. Gug, D.C. Dimitriu, E.V. Gorduza, Circular RNA-is the circle perfect? Biomolecules 11 (12) (2021).
[125] Z. Cheng, Y. Zhang, S. Wu, R. Zhao, Y. Yu, Y. Zhou, Z. Zhou, Y. Dong, A. Qiu, H. Xu, et al., Peripheral blood circular RNA hsa_circ_0058493 as a potential novel biomarker for silicosis and idiopathic pulmonary fibrosis, Ecotoxicol. Environ. Saf. 236 (2022) 113451.
[126] Z. Mi, C. Zhongqiang, J. Caiyun, L. Yanan, W. Jianhua, L. Liang, Circular RNA detection methods: a minireview, Talanta 238 (Pt 2) (2022) 123066.
[127] X. Cui, W. Niu, L. Kong, M. He, K. Jiang, S. Chen, A. Zhong, W. Li, J. Lu, L. Zhang, hsa_circRNA_103636: potential novel diagnostic and therapeutic biomarker in Major depressive disorder, Biomarkers Med. 10 (9) (2016) 943–952.
[128] R. Song, Y. Bai, X. Li, J. Zhu, H. Zhang, Y. Shi, K. Li, B. Wang, H. Zhang, Y. Yang, et al., Plasma circular RNA DYM related to major depressive disorder and rapid antidepressant effect treated by visual cortical repetitive transcranial magnetic stimulation, J. Affect. Disord. 274 (2020) 486–493.
[129] D. Zhang, Y. Ji, X. Chen, R. Chen, Y. Wei, Q. Peng, J. Lin, J. Yin, H. Li, L. Cui, et al., Peripheral blood circular RNAs as a biomarker for major depressive disorder and prediction of possible pathways, Front. Neurosci. 16 (2022) 844422.
[130] Y. Shi, R. Song, Z. Wang, H. Zhang, J. Zhu, Y. Yue, Y. Zhao, Z. Zhang, Potential clinical value of circular RNAs as peripheral biomarkers for the diagnosis and treatment of major depressive disorder, EBioMedicine 66 (2021) 103337.
[131] J. Mao, T. Li, D. Fan, H. Zhou, J. Feng, L. Liu, C. Zhang, X. Wang, Abnormal expression of rno_circRNA_014900 and rno_circRNA_005442 induced by ketamine in the rat hippocampus, BMC Psychiatr. 20 (1) (2020) 1.
[132] T.L. Greer, Circular RNAs as putative biomarkers for depression diagnosis and treatment, EBioMedicine 68 (2021) 103362.
[133] H. Zhang, Z. Chen, Z. Zhong, W. Gong, J. Li, Total saponins from the leaves of Panax notoginseng inhibit depression on mouse chronic unpredictable mild stress model by regulating circRNA expression, Brain Behav. 8 (11) (2018) e01127.
[134] W. Alshaer, H. Zureigat, A. Al Karaki, A. Al-Kadash, L. Gharaibeh, M.M. Hatmal, A.A.A. Aljabali, A. Awidi, siRNA: mechanism of action, challenges, and therapeutic approaches, Eur. J. Pharmacol. 905 (2021) 174178.
[135] R.R. Nikam, K.R. Gore, Journey of siRNA: clinical developments and targeted delivery, Nucleic Acid Therapeut. 28 (4) (2018) 209–224.
[136] N. Fullana, J. Gasull-Camós, M. Tarrés-Gatius, A. Castañé, A. Bortolozzi, F. Artigas, Astrocyte control of glutamatergic activity: downstream effects on serotonergic function and emotional behavior, Neuropharmacology 166 (2020) 107914.
[137] L.T. Guo, S.Q. Wang, J. Su, L.X. Xu, Z.Y. Ji, R.Y. Zhang, Q.W. Zhao, Z.Q. Ma, X.Y. Deng, S.P. Ma, Baicalin ameliorates neuroinflammation-induced depressive-like behavior through inhibition of toll-like receptor 4 expression via the PI3K/AKT/FoxO1 pathway, J. Neuroinflammation 16 (1) (2019) 95.
[138] W. Liao, Y. Liu, H. Huang, H. Xie, W. Gong, D. Liu, F. Tian, R. Huang, F. Yi, J. Zhou, Intersectional analysis of chronic mild stress-induced lncRNA-mRNA interaction networks in rat hippocampus reveals potential anti-depression/anxiety drug targets, Neurobiol. Stress 15 (2021) 100347.
[139] L. Liu, H. Wang, X. Chen, Y. Zhang, W. Li, X. Rao, Y. Liu, L. Zhao, J. Pu, S. Gui, et al., Integrative analysis of long non-coding RNAs, messenger RNAs, and MicroRNAs indicates the neurodevelopmental dysfunction in the Hippocampus of gut microbiota-dysbiosis mice, Front. Mol. Neurosci. 14 (2021) 745437.
[140] A. Bahi, Hippocampal BDNF overexpression or microR124a silencing reduces anxiety- and autism-like behaviors in rats, Behav. Brain Res. 326 (2017) 281–290.
[141] E. Pascale, C. Beclin, A. Fiorenzano, G. Andolfi, A. Erni, S. De Falco, G. Minchiotti, H. Cremer, A. Fico, Long non-coding RNA T-UCstem1 controls progenitor proliferation and neurogenesis in the postnatal mouse olfactory bulb through interaction with miR-9, Stem Cell Rep. 15 (4) (2020) 836–844.
[142] L. Torner, Actions of prolactin in the brain: from physiological adaptations to stress and neurogenesis to psychopathology, Front. Endocrinol. 7 (2016) 25.
[143] T. Bu, Z. Qiao, W. Wang, X. Yang, J. Zhou, L. Chen, J. Yang, J. Xu, Y. Ji, Y. Wang, et al., Diagnostic biomarker Hsa_circ_0126218 and functioning prediction in peripheral blood monocular cells of female patients with major depressive disorder, Front. Cell Dev. Biol. 9 (2021) 651803.
[144] E. Marfil-Marin, M. Santamaría-Olmedo, A. PerezGrovas-Saltijeral, M. Valdes-Flores, A. Ochoa-Morales, A. Jara-Prado, R. Sevilla-Montoya, A. Camacho-Molina, A. Hidalgo-Bravo, circRNA regulates dopaminergic synapse, MAPK, and long-term depression pathways in huntington disease, Mol. Neurobiol. 58 (12) (2021) 6222–6231.
[145] H. Gan, Y. Lei, N. Yuan, K. Tang, W. Hao, Q. Ma, M. Wu, X. Zhou, X. Li, J. Huang, et al., Circular RNAs in depression: biogenesis, function, expression, and therapeutic potential, Biomed. Pharmacother. 137 (2021) 111244.
[146] H. Gao, H. Ma, M. Gao, A. Chen, S. Zha, J. Yan, Long non-coding RNA GAS5 aggravates myocardial depression in mice with sepsis via the microRNA-449b/HMGB1 axis and the NF-κB signaling pathway, Biosci. Rep. 41 (4) (2021).
[147] V. Micale, M. Di Bartolomeo, S. Di Martino, T. Stark, B. Dell'Osso, F. Drago, C. D'Addario, Are the epigenetic changes predictive of therapeutic efficacy for psychiatric disorders? A translational approach towards novel drug targets, Pharmacol. Ther. 241 (2023) 108279.
[148] F. Wu, Y. An, L. Zhou, Y. Zhao, L. Chen, J. Wang, G. Wu, Whole-transcriptome sequencing and ceRNA interaction network of temporomandibular joint osteoarthritis, Front. Genet. 13 (2022) 962574.
[149] T. Zhou, M. Li, Z. Xiao, J. Cai, W. Zhao, J. Duan, Z. Yang, Z. Guo, Y. Chen, W. Cai, et al., Chronic stress-induced gene changes in vitro and in vivo: potential biomarkers associated with depression and cancer based on circRNA- and lncRNA-associated ceRNA networks, Front. Oncol. 11 (2021) 744251.
[150] X. Wang, H. Song, Y. Du, Y. Zhao, Y. Fu, Q. Meng, Y. Gao, M. Gong, L. Song, S. Wang, et al., CircSYNDIG1 ameliorates stress-induced abnormal behaviors by suppressing miR-344-5p in mice, Brain Res. Bull. 195 (2023) 66–77.
[151] Y. Chen, P. Cao, Circ-Bnc2 alleviates neuroinflammation in LPS-stimulated microglial cells to inhibit neuron cell apoptosis through regulating miR-497a-5p/HECTD1 axis, Brain Behav. 13 (5) (2023) e2935.
[152] T. Yu, B. Xu, M. Bao, Y. Gao, Q. Zhang, X. Zhang, R. Liu, Identification of potential biomarkers and pathways associated with carotid atherosclerotic plaques in type 2 diabetes mellitus: a transcriptomics study, Front. Endocrinol. 13 (2022) 981100.
[153] H. Bian, G. Wang, J. Huang, L. Liang, Y. Zheng, Y. Wei, H. Wang, L. Xiao, H. Wang, Dihydrolipoic acid protects against lipopolysaccharide-induced behavioral deficits and neuroinflammation via regulation of Nrf2/HO-1/NLRP3 signaling in rat, J. Neuroinflammation 17 (1) (2020) 166.
[154] X.H. Tang, G.F. Zhang, N. Xu, G.F. Duan, M. Jia, R. Liu, Z.Q. Zhou, J.J. Yang, Extrasynaptic CaMKIIα is involved in the antidepressant effects of ketamine by downregulating GluN2B receptors in an LPS-induced depression model, J. Neuroinflammation 17 (1) (2020) 181.

[155] Y. Wang, Y. Xie, K.V. Kilchrist, J. Li, C.L. Duvall, D. Oupický, Endosomolytic and tumor-penetrating mesoporous silica nanoparticles for siRNA/miRNA combination cancer therapy, ACS Appl. Mater. Interfaces 12 (4) (2020) 4308–4322.
[156] E.M. Park, S. Gelber, S.M. Rosenberg, D.S.E. Seah, L. Schapira, S.E. Come, A.H. Partridge, Anxiety and depression in young women with metastatic breast cancer: a cross-sectional study, Psychosomatics 59 (3) (2018) 251–258.
[157] E. Maffioletti, A. Salvi, I. Conde, C. Maj, M. Gennarelli, G. De Petro, L. Bocchio-Chiavetto, Study of the in vitro modulation exerted by the antidepressant drug escitalopram on the expression of candidate microRNAs and their target genes, Mol. Cell. Neurosci. 85 (2017) 220–225.
[158] W.H. Kuang, Z.Q. Dong, L.T. Tian, J. Li, MicroRNA-451a, microRNA-34a-5p, and microRNA-221-3p as predictors of response to antidepressant treatment, Braz. J. Med. Biol. Res. 51 (7) (2018) e7212.
[159] J. Li, H. Meng, W. Cao, T. Qiu, MiR-335 is involved in major depression disorder and antidepressant treatment through targeting GRM4, Neurosci. Lett. 606 (2015) 167–172.
[160] C. Chen, Y.J. Xu, S.R. Zhang, X.H. Wang, Y. Hu, D.H. Guo, X.J. Zhou, W.Y. Zhu, A.D. Wen, Q.R. Tan, et al., MiR-1281 is involved in depression disorder and the antidepressant effects of Kai-Xin-San by targeting ADCY1 and DVL1, Heliyon 9 (3) (2023) e14265.
[161] E. Ivanova, R. Bozhilova, R. Kaneva, V. Milanova, The dysregulation of microRNAs and the role of stress in the pathogenesis of mental disorders, Curr. Top. Med. Chem. 18 (21) (2018) 1893–1907.
[162] B. Miller, Z. Zeier, L. Xi, T. Lanz, S. Deng, J. Strathmann, D. Willoughby, P. Kenny, J. Elsworth, M. Lawrence, et al., MicroRNA-132 dysregulation in schizophrenia has implications for both neurodevelopment and adult brain function, Bio. Sci. 109 (8) (2012) 3125–3130.
[163] J. Ma, S. Shang, J. Wang, T. Zhang, F. Nie, X. Song, Heping Zhao, C. Zhu, R. Zhang, D. Hao, Identification of miR-22-3p, miR-92a-3p, and miR-137 in peripheral blood as biomarker for schizophrenia, Psychiatry Res. 265 (2018) 70–76.
[164] J. Wong, C. Duncan, N. Beveridge, M. Webster, M. Cairns, C. Weickert, Expression of NPAS3 in the human cortex and evidence of its posttranscriptional regulation by miR-17 during development, with implications for schizophrenia, Schizophr Bull. 39 (2) (2013) 396–406.
[165] W. Wang, B. Rajeev, A. Stromberg, N. Ren, G. Tang, Q. Huang, I. Rigoutsos, P.J.T. Nelson, The expression of microRNA miR-107 decreases early in Alzheimer's disease and may accelerate disease progression through regulation of beta-site amyloid precursor protein-cleaving enzyme 1, J. Neurosci. 28 (5) (2008) 1213–1223.
[166] C. Cheng, W. Li, Z. Zhang, S. Yoshimura, Q. Hao, C. Zhang, Z.J.T. Wang, MicroRNA-144 is regulated by activator protein-1 (AP-1) and decreases expression of Alzheimer disease-related a disintegrin and metalloprotease 10 (ADAM10), J. Biol. Chem. 288 (19) (2013) 13748–13761.
[167] C. Sala Frigerio, P. Lau, E. Salta, J. Tournoy, K. Bossers, R. Vandenberghe, A. Wallin, M. Bjerke, H. Zetterberg, K. Blennow, et al., Reduced expression of hsa-miR-27a-3p in CSF of patients with Alzheimer disease, Neurology 81 (24) (2013) 2103–2106.
[168] H. Geekiyanage, C.J.T. Chan, MicroRNA-137/181c regulates serine palmitoyltransferase and in turn amyloid β, novel targets in sporadic Alzheimer's disease, J. Neurosci. 31 (41) (2011) 14820–14830.
[169] T. Jiang, Y. Yang, C. Wu, C. Qu, J. Chen, H. Cao, MicroRNA-218 regulates neuronal radial migration and morphogenesis by targeting Satb2 in developing neocortex, Biochem. Biophys. Res. Commun. 647 (2023) 9–15.
[170] H. Atwan, M. Assarehzadegan, M. Shekarabi, S. Jazayeri, S. Barfi, R. Shokouhi Shoormasti, N. Chimeh, H. Pouretemad, Tayebi BJIjoa, asthma, immunology, Assessment of miR-181b-5p, miR-23a-3p, BCL-2, and IL-6 in peripheral blood mononuclear cells of autistic patients, Likelihood Reliable Biomark. 19 (1) (2020) 74–83.
[171] B.M. Zamil, R. Ali-Labib, W.Y. Youssef, E. Khairy, Evaluation of miR-106a and ADARB1 in autistic children, Gene Rep. 18 (2020) 100586.
[172] J. Zhou, P. Nagarkatti, Y. Zhong, J. Ginsberg, N. Singh, J. Zhang, M. Nagarkatti, Dysregulation in microRNA expression is associated with alterations in immune functions in combat veterans with post-traumatic stress disorder, PLoS One 9 (4) (2014) e94075.
[173] R. Wang, R. Phang, P. Hsu, W. Wang, H. Huang, I. Liu, In vivo knockdown of hippocampal miR-132 expression impairs memory acquisition of trace fear conditioning, Hippocampus 23 (7) (2013) 625–633.
[174] B.I. Arioz, B. Tastan, E. Tarakcioglu, K.U. Tufekci, M. Olcum, N. Ersoy, A. Bagriyanik, K. Genc, S. Genc, Melatonin attenuates LPS-induced acute depressive-like behaviors and microglial NLRP3 inflammasome activation through the SIRT1/nrf2 pathway, Front. Immunol. 10 (2019) 1511.
[175] B. Khavari, M. Cairns, Epigenomic dysregulation in schizophrenia: in search of disease etiology and biomarkers, Cells 9 (8) (2020).
[176] A. Kim, M. Reimers, B. Maher, V. Williamson, O. McMichael, J. McClay, E. van den Oord, B. Riley, K. Kendler, V. Vladimirov, MicroRNA expression profiling in the prefrontal cortex of individuals affected with schizophrenia and bipolar disorders, Schizophr Res. 124 (2010) 183–191.
[177] S. Liu, F. Zhang, Y. Shugart, L. Yang, X. Li, Z. Liu, N. Sun, C. Yang, X. Guo, J. Shi, et al., The early growth response protein 1-miR-30a-5p-neurogenic differentiation factor 1 axis as a novel biomarker for schizophrenia diagnosis and treatment monitoring, Hereditas 7 (1) (2017) e998.
[178] P. Nelson, W.J. Wang, MiR-107 is reduced in Alzheimer's disease brain neocortex: validation study, J. Alzheimers Dis. 21 (1) (2010) 75–79.
[179] G. Yang, Y. Song, X. Zhou, Y. Deng, T. Liu, G. Weng, D. Yu, S. Pan, MicroRNA-29c targets β-site amyloid precursor protein-cleaving enzyme 1 and has a neuroprotective role in vitro and in vivo, Mol. Med. Rep. 12 (2) (2015) 3081–3088.
[180] J. Zhang, M. Hu, Z. Teng, Y. Tang, C.J.T. Chen, Synaptic and cognitive improvements by inhibition of 2-AG metabolism are through upregulation of microRNA-188-3p in a mouse model of Alzheimer's disease, J. Neurosci. 34 (45) (2014) 14919–14933.
[181] J. Long, B. Ray, D.J.T. Lahiri, MicroRNA-339-5p down-regulates protein expression of β-site amyloid precursor protein-cleaving enzyme 1 (BACE1) in human primary brain cultures and is reduced in brain tissue specimens of Alzheimer disease subjects, J. Biol. Chem. 289 (8) (2014) 5184–5198.
[182] J. Kim, H. Yoon, T. Horie, J. Burchett, J. Restivo, N. Rotllan, C. Ramírez, P. Verghese, M. Ihara, H. Hoe, et al., microRNA-33 regulates ApoE lipidation and amyloid-β metabolism in the brain, J. Neurosci. 35 (44) (2015) 14717–14726.
[183] G. Vetere, C. Barbato, S. Pezzola, P. Frisone, M. Aceti, M. Ciotti, C. Cogoni, M. Ammassari-Teule, F. Ruberti, Selective inhibition of miR-92 in hippocampal neurons alters contextual fear memory, Hippocampus 24 (12) (2014) 1458–1465.
[184] H. Zhao, R. Yao, X. Cao, G.J. Wu, Neuroimmune modulation following traumatic stress in rats: evidence for an immunoregulatory cascade mediated by c-Src, miRNA222 and PAK1, J. Neuroinflamm. 8 (2011) 159.
[185] E. Griggs, E. Young, G. Rumbaugh, C.J.T. Miller, MicroRNA-182 regulates amygdala-dependent memory formation, J. Neurosci. 33 (4) (2013) 1734–1740.
[186] Y. Ozkul, S. Taheri, K. Bayram, E. Sener, E. Mehmetbeyoglu, D. Öztop, F. Aybuga, E. Tufan, A. Bayram, N. Dolu, et al., A heritable profile of six miRNAs in autistic patients and mouse models, Scientific Rep. 10 (1) (2020) 9011.