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Review

Epigenetics of Alzheimer's Disease

Matea Nikolac Perkovic [1,†], Alja Videtic Paska [2,†], Marcela Konjevod [1], Katarina Kouter [2], Dubravka Svob Strac [1], Gordana Nedic Erjavec [1] and Nela Pivac [1,*]

[1] Laboratory for Molecular Neuropsychiatry, Division of Molecular Medicine, Ruder Boskovic Institute, HR-10000 Zagreb, Croatia; mnikolac@irb.hr (M.N.P.); mkonjev@irb.hr (M.K.); dsvob@irb.hr (D.S.S.); gnedic@irb.hr (G.N.E.)

[2] Medical Center for Molecular Biology, Institute of Biochemistry and Molecular Genetics, Faculty of Medicine, University of Ljubljana, SI-1000 Ljubljana, Slovenia; alja.videtic@mf.uni-lj.si (A.V.P.); katarina.kouter@mf.uni-lj.si (K.K.)

* Correspondence: npivac@irb.hr; Tel.: +38-514-571-207

† M.N.P. and A.V.P. equally contributed to this work.

Abstract: There are currently no validated biomarkers, which can be used to accurately diagnose Alzheimer's disease (AD), and to distinguish it from other dementia-causing neuropathologies. Moreover, to date, only symptomatic treatments exist for this progressive neurodegenerative disorder. In the search for new, more reliable biomarkers, and potential therapeutic options, epigenetic modifications have emerged as important players in the pathogenesis of AD. The aim of the article was to provide a brief overview of the current knowledge regarding the role of epigenetics (including mitoepigenetics) in AD, and the possibility of applying these advances for future AD therapy. Extensive research has suggested an important role of DNA methylation and hydroxymethylation, histone posttranslational modifications, and noncoding RNA regulation (with the emphasis on microRNAs) in the course and development of AD. Recent studies also indicated mitochondrial DNA (mtDNA) as an interesting biomarker of AD, since dysfunctions in the mitochondria, as well as lower mtDNA copy number, have been associated with AD pathophysiology. The current evidence suggest that epigenetic changes can be successfully detected, not only in the central nervous system, but also in the cerebrospinal fluid and on the periphery, contributing further to their potential as both biomarkers and therapeutic targets in AD.

Keywords: epigenetics; mitoepigenetics; DNA methylation; DNA hydroxymethylation; miRNA; histone modifications; Alzheimer's disease

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Table S1. Overview of studies investigating miRNA expression in AD.

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
let-7b	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-let-7b-5p&full=1	AD (*n* = 25), MCI (*n* = 30), Ctrl (*n* = 31); Longitudinal cohort: MCI-MCI-Dementia (*n* = 6), Ctrl-MCI-Dementia (*n* = 6), Ctrl-MCI-MCI (*n* = 6)	Plasma Array/RT-qPCR	Expression of let-7b increased in MCI subjects. Expression of miR-206 increased in AD subjects.	[217]
			AD (*n* = 17), SMC (*n* = 41), MCI (*n* = 36)	CSF RT-qPCR	Expression of let-7b increased in association with the progression of AD.	[290]
let-7d-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-let-7d-5p&full=1	AD (*n* = 11/20), MCI (*n* = 9/0), Ctrl (*n* = 20/17)	Plasma miRNA-seq/RT-qPCR	Expression of let-7d-5p, let-7g-5p, miR-15b-5p, miR-142-3p, miR-191-5p, miR-301a-3p and miR-545-3p deregulated in AD.	[291]
let-7f-5p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-let-7f-5p&full=1	AD (*n* = 27), Ctrl (*n* = 18)	Serum miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
let-7g-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-let-7g-5p&full=1	AD (*n* = 11/20), MCI (*n* = 9/0), Ctrl (*n* = 20/17)	Plasma miRNA-seq/RT-qPCR	Expression of let-7d-5p, let-7g-5p, miR-15b-5p, miR-142-3p, miR-191-5p, miR-301a-3p and miR-545-3p deregulated in AD.	[291]
let-7i-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-let-7i-5p&full=1	Aβ(−)MCI (*n* = 12), Aβ(+)MCI (*n* = 11), Ctrl (*n* = 9)	Platelets Array/RT-qPCR	Expression of let-7i-5p, miR-125a, miR-1233-5p, and miR-6787-5p downregulated in AD, miR-6880-5p upregulated in AD.	[292]
miR-9-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-9-5p&full=1	AD (*n* = 69), PD (*n* = 67), Ctrl (*n* = 78)	CSF miRNA-seq	Expression of 41 miRNAs deregulated in AD CSF, and 20 miRNAs in AD serum.	[164]
			Braak III-VI (*n* = 20), Braak 0-I (*n* = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
	↓		AD (*n* = 7), Ctrl (*n* = 7)	CNS (Neocortex) RT-qPCR	Expression of miR-137, miR-181c, miR-9, miR-29a, miR-29b-1, miR-15 and miR-124 downregulated in AD FCx.	[166]
			AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
miR-9-5p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-9-5p&full=1	AD (*n* = 10/18), Ctrl (*n* = 10/18)	CSF RT-qPRC	Expression of 15 microRNAs deregulated in AD. miR-9-5p and miR-598 suggested as potential biomarkers for AD.	[168]
			AD (*n* = 6), Ctrl (*n* = 6)	CNS (TCx) Array/RT-qPCR	Expression of miRNA-9, miRNA-125b, miRNA-146a, miRNA-155 increased in AD CSF and brain tissue-derived extracellular fluid.	[169]
			AD (*n* = 6), Ctrl (*n* = 6)	CNS (TCx) Array	Expression of miRNA-9, miRNA-125b and miRNA-146a up-regulated in AD TCx.	[170]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-9-5p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-9-5p&full=1	AD (*n* = 5), Ctrl (*n* = 5)	CNS (TCx) RT-qPCR	Expression of miR-146a, miR-155, miR-9, miR-125b, miR-34a, miR-25, miR-128, miR-15b, miR-454, miR-642, miR-20a, and miR-106a increased in AD neocortical extracellular fluid and CSF.	[171]
			AD (*n* = 5), Ctrl (*n* = 5)	CNS (HPC) Array	Expression of miR-9, miR-125b and miR-128 elevated and of miR-124a reduced in AD.	[172]
miR-15b-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-15b-5p&full=1	AD (*n* = 23/16), MCI (*n* = 3/8), Ctrl (*n* = 23/36)	Serum (Exosomes) miRNA-seq/RT-qPCR	Expression of 17 miRNA deregulated (14 miRNAs upregulated and 3 downregulated) in AD.	[293]
			AD (*n* = 11/20), MCI (*n* = 9/0), Ctrl (*n* = 20/17)	Plasma miRNA-seq/RT-qPCR	Expression of let-7d-5p, let-7g-5p, miR-15b-5p, miR-142-3p, miR-191-5p, miR-301a-3p and miR-545-3p deregulated in AD.	[291]
			AD (*n* = 40), Ctrl (*n* = 31); Validation cohort: publicly available dataset of miRNA data	Blood miRNA-seq	Expression of 71 deregulated in AD, including miR-146b-5p and miR-15b-5p.	[210]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-16-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-16-5p&full=1	AD (*n* = 10), Ctrl (*n* = 11)	CNS (HPC) RT-qPCR	Expression of miR-16, miR-34c, miR-107, miR-128a, and miR-146a were differentially regulated in AD HPC.	[196]
			Braak III-VI (*n* = 20), Braak 0-I (*n* = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
			AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-16-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-16-5p&full=1	AD (n = 12), Ctrl (n = 12)	CNS (HPC, TCx, CB) RT-qPCR	Expression of miR-103, miR-107, miR-15b, miR-16 and miR-195 reduced in AD HPC and TCx (including miR-15a), but not in CB.	[195]
miR-19b-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-19b-3p&full=1	AD (n = 20), Ctrl (n = 20)	Serum miRNA-seq/RT-qPCR	Expression of 72 miRNAs deregulated in AD (miR-146a-5p, miR-106b-3p, miR-195-5p, miR-20b-5p, and miR-497-5p upregulated, miR-125b-3p, miR-29c-3p, miR-93-5p and miR-19b-3p downregulated).	[182]
miR-22-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-22-3p&full=1	AD (n = 19/121), Ctrl (n = 9/86)	Serum miRNA-seq/RT-qPCR	Expression of miR-26a-5p, miR-181c-3p, miR-126-5p, miR-22-3p, miR-148b-5p, miR-106b-3p, miR-6119-5p, miR-1246, and miR-660-5p can be utilized as biomarker for detecting AD.	[294]
miR-27a-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-27a-3p&full=1	AD (n = 20/15), Ctrl (n = 19/18)	CSF RT-qPCR	Expression of miR-27a-3p level reduced in AD CSF.	[295]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-29a(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-29a-3p&full=1	AD (*n* = 10), Ctrl (*n* = 10)	CSF RT-qPCR	Expression of miR-34a and miR-146a decreased in AD plasma, and of miR-34a, miR-125b, and miR-146a in CSF.	[173]
			AD (*n* = 50/16); Ctrl (*n* = 49/16)	CSF Array/RT-qPCR	Expression of 36 miRNAs (20 in validation cohort) discriminate AD from control CSF.	[174]
		http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-29a-3p&full=1	AD (*n* = 7), Ctrl (*n* = 7)	CNS (Neocortex) RT-qPCR	Expression of miR-137, miR-181c, miR-9, miR-29a, miR-29b-1, miR-15 and miR-124 downregulated in AD FCx.	[166]
	↑		AD (*n* = 18), Ctrl (*n* = 20)	CSF RT-qPCR	Expression of miR-29a increased in AD CSF.	[175]

Epigenetic mechanism	**Effect**	**Gene/Target pathway involved** [1]	**Study model** [2]	**Tissue Study/design**	**Main results**	**References**
miR-29a(-3p)	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-29a-3p&full=1	Braak III-VI (*n* = 20), Braak 0-I (*n* = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
miR-29b(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-29b-3p&full=1	Probable AD (*n* = 7), aMCI/Probable Early AD (*n* = 7), Ctrl (*n* = 7)	Serum RT-qPCR	Expression of miR-137, miR-181c, miR-9, miR-29a/b down-regulated in probable AD patients.	[176]
			AD (*n* = 35), Ctrl (*n* = 35)	Plasma (Exosomes) miRNA-seq	Expression of 20 miRNAs deregulated in AD group.	[177]
			AD (*n* = 48), Ctrl (*n* = 22)	BloodomiRas and DIANA miRPath	Expression of 27 miRNAs discriminate between two groups.	[178]
			AD (*n* = 28), Ctrl (*n* = 25)	PBMC RT-qPCR	Expression of miR-29b downregulated in AD.	[179]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-29b(-3p)	↓		AD (n = 10), Ctrl (n = 5)	CNS (FCx) RT-qPCR	Expression of miR-125b increased in AD brains. Expression of miR-29a and 29b downregulated in AD.	[158]
			AD (n = 5), Ctrl (n = 5)	CNS (PCx) Array	Expression of 48 miRNAs differentially regulated in AD brain.	[180]
	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-29b-3p&full=1	Braak III–VI (n = 20), Braak 0–I (n = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
miR-29c(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-29c-3p&full=1	AD (n = 30), Ctrl (n = 30)	Blood RT-qPCR	Expression of miR-29c decreased in AD.	[181]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-29c(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-29c-3p&full=1	AD (*n* = 20), Ctrl (*n* = 20)	Serum miRNA-seq/RT-qPCR	Expression of 72 miRNAs deregulated in AD (miR-146a-5p, miR-106b-3p, miR-195-5p, miR-20b-5p, and miR-497-5p upregulated, miR-125b-3p, miR-29c-3p, miR-93-5p and miR-19b-3p downregulated).	[182]
			AD (*n* = 28), PD (*n* = 47), Ctrl (*n* = 27)	CSF (Exosomes) Array/RT-qPCR	Expression of miR-16-2, miR-331-5p, miR-132-5p, miR-485-5p, miR-151, miR-136-3p, and miR-29c were deregulated in AD CSF.	[183]
			AD (*n* = 30), Ctrl (*n* = 30)	CSF RT-qPCR	Expression of miR-29c decreased in AD CSF.	[184]
			AD (*n* = 31), Ctrl (*n* = 29)	CNS (FCx) RT-qPCR	Expression of miR-29c downregulated in sporadic AD brains.	[185]
			AD (*n* = 5), Ctrl (*n* = 5)	CNS (PCx) Array	Expression of 48 miRNA deregulated in AD brains.	[180]
	↑		AD (*n* = 10), VD (*n* = 4), FTD (*n* = 4), DLB (*n* = 2)	CSF RT-qPCR	Expression of let-7i-5p and miR-15a-5p upregulated and of miR-29c-3p downregulated in AD.	[186]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-30a-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-30a-3p&full=1	AD (n = 50/16), Ctrl (n = 49/16)	CSF Array/RT-qPCR	Expression of 36 miRNAs (20 in validation cohort) discriminate AD from control CSF.	[174]
	↑		Braak V (n = 10), Braak I (n = 10)	CSF RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
miR-34a(-5p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-34a-5p&full=1	AD (n = 10), Ctrl (n = 10)	Plasma RT-qPCR	Expression of miR-34a and miR-146a decreased in AD plasma, and of miR-34a, miR-125b, and miR-146a in CSF.	[173]
			AD (n = 21/15), preclinical AD (n = 21/15), Ctrl (n = 21/15), PD (n = 21/0)	Plasma RT-qPCR	Expression levels of miR-15b-5p, miR-34a-5p, miR-142-3p, and miR-545-3p distinguished AD from PD and HC subjects.	[187]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
	↓		AD (*n* = 10), Ctrl (*n* = 10)	CSF RT-qPCR	Expression of miR-34a and miR-146a decreased in AD plasma, and of miR-34a, miR-125b, and miR-146a in CSF.	[173]
	↑		AD (*n* = 16), Ctrl (*n* = 16)	PBMC Array/RT-qPCR	Expression of 22 miRNAs upregulated in AD subjects.	[188]
miR-34a(-5p)		http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-34a-5p&full=1	AD (*n* = 5), Ctrl (*n* = 5)	CNS (TCx) RT-qPCR	Expression of miR-146a, miR-155, miR-9, miR-125b, miR-34a, miR-25, miR-128, miR-15b, miR-454, miR-642, miR-20a, and miR-106a increased in AD neocortical extracellular fluid and CSF samples.	[171]
			AD (*n* = 26), Ctrl (*n* = 19)	CNS (TCx) Array	Expression of miR-7, miR-9-1, miR-23a/miR-27a, miR-34a, miR-125b-1, miR-146a, and miR-155 increased in AD-affected superior TCx.	[189]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-34a(-5p)	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-34a-5p&full=1	AD (*n* = 29), Ctrl (*n* = 20)	CNS (HPC) RT-qPCR	Expression of miR-34a increased in the AD HPC.	[190]
			AD (*n* = 3), Ctrl (*n* = 3)	CNS (HPC) Array	Expression of miR-34a, miR-125b, miR-146a, miR-155 upregulated in AD brain samples.	[170]
miR-34c	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-34c-5p&full=1	AD (*n* = 110), Ctrl (*n* = 123)	Plasma, PBMC RT-qPCR	Expression of miR-34c increased in both AD PBMCs and plasma.	[296]
			aMCI (*n* = 71), Ctrl (*n* = 69)	Plasma RT-qPCR	Expression of miR-34c increased in patients with aMCI.	[297]
miR-92a-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-92a-3p&full=1	AD (*n* = 56/0), MCI (*n* = 26/0), FTD (*n* = 0/27), Ctrl (*n* = 14/24)	Plasma RT-qPCR	Expression of miR-92a-3p, miR-181c-5p and miR-210-3p increased in AD and MCI plasma.	[216]
miR-98-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-98-5p&full=1	AD (*n* = 50/158), Ctrl (*n* = 50/155)	Serum miRNA-seq/RT-qPCR	Expression of miR-98-5p, miR-885-5p, miR-483-3p, miR-342-3p, miR-191-5p, and miR-let-7d-5p deregulated in AD patients.	[198]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-103a-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-103a-3p&full=1	AD (*n* = 48/106), MCI (*n* = 18/0), MS (*n* = 16/0), PD (*n* = 9/0), DEP (*n* = 15/0), BD (*n* = 15/0), SCH (*n* = 14/0), Ctrl (*n* = 22/22)	Blood miRNA-seq/RT-qPCR	Expression of 82 miRNAs upregulated and 58 downregulated in AD patient samples.	[192]
			AD (*n* = 7/13), MCI-AD (*n* = 7/8), Ctrl (*n* = 6/9)	Plasma RT-qPCR	Expression of miR-151a-5p, miR-30b-5p, miR-486-5p, miR-33a-5p, miR-483-5p, miR-18a-5p, miR-320a, miR-320b, miR-320c, miR-502-3p, miR-103a-3p, miR-301a-3p, miR-142-3p, and miR-200a-3p deregulated in AD.	[298]
miR-106b	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-106b-5p&full=1	AD (*n* = 56), Ctrl (*n* = 60)	Serum RT-qPCR	Expression of miR-106b downregulated in AD serum samples.	[299]
miR-106b-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-106b-3p&full=1	AD (*n* = 20), Ctrl (*n* = 20)	Serum miRNA-seq/RT-qPCR	Expression of 72 miRNAs deregulated in AD (miR-146a-5p, miR-106b-3p, miR-195-5p, miR-20b-5p, and miR-497-5p upregulated, miR-125b-3p, miR-29c-3p, miR-93-5p and miR-19b-3p downregulated).	[182]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-107	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-107&full=1	AD (*n* = 48/106), MCI (*n* = 18/0), MS (*n* = 16/0), PD (*n* = 9/0), DEP (*n* = 15/0), BD (*n* = 15/0), SCH (*n* = 14/0), Ctrl (*n* = 22/22)	Blood miRNA-seq/RT-qPCR	Expression of 82 miRNAs upregulated and 58 downregulated in AD patient samples.	[192]
			AD (*n* = 97), aMCI (*n* = 116), Ctrl (*n* = 81)	Plasma RT-qPCR	Expression of miR-107 in plasma had a high capability to discriminate between patients with aMCI and healthy controls.	[193]
			AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
			AD (*n* = 6), MCI (*n* = 6), Ctrl (*n* = 11)	CNS (TCx) Array	Expression of miR-107 decreased in the progression of AD.	[194]
			AD (*n* = 12), Ctrl (*n* = 12)	CNS (HPC, TCx, CB) RT-qPCR	Expression of miR-103, miR-107, miR-15b, miR-16 and miR-195 reduced in AD HPC and TCx (including miR-15a), but not in CB.	[195]

Epigenetic mechanism	Effect	Gene/Target pathway involved ¹	Study model ²	Tissue Study/design	Main results	References
miR-107	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-107&full=1	AD (*n* = 10), Ctrl (*n* = 11)	CNS (HPC) RT-qPCR	Expression of miR-16, miR-34c, miR-107, miR-128a, and miR-146a were differentially regulated in AD HPC.	[196]
miR-125a-5p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-125a-5p&full=1	AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
miR-125b	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-125b-5p&full=1	AD (*n* = 69), PD (*n* = 67), Ctrl (*n* = 78)	Serum miRNA-seq	Expression of 41 miRNAs deregulated in AD CSF, and 20 miRNAs in AD serum.	[164]
			AD (*n* = 22), FTD (*n* = 10), Ctrl (*n* = 26)	Serum Array/RT-qPCR	Expression of miR-26b, miR-23a and miR-126b downregulated in AD serum, and of miR-26b and miR-126b in AD CSF.	[197]
			AD (*n* = 10), Ctrl (*n* = 10)	Plasma RT-qPCR	Expression of miR-34a and miR-146a decreased in AD plasma, and of miR-34a, miR-125b, and miR-146a in CSF.	[173]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-125b	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-125b-5p&full=1	AD (n = 35), Ctrl (n = 35)	Plasma (Exosomes) miRNA-seq	Expression of 20 miRNAs deregulated in AD group.	[177]
			Probable AD (n = 105), Ctrl (n = 150)	Serum RT-qPCR	Expression of miR-125b and miR-181c downregulated, and of miR-9 upregulated in serum of AD patients.	[198]
			AD (n = 22), FTD (n = 10), Ctrl (n = 26)	CSF Array/RT-qPCR	Expression of miR-26b, miR-23a and miR-126b downregulated in AD serum, and of miR-26b and miR-126b in AD CSF.	[197]
			AD (n = 50/16), Ctrl (n = 49/16)	CSF Array/RT-qPCR	Expression of 36 miRNAs (20 in validation cohort) discriminate AD from control CSF.	[174]
	↑		AD (n = 6), Ctrl (n = 6)	CSF Array/RT-qPCR	Expression of miRNA-9, miRNA-125b, miRNA-146a, miRNA-155 increased in AD CSF and brain tissue-derived extracellular fluid.	[169]
			AD (n = 10/37), Ctrl (n = 10/32)	CSF Array/RT-qPCR	Expression of miR-222 and miR-125b upregulated in AD CSF.	[199]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-125b	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-125b-5p&full=1	AD (*n* = 10); Ctrl (*n* = 10)	CSF RT-qPCR	Expression of miR-34a and miR-146a decreased in AD plasma, and of miR-34a, miR-125b, and miR-146a in CSF.	[173]
			YOAD (*n* = 17/17), LOAD (*n* = 13/13), Ctrl (*n* = 12/12)	CSF (Exosomes) RT-qPCR	Expression of miR-16-5p, miR-125b-5p, miR-451a, and miR-605-5p deregulated in AD CSF-derived exosomes.	[200]
miR-125b-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-125b-3p&full=1	AD (*n* = 20), Ctrl (*n* = 20)	Serum miRNA-seq/RT-qPCR	Expression of 72 miRNAs deregulated in AD (miR-146a-5p, miR-106b-3p, miR-195-5p, miR-20b-5p, and miR-497-5p upregulated, miR-125b-3p, miR-29c-3p, miR-93-5p and miR-19b-3p downregulated).	[182]
	↑		AD (*n* = 6), Ctrl (*n* = 6)	CNS (TCx) Array/RT-qPCR	Expression of miRNA-9, miRNA-125b, miRNA-146a, miRNA-155 increased in AD CSF and brain tissue-derived extracellular fluid.	[169]
			AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-125b-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-125b-3p&full=1	AD (*n* = 5), Ctrl (*n* = 5)	CNS (TCx) RT-qPCR	Expression of miR-146a, miR-155, miR-9, miR-125b, miR-34a, miR-25, miR-128, miR-15b, miR-454, miR-642, miR-20a, and miR-106a increased in AD neocortical extracellular fluid and CSF samples.	[171]
			AD (*n* = 26), Ctrl (*n* = 19)	CNS (TCx) Array	Expression of miR-7, miR-9-1, miR-23a/miR-27a, miR-34a, miR-125b-1, miR-146a, and miR-155 increased in AD-affected superior TCx.	[189]
			AD (*n* = 6), Ctrl (*n* = 6)	CNS (TCx) Array	Expression of miRNA-9, miRNA-125b and miRNA-146a upregulated in AD TCx.	[170]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-125b-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-125b-3p&full=1	Braak III–VI (*n* = 20), Braak 0–I (*n* = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b..	[165]
			AD (*n* = 3), Ctrl (*n* = 3)	CNS (HPC) Array	Expression of miR-34a, miR-125b, miR-146a, miR-155 upregulated in AD brain samples	[191]
			AD (*n* = 10), Ctrl (*n* = 5)	CNS (FCx) RT-qPCR	Expression of miR-125b increased and of miR-29a and miR-29b decreased in AD.	[158]
			AD (*n* = 9), MCI (*n* = 8), Ctrl (*n* = 10)	CNS RT-qPCR	Expression of miR-125b upregulated in AD.	[159]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-127-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-127-3p&full=1	AD (*n* = 69), PD (*n* = 67), Ctrl (*n* = 78)	CSF miRNA-seq	Expression of 41 miRNAs deregulated in AD CSF, and 20 miRNAs in AD serum.	[164]
			AD (*n* = 19/19), Ctrl (*n* = 19/19)	CSF Array/RT-qPCR	Expression of miRNA-139-5p, miRNA-181-5p, miRNA-127-3p, miRNA-140-3p, miRNA-374b, miRNA-376c, miRNA-532-3p, miRNA-758, miRNA-744, miRNA-642 downregulated, miRNA-129-3p, miRNA-206 upregulated in EOAD. Let-7a, miRNA-210, miRNA-224 downregulated and miRNA-223-5p, miRNA-486-5p, miRNA-424-3p and miRNA-625-3p upregulated in LOAD.	[218]
	↑		AD (*n* = 210), Probable FTD (*n* = 54), Ctrl (*n* = 53)	Plasma RT-qPCR	Expression of miR-127-3p downregulated in FTD compared to controls and AD.	[300]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-128b	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-155-5p&full=1	AD (*n* = 12), Ctrl (*n* = 6)	CNS (FCx, TCx) RT-qPCR	Expression of miR-128a/b reduced in AD TCx and of miR-128b in AD FCx.	[301]
miR-132(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-132-3p&full=1	AD (*n* = 31), AD-MCI (*n* = 16), Ctrl (*n* = 16)	Plasma (Exosomes) Array/RT-qPCR	Expression of miR-132-3p and miR-212 was decreased in neurally-derived plasma EVs from AD patients.	[201]
			AD (*n* = 11), Ctrl (*n* = 8)	CNS Array/RT-qPCR	Expression of miR-132-3p and miR-212 was decreased in neurally-derived plasma EVs from AD patients.	[201]
			AD (*n* = 6), PD (*n* = 6), Ctrl (*n* = 6)	CNS (HPC, TCx, FCx) miRNA-seq/RT-qPCR	Expression of miR-184, miR-34c-3p, miR-375 and miR-132-5p, and of the other members of the 132/212 cluster downregulated in AD brain.	[202]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-132(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-132-3p&full=1	Braak III–VI (*n* = 20), Braak 0–I (*n* = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b..	[165]
			AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
			AD (*n* = 5), DLB (*n* = 4), FTD (*n* = 5), HS-aging (*n* = 4), Ctrl (*n* = 2)	CNS (TCx) RNA deep seq/RT-qPCR	Expression of miR-132 altered in AD and FTD cases.	[203]
			HPC: AD (*n* = 41), Ctrl (*n* = 23); FCx: AD (*n* = 21), Ctrl (*n* = 28), TCx: AD (*n* = 8), Ctrl (*n* = 8)	CNS (HPC, FCx, TCx) RNA deep seq/RT-qPCR	Expression of 41 miRNAs deregulated in AD HPC.	[204]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-132(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-132-3p&full=1	TCx: AD (n = 39/8), Ctrl (n = 25/8); FCx: AD (n = 225/8), Ctrl (n = 87/8)	CNS (FCx, TCx) Array/RT-qPCR	Expression of 102 miRNAs deregulated in AD temporal cortical brain regions, including downregulated expression of miR132-3p and miR-212-3p in AD FCx and TCx.	[162]
			FCx: AD (n = 7), Ctrl (n = 5); TCx: AD (n = 8/11), MCI (n = 0/10), Ctrl (n = 8/11); HPC: AD (n = 10), Ctrl (n = 13)	CNS (HPC, TCx, FCx) RT-qPCR	Expression of miR-132 is downregulated in AD.	[205]
			AD (n = 3/10), MCI (n = 0/10), Ctrl (n = 3/12)	CNS (FCx) Array/RT-qPCR	Expression of miR-498, miR-150, miR-886-3p, miR-132, miR-21, miR-23a, miR-140-3p, miR-212, miR-23b, miR-181a and let-7d upregulated in AD FCx, and of miR-212, miR-132 and miR-150 upregulated in AD TCx.	[206]
			Braak IV (n = 18), Braak III/IV (n = 14), Ctrl (n = 18)	CNS (TCx) RT-qPCR	Expression of miR-132 and miR-212 downregulated in AD TCX and CA1 HPC neurons.	[207]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-132(-3p)	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-132-3p&full=1	MCI (*n* = 66), Ctrl (*n* = 76)	Serum RT-qPCR	Expression of miR-206 and miR-132 elevated in MCI patients.	[208]
miR-133b	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-133b&full=1	AD (*n* = 105), Ctrl (*n* = 98)	Serum RT-qPCR	Expression of miR-133b downregulated in AD.	[302]
miR-135a	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-135a-5p&full=1	AD (*n* = 5), Ctrl (*n* = 5)	CSF RT-qPCR	Expression of miR-135a and miR-200b downregulated in AD.	[303]
			AD (*n* = 107), MCI (*n* = 101), PD (*n* = 30), VD (*n* = 20), Ctrl (*n* = nR)	Serum (Exosomes) RT-qPCR	Expression of miR-135a and miR-384 upregulated, and of miR-193b downregulated in AD.	[304]

Epigenetic mechanism	Effect	Gene/Target pathway involved ¹	Study model ²	Tissue Study/design	Main results	References
miR-135a	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-135a-5p&full=1	Braak V (*n* = 10), Braak 0 (*n* = 10)	CSF RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
miR-135b	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-135b-5p&full=1	AD (*n* = 25), Ctrl (*n* = 25)	Blood RT-qPCR	Expression of miR-135b reduced AD patients.	[155]
miR-136-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-136-3p&full=1	AD (*n* = 69), PD (*n* = 67), Ctrl (*n* = 78)	CSF miRNA-seq	Expression of 41 miRNAs deregulated in AD CSF, and 20 miRNAs in AD serum.	[164]
			AD (*n* = 28), PD (*n* = 47), Ctrl (*n* = 27)	CSF (Exosomes) Array/RT-qPCR	Expression of miR-16-2, miR-331-5p, miR-132-5p, miR-485-5p, miR-151, miR-136-3p, and miR-29c deregulated in AD CSF.	[183]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
	↓		AD (*n* = 69), PD (*n* = 67), Ctrl (*n* = 78)	CSF miRNA-seq	Expression of 41 miRNAs deregulated in AD CSF, and 20 miRNAs in AD serum.	[164]
miR-139-5p		http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-139-5p&full=1	AD (*n* = 19/19), Ctrl (*n* = 19/19)	CSF Array/RT-qPCR	Expression of miR-139-5p, miR-181-5p, miR-127-3p, miR-140-3p, miR-374b, miR-376c, miR-532-3p, miR-758, miR-744, and miR-642 downregulated miR-129-3p, and miR-206 upregulated in EOAD. Let-7a, miR-210 and miR-224 downregulated, and miR-223-5p, miR-486-5p, miR-424-3p and miR-625-3p upregulated in LOAD.	[218]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-141	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-141-3p&full=1	Braak V (*n* = 10), Braak 0 (*n* = 10)	CSF RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
			AD (*n* = 10/18), Ctrl (*n* = 10/18)	CSF RT-qPRC	Expression of 15 miRNAs deregulated in AD, miR-9-5p and miR-598 suggested as potential biomarkers for AD.	[168]
miR-142-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-142-3p&full=1	AD (*n* = 21/15), preclinical AD (*n* = 21/15), Ctrl (*n* = 21/15), PD (*n* = 21/0)	Plasma RT-qPCR	Expression levels of miR-15b-5p, miR-34a-5p, miR-142-3p, and miR-545-3p distinguished AD from PD and HC subjects.	[187]
			AD (*n* = 11/20), MCI (*n* = 9/0), Ctrl (*n* = 20/17)	Plasma miRNA-seq/RT-qPCR	Expression of let-7d-5p, let-7g-5p, miR-15b-5p, miR-142-3p, miR-191-5p, miR-301a-3p and miR-545-3p deregulated in AD.	[291]

Epigenetic mechanism	**Effect**	**Gene/Target pathway involved** [1]	**Study model** [2]	**Tissue Study/design**	**Main results**	**References**
miR-142-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-142-3p&full=1	AD (*n* = 7/13), MCI-AD (*n* = 7/8), Ctrl (*n* = 6/9)	Plasma RT-qPCR	Expression of miR-151a-5p, miR-30b-5p, miR-486-5p, miR-33a-5p, miR-483-5p, miR-18a-5p, miR-320a, miR-320b, miR-320c, miR-502-3p, miR-103a-3p, miR-301a-3p, miR-142-3p, and miR-200a-3p deregulated in AD.	[298]
miR-146a(-5p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-146a-5p&full=1	AD (*n* = 127), MCI (*n* = 30), VD (*n* = 30)	Serum miRNA-seq/RT-qPCR	Expression of miR-31, miR-93, miR-143, and miR-146a decreased in AD serum, and of miR-93, and miR-146a increased in MCI. The panel of miR-31, miR-93 and miR-146a can be used to discriminate AD from VD.	[209]
			AD (*n* = 10), Ctrl (*n* = 10)	Plasma RT-qPCR	Expression of miR-34a and miR-146a decreased in AD plasma, and of miR-34a, miR-125b, and miR-146a in CSF.	[173]
			AD (*n* = 40), Ctrl (*n* = 31); Validation cohort: publicly available dataset of miRnA data	Blood miRNA-seq	Expression of 71 deregulated in AD, including miR-146b-5p and miR-15b-5p.	[210]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-146a(-5p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-146a-5p&full=1	AD ($n = 10$), Ctrl ($n = 10$)	CSF RT-qPCR	Expression of miR-34a and miR-146a decreased in AD plasma, and of miR-34a, miR-125b, and miR-146a in CSF.	[173]
			AD ($n = 50/16$), Ctrl ($n = 49/16$)	CSF Array/RT-qPCR	Expression of 36 miRNAs (20 in validation cohort) discriminate AD from control CSF.	[174]
			AD ($n = 20$), Ctrl ($n = 20$)	CSF RT-qPCR	Expression of miR-16, miR-34c, miR-107, miR-128a, and miR-146a were differentially regulated in AD HPC.	[196]
			AD ($n = 60$), MCI-AD ($n = 39$), FTD ($n = 37$), DLB ($n = 37$), Ctrl ($n = 40$)	CSF RT-qPCR	Expression of miR-29a increased in AD CSF.	[175]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-146a(-5p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-146a-5p&full=1	Braak III–VI (n = 20), Braak 0–I (n = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
			AD (n = 27), Ctrl (n = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
			AD (n = 10), Ctrl (n = 11)	CNS (HPC) Array	Expression of miR-16, miR-34c, miR-107, miR-128a, and miR-146a were differentially regulated in AD HPC.	[196]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-146a(-5p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-146a-5p&full=1	Braak III–VI (n = 20), Braak 0–I (n = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]
			AD (n = 27), Ctrl (n = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
	↑		AD (n = 20), Ctrl (n = 20)	Serum miRNA-seq/RT-qPCR	Expression of 72 miRNAs deregulated in AD (miR-146a-5p, miR-106b-3p, miR-195-5p, miR-20b-5p, and miR-497-5p upregulated, miR-125b-3p, miR-29c-3p, miR-93-5p and miR-19b-3p downregulated).	[182]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-146a(-5p)	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-146a-5p&full=1	AD (*n* = 6), Ctrl (*n* = 6)	CSF Array/RT-qPCR	Expression of miRNA-9, miRNA-125b, miRNA-146a, miRNA-155 increased in AD CSF and brain tissue-derived extracellular fluid.	[169]
			AD (*n* = 22), Ctrl (*n* = 28)	CSF RT-qPCR	Expression of 74 down- and 74 up-regulated miRNAs detected in AD, including miR-100, miR-146a and miR-1274a.	[211]
			AD (*n* = 6), Ctrl (*n* = 6)	CNS (TCx) Array/RT-qPCR	Expression of miRNA-9, miRNA-125b, miRNA-146a, miRNA-155 increased in AD CSF and brain tissue-derived extracellular fluid.	[169]
			AD (*n* = 36), Ctrl (*n* = 30)	CNS (HPC, TCx) Array	Expression of miRNA-146a upregulated in AD superior TCx.	[212]
			AD (*n* = 5), Ctrl (*n* = 5)	CNS (TCx) RT-qPCR	Expression of miR-146a, miR-155, miR-9, miR-125b, miR-34a, miR-25, miR-128, miR-15b, miR-454, miR-642, miR-20a, and miR-106a increased in AD neocortical extracellular fluid and CSF samples.	[171]

Epigenetic mechanism	Effect	Gene/Target pathway involved ¹	Study model ²	Tissue Study/design	Main results	References
miR-146a(-5p)	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-146a-5p&full=1	AD (*n* = 26), Ctrl (*n* = 19)	CNS (TCx) Array	Expression of miR-7, miR-9-1, miR-23a/miR-27a, miR-34a, miR-125b-1, miR-146a, and miR-155 increased in AD-affected superior TCx.	[189]
			AD (*n* = 6), Ctrl (*n* = 6)	CNS (TCx) Array	Expression of miRNA-9, miRNA-125b and miRNA-146a upregulated in AD TCx.	[170]
			AD (*n* = 12), Ctrl (*n* = 6)	CNS Array	Expression of miR-7, miR-146a, and miR-155 increased in AD.	[213]
			AD (*n* = 23), Ctrl (*n* = 23)	CNS (TCx) Array	Expression of miR-146a coupled to down-regulation of CFH observed in AD brain.	[214]
			AD (*n* = 3), Ctrl (*n* = 3)	CNS (HPC) Array	Expression of miR-34a, miR-125b, miR-146a, miR-155 upregulated in AD brain samples.	[191]
miR-151a-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-151a-3p&full=1	AD (*n* = 48/106), MCI (*n* = 18/0), MS (*n* = 16/0), PD (*n* = 9/0), DEP (*n* = 15/0), BD (*n* = 15/0), SCH (*n* = 14/0), Ctrl (*n* = 22/22)	Blood miRNA-seq/RT-qPCR	Expression of 82 miRNAs upregulated and 58 downregulated in AD patient samples.	[192]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-151a-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-151a-3p&full=1	AD (*n* = 48), Ctrl (*n* = 22)	BloodomiRas and DIANA miRPath	Expression of 27 miRNAs discriminate between two groups.	[178]
miR-155	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-155-5p&full=1	AD (*n* = 36), MCI (*n* = 52), Ctrl (*n* = 6)	PBMC RT-qPCR	Expression of immune-related miRNAs, including miR-155, miR-154, miR-200b, miR-27b, and miR-128, differentially expressed in PBMCs from AD and MCI subjects.	[215]
			AD (*n* = 16), Ctrl (*n* = 16)	PBMC Array/RT-qPCR	Expression of 22 miRNAs upregulated in AD.	[188]
			AD (*n* = 6), Ctrl (*n* = 6)	CNS (TCx) Array/RT-qPCR	Expression of miR-9, miR-125b, miR-146a, miR-155 increased in AD CSF and brain tissue-derived extracellular fluid.	[169]
			AD (*n* = 12), Ctrl (*n* = 6)	CNS Array	Expression of miR-7, miR-146a, and miR-155 increased in AD.	[213]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-155	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-155-5p&full=1	AD ($n = 5$), Ctrl ($n = 5$)	CNS (TCx) RT-qPCR	Expression of miR-146a, miR-155, miR-9, miR-125b, miR-34a, miR-25, miR-128, miR-15b, miR-454, miR-642, miR-20a, and miR-106a increased in AD neocortical extracellular fluid and CSF samples.	[171]
			AD ($n = 3$), Ctrl ($n = 3$)	CNS (HPC) Array	Expression of miR-34a, miR-125b, miR-146a, miR-155 upregulated in AD brain samples.	[191]
			Braak III–VI ($n = 20$), Braak 0–I ($n = 7$)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]

Epigenetic mechanism	Effect	Gene/Target pathway involved ¹	Study model ²	Tissue Study/design	Main results	References
miR-155	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-155-5p&full=1	AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
			AD (*n* = 26), Ctrl (*n* = 19)	CNS (TCx) Array	Expression of miR-7, miR-9-1, miR-23a/miR-27a, miR-34a, miR-125b-1, miR-146a, and miR-155 increased in AD-affected superior TCx.	[189]
miR-181a-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-181a-5p&full=1	Braak III–VI (*n* = 20), Braak 0–I (*n* = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-181a-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-181a-5p&full=1	AD (*n* = 3/10), MCI (*n* = 0/10), Ctrl (*n* = 3/12)	CNS (FCx) Array/RT-qPCR	Expression of miR-498, miR-150, miR-886-3p, miR-132, miR-21, miR-23a, miR-140-3p, miR-212, miR-23b, miR-181a and let-7d upregulated in AD FCx, and of miR-212, miR-132 and miR-150 upregulated in AD TCx.	[206]
miR-181c(-5p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-181c-5p&full=1	Probable AD (*n* = 7), aMCI/Probable Early AD (*n* = 7), Ctrl (*n* = 7)	Serum RT-qPCR	Expression of miR-137, miR-181c, miR-9, miR-29a/b downregulated in serum of probable AD patients.	[176]
			Probable AD (*n* = 105), Ctrl (*n* = 150)	Serum RT-qPCR	Expression of miR-125b and miR-181c downregulated, and of miR-9 upregulated in serum of AD patients.	[198]
			AD (*n* = 7), Ctrl (*n* = 7)	CNS (Neocortex) RT-qPCR	Expression of miR-137, miR-181c, miR-9, miR-29a, and miR-29b-1, miR-15 and miR-124 downregulated in the FCx of the subgroup of sporadic AD patient.	[166]
			AD (*n* = 5), Ctrl (*n* = 5)	CNS (PCx) Array	Expression of 48 miRNAs deregulated in AD brain.	[180]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-181c(-5p)	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-181c-5p&full=1	AD (*n* = 56/0), MCI (*n* = 26/0), FTD (*n* = 0/27), Ctrl (*n* = 14/24)	Plasma RT-qPCR	Expression of miR-92a-3p, miR-181c-5p and miR-210-3p increased in AD and MCI subjects.	[216]
miR-181d-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-181d-5p&full=1	AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
miR-191-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-191-5p&full=1	AD (*n* = 11/20), MCI (*n* = 0/9), Ctrl (*n* = 20/17)	Plasma miRNA-seq/RT-qPCR	Expression of let-7d-5p, let-7g-5p, miR-15b-5p, miR-142-3p, miR-191-5p, miR-301a-3p and miR-545-3p deregulated in AD.	[291]
			AD (*n* = 50/158), Ctrl (*n* = 50/155)	Serum miRNA-seq/RT-qPCR	Expression of miR-98-5p, miR-885-5p, miR-483-3p, miR-342-3p, miR-191-5p, and miR-let-7d-5p deregulated in AD patients.	[198]
miR-193a-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-193a-3p&full=1	AD (*n* = 108), Ctrl (*n* = 93)	Serum RT-qPCR	Expression of miR-193a-3p downregulated in AD.	[305]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-193b	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-193b-3p&full=1	AD (*n* = 107), MCI (*n* = 101), PD (*n* = 30), VD (*n* = 20), Ctrl (*n* = nR)	Serum (Exosomes) RT-qPCR	Expression of miR-135a and miR-384 upregulated, and of miR-193b downregulated in AD.	[304]
miR-200a-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-200a-3p&full=1	AD (*n* = 7), Ctrl (*n* = 5)	Plasma RT-qPCR	Expression of miR-200a-3p levels downregulated in AD blood plasma.	[306]
	↑		AD (*n* = 7/13), MCI-AD (*n* = 7/8), Ctrl (*n* = 6/9)	Plasma RT-qPCR	Expression of miR-151a-5p, miR-30b-5p, miR-486-5p, miR-33a-5p, miR-483-5p, miR-18a-5p, miR-320a, miR-320b, miR-320c, miR-502-3p, miR-103a-3p, miR-301a-3p, miR-142-3p, and miR-200a-3p deregulated in AD.	[298]
miR-206	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-206&full=1	AD (*n* = 25), MCI (*n* = 30), Ctrl (*n* = 31); Longitudinal cohort: MCI-MCI-Dementia (*n* = 6), Ctrl-MCI-Dementia (*n* = 6), Ctrl-MCI-MCI (*n* = 6)	Plasma Array/RT-qPCR	Expression of let-7b increased in MCI subjects. Expression of miR-206 increased in AD subjects.	[217]
			MCI (*n* = 66), Ctrl (*n* = 76)	Serum RT-qPCR	Expression of miR-206 and miR-132 elevated in MCI patients.	[208]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
	↑		AD (n = 10/18), Ctrl (n = 10/18)	CSF RT-qPRC	Expression of 15 miRNAs deregulated in AD. miR-9-5p and miR-598 suggested as potential biomarkers for AD.	[168]
miR-206		http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-206&full=1	AD (n = 19/19); Ctrl (n = 19/19)	CSF Array/RT-qPCR	Expression of miR-139-5p, miR-181-5p, miR-127-3p, miR-140-3p, miR-374b, miR-376c, miR-532-3p, miR-758, miR-744, and miR-642 downregulated miR-129-3p, and miR-206 upregulated in EOAD. Let-7a, miR-210 and miR-224 downregulated, and miR-223-5p, miR-486-5p, miR-424-3p and miR-625-3p upregulated in LOAD.	[218]
miR-210-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-210-3p&full=1	AD (n = 56/0), MCI (n = 26/0), FTD (n = 0/27), Ctrl (n = 14/24)	Plasma RT-qPCR	Expression of miR-92a-3p, miR-181c-5p and miR-210-3p increased in AD and MCI subjects.	[216]
miR-212(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-212-3p&full=1	AD (n = 31), AD-MCI (n = 16), Ctrl (n = 16)	Plasma (Exosomes) Array/RT-qPCR	Expression of miR-132-3p and miR-212 decreased in neurally-derived plasma exosomes from AD patients.	[201]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-212(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-212-3p&full=1	AD (*n* = 11), Ctrl (*n* = 8)	CNS Array/RT-qPCR	Expression of miR-132-3p and miR-212 decreased in neurally-derived plasma exosomes from AD patients.	[201]
			AD (*n* = 6), PD (*n* = 6), Ctrl (*n* = 6)	CNS (HPC, TCx, FCx) miRNA-seq/RT-qPCR	Expression of miR-184, miR-34c-3p, miR-375, miR-132-5p, and other members of the 132/212 cluster downregulated in AD brain.	[202]
			Braak III–VI (*n* = 20), Braak 0–I (*n* = 7)	CNS (HPC, MFG, CB) RT-qPCR	Expression of miR-145, miR-148a, miR-200c, miR-210, miR-26a, miR-30c, miR-30e-5p, miR-423, and miR-92 deregulated in HPC and/or MFG. Expression of miR-100, miR-125b, miR-132, miR-146b, miR-212, miR-27a, miR-27b, miR-34a, miR-381, miR-422a, miR-425, miR-9 deregulated in CB. Increased expression of miR-29a and miR-29b.	[165]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-212(-3p)	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-212-3p&full=1	AD (*n* = 3/10), MCI (*n* = 10), Ctrl (*n* = 3/12)	CNS (FCx) Array/RT-qPCR	Expression of miR-498, miR-150, miR-886-3p, miR-132, miR-21, miR-23a, miR-140-3p, miR-212, miR-23b, miR-181a and let-7d upregulated in AD FCx, and of miR-212, miR-132 and miR-150 upregulated in AD TCx.	[206]
			Braak IV (*n* = 18), Braak III/IV (*n* = 14), Ctrl (*n* = 18)	CNS (TCx) RT-qPCR	Expression of miR-132 and miR-212 downregulated in AD TCx areas and CA1 HPC neurons.	[207]
			TCx: AD (*n* = 39/8), Ctrl (*n* = 25/8); FCx: AD (*n* = 225/8), Ctrl (*n* = 87/8)	CNS (FCx, TCx) Array/RT-qPCR	Expression of 102 miRNAs deregulated in AD temporal cortical brain regions, including downregulated expression of miR132-3p and miR-212-3p in AD FCx and TCx.	[162]
			AD (*n* = 27), Ctrl (*n* = 18)	CNS (TCx) miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]

Epigenetic mechanism	**Effect**	**Gene/Target pathway involved** [1]	**Study model** [2]	**Tissue Study/design**	**Main results**	**References**
miR-222	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-222-3p&full=1	Mild AD (*n* = 30), Moderate AD (*n* = 30), Ctrl (*n* = 30)	Serum miRNA-seq/RT-qPCR	Expression of miR-222 decreased in the mild and moderate AD.	[307]
	↑		AD (*n* = 70), VD (*n* = 17), tauopathies other than AD (*n* = 23), Ctrl (*n* = 43)	CSF RT-qPCR	Expression of miR-222 increased in VD patients compared to both control and AD subjects.	[308]
miR-223	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-223-3p&full=1	Probable AD (*n* = 84), Ctrl (*n* = 62)	Serum RT-qPCR	Expression of miR-29, miR-125b and miR-223 decreased, and of miR-519 increased in AD patients.	[309]
			AD - no treatment (*n* = 11), AD - with treatment (*n* = 11), VD (*n* = 10), Ctrl (*n* = 16)	Serum (Exosomes) RT-qPCR	Expression of miR-223 decreased in dementia patients.	[310]
miR-301a-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-301a-3p&full=1	AD (*n* = 11/20), MCI (*n* = 9), Ctrl (*n* = 20/17)	Plasma miRNA-seq/RT-qPCR	Expression of let-7d-5p, let-7g-5p, miR-15b-5p, miR-142-3p, miR-191-5p, miR-301a-3p and miR-545-3p deregulated in AD.	[291]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-301a-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-301a-3p&full=1	AD (*n* = 7/13), MCI-AD (*n* = 7/8), Ctrl (*n* = 6/9)	Plasma RT-qPCR	Expression of miR-151a-5p, miR-30b-5p, miR-486-5p, miR-33a-5p, miR-483-5p, miR-18a-5p, miR-320a, miR-320b, miR-320c, miR-502-3p, miR-103a-3p, miR-301a-3p, miR-142-3p, and miR-200a-3p deregulated in AD.	[298]
miR-342-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-34a-3p&full=1	AD (*n* = 23/16), MCI (*n* = 3/8), Ctrl (*n* = 23/36)	Serum (Exosomes) miRNA-seq/RT-qPCR	Expression of 17 miRNA deregulated (14 miRNAs upregulated and 3 downregulated) in AD.	[293]
			AD (*n* = 35), Ctrl (*n* = 35)	Plasma (Exosomes) miRNA-seq	Expression of 20 miRNAs deregulated in AD group.	[177]
miR-384	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-384&full=1	AD (*n* = 107), MCI (*n* = 101), PD (*n* = 30), VD (*n* = 20), Ctrl (*n* = nR)	Serum (Exosomes) RT-qPCR	Expression of miR-135a and miR-384 upregulated, and of miR-193b downregulated in AD.	[304]
miR-425	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-425-5p&full=1	AD (*n* = 4 severe+4 mild/45), Ctrl (*n* = 4/41)	PBMC Array/RT-qPCR	Expression of miR-339 and miR-425 altered in AD.	[311]
			AD (*n* = 48), Ctrl (*n* = 22)	BloodomiRas and DIANA miRPath	Expression of 27 miRNAs discriminate between two groups.	[178]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-451a	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-451a&full=1	YOAD (*n* = 17/17), LOAD (*n* = 13/13), Ctrl (*n* = 12/12)	CSF (Exosomes) RT-qPCR	Expression of miR-16-5p, miR-125b-5p, miR-451a, and miR-605-5p deregulated in AD CSF-derived exosomes.	[200]
miR-455-3p	↑	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-455-3p&full=1	AD (*n* = 10/11), MCI (*n* = 16/20), Ctrl (*n* = 14/18)	Serum Array/RT-qPCR	Expression of miR-455-3p, miR-4668-5p, miR-3613-3p, miR-4674 upregulated, and of mir-6722 downregulated in AD and MCI.	[312]
miR-501-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-501-3p&full=1	AD (*n* = 27), Ctrl (*n* = 18)	Serum miRNA-seq/RT-qPCR	Expression of 20 miRNAs deregulated in AD, including miR-501-3p, let-7f-5p, and miR-26b-5p.	[167]
miR-545-3p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-545-3p&full=1	AD (*n* = 21/15), preclinical AD (*n* = 21/15), PD (*n* = 21/0), Ctrl (*n* = 21/15)	Plasma, CSF RT-qPCR	Expression levels of miR-15b-5p, miR-34a-5p, miR-142-3p, and miR-545-3p distinguished AD from PD and HC subjects.	[187]
			AD (*n* = 11/20), MCI (*n* = 9/0), Ctrl (*n* = 20/17)	Plasma miRNA-seq/RT-qPCR	Expression of let-7d-5p, let-7g-5p, miR-15b-5p, miR-142-3p, miR-191-5p, miR-301a-3p and miR-545-3p deregulated in AD.	[291]

Epigenetic mechanism	Effect	Gene/Target pathway involved [1]	Study model [2]	Tissue Study/design	Main results	References
miR-598	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-598-5p&full=1	AD (*n* = 69); PD (*n* = 67); Ctrl (*n* = 78)	CSF miRNA-seq	Expression of 41 miRNAs deregulated in AD CSF, and 20 miRNAs in AD serum.	[164]
	↑		AD (*n* = 10/18), Ctrl (*n* = 10/18)	CSF RT-qPRC	Expression of 15 microRNAs deregulated in AD. miR-9-5p and miR-598 suggested as potential biomarkers for AD.	[168]
miR-1233-5p	↓	http://www.mirdb.org/cgi-bin/search.cgi?searchType=miRNA&searchBox=hsa-miR-1233-5p&full=1	Aβ(−)MCI (*n* = 12), Aβ(+)MCI (*n* = 11), Ctrl (*n* = 9)	Platelets Array/RT-qPCR	Expression of let-7i-5p, miR-125a, miR-1233-5p, and miR-6787-5p downregulated, and of miR-6880-5p upregulated in AD.	[292]

↓—decreased levels; ↑—increased levels; AD—Alzheimer's disease; BD—Bipolar disorder; CB—Cerebellum; CNS—Central nervous system; Ctrl—Control subjects; DEP—Depression; DLB—Dementia with Lewy bodies; FCx—Frontal cortex; FTD—Frontotemporal dementia; HPC—Hippocampus; HS-aging—Hippocampal sclerosis of aging; LOAD—Late-onset AD; MCI—Mild cognitive impairment; MFG—Medial frontal gyrus; aMCI—amnestic MCI; MS—Multiple sclerosis; *n*—Number of subjects; PD—Parkinson's disease; PCx—Parietal cortex; RT-qPCR—Reverse transcription quantitative real-time PCR; SCH—Schizophrenia; SMC—subjective memory complaints; TCx—Temporal cortex; VD—Vascular dementia; YOAD—Young-onset AD.

[1] Link to miRDB online database (http://www.mirdb.org/) which uses bioinformatics tool, MirTarget, for prediction of functional microRNA targets [313,314]

[2] Number of subjects per group is presented as Discovery cohort/Validation cohort

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