

Supplementary Materials: MicroRNAs-Based Theranostics against Anesthetic-Induced Neurotoxicity

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Table S1. Potential miRNAs as alleviative target for neurotoxicity.

Sr. No.	Neurotoxicity	miRNAs	Targets/ Signalling Pathways	Experimental Validation Approach	References
1.	Sevoflurane-induced neurotoxicity	miR-27a-3p	PPAR- γ signalling pathway	Mouse model	[1]
2.	MPP (+)-induced neurotoxicity	miR-124-3p	STAT3	SH-SY5Y cells	[2]
3.	Bupivacaine-induced neurotoxicity	miR-137	LSD1	Cultured in vitro Murine DRGNs	[3]
4.	Glutamate-induced neurotoxicity	miR-219	CaMKII γ	Rat hippocampal neurons	[4]
5.	β -amyloid-induced neurotoxicity	miR-16	BACE1	AD tissues and the cellular AD model of PC12	[5]
6.	Arsenic-induced - neurotoxicity	miR-219	CaMKII	Mouse hippocampus	[6]
7.	6-Hydroxydopamine-Induced Cell Model of PD	miR-124-3p	ANAX5	PC12 and SH-SY5Y cells	[7]
8.	Triazophos-induced toxicity	miR-217	nup43	Adult zebrafish and ZF4 cells	[8]
9.	Sevoflurane-induced neurotoxicity	hsa-miR-302e	OXR1	Human hippocampal cells (HN-h)	[9]
10.	Parkinson's Disease	miR-124	MEKK3	BV2 cells	[10]
11.	Amyloid- β -induced neurotoxicity	miR-107	BDNF-TrkB signaling pathway	Mice	[11]
12.	Manganese induced neurotoxic	miR-7 and miR-433	SNCA and FGF-20 mRNA	SH-SY5Y cells	[12]
13.	Propofol-induced neurotoxicity	miR-34a	MAPK/ERK signaling pathway	In vivo and in vitro (Sprague-Dawley rats and SH-SY5Y cells)	[13]
14.	Ketamine-induced neurotoxicity	miR-107	BDNF	ESC-derived neurons	[14]
15.	MPTP-induced Parkinson's disease	miR-190	Nlrp3	PD mouse model and BV2 cells	[15]
16.	Ketamine-induced neurotoxicity	hsa-miR-375	BDNF	Human embryonic stem cell (hESC)-derived neuron model	[16]
17.	A β -induced neurotoxicity	miR-34a	Caspase-2	SH-SY5Y cells	[17]
18.	A β -induced neurotoxicity	miR-409-5p	Plek	APP/PS1 mice cortexes	[18]
19.	Atrazine-induced Parkinson's disease	miR-7	BDNF/ α -syn axis	Peripheral blood and brain tissue in a rat model of PD	[19]
20.	METH-mediated neurotoxicity	miR-142a-3p/miR-155-5p	Peli1	BV2 cells and brain of mouse	[20]

21.	MPP (+)-induced neurotoxicity	miR-9-5p	SIRT1	SH-SY5Y cells	[21]
22.	MPP (+)- neurotoxicity	miR-200a and miR-204	Sirt1 and BCL2	PC12 cells	[22]
23.	Isoflurane-induced neurotoxicity	miR-214	PTEN	Human neuroblastoma cell line SH-SY5Y	[23]
24.	Parkinson's Disease	miR-326	KLK7-Mediated MAPK Signaling Pathway	Mice with PD	[24]
25.	Isoflurane-induced neurotoxicity	miRNA-153	Nrf2/ARE	Vitro mice model	[25]
26.	Bupivacaine-induced neurotoxicity	miR-132	IGF1R	Human neuroblastoma cell line (SH-SY5Y)	[26]
27.	Pb neurotoxicity	miR-106b-5p	XIAP	HT-22 and PC12 cells	[27]
28.	A β -induced neurotoxicity	miR-29c-3p	TNFAIP1/ NF- κ B signalling pathway	Neuroblastoma Cells	[28]
29.	Parkinson's disease	miR-103a-3p	Parkin/Ambra1 signaling	SH-SY5Y cells	[29]
30.	T helper cell 1 (Th1)-skewed neurotoxicity	miR-494	HDAC2-STAT4 pathway	Blood from AIS (acute ischemic stroke) patients and controls	[30]
31.	Sevoflurane-induced neurotoxicity	miR-204-5p	BDNF/TrkB/Akt pathway	Mouse hippocampal neuronal cell line (HT22)	[31]
32.	Sevoflurane-induced neurotoxicity	miR-325-3p	Nupr1 and C/EBP β /IGFBP5 signaling	Neonatal rats and HCN-2 human cortical neuronal cells	[32]
33.	Isoflurane-induced neurotoxicity	miR-140-5p	SNX12	Diabetic rat model	[33]
34.	A β (25-35)-induced neurotoxicity	miR-212	PDCD4/ PI3K/AKT signaling pathway	Plasma from AD patients, SH-SY5Y and IMR-32 cells	[34]
35.	A β ₂₅₋₃₅ -induced	miR-33	Akt/mTOR pathway	SH-SY5Y cells	[35]
36.	Propofol-induced neurotoxicity	miR-496	ROCK2	Primary Prefrontal Cortical (PFC) neurons of neonatal rats	[36]
37.	A β -induced neurotoxicity	miR-34a-5p and miR-125b-5p	BACE1	Serum samples AD patients and Primary mouse cortical neurons (MCN) and Neuro2a (N2a) cells	[37]
38.	Propofol-induced Neurotoxicity	miR-215	LATS2	Neonatal rat hippocampal neuron	[38]
39.	Neurotoxicity induced by 6-hydroxydopamine	miR-107	PDCD10	In vitro and in vivo (Mouse, SH-SY5Y and PC12 cells)	[39]
40.	Arsenic-induced Endoplasmic Reticulum Stress and Neurotoxicity	miR-124	SNPs - rs67543816 and rs35418153	Neural cells	[40]
41.	Amyloid- β induced neurotoxicity	miR-193a-3p	PTEN	Serum, cellular AD model of PC12 and SH-SY5Y	[41]

42.	A β -induced neurotoxicity	miR-433	JAK2	Serum and cerebrospinal fluid (CS) of AD patients and AD cell model	[42]
43.	Propofol-induced neurotoxicity	miR-455-3p	EphA4	Primary hippocampal neurons of SD (Sprague-Dawley) rats	[43]
44.	Propofol-induced neurotoxicity	miR-582-5p	ROCK1	Primary rat hippocampal neurons	[44]
45.	Isoflurane-induced neurotoxicity	miR-24	p27kip1	Rat hippocampal neurons	[45]
46.	MPP (+)-induced neurotoxicity	miR-30b	SNCA	SH-SY5Y	[46]
47.	MPP (+)-induced neurotoxicity	miR-20a-5p	IRF9/NF- κ B Axis	Hippocampal cell line-HT22 cells	[47]
48.	Isoflurane-induced neurotoxicity	miR-497	PLD1	Neonatal rat's hippocampus and hippocampal primary neuronal cell	[48]
49.	PD Neurotoxicity	miR-3473b	TREM2/ULK1	Mouse microglia cell line (BV2) cells	[49]
50.	Lidocaine induces neurotoxicity	miR-199a-5p	MYRF	Rat model	[50]
51.	Oxygen-glucose deprivation/reoxygenation (OGD/R) -induced neurotoxicity	miR-126	SIRT1/Nrf2 signaling pathway	Human umbilical vein endothelial cell (HUVEC)	[51]
52.	Sevoflurane-induced neurotoxicity	miR-1297	PTEN	Mice	[52]
53.	Bupivacaine-induced neurotoxicity	miR-494-3p	CDK6-PI3K/AKT Signaling	Primary mouse hippocampal neuronal cells (C57BL/6 mice)	[53]
54.	Ketamine-induced neurotoxicity	miR-429	BAG5	PC12 cells	[54]
55.	PD Neurotoxicity	miR-421	MEF2D	Cellular model of PD (Parkinson's disease)	[55]
56.	Amyloid- β induced neurotoxicity	miR-148a-3p	ROCK1	Serum of AD patients	[56]
57.	Isoflurane-induced neurotoxicity	miR-191	BDNF	In vitro and in vivo (hippocampal tissues of rats)	[57]
58.	A β 1-42-induced neurotoxicity	miR-204-3p	Nox4	Hippocampus of APP/PS1 mice	[58]
59.	A β -induced neurotoxicity	miR-130a-3p	DAPK1	SH-SY5Y cells and hippocampus tissues of AD mice	[59]
60.	Isoflurane-induced neurotoxicity	miR-424-5p	FASN	hESC-derived neurons	[60]
61.	Sevoflurane-induced neurotoxicity	miR-221-3p	CDKN1B	Rat hippocampal neuron cells	[61]
62.	Sevoflurane-induced neurotoxicity	miR-128-3p	NOVA1	Rat hippocampal neuron cells	[62]
63.	Hypoxia/ischemia-induced	miR-381-3p	CCR2/NF- κ B pathway	BV2 cells and HT-22 neurons	[63]

64.	Neurotoxicity induced by MPP+	miR-126-5p	SP1	SH-SY5Y and SK-N-SH cells	[64]
65.	Isoflurane-induced neurotoxicity	miR-128-3p	specificity protein 1 (SP1)	Sprague-Dawley (SD) rats	[65]
66.	Ischemic stroke (IS).	miR-107	FGF9/FGF12/ PI3K-AKT signaling pathway	Oxygen-Glucose Deprivation/Reoxygenation (OGD/R)-induced PC12 cells	[66]
67.	Sevoflurane-induced neurotoxicity	miR-384-3p	Aak1	Rat hippocampus	[67]
68.	Sevoflurane-induced neurotoxicity	miR-424	TLR4/MyD88/NF-κB pathway	Mouse and in PC12 cells	[68]
69.	Amyloid-β Induced Neurotoxicity	miR-26a-5p	PTGS2	Peripheral blood of AD patients and AD model cells (SH-SY5Y cells)	[69]
70.	Ketamine-induced neurotoxicity	miR-384-5p	GABRB1	Neonatal hippocampal neurons from rats	[70]
71.	Propofol-induced neurotoxicity	miR-17-5p	BCL2L11	SH-SY5Y cells	[71]
72.	Beta-Amyloid-Induced Neurotoxicity	miR-381-3p	PTGS2	Serum of AD patients and AD cell model- SH-SY5Y cells	[72]

Table S2. Potential modulator of miRNA as alleviative target for neurotoxicity.

Sr. No.	Modulators	MicroRNA	Neurotoxicity	References
1.	lncRNA-ATB	miR-200/ZNF217 axis	Amyloid-β-induced neurotoxicity	[73]
2.	Melatonin	miR-132/PTEN/AKT/FOXO3a pathway	Aβ-induced neurotoxicity	[74]
3.	LncRNA Rik-203	miR-101a-3p	Anesthesia neurotoxicity	[75]
4.	Baicalin	miR-192-5p	6-hydroxydopamine-induced neurotoxicity	[76]
5.	lncRNA MALAT1	miR-101-3p/PDCD4 axis	Bupivacaine-induced neurotoxicity	[77]
6.	Pramipexole	miR-494-3p/BDNF	MPP (+)-Induced Neurotoxicity	[78]
7.	LncRNA Rik-203	miR-466l-3p	Sevoflurane Induced Neurotoxicity	[79]
8.	Long-Noncoding RNA TUG1	MiR-152-3p/PTEN Pathway	Parkinson's Disease	[80]
9.	LncRNA H19	miR-585-3p/PIK3R3	MPTP-Induced Parkinson's Disease	[81]
10.	Vitexin	miR-409	Isoflurane-induced neurotoxicity	[82]
11.	Oxytocin	miR-26a/DAPK1 signaling pathway	MPTP-Induced Neurotoxicity	[83]
12.	Long Non-Coding RNA BACE1-AS	miR-214-3p	Isoflurane-Induced Neurotoxicity	[84]
13.	Dexmedetomidine	miR-381/LRRC4 /SDF-1/CXCR4 signaling pathway	Ropivacaine	[85]
14.	Long non-coding RNA Peg13	miR-128-3p	Sevoflurane toxicity	[86]

15.	lncRNA Gm15621	miR-133a/Sox4	Sevoflurane-induced neurotoxicity	[87]
16.	LncRNA KCNQ1OT1	miR-206	Ketamine-induced	[88]
17.	Berberine	circHDAC9/miR-142-5p axis	A β 42-induced	[89]
18.	Long noncoding RNA small nucleolar RNA host gene 1 (SNHG1)	miR-181b	Sevoflurane-induced neurotoxicity	[90]
19.	Circular RNA circDLGAP4	miR-134-5p/CREB pathway	Parkinson's disease	[91]
20.	Neuron-derived exosomes	miR-124-3p	Neurotoxic microglia and astrocytes in Spinal cord injury (SCI)	[92]
21.	Syringin	miR-124-3p/BID Pathway	A β (25-35)-Induced Neurotoxicity	[93]
22.	lncRNA MAGI2-AS3	sponging miR-374b-5p	Amyloid- β induced neurotoxicity	[94]
23.	Dexmedetomidine	miR-330-3p/ULK1 axis	Sevoflurane-induced neurotoxicity	[95]
24.	LncRNA Neat1	miR-298-5p/Srpk1	Sevoflurane-Induced Neurotoxicity	[96]
25.	LINC00665	has-miR-34a-5p	Bupivacaine induced neurotoxicity	[97]
26.	lncRNA NEAT1	miR-374c-5p	MPTP-induced PD	[98]
27.	LncRNA Rian	miR-143-3p	Sevoflurane anesthesia-induced	[99]
28.	lipoxin A4 methyl ester (LXA4 ME)	miR-22/BAG5 pathway	Ketamine-induced neurotoxicity	[100]
29.	lncRNA ZFAS1	miR-421/zinc finger protein564 (ZNF564) axis	Bupivacaine-induced neurotoxicity	[101]
30.	LncRNA SNHG1	miR-181a-5p/CXCL12 axis	Neuronal injury in Parkinson's disease	[102]
31.	HOTAIR	miR-455-3p/NLRP1 axis	Propofol-induced neurotoxicity	[103]
32.	lncSh2d3c	mmu-miR-675-5p/Chmp4b/Bax axis	Mn-induced neurotoxicity	[104]
33.	Dexmedetomidine	miR-377-5p/Arc pathway	Propofol-induced	[105]
34.	Apple phenolic extracts	miR-22-3p/SIRT1 axis	Lead neurotoxicity	[106]
35.	Long Noncoding RNA H19	miR-17-5p	Isoflurane (ISO) neurotoxicity	[107]
36.	trametenolic acid B	mir-329-3p	Sevoflurane-induced	[108]
37.	Benzodiazepines	miR-133a-3p/EGFR pathway	Toxicity of lidocaine	[109]
38.	Long Noncoding RNA SNHG14	miR-519a-3p	MPP+ toxicity	[110]
39.	Bone Marrow Stem Cell-Exo-Derived TSG-6	STAT3/miR-7/NEDD4/LRRK2 Axis	1-Methyl-4-Phenylpyridinium+-Induced Neurotoxicity	[111]
40.	CircAXL	miR-1306-5p	A β (1-42)-Induced Neurotoxicity	[112]

41.	Myocardia-Related Transcription Factors-A (MRTF-A)	miR-1273g-3p/mTOR axis	A β -Induced Neurotoxicity	[113]
42.	LncRNA BDNF-AS	miR-9-5p/BACE1 pathway	neurotoxicity in Alzheimer's disease	[114]
43.	Circular RNA circ_0070441	miR-626/IRS2 axis.	MPP (+)-triggered neurotoxic effect	[115]
44.	LncRNA SNHG12	miR-497-5p	bupivacaine-induced neurotoxicity	[116]
45.	LncRNA Riken	MicroRNA-101a/MKP-1/JNK Pathway	sevoflurane-induced neurotoxic effects	[117]
46.	Resveratrol-Selenium Nanoparticles	Sirt1/miRNA-134/GSK3 β	Neurotoxicity in a Rat Model of Alzheimer's Disease	[118]

Table S3. Potential miRNAs as alleviative target for AD related neurotoxicity.

Sr. No.	Neurotoxicity	miRNAs	Targets/Signalling Pathways	Experimental Validation Approach	References
1.	β -amyloid-induced neurotoxicity	miR-16	BACE1	AD tissues and the cellular AD model of PC12	[5]
2.	Amyloid- β -induced neurotoxicity	miR-107	BDNF-TrkB signaling pathway	mice	[11]
3.	A β -induced neurotoxicity	miR-34a	Caspase-2	SH-SY5Y cells	[17]
4.	A β -induced neurotoxicity	miR-409-5p	Plek	APP/PS1 mice cortexes	[18]
5.	A β -induced neurotoxicity	miR-29c-3p	TNFAIP1/ NF- κ B signalling pathway	Neuroblastoma Cells	[28]
6.	A β (25-35)-induced neurotoxicity	miR-212	PDCD4/ PI3K/AKT signaling pathway	plasma from AD patients, SH-SY5Y and IMR-32 cells	[34]
7.	A β (25-35)-induced neurotoxicity	miR-33	Akt/mTOR pathway	SH-SY5Y cells	[35]
8.	A β -induced neurotoxicity	miR-34a-5p and miR-125b-5p	BACE1	Serum samples AD patients and Primary mouse cortical neurons (MCN) and Neuro2a (N2a) cells	[37]
9.	Amyloid- β induced neurotoxicity	miR-193a-3p	PTEN	Serum, cellular AD model of PC12 and SH-SY5Y	[41]
10.	A β -induced neurotoxicity	miR-433	JAK2	serum and cerebrospinal fluid (CS) of AD patients and AD cell model	[42]
11.	Amyloid- β induced neurotoxicity	miR-148a-3p	ROCK1	Serum of AD patients	[56]

12.	A β 1-42-induced neurotoxicity	miR-204-3p	Nox4	hippocampus of APP/PS1 mice	[58]
13.	A β -induced neurotoxicity	miR-130a-3p	DAPK1	SH-SY5Y cells and hippocampus tissues of AD mice	[59]
14.	Amyloid- β Induced Neurotoxicity	miR-26a-5p	PTGS2	peripheral blood of AD patients and AD model cells (SH-SY5Y cells)	[69]
15.	Beta-Amyloid-Induced Neurotoxicity	miR-381-3p	PTGS2	Serum of AD patients and AD cell model- SH-SY5Y cells	[72]

Table S4. Potential miRNAs as alleviative target for PD related neurotoxicity.

Sr. No.	Neurotoxicity	miRNAs	Targets/ Signalling Pathways	Experimental Validation Approach	References
1.	MPP (+)-induced 6-Hydroxydopamine-Induced Cell Model of PD	miR-124-3p	STAT3	SH-SY5Y cells	[2]
2.	Parkinson's Disease	miR-124-3p	ANAX5	PC12 and SH-SY5Y cells	[7]
3.	MPTP-induced Parkinson's disease	miR-124	MEKK3	BV2 cells	[10]
4.	Atrazine-induced Parkinson's disease	miR-190	Nlrp3	PD mouse model and BV2 cells	[15]
5.	(MPP+-) induced neurotoxicity	miR-7	BDNF/ α -syn axis	peripheral blood and brain tissue in a rat model of PD	[19]
6.	MPP+ neurotoxicity	miR-9-5p	SIRT1	SH-SY5Y cells	[21]
7.	Parkinson's Disease	miR-200a and miR-204	Sirt1 and BCL2	PC12 cells	[22]
8.	Parkinson's disease	miR-326	KLK7-Mediated MAPK Signaling Pathway	mice with PD	[24]
9.	Neurotoxicity induced by 6-hydroxydopamine	miR-103a-3p	Parkin/Ambra1 signaling	SH-SY5Y cells	[29]
10.	MPP (+)-induced neurotoxicity	miR-107	PDCD10	in vitro and in vivo (Mouse, SH-SY5Y and PC12 cells)	[39]
11.	(MPP+-) induced neurotoxicity	miR-30b	SNCA	SH-SY5Y	[46]
12.	PD	miR-20a-5p	IRF9/NF- κ B Axis	hippocampal cell line-HT22 cells	[47]
13.	PD Neurotoxicity	miR-3473b	TREM2/ULK1	moues microglia cell line (BV2) cells	[49]
14.	Neurotoxicity induced by MPP+	miR-421	MEF2D	cellular model of PD (Parkinson's disease)	[55]
15.		miR-126-5p	SP1	SH-SY5Y and SK-N-SH cells	[64]

Table S5. Potential miRNAs as alleviative target for IS related neurotoxicity.

Sr. No.	Neurotoxicity	miRNAs	Targets/ Signalling Pathways	Experimental Validation Approach	References
1.	Hypoxia/ischemia-induced	miR-381-3p	CCR2/NF- κ B pathway	BV2 cells and HT-22 neurons	[63]
2.	Ischemic stroke (IS)	miR-107	FGF9/FGF12/ PI3K-AKT signaling pathway	Oxygen-Glucose Deprivation/Reoxygenation (OGD/R)-induced PC12 cells	[66]

Table S6. Potential miRNAs as alleviative target for heavy metals related neurotoxicity.

Sr. No.	Neurotoxicity	miRNAs	Targets/ Signalling Pathways	Experimental Validation Approach	References
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1.	Arsenic-Induced - neurotoxicity	miR-219	CaMKII	mouse hippocampus	[6]
2.	manganese induced neurotoxic	miR-7 and miR-433	SNCA and FGF-20 mRNA	SH-SY5Y cells	[12]
3.	Pb neurotoxicity	miR-106b-5p	XIAP	HT-22 and PC12 cells	[27]
4.	Arsenic-induced Endoplasmic Reticulum Stress and Neurotoxicity	miR-124	SNPs - rs67543816 and rs35418153	neural cells	[40]

Table S7. Potential miRNAs as alleviative target for other types of neurotoxicity.

Sr. No.	Neurotoxicity	miRNAs	Targets/ Signalling Pathways	Experimental Validation Approach	References
1.	Glutamate-induced neurotoxicity	miR-219	CaMKII γ	rat hippocampal neurons	[4]
2.	Triazophos-induced toxicity	miR-217	nup43	adult zebrafish and ZF4 cells	[8]
3.	METH-mediated neurotoxicity	miR-142a-3p/miR-155-5p	Peli1	BV2 cells and brain of mouse	[20]
4.	T helper cell 1 (Th1)-skewed neurotoxicity	miR-494	HDAC2-STAT4 pathway	blood from AIS (acute ischemic stroke) patients and controls	[30]
5.	Lidocaine induces neurotoxicity	miR-199a-5p	MYRF	rat model	[50]
6.	Oxygen-glucose deprivation/reoxygenation (OGD/R) -induced neurotoxicity	miR-126	SIRT1/Nrf2 signaling pathway	human umbilical vein endothelial cell (HUVEC)	[51]

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