Supplementary Table 4- KEGG pathway analysis of genes targeted by pathogenic and protective miRNAs

Upregulated Pathogenic miRNAs in WMLs			
KEGG pathway	**p-value**	**#genes**	**#miRNAs**
PI3K-Akt signaling pathway	0.038099	69	7
MAPK signaling pathway	0.0131893	59	7
Ras signaling pathway	0.0025175	51	7
Rap1 signaling pathway	0.0025175	50	7
Regulation of actin cytoskeleton	0.0226995	47	6
cAMP signaling pathway	0.0212892	46	7
Focal adhesion	0.0306889	46	7
Endocytosis	0.0145157	45	7
Proteoglycans	0.0049956	40	7
Viral carcinogenesis	0.0495451	40	7
Transcriptional misregulation in cancer	0.0355647	39	7
FoxO signaling pathway	0.0009886	38	7
cGMP-PKG signaling pathway	0.0256075	37	6
Oxytocin signaling pathway	0.0489916	37	7
Axon guidance	0.0023943	36	7
Ubiquitin mediated proteolysis	0.01593	35	7
Signaling pathways regulating pluripotency of stem cells	0.0270347	32	6
Neurotrophin signaling pathway	0.0134247	31	7
AMPK signaling pathway	0.0226995	31	6
Glutamatergic synapse	0.0047646	29	7

Downregulated Pathogenic miRNAs in WMLs			
KEGG pathway	p-value	#genes	#miRNAs
Pathways in cancer	0.0017319	66	4
Ras signaling pathway	0.0455952	39	4
Rap1 signaling pathway	0.0473378	39	4
Signaling pathways regulating pluripotency of stem cells	7.76E-06	36	4
Proteoglycans in cancer	0.0016556	36	4
Adrenergic signaling in cardiomyocytes	0.0149366	28	4
AMPK signaling pathway	0.004942	27	4
Wnt signaling pathway	0.0264365	27	4

FoxO signaling pathway	0.0401161	27	4
Prostate cancer	0.000174	25	4
Neurotrophin signaling pathway	0.0214238	25	4
Sphingolipid signaling pathway	0.0361575	22	3
HIF-1 signaling pathway	0.0410532	22	3
Oocyte meiosis	0.0203943	21	4
Glioma	3.878E-07	20	3
mTOR signaling pathway	0.000174	20	3
Melanoma	0.0013895	20	3
ErbB signaling pathway	0.0330705	20	3
Progesterone-mediated oocyte maturation	0.0361575	20	4
Long-term depression	0.0008606	18	4

*Pathways in shadow boxes are common between pathogenic and protective groups.

Downregulated Protective miRNAs in WMLs			
KEGG pathway	**p-value**	**#genes**	**#miRNAs**
MAPK signaling pathway	0.037136	64	5
Proteoglycans	0.001217	58	5
Ras signaling pathway	0.046795	57	5
Rap1 signaling pathway	0.014478	56	5
Focal adhesion	0.018506	56	5
cAMP signaling pathway	0.040156	52	5
Transcriptional misregulation in cancer	0.046795	45	6
Insulin signaling pathway	0.026389	40	5
Wnt signaling pathway	0.005565	39	6
FoxO signaling pathway	0.024963	39	5
Signaling pathways regulating pluripotency of stem c	0.021797	38	5
Thyroid hormone signaling pathway	0.005565	35	6
Hippo signaling pathway	0.021797	34	6
ErbB signaling pathway	9.14E-06	33	5
Choline metabolism in cancer	0.014857	33	5
GnRH signaling pathway	0.037136	27	5
Estrogen signaling pathway	0.010758	26	5
Long-term potentiation	0.005565	25	5
Amphetamine addiction	2.74E-05	24	5
Central carbon metabolism in cancer	0.003743	24	5

Upregulated Protective miRNAs in WMLs			
KEGG pathway	p-value	#genes	#miRNAs
Regulation of actin cytoskeleton	0.048121	44	5
cGMP-PKG signaling pathway	0.00616	39	4
Dopaminergic synapse	0.000853	36	5
Protein processing in endoplasmic reticulum	0.043061	33	5
Axon guidance	0.00802	32	5
Adrenergic signaling in cardiomyocytes	0.00802	31	4
FoxO signaling pathway	0.015049	30	5
Wnt signaling pathway	0.04829	29	5

Choline metabolism in cancer	0.006517	27	5
ErbB signaling pathway	0.030651	23	5
Amphetamine addiction	7.98E-05	19	5
B cell receptor signaling pathway	0.031121	19	5
Gap junction	0.018338	18	5
Long-term depression	0.000853	17	4
Glioma	0.030651	15	5
N-Glycan biosynthesis	7.98E-05	14	5
Mucin type O-Glycan biosynthesis	1.90E-05	7	4
Glycosaminoglycan biosynthesis - keratan sulfate	0.000122	5	3

*Pathways in shadow boxes are common between pathogenic and protective groups.