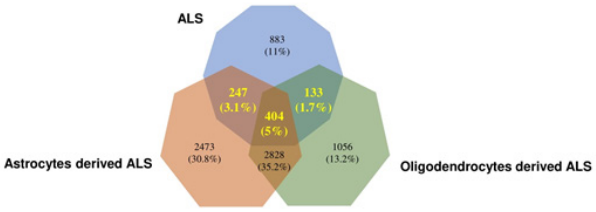
A

Term	P-value	Genes
Regulation of actin cytoskeleton	0.005844482	ARHGEF12,ABI2,PDGFD,BRK1,ITGAV,KRAS,EZR,MYH10
Steroid hormone biosynthesis	0.00683156	STS,AKR1C1,AKR1C3,HSD17B12
Inositol phosphate metabolism	0.01270949	MTMR2,IMPA1,IPMK,PLCH1
N-Glycan biosynthesis	0.023820769	ALG8,ALG14,ALG13
Phosphatidylinositol signaling system	0.032250230	MTMR2,IMPA1,IPMK,DGKH

Term	P-value	Genes
p53 signaling pathway	0.00001556	SESN3,ZMAT3,GADD45A,MDM2,PMAIP1,TNFRSF10B,MDM4,PPM1D,TP53
Cell cycle	0.000925657	TGFB2,HDAC2,ANAPC7,GADD45A,MDM2,E2F3,TP53,YWHAZ,ANAPC10
Cellular senescence	0.00127543	TGFB2,RBBP4,GADD45A,ITPR1,MDM2,PIK3R3,MAPK1,TRPM7,E2F3,TP53
Adherens junction	0.003065	LEF1,MAPK1,LMO7,WASL,NLK,WASF2
Glioma	0.0040309	GADD45A,MDM2,PIK3R3,MAPK1,E2F3,TP53

Term	P-value	Genes
p53 signaling pathway	0.381581782	CD82
Glioma	0.389686200	CAMK2D
cAMP signaling pathway	0.41449744	AFDN,CAMK2D
Protein digestion and absorption	0.4926760	COL21A1
T cell receptor signaling pathway	0.49601619	PTPRC



B

Term	P-value	Genes
Regulation of lipolysis in adipocytes	0.000221863	ADCY9,IRS1,INSR,MGLL
Insulin signaling pathway	0.0008882512	PPP1R3C,IRS1,INSR,EIF4EBP1,GCK
Longevity regulating pathway	0.0022771277	ADCY9,IRS1,INSR,EIF4EBP1
AMPK signaling pathway	0.0040881826	IRS1,INSR,EIF4EBP1,PPP2R3B
Galactose metabolism	0.01213080	B4GALT2,GCK

Term	P-value	Genes
Aldosterone synthesis and secretion	0.004566554	SCARB1,NR4A1,GNA11,ATP2B2,CAMK2G
Glucagon signaling pathway	0.006604896	LDHA,PPP3CB,PKM,ACACB,CAMK2G
HIF-1 signaling pathway	0.0071322027	LDHA,PGK1,GAPDH,CAMK2G,IGF1R
Inositol phosphate metabolism	0.00858045367	ALDH6A1,TPI1,INPP5A,PIP4K2B
PPAR signaling pathway	0.0089942617	SLC27A1,RXRA,PLIN4,PLIN2

Term	P-value	Genes
Pathways of neurodegeneration	0.00400429	FZD1,ACTR1A,PSMD2,MFN2,CACNA1S,MAP2K7,TUBA4A,UBE2L3
Butanoate metabolism	0.009789146	ACADS,ACSM2B
Salmonella infection	0.010929295	ACTR1A,PLEKHM2,MAP2K7,TUBA4A,DNM2
Tight junction	0.01294962	PPP2R1A,MAP2K7,TUBA4A,LLGL1
GnRH signaling pathway	0.01363996	CACNA1S,MAP2K7,HBEGF

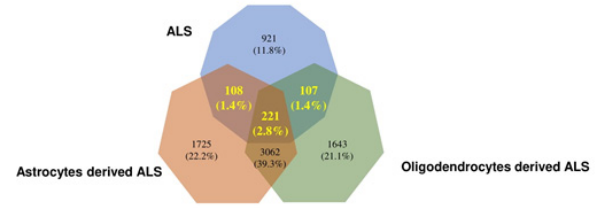


Fig. S1. Identification of shared and unique genes between astrocyte- and oligodendrocyte-derived ALS. Shared genes were identified using a Venn diagram, followed by pathway analysis of genes unique to each cell type. (A) Upregulated genes. (B) Downregulated genes.

A

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Regulation of actin cytoskeleton	0.005844482	ARHGEF12,ABI2,PDGFD,BRK1,ITGAV,KRAS,EZR,MYH10
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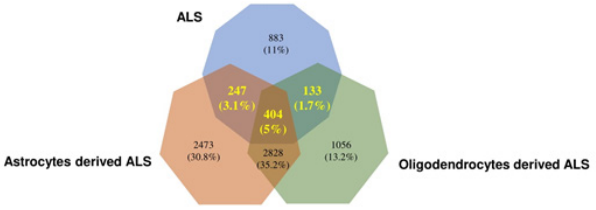

B

Term	P-value	Genes
Regulation of lipolysis in adipocytes	0.000221863	ADCY9,IRS1,INSR,MGLL
Insulin signaling pathway	0.0008882512	PPP1R3C,IRS1,INSR,EIF4EBP1,GCK
Longevity regulating pathway	0.0022771277	ADCY9,IRS1,INSR,EIF4EBP1
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Galactose metabolism	0.01213080	B4GALT2,GCK

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GnRH signaling pathway	0.01363996	CACNA1S,MAP2K7,HBEGF

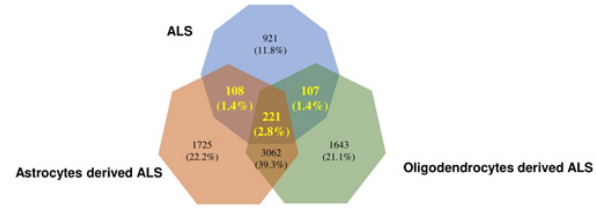

Fig. S2. Shared and unique genes between astrocyte- and oligodendrocyte-derived ALS were identified using a Venn diagram. Unique genes were subsequently analyzed for involvement in key signaling pathways. (A) Upregulated genes. (B) Downregulated genes.

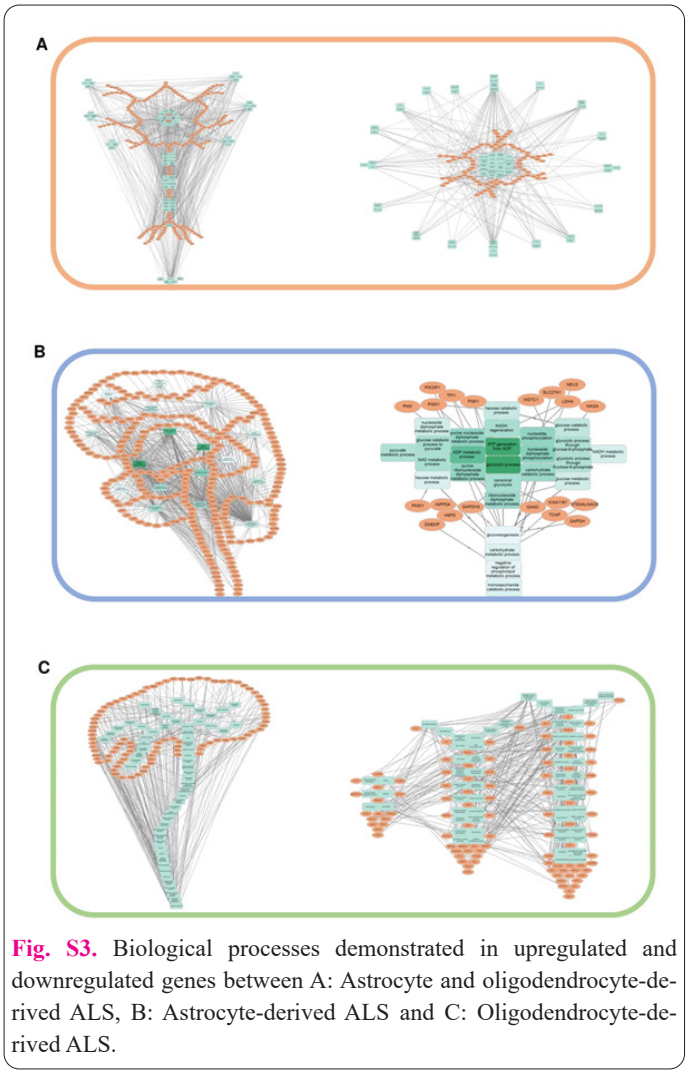

Fig. S3. Biological processes demonstrated in upregulated and downregulated genes between A: Astrocyte and oligodendrocyte-derived ALS, B: Astrocyte-derived ALS and C: Oligodendrocyte-derived ALS.

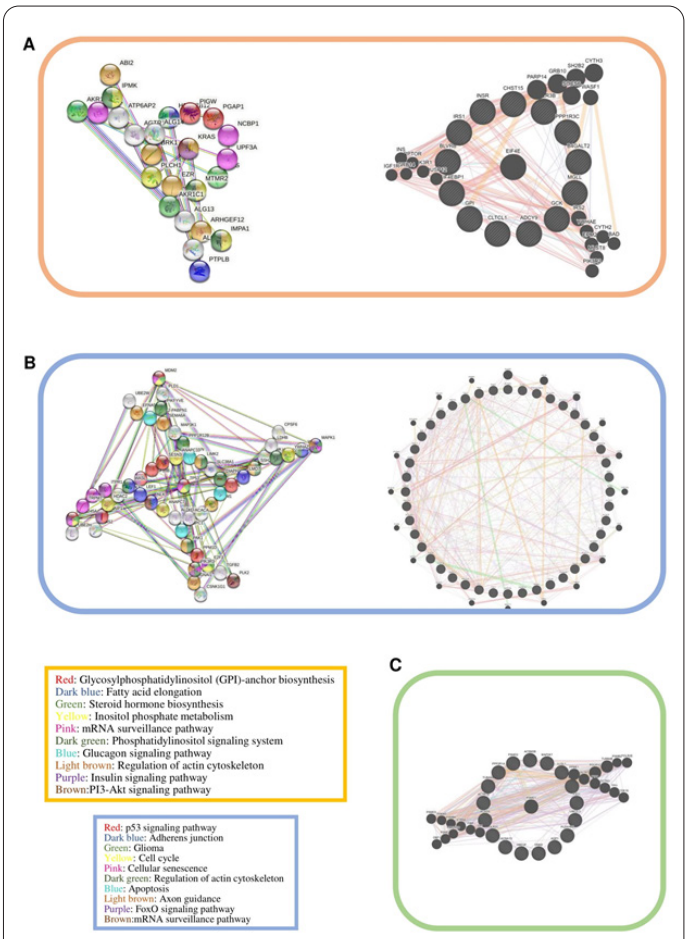

Fig. S4. Hub proteins identified in (A) astrocyte- and oligodendrocyte-derived ALS, (B) astrocyte-derived ALS, and (C) oligodendrocyte-derived ALS. These data highlight key proteins associated with each condition.

A

Node	Node degree
MLLT4	2
PTPRC	2
PTK2	1
PTPRJ	1
CAMK2D	0
CD82	0
CYLD	0
CYP2R1	0
FZD3	0
MFSD8	0

B

Node	Node degree
PPP2R1A	2
ACADS	1
ACSM2B	1
CACNA1S	1
DNM2	1
FZD1	1
HBEGF	1
MAP2K7	1
MFN2	1
ACTR1A	0

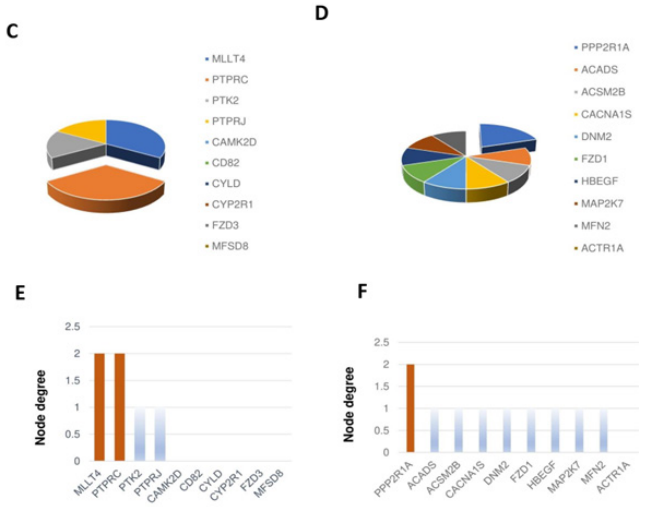

Fig. S5. Node degree analysis of key hub genes in astrocyte- and oligodendrocyte-derived ALS. (A–C) Analysis of ACE upregulated hub genes: (A) Node degree table, (C) pie chart, and (E) bar plot visualization showing the distribution of node degrees among upregulated genes. (B–D) Analysis of BDF downregulated hub genes: (B) Node degree table, (D) pie chart, and (F) bar plot visualization representing the node degree distribution among downregulated genes. Higher node degrees indicate a greater number of direct connections, suggesting central roles in the respective regulatory networks.

A

Node	Node degree
TP53	24
MDM2	14
GADD45A	9
YWHAZ	9
MAPK1	8
CSNK1A1	7
MDM4	7
PMAIP1	7
TNFRSF10B	7
ZMAT3	6

B

Node	Node degree
GAPDH	20
PKM	8
LDHA	7
PGM1	7
TPI1	7
GAPDHS	6
PGK1	6
IGF1R	5
NFATC1	5
ACACB	4

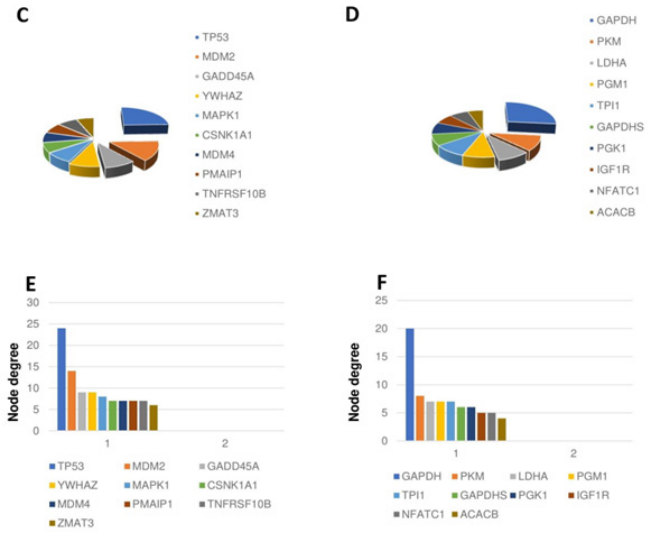

Fig. S6. Node degree analysis of hub genes in astrocyte-derived and oligodendrocyte-derived ALS. (A–C) Analysis of ACE upregulated hub genes: (A) Node degree table, (C) pie chart, and (E) bar plot representation highlighting the node degrees of upregulated genes. (B–D) Analysis of BDF downregulated hub genes: (B) Node degree table, (D) pie chart, and (F) bar plot representation showing the node degree distribution among downregulated genes. Genes with higher node degrees are likely to play more central roles in the regulatory networks.

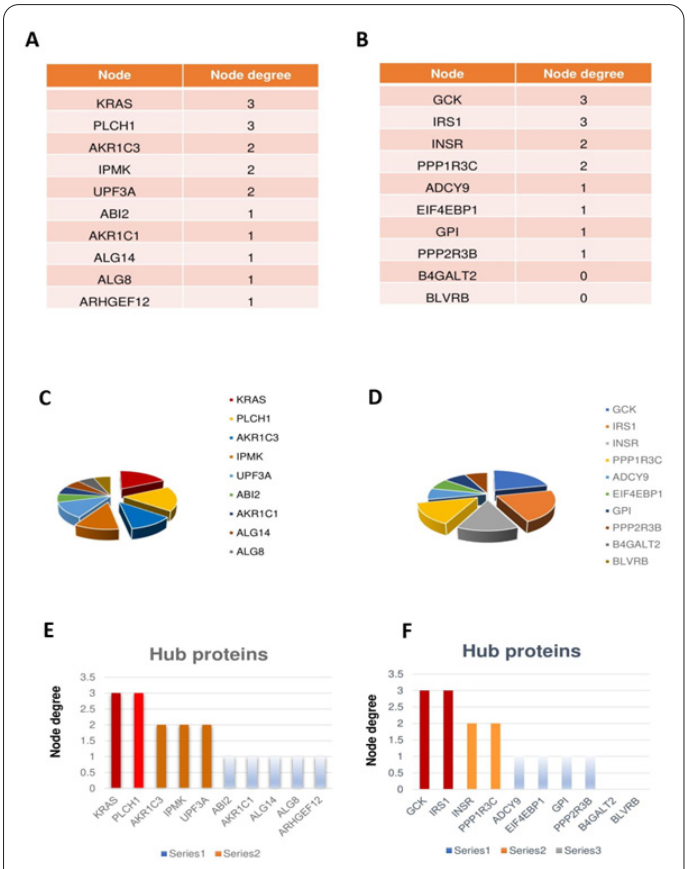

Fig. S7. Node degree analysis of additional hub genes identified in astrocyte- and oligodendrocyte-derived ALS. (A–C) Analysis of ACE upregulated hub genes: (A) Node degree table, (C) pie chart, and (E) bar plot showing node degree distribution among upregulated genes. (B–D) Analysis of BDF downregulated hub genes: (B) Node degree table, (D) pie chart, and (F) bar plot representing node degree distribution among downregulated genes. Node degree indicates the number of direct interactions, highlighting genes with potentially important regulatory roles in the disease network.

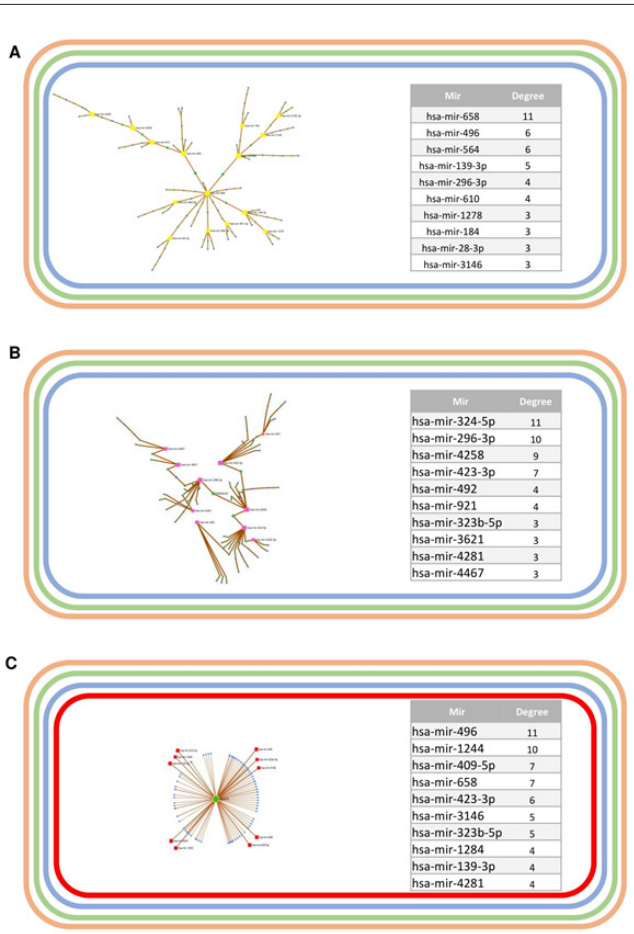

Fig. S8. Network illustrating the relationships between key extracellular vesicle miRNAs in (A) astrocyte-derived and oligodendrocyte-derived ALS, (B) astrocyte-derived ALS, and (C) oligodendrocyte-derived ALS.