

SUPPLEMENTARY FIGURES

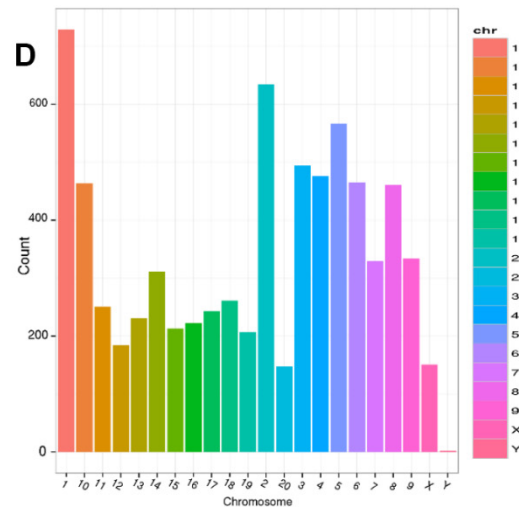
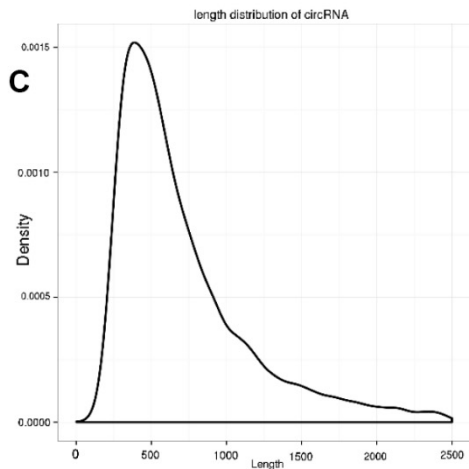
A **Base information TAB after filter**

Sample	After Filter				
	HQ Clean Data(bp)	Q20(%)	Q30(%)	N(%)	GC(%)
D0	16539966600 (75.55%)	15968305623 (96.54%)	15356332640 (92.84%)	28755004 (0.17%)	8751536597 (52.91%)
D1	16613502900 (76.55%)	16044928674 (96.58%)	15432168840 (92.89%)	27238712 (0.16%)	8984970973 (54.08%)
D2	14333866200 (76.09%)	13893647821 (96.93%)	13401904472 (93.50%)	23430073 (0.16%)	7968099663 (55.59%)
D3	13996249200 (74.71%)	13528794735 (96.66%)	13025089708 (93.06%)	22978314 (0.16%)	7413860886 (52.97%)

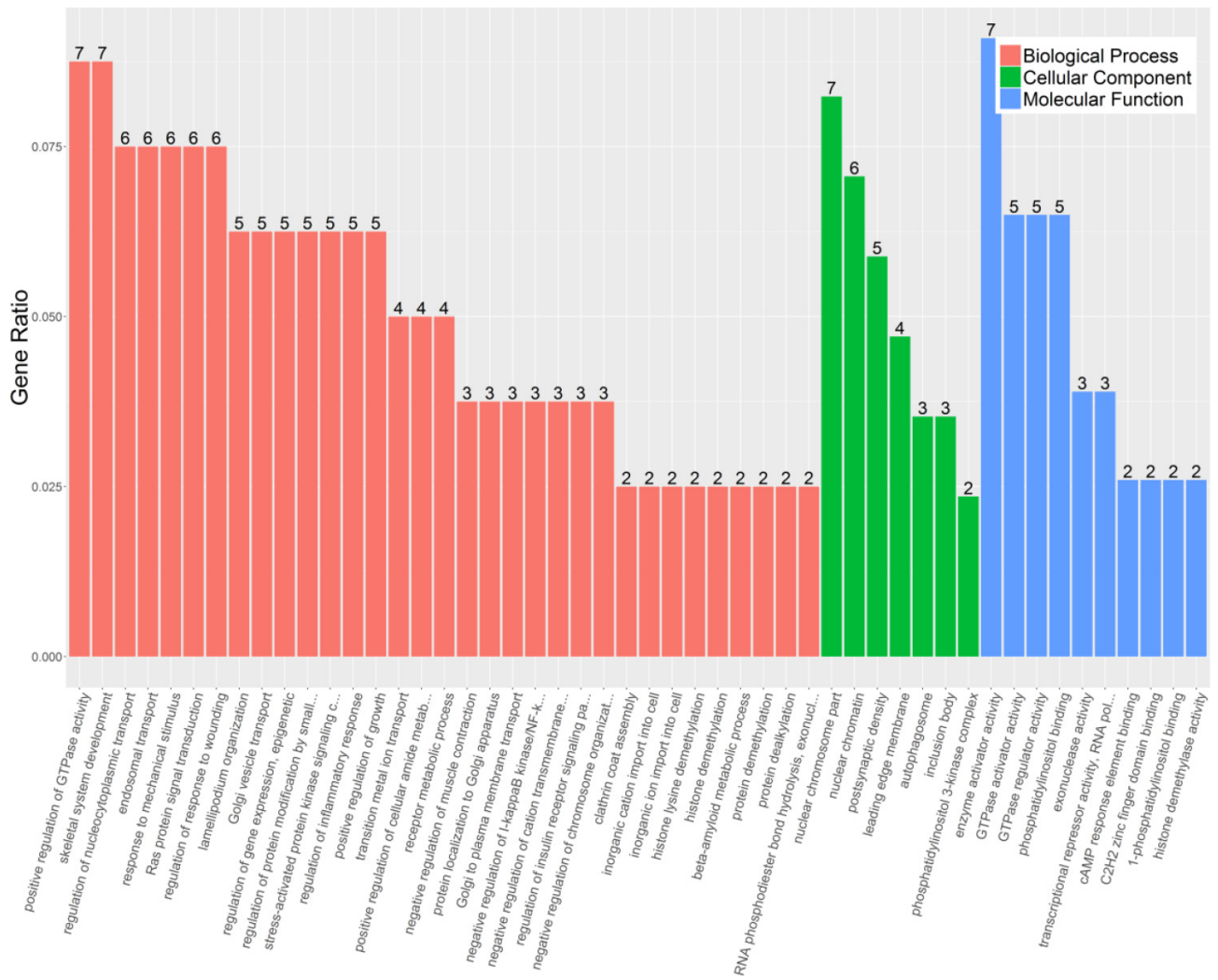
B **Genomic alignment data quality assessment**

Sample	Total Reads	Mapped Reads	Ribosome Reads	Coding Reads	UTR Reads	Intronic Reads	Intergenic Reads
D0	66747201	20348617	9263365	1119012	909578	2052950	4130737
D1	65974519	25650918	12500089	1303876	1541039	2154409	4639657
D2	57663232	39867408	5727149	4592629	4949105	7385101	12573045
D3	57284221	34232254	4093082	2937374	3382552	5651032	14123865

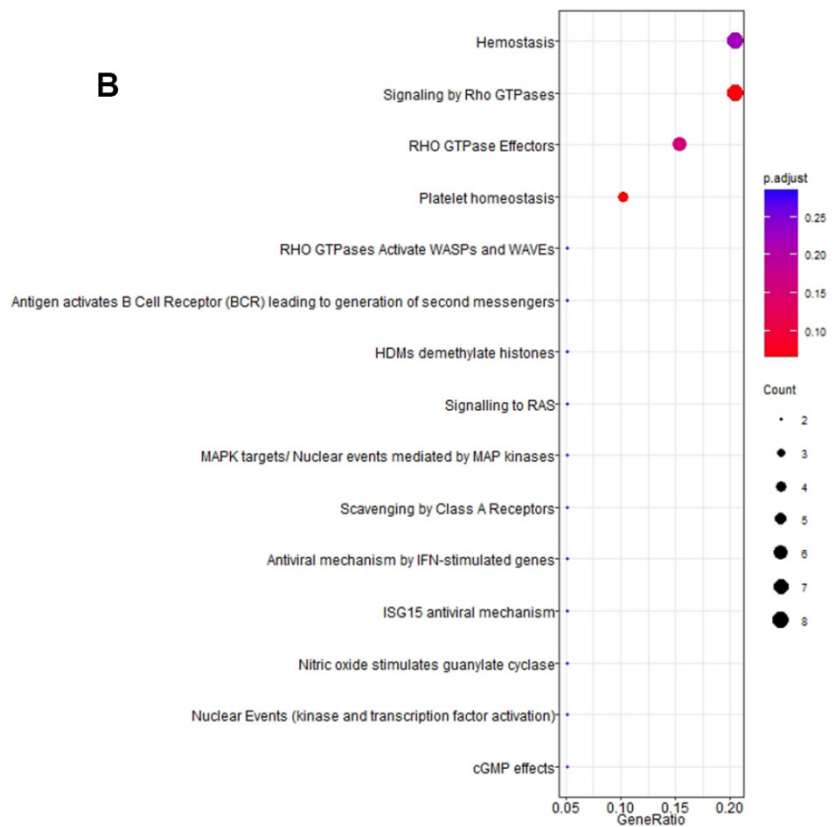
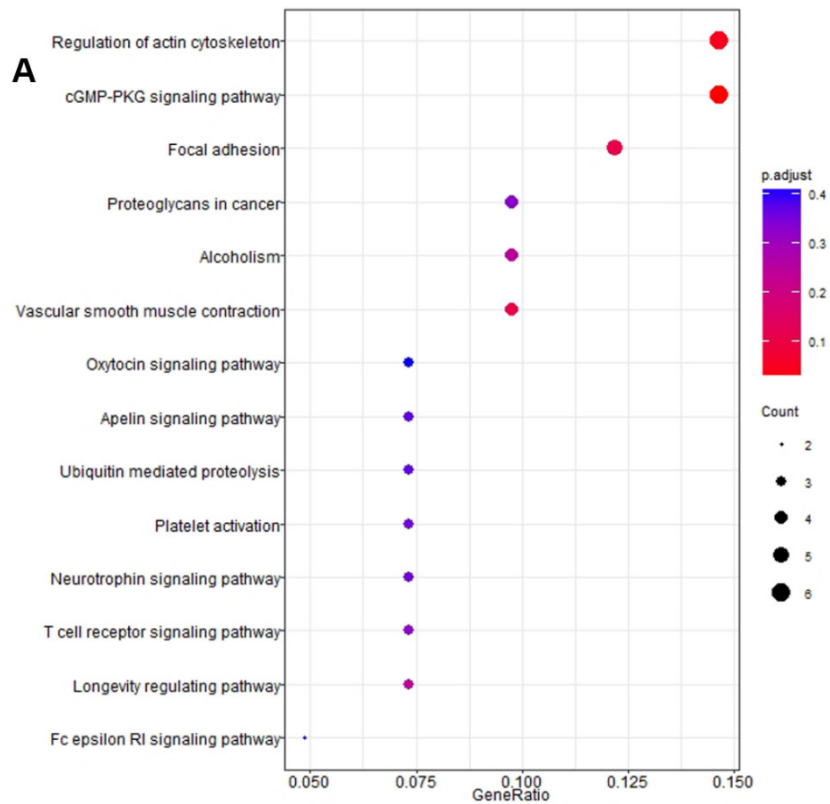
PCT Ribosome Reads	PCT Coding Reads	PCT UTR Reads	PCT Intronic Reads	PCT Intergenic reads	PCT mRNA Reads
0.530078	0.064033	0.052049	0.117476	0.236373	0.116082
0.564622	0.058895	0.069608	0.097314	0.209571	0.128503
0.162579	0.130373	0.140492	0.209644	0.356916	0.270865
0.135587	0.097303	0.11205	0.187196	0.467866	0.209353



Supplementary Figure 1. Senescence-regulated astroglial circRNAs. (A) Base information TAB after filter; (B) Genomic alignment data quality assessment; (C) Length distribution of circRNA; (D) circRNAs distribution on chromosome. Sequencing libraries were constructed using Illumina TruSeq RNA Sample Preparation Kits and were sequenced with an Illumina HiSeq™ 2500 flowcell.



Supplementary Figure 2. The enrichment of different expression circRNAs in the senescence-regulated astrocyte.



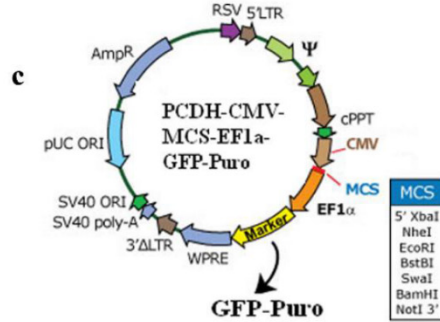
Supplementary Figure 3. The KEGG enrichment (A) and reactome enrichment (B) of different expression circRNAs in the senescence-regulated astrocyte.

A Full length sequence of genes 575bp:

TCTAGAAGTGCTGAGATTACAGGCGTGAGCCACCACCCCGGCCACTTTTTGTAAAGGTACGTAATAAGTACTTTTTTTTAT
 ACTTCAAGCTTTCCAATAAAAAACAGGACAGCAGAAACACACATACCAAAGTCAGCAGCGGAGCACAAACAGGAGTGTCTGATCAACA
 TTCCAAAGTACAAGTTTTCTTGGTCATCAGTGGACTCACCACCATTCTAAAGAATGTTAACAAATATGAGGATATTTGGAGAAG
 CTGCTGAAAAAATTTGTATCTCTCAGTTGATCATATTGGATACACTGGAAAAATGCTTGTCTGGGCAACCAAAGGACACAA
 TGAGATTAGTAAACAATGCTGGTCAAACAGTTGCTACCAGAAATCTGCCATTTTCTCACCTGCCGTGAAGGAAACCAAC
 ATGCAGCCGAACCTCGGAATTCTGCTTCTGGGGTTTTATTTCTCTCAGCTGCAACAACCTCAATGCAGTCTTTAGTCGAATTC
 TACAAGGTAAGAAGCAAGGAAAGAATTAGGCTCGGACGGTAGCTCACACTGTAATCCACGAGGATCC

b Reference Sequence, >rho_circ_000978 (NF1-419)

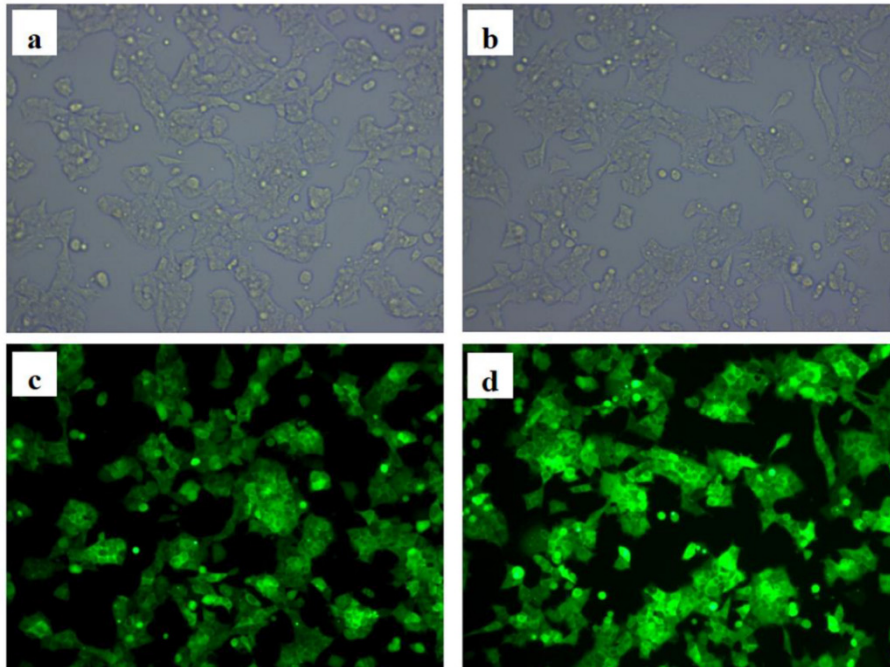
CTTCCAATAAAAAACAGGACAGCAGAAACACACATACCAAAGTCAGCAGCGGAGCACAAACAGGAGTGTCTGATCAACATTCCAA
 GTACAAGTTTTCTTGGTCATCAGTGGACTCACCACCATTCTAAAGAATGTTAACAAATATGAGGATATTTGGAGAAGCTGCTGA
 AAAAAATTTGTATCTCTCAGTTGATCATATTGGATACACTGGAAAAATGCTTGTCTGGGCAACCAAAGGACACAAATGAGATT
 AGATGAAACAATGCTGGTCAAACAGTTGCTACCAGAAATCTGCCATTTTCTCACCTGCCGTGAAGGAAACCAACATGCAGC
 CGAACTTCGGAATTCTGCTTCTGGGGTTTTATTTCTCTCAGCTGCAACAACCTCAATGCAGTCTTTAGTCGAATTTTACAAG



d The sequencing of over-expression vector

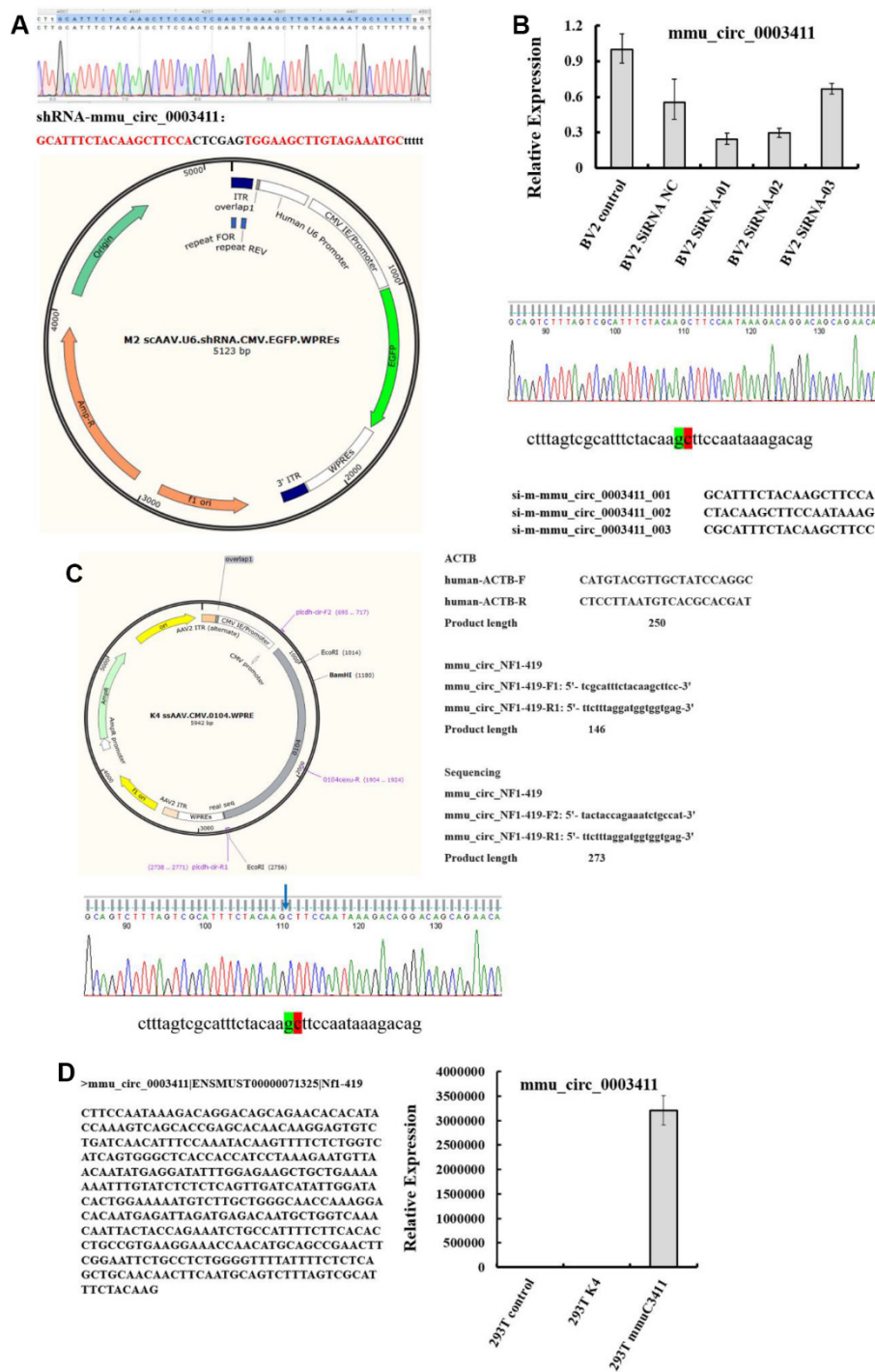
GCGCGGTTGACTCATAGAAGATTCTAGAAGTGCTGAGATTACAGGCGTGAGCCACCACCCCGGCCACTTTTTGTAAAGGT
 ACGTACTAATGACTTTTTTTTATACTTCTCAGCTTCCAATAAAAAACAGGACAGCAGAAACACACATACCAAAGTCAGCAGCGGAGC
 ACAACAAGGAGTGTCTGATCAACATTTCCAAGTACAAGTTTTCTTGGTCATCAGTGGACTCACCACCATTCTAAAGAATGTT
 AACAAATGAGGATATTTGGAGAAGCTGCTGAAAAAATTTGTATCTCTCAGTTGATCATATTGGATACACTGGAAAAATG
 TCTTGTCTGGGCAACCAAAGGACACAATGAGATTAGATGAAACAATGCTGGTCAAACAGTTGCTACCAGAAATCTGCCATTT
 TCTCACCTGCCGTGAAGGAAACCAACATGCAGCCGAACCTCGGAATCTGCTTCTGGGGTTTTATTTCTCTCAGCTGCA
 ACAACTTCAATGCAGTCTTAGTCGAATTTCTACAAGGTAAGAAGCAAGGAAAGAATTAGGCTCGGCACGGTAGCTCACAC
 CTGTAATCCAGCAGGATCCGCGGCCGCAAGGATCTGCGATCGCTCCGGTGCCTGTCAGTGGGAGAGCGCACATCGCCC
 ACAGTCCCGAGAAAGTTGGGGGAGGGGTCGGCAATTGAACGGGTGCTAGAGAAGGTGGCGGGGTAACCTGGGAAAG
 TGATGTCGTACTGGCTCCGCCTTTTCCCGAGGGTGGGGGAGAACCCTATATAAGTCGAGTAGTCGCCGTGAACGTTCT
 TTTCCGCAACGGGTTTCCGCCAGAACACAGCTGAAGCTTCGAGGGGCTCGCATCTCTCTTACCGCCCGCCGCTACCT
 GAGGCCCATCCAGCCGGTTAGTCGGCTTCTGCCGCTCCGCTGTGGTGCTCTGAACTGGTCCGCGCTC

B

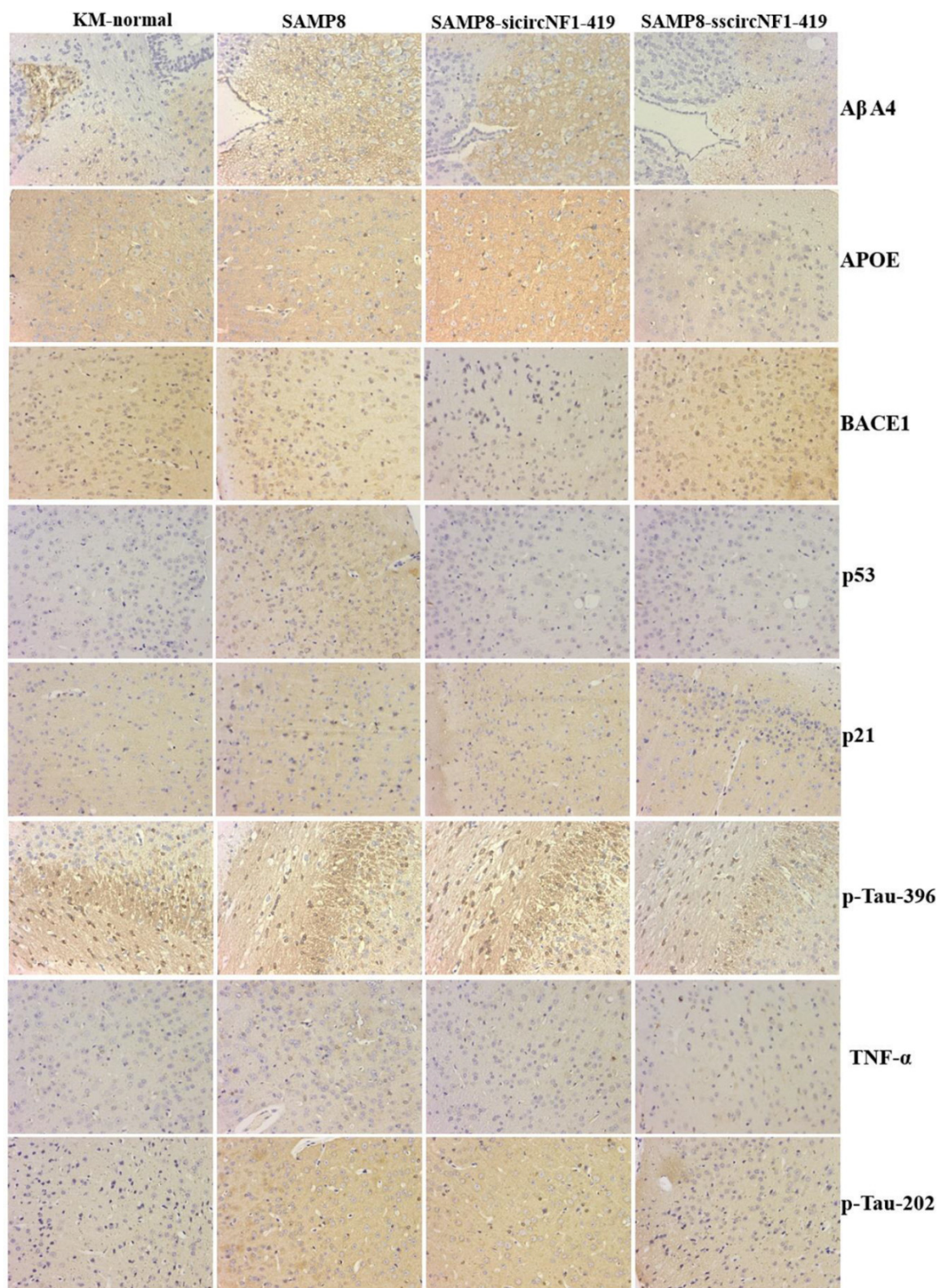


B cells image of pCDH-CMV-MCS-EF1-GFP+Puro (CD513B-1) at bright-field (a) and fluorescence image(c), over-circNF1-419- transfected cell (b, c)

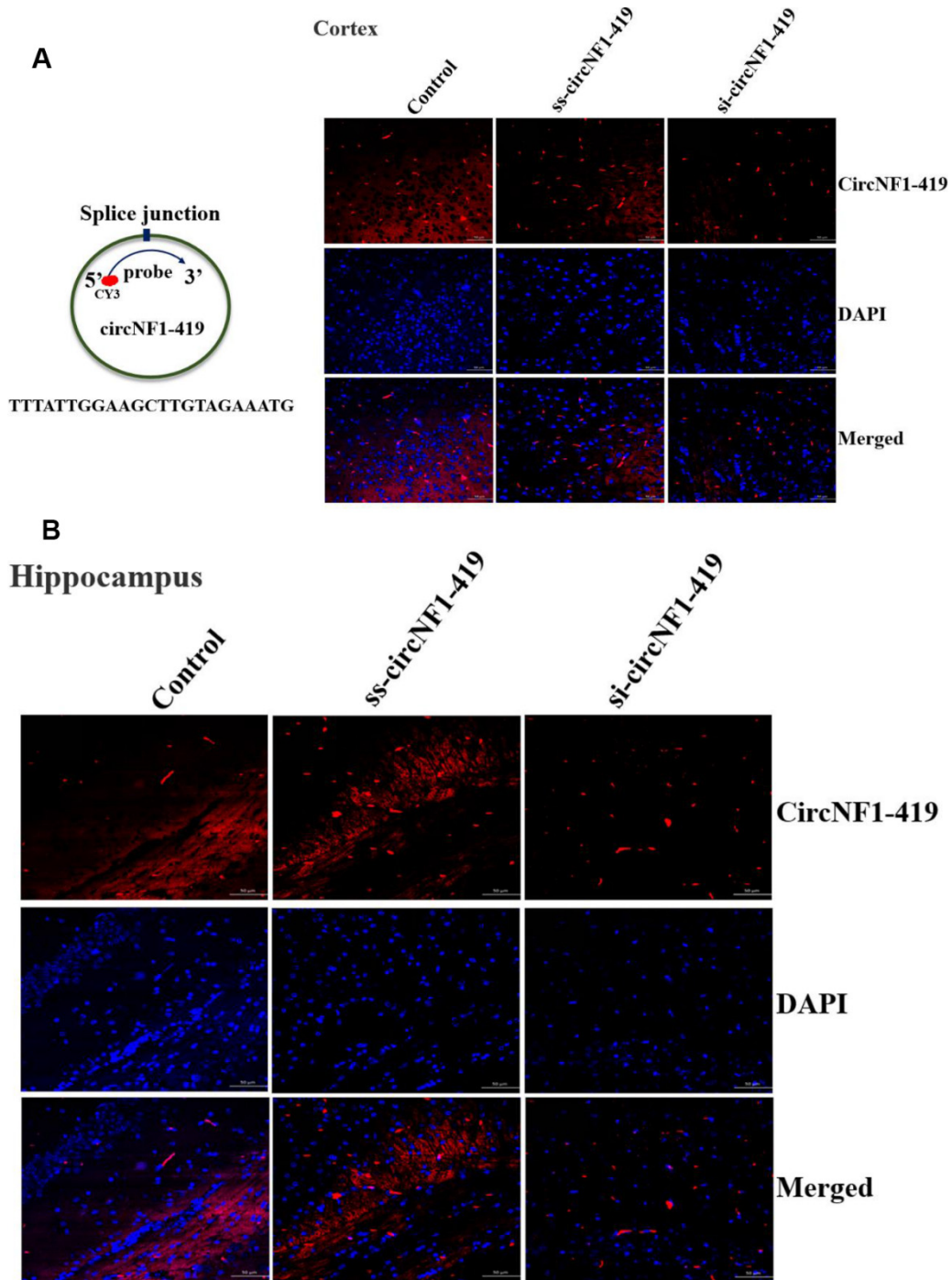
Supplementary Figure 4. The construction of over-expression circNF1-419-transfected rat astrocyte. (A) vector of over-expression circNF1-419 construction; **(B)** Lentivirus packaging and circNF1-419- transfected astrocytes.



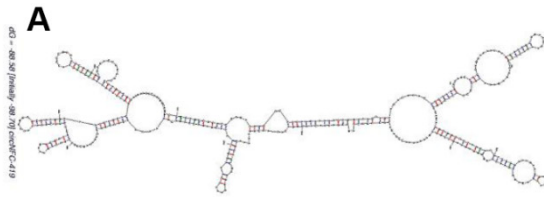
Supplementary Figure 5. AAV viral transduction system with RNA interference (*scircNF1-419*-AAV, **A, B**) and separately an over-expressing *circNF1-419* (*sscircNF1-419*-AAV, **C, D**).



Supplementary Figure 6. The AD marker proteins such as Tau, p-Tau, Aβ A4, APOE, and BACE1 were inhibited, and the senescence-associated biomarkers p21 and p35 were improved after treatment with *circNF1-419-OV-AAV* for 2 months, also some inflammatory factors, NF-κB and TNF-α were inhibited.



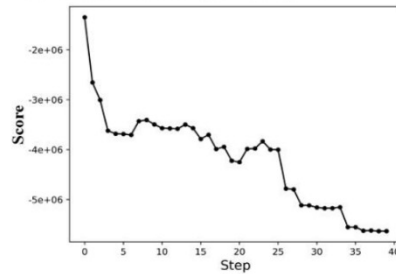
Supplementary Figure 7. Fluorescent *in situ* hybridization (FISH) was used to detect *circNF1-419-OV-AAV* in infected brain tissue, (A) cortex and (B) hippocampus.



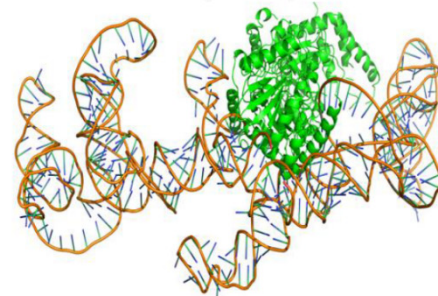
C1 circNF1-419 and dynamin-1 protein

A 108 C N1 B 196 GLN OE1 2.33 HS -1.00
 A 208 C N4 B 3 GLU OE2 2.80 HS -1.00
 Number of interacting residues Molecule1 78
 Number of interacting residues Molecule2 164
 Number of hydrophilic-hydrophobic interaction 282
 Number of hydrophilic-hydrophilic interaction 426
 Number of hydrophobic-hydrophobic interaction 0
 Buried area upon the complex formation (A) 6732.3
 Buried area upon the complex formation (%) 7.35
 Interface area (A) 3366.15
 Interface area MOL1 (%) 4.47
 Interface area MOL2 (%) 20.57
 POLAR Buried area upon the complex formation (A) 2766.5
 POLAR Buried area upon the complex formation (%) 41.09
 POLAR Interface area (A) 1383.25
 NO POLAR Buried area upon the complex formation (A²) 3965.7
 NO POLAR Buried area upon the complex formation (%) 58.91
 NO POLAR Interface area (A) 1982.85
 Residues at the interface_TOT (n) 152
 Residues at the interface_Mol1 (n) 58
 Residues at the interface_Mol2 (n) 94

C2 circNF1-419 and dynamin-1 protein



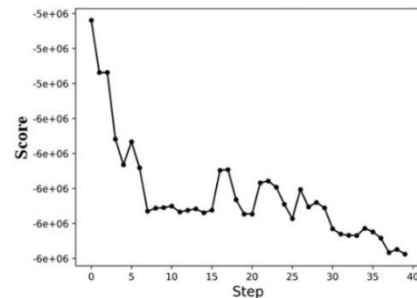
C3 circNF1-419 and dynamin-1 protein



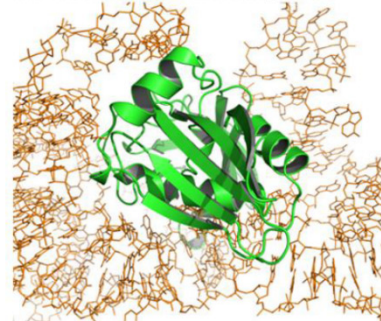
D1 circNF1-419 and AP2B1 protein

A 224 C N4 B 783 ASP O 2.64 HM -1.00
 A 248 G N2 B 707 TYR OH 2.34 HS -1.00
 B 892 LYS NZ A 368 U O2 1.74 SH -1.00
 A 388 U N3 B 811 ILE O 2.33 HM -1.00
 A 391 A N6 B 717 ALA O 2.41 HM -1.00
 B 745 LYS NZ A 392 A N1 2.69 SH -1.00
 B 817 SER OG A 396 A N1 3.24 SH -1.00
 B 707 TYR OH A 406 C O2 2.49 SH -1.00
 A 408 C N1 B 936 LYS O 2.12 HM -1.00
 Number of interacting residues Molecule 1 80
 Number of interacting residues Molecule 2 158
 Number of hydrophilic-hydrophobic interaction 264
 Number of hydrophilic-hydrophilic interaction 355
 Number of hydrophobic-hydrophobic interaction 0
 Buried area upon the complex formation (A) 5827.4
 Buried area upon the complex formation (%) 6.70
 Interface area (A) 2913.7
 Interface area MOL1 (%) 3.88
 Interface area MOL2 (%) 24.67
 POLAR Buried area upon the complex formation (A) 2637.9
 POLAR Buried area upon the complex formation (%) 45.27
 POLAR Interface area (A) 1318.95
 NO POLAR Buried area upon the complex formation (A²) 3189.6
 NO POLAR Buried area upon the complex formation (%) 54.73
 NO POLAR Interface area (A) 1594.8
 Residues at the interface_TOT (n) 141
 Residues at the interface_Mol1 (n) 56
 Residues at the interface_Mol2 (n) 85

D2 circNF1-419 and AP2B1 protein

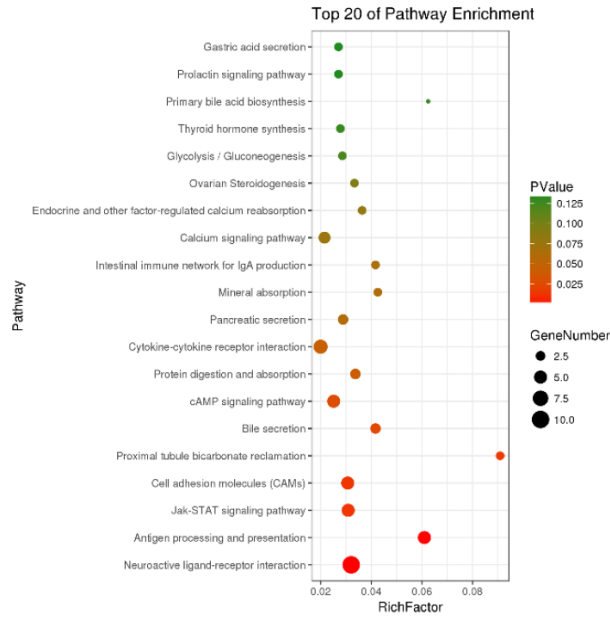


D3 circNF1-419 and AP2B1 protein

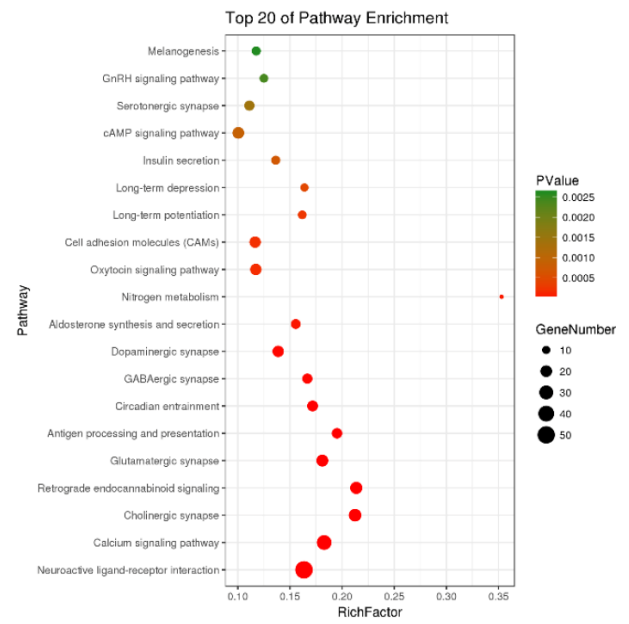


Supplementary Figure 8. The computer-aided molecular simulation demonstrated that the dynamin-1 and AP2B1 protein binds the circNF1-419.

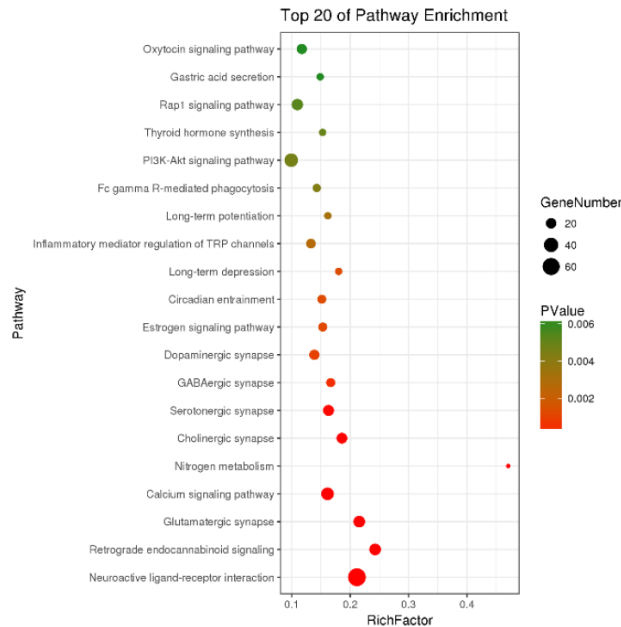
KM vs SAMP8



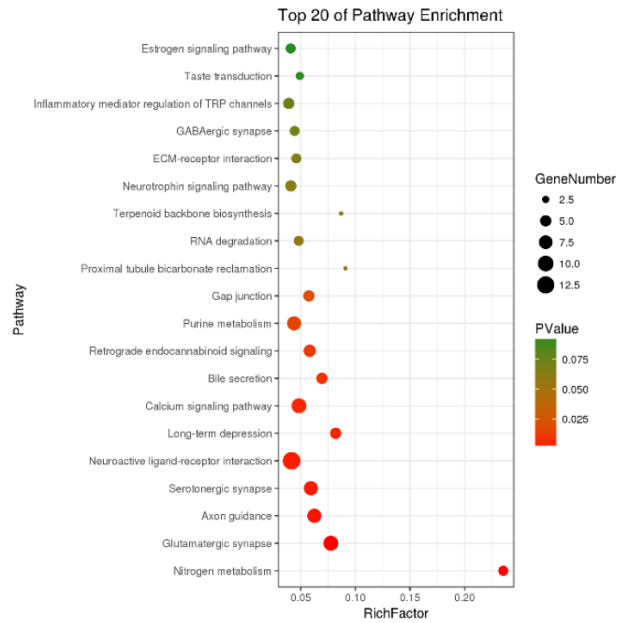
SAMP8 vs SAMP8-sicircNF1



SAMP8 vs SAMP8-sscircNF1



KM vs SAMP8-sicircNF1



Supplementary Figure 9. *CircNF1-419* improves the brain transcriptome of AD mice. The KEGG pathway analysis of different expressed mRNA of brain tissues were showed after injection of an AAV viral transduction system with RNA interference (*sicircNF1-419*-AAV) and separately an over-expressing *circNF1-419* (*sscircNF1-419*-AAV).