

Supplementary Materials

Transcriptome Sequencing Reveals Astrocytes as a Therapeutic Target in Heat-Stroke

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Table S1. Primers for qPCR

Gene name	Primer sequence (5' to 3')
GAPDH-F	ACTTTGGCATCGTGGAAGGG
GAPDH-R	TGCAGGGATGATGTTCTGGG
HSP70-F	GGACCAACCACCTCAAGCA
HSP70-R	TCATTCTCTGTGTACAGGCCG
CCR1-F	GCCATTGTCCATGCAGTGTT
CCR1-R	GTCTTCAGGCTCTCATCGGG
CCL3-F	ATGGACGGCAAATTCCACGA

CCL3-R	GGGTTCCCTTGCTGCCTCTAA
CCL4-F	CACCTCCCGGAAGATTCATCG
CCL4-R	CTGGGGTTCGGCACAGATTT
IL2RB-F	ACCAATAGCTCTGGGCAACAG
IL2RB-R	GGCATCAGTGTTTAGAGTCAGG
GDF5-F	CGGCTGAGTCCCATTAGCAT
GDF5-R	AGCCACAAGATTCCACGACC
CXCL2-F	GTCAATGCCTGACGACCCTA
CXCL2-R	GACGATCCTCTGAACCAAGGG
C6-F	AAGCAGATTCAGGGTGCCTC
C6-R	ATCCCACAGCTTTGAATCCAG
FGA-F	GTGGTCACTTCGGATGATGGT
FGA-R	CTTGTGAGTGAACCAAAGCGG
F9-F	GAGTTCCACTGGTTGACCGA

F9-R	CCTTCACGGTAACCTGCACA
C2-F	CTTGAGCGGAGGTACAGGTTT
C2-R	TTGTTGGAGGAACCGTGACAA
IL7-F	TGTAGTAGCAACCTCCAAGAACT
IL7-R	CCAGGAGGCATCCAGAACTT
IL6R-F	ATTCGAGCTTCGATACCGACC
IL6R-R	CTCTGCTAGCCAAGGAGTGC
Aqp4-F	TTCCACATCTCAGAGACACTGC
Aqp4-R	GCCATCAGTGGGGTTAGAGC
Slc1a3-F	GCCGGGATTGTTGAACACTTG
Slc1a3-R	CCTCAATCACGGAGTTCCCC
Cldn5-F	TTCGAAAGACCGATGTGGG
Cldn5-R	TCAACGACCCCTCTCTGTGA
Flt1-F	ATGTGCCAAACGGCTTTCAC

Flt1-R	TGGTGCATGGTCCTGTTGTT
Tnf-F	CATCCGTTCTCTACCCAGCC
Tnf-R	AATTCTGAGCCCGGAGTTGG
Mbp-F	GTGGGGGTAAGAGAAACGCA
Mbp-R	CGAACACTCCTGTGGAACGA
Tubb3-F	CCTTCCTCCACTGGTACACG
Tubb3-R	TGCAAGCAACTTCACTTGGG
Enpp6-F	GCCTTCGGACCTGCTATCTG
Enpp6-R	AGCCTCCAGGAAGCAATCTT
Nfasc-F	GACGCATTCAGGAGAGGACA
Nfasc-R	GCTAGACGCCTTGTGTCTGT
Cspg4-F	GCAAACGCAACAAGACAGGT
Cspg4-R	GTGTCACCAGCTAGGCCATT
Igf2-F	TTGGCCCTCCTGGAGACATA

Igf2-R

GTATCTGGGGAAGTCGTCCG

Rdh10-F

TTCAGAGGCTGCCGAATCAG

Rdh10-R

GTACATGAGACGAGGGGTGC

Table S3. Functional annotation clustering of astrocytic DEGs

Annotation Cluster	Enrichment Score	Category	Term	Count	Genes	PValue	Fold Enrichment	Bonferroni	Benjamini	FDR
1	2.78525006	UP_KEYWORDS	Monooxygenase	7	CYP2AC1, CYP2J16, CYP2D5, CYP2J10, CH25H, CYP11B2, CYP26A1	1.80E-05	12.72298951	0.00232116	0.00232116	0.020947609
		GOTERM_MF_DIRECT	GO:0005506-iron ion binding	8	CYP2AC1, CYP2J16, CYP2D5, CYP2J10, CH25H, CYP11B2, CYP26A1, AOX4	4.83E-05	8.242574257	0.00894116	0.00894116	0.059785057
		UP_KEYWORDS	Iron	8	CYP2AC1, CYP2J16, CYP2D5, CYP2J10, CH25H, CYP11B2, CYP26A1, AOX4	5.12E-04	5.671849427	0.063935733	0.032495857	0.593867297
		GOTERM_MF_DIRECT	GO:0016712-oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen	4	CYP2AC1, CYP2J16, CYP2D5, CYP2J10	5.53E-04	24.48529412	0.097827076	0.050172161	0.683147629
		UP_KEYWORDS	Oxidoreductase	10	CYP2AC1, FAR2, CYP2J16, CYP2D5, DOXL1, CYP2J10, CH25H, CYP11B2, CYP26A1, AOX4	7.81E-04	4.047220492	0.095819479	0.033018017	0.903946406
		GOTERM_BP_DIRECT	GO:0055114-oxidation-reduction process	11	CYP2AC1, FAR2, CYP2J16, CYP2D5, DOXL1, CYP2J10, CH25H, CYP11B2, CYP26A1, AOX4, LOC100361934	8.11E-04	3.613296617	0.293828426	0.067213942	1.136129314
		UP_KEYWORDS	Heme	6	CYP2AC1, CYP2J16, CYP2D5, CYP2J10, CYP11B2, CYP26A1	8.28E-04	8.160518053	0.101369165	0.026366902	0.958932859
		GOTERM_MF_DIRECT	GO:0008395-steroid hydroxylase activity	4	CYP2AC1, CYP2D5, CYP2J10, CH25H	8.31E-04	21.34615385	0.143235415	0.037910718	1.024079818
		GOTERM_MF_DIRECT	GO:0020037-heme binding	6	CYP2AC1, CYP2J16, CYP2D5, CYP2J10, CYP11B2, CYP26A1	0.001153357	7.522590361	0.193174731	0.0420212	1.419080783
		GOTERM_MF_DIRECT	GO:0008392-arachidonic acid epoxidase activity	3	CYP2AC1, CYP2D5, CYP2J10	0.011302997	18.36397059	0.879285773	0.260696714	13.13228378
		KEGG_PATHWAY	rn04726:Serotonergic synapse	4	CYP2J16, CYP2D5, CYP2J10, KCNJ3	0.019244869	6.782911944	0.776042633	0.312074611	18.53721882
UP_KEYWORDS	Metal-binding	17	S100A3, CYP2D5, DOXL1, CYP11B2, CYP26A1, WT1, MMP12, CYP2AC1, CYP2J16, DYT1, ZSCAN10, CYP2J10, RASGRP4, CH25H, PLA2G2C, AOX4,	0.058942363	1.597957578	0.999605095	0.452742455	50.66324709		
KEGG_PATHWAY	rn01100:Metabolic pathways	8	CYP2J16, CYP2J10, CHSY3, CYP11B2, CYP26A1, AOX4, PLA2G2C, ACSM5	0.390193956	1.30097615	1	0.985472333	99.45844083		
2	2.088613795	GOTERM_BP_DIRECT	GO:0030595-leukocyte chemotaxis	4	CCL3, CCR1, CXCL2, CCL4	4.15E-05	57.02439024	0.017651183	0.017651183	0.05847417
		GOTERM_BP_DIRECT	GO:0070098-chemokine-mediated signaling pathway	5	CCL12, CCL3, CCR1, CXCL2, CCL4	1.39E-04	18.75802311	0.057712152	0.029284878	0.195048898
		GOTERM_BP_DIRECT	GO:0030593-neutrophil chemotaxis	5	CCL12, EDN3, CCL3, CXCL2, CCL4	1.48E-04	18.43460892	0.06164315	0.020985007	0.208751554
		GOTERM_MF_DIRECT	GO:0008009-chemokine activity	4	CCL12, CCL3, CXCL2, CCL4	6.56E-04	23.125	0.114858994	0.039853536	0.809107759
		GOTERM_BP_DIRECT	GO:0007204-positive regulation of cytosolic calcium ion concentration	6	CCL3, PTGIR, CCR1, NPY2R, CXCL2, UTS2R	7.77E-04	8.22467167	0.283630802	0.080007629	1.089563477
		GOTERM_BP_DIRECT	GO:0006816-calcium ion transport	5	CCL12, CCL3, CCR1, TRPC7, RAMP1	8.67E-04	11.62181866	0.310797504	0.060151599	1.215076926
		UP_KEYWORDS	Chemotaxis	4	CCL12, CCL3, CXCL2, CCL4	0.001953926	15.99461538	0.222990755	0.049208617	2.248863483
		GOTERM_BP_DIRECT	GO:0006954-inflammatory response	7	CCL12, CCL3, PTGIR, CCR1, CRHBP, CXCL2, CCL4	0.002515449	5.040034491	0.66056987	0.143032521	3.486520618
		GOTERM_BP_DIRECT	GO:0050729-positive regulation of inflammatory response	4	CCL12, CCL3, FABP4, CCL4	0.003089187	13.57723577	0.734810962	0.152880954	4.265765857
		GOTERM_BP_DIRECT	GO:0071356-cellular response to tumor necrosis factor	5	CCL12, CCL3, CRHBP, FABP4, CCL4	0.003352616	8.03915276	0.763235303	0.147921395	4.621590775
		GOTERM_MF_DIRECT	GO:0048020-CCR chemokine receptor binding	3	CCL12, CCL3, CCL4	0.003607263	32.86184211	0.48939754	0.105980173	4.376959972
		GOTERM_BP_DIRECT	GO:0048247-lymphocyte chemotaxis	3	CCL12, CCL3, CCL4	0.004585146	29.16019956	0.860759305	0.178936742	6.270161484
		KEGG_PATHWAY	rn04062:Chemokine signaling pathway	5	CCL12, CCL3, CCR1, CXCL2, CCL4	0.008644208	9.939838143	0.487521998	0.487521998	8.752807592
		GOTERM_BP_DIRECT	GO:0051928-positive regulation of calcium ion transport	3	CCL3, CCR1, CCL4	0.008985264	20.69433517	0.979185393	0.296726288	11.94206231
		GOTERM_BP_DIRECT	GO:0002548-monocyte chemotaxis	3	CCL12, CCL3, CCL4	0.009555774	20.0476372	0.983741497	0.290547408	12.6536512
		GOTERM_BP_DIRECT	GO:0006874-cellular calcium ion homeostasis	4	CCL12, EDN3, CCL3, CCR1	0.010254123	8.818204677	0.987986545	0.288324283	13.51741933
		GOTERM_BP_DIRECT	GO:0071347-cellular response to interleukin-1	4	CCL12, CCL3, CXCL2, CCL4	0.010543263	8.728222997	0.989401819	0.277321563	13.87272103
		GOTERM_BP_DIRECT	GO:0070374-positive regulation of ERK1 and ERK2 cascade	5	CCL12, CCL3, CCR1, NPSR1, CCL4	0.010816111	5.748426436	0.990584405	0.267305075	14.20675702
		UP_KEYWORDS	Cytokine	4	CCL12, CCL3, CXCL2, CCL4	0.016967917	7.336979534	0.890040617	0.181838009	18.04675189
		KEGG_PATHWAY	rn04060:Cytokine-cytokine receptor interaction	5	CCL12, CCL3, IL2RB, CCR1, CCL4	0.016981556	4.867367367	0.73254648	0.355707949	16.53177246
		GOTERM_BP_DIRECT	GO:0071346-cellular response to interferon-gamma	3	CCL12, CCL3, CCL4	0.032353005	10.51679328	0.99999254	0.543345902	37.08548429
KEGG_PATHWAY	rn05132:Salmonella infection	3	CCL3, CXCL2, CCL4	0.05608021	7.600130251	0.988250969	0.523202824	45.60607196		
GOTERM_CC_DIRECT	GO:0005615-extracellular space	11	CCL12, EDN3, CCL3, LOC689081, SCUBE2, C6, CRHBP, CXCL2, DCN, CCL4, RAMP1	0.05649448	1.911141131	0.991507325	0.907844287	46.27320078		
GOTERM_BP_DIRECT	GO:0007267-cell-cell signaling	3	CCL12, CCL3, CCR1	0.058821666	7.547345768	1	0.745586769	57.43667664		
UP_KEYWORDS	Inflammatory response	3	CCL3, CXCL2, CCL4	0.059845214	7.497475962	0.999651087	0.433693879	51.21091535		
GOTERM_BP_DIRECT	GO:0006887-exocytosis	3	CCL12, CCL3, CCR1	0.062522391	7.290049889	1	0.749642053	59.73504921		
UP_KEYWORDS	Secreted	10	CCL12, EDN3, CCL3, C6, CRHBP, CXCL2, PLA2G2C, DCN, CCL4, MMP12	0.074472141	1.913231505	0.999953842	0.444152593	59.34373128		
GOTERM_BP_DIRECT	GO:0006955-immune response	4	C6, CCR1, CXCL2, CCL4	0.126111411	3.203617429	1	0.910148109	85.03378729		
GOTERM_BP_DIRECT	GO:0043547-positive regulation of GTPase activity	4	CCL12, CCL3, RASGRP4, CCL4	0.279077035	2.149160436	1	0.995479711	99.00540994		
GOTERM_BP_DIRECT	GO:0007186-G-protein coupled receptor signaling pathway	11	CCL12, CCL3, OLR1595, CCR1, NPY2R, CXCL2, VOM1R66, GNRHR, OLR1588, CCL4, RAMP1	0.467799055	1.156468091	1	0.999955573	99.98618386		
3	1.50449054	UP_KEYWORDS	Transmembrane helix	43	MILL1, CYP2D5, SYNDIG1, RGD1304770, NPY2R, CCR1, GNRHR, LY9, KCNJ3, SLC5A3, CLEC10A, CNTNAP5B, FAR2, PTGIR, CYP2J16, CYP2J10, CH25H, OLR1595, NPSR1, MUC15, RAMP1, IL2RB, TMCO5A, CLCA5, TRPC7, TMEM200A, SLC7A10, LOC100361934, SLC6A16, CACNG1, GJB1, PKD2L2, SYNGR4, CYP2AC1, CLIC5, VOM1R66, SCN11A, PLA2G2C, UTS2R, EQTN, OLR1588, SMPD5, TMCO3	0.01078468	1.39066738	0.75310189	0.1604149	11.8474471
		UP_KEYWORDS	Transmembrane	43	MILL1, CYP2D5, SYNDIG1, RGD1304770, NPY2R, CCR1, GNRHR, LY9, KCNJ3, SLC5A3, CLEC10A, CNTNAP5B, FAR2, PTGIR, CYP2J16, CYP2J10, CH25H, OLR1595, NPSR1, MUC15, RAMP1, IL2RB, TMCO5A, CLCA5, TRPC7, TMEM200A, SLC7A10, LOC100361934, SLC6A16, CACNG1, GJB1, PKD2L2, SYNGR4, CYP2AC1, CLIC5, VOM1R66, SCN11A, PLA2G2C, UTS2R, EQTN, OLR1588, SMPD5, TMCO3	0.01162878	1.38484307	0.7788477	0.15435528	12.7182778
		UP_KEYWORDS	Membrane	45	MILL1, CYP2D5, SYNDIG1, RGD1304770, CYP11B2, NPY2R, CCR1, GNRHR, LY9, KCNJ3, SLC5A3, CLEC10A, CNTNAP5B, FAR2, PTGIR, CYP2J16, CYP2J10, RASGRP4, CH25H, OLR1595, NPSR1, MUC15, RAMP1, IL2RB, TMCO5A, CLCA5, TRPC7, TMEM200A, SLC7A10, LOC100361934, SLC6A16, CACNG1, GJB1, PKD2L2, SYNGR4, CYP2AC1, CLIC5, VOM1R66, SCN11A, PLA2G2C, UTS2R, EQTN, OLR1588, SMPD5,	0.0629416	1.2361873	0.99977202	0.42826702	53.0472463
		GOTERM_CC_DIRECT	GO:0016021-integral component of membrane	31	MILL1, CYP2D5, RGD1304770, CCR1, GNRHR, LY9, CLEC10A, CNTNAP5B, FAR2, CYP2J16, CYP2J10, CH25H, OLR1595, MUC15, RAMP1, IL2RB, TRPC7, TMCO5A, TMEM200A, SLC7A10, LOC100361934, GJB1, PKD2L2, SYNGR4, CYP2AC1, VOM1R66, PLA2G2C, EQTN,	0.12155102	1.24109635	0.99997575	0.9710542	74.9553451
4	1.16521401	KEGG_PATHWAY	rn00591:Linoleic acid metabolism	3	CYP2J16, CYP2J10, PLA2G2C	0.01524428	15.3856295	0.69359533	0.44646168	14.9622308
		KEGG_PATHWAY	rn00590:Arachidonic acid metabolism	3	CYP2J16, CYP2J10, PLA2G2C	0.05369953	7.78778779	0.98573613	0.57258726	44.1410979
		KEGG_PATHWAY	rn01100:Metabolic pathways	8	CYP2J16, CYP2J10, CHSY3, CYP11B2, CYP26A1, AOX4, PLA2G2C, ACSM5	0.39019396	1.30097615	1	0.98547233	99.4584408
5	1.04968679	GOTERM_BP_DIRECT	GO:0034765-regulation of ion transmembrane transport	4	CLIC5, SCN11A, CACNG1, KCNJ3	0.01113567	8.55365854	0.9918031	0.25936695	14.5964486
		UP_KEYWORDS	Voltage-gated channel	4	CLIC5, SCN11A, CACNG1, KCNJ3	0.02632655	6.19946333	0.96798752	0.24933999	26.6748256
		UP_KEYWORDS	Ion channel	4	CLIC5, SCN11A, CACNG1, KCNJ3	0.18143537	2.70179314	1	0.76183407	90.2534295
		UP_KEYWORDS	Transport	10	LOC690507, RGD1304770, CLIC5, SLC7A10, FABP4, SCN11A, CACNG1, KCNJ3, SLC5A3, RAMP1	0.22451635	1.48208074	1	0.79027001	94.802578
		UP_KEYWORDS	Ion transport	4	CLIC5, SCN11A, CACNG1, KCNJ3	0.47259147	1.54986583	1	0.97651601	99.9412893
6	0.69996768	GOTERM_BP_DIRECT	GO:0007204-positive regulation of cytosolic calcium ion concentration	6	CCL3, PTGIR, CCR1, NPY2R, CXCL2, UTS2R	7.77E-04	8.22467167	0.2836308	0.08000763	1.08956348
		GOTERM_BP_DIRECT	GO:0007218-neuropeptide signaling pathway	3	NPY2R, NPSR1, UTS2R	0.07407738	6.61365351	1	0.79242803	66.190786
		KEGG_PATHWAY	rn04080:Neuroactive ligand-receptor interaction	4	PTGIR, NPY2R, GNRHR, UTS2R	0.15144746	2.88041466	0.99999678	0.79415854	82.3185207
		GOTERM_CC_DIRECT	GO:0005886-plasma membrane	17	MILL1, CCR1, NPY2R, CLCA5, GNRHR, LY9, GJB1, PTGIR, CD163L1, RASGRP4, OLR1595, SCN11A, C2CD4A, EQTN, UTS2R, OLR1588, RAMP1	0.66301332	0.9808008	1	0.99998561	99.9991017
		UP_KEYWORDS	Receptor	12	PTGIR, IL2RB, OLR1595, CCR1, NPY2R, TRPC7, VOM1R66, GNRHR, NPSR1, UTS2R, OLR1588, RAMP1	0.72381115	0.94717422	1	0.99900807	99.9999683
		UP_KEYWORDS	G-protein coupled receptor	8	PTGIR, OLR1595, CCR1, NPY2R, GNRHR, NPSR1, UTS2R, OLR1588	0.78790489	0.89958467	1	0.99954443	99.9999985
		UP_KEYWORDS	Transducer	8	PTGIR, OLR1595, CCR1, NPY2R, GNRHR, NPSR1, UTS2R, OLR1588	0.81446598	0.87164117	1	0.99957389	99.9999997
UP_KEYWORDS	Cell membrane	11	PTGIR, SYNDIG1, RASGRP4, OLR1595, SCN11A, GNRHR, NPSR1, UTS2R, OLR1588, SLC5A3, GJB1	0.93598591	0.74024221	1	0.99998922	100		
7	0.42445962	GOTERM_CC_DIRECT	GO:0022625-cytosolic large ribosomal subunit	3	RPL32, LOC680700, LOC306079	0.17024119	3.98794143	0.99999977	0.97819714	86.3808438
		GOTERM_BP_DIRECT	GO:0006412-translation	3	RPL32, LOC680700, LOC306079	0.52393102	1.69715447	1	0.99998848	99.9971269
		GOTERM_MF_DIRECT	GO:0003735-structural constituent of ribosome	3	RPL32, LOC680700, LOC306079	0.59742361	1.48307601	1	0.99999996	99.9987233
8	0.09034559	UP_KEYWORDS	Zinc	6	S100A3, DYT1, ZSCAN10, RASGRP4, MMP12, WT1	0.74582191	0.96353105	1	0.99914786	99.9999879
		UP_KEYWORDS	Zinc-finger	4	DYT1, ZSCAN10, RASGRP4, WT1	0.79724718	0.94196793	1	0.99951153	99.9999991
		GOTERM_MF_DIRECT	GO:0046872-metal ion binding	5	ZSCAN10, RASGRP4, AOX4, ACSM5, WT1	0.90102139	0.75571895	1	1	100
9	0.03277957	GOTERM_BP_DIRECT	GO:0006355-regulation of transcription, DNA-templated	4	ZSCAN10, RHOX5, PERM1, WT1	0.87241314	0.81154256	1	1	100
		UP_KEYWORDS	Transcription regulation	3	ZSCAN10, RHOX5, WT1	0.92063013	0.72352	1	0.99998725	100
		UP_KEYWORDS	Transcription	3	ZSCAN10, RHOX5, WT1	0.93533515	0.68314132	1	0.99999231	100
		UP_KEYWORDS	Nucleus	7	ZSCAN10, RHOX5, ETV2, FABP4, LOC100360260, WT1, PSMB11	0.9842538	0.58023584	1	0.99999977	100