Supplementary Table 3. Altered molecular composition of astrocytes in ALS. Abbreviations: 2D-HPLC, two-dimensional high performance liquid chromatography; ACM, astrocyte conditioned medium; ALS, amyotrophic lateral sclerosis; Cx43, connexin 43; EAAT2, excitatory amino acid transporter 2; ELISA, enzyme-linked immunosorbent assay; ES, embryonic stem; ESC, embryonic stem cell; ER, endoplasmic reticulum; fALS, familial ALS; GDNF, glial-derived neurotrophic factor; IFN, interferon; IFN- αR1, interferon α receptor 1; IHC, immunohistochemistry; IPSCs, induced pluripotent stem cells; IF, immunofluorescence; iNOS, inducible nitric oxide synthase; ISG, IFN-stimulated gene; Kir 4.1, inward-rectifying potassium channel 4.1; LC-HRMS, liquid chromatography coupled with high resolution mass spectrometry; LMN, lower motor neuron; LDH, lactate dehydrogenase; mPTP-I, mitochodria permeability transition pore inhibitor; NMDA, N-methyl-D-aspartate; n.a, not applicable; n.s., not specified; NOS, nitric oxide synthase; NOX2, NADPH oxidase 2; PDC, parkinsonism dementia complex; PDG2, Prostaglandin D2; RCR, respiratory control ratio; ROS, reactive oxygen species; RT RT-qPCR, Real-Time quantitative reverse transcription polymerase chain reaction; SOD1, superoxide dismutase 1; sALS, sporadic ALS; SOCE, ER store-operated calcium entry; TGF-β, transforming growth factor β; TNF, neurotrophic factor; TNFR1, TNF receptor 1; WB, western blotting.

	ALS model	disease stage	region	method of investigation	findings	references
rodent models of ALS	ALS-PDC	symptomatic	motor cortex spinal cord	WB and IHC	GLT-1 ↓	(Wilson et al., 2003)
	$SOD1^{G85R}$	end-stage	spinal cord	WB		(Bruijn et al., 1997)
	$SOD1^{G93A}$	presymptomatic, symptomatic and end-stage	spinal cord ventral horn	IHC		(Howland et al., 2002)
	TDP-43	disease onset and symptomatic	spinal cord	IHC		(Tong et al., 2013)
	$SOD1^{G93A}$	presymptomatic, symptomatic and end-stage	spinal cord ventral horn	IF and WB	Kir 4.1 ↓	(Kaiser et al., 2006)
		symptomatic	brainstem and cortex	IF, WB and whole-cell patch-clamp recordings in cultured cortical astrocytes		(Bataveljic et al., 2012)
	$SOD1^{G93A}$	presymptomatic, symptomatic and end-stage	spinal cord ventral horn	WB	AQP4 ↑	(Kaiser et al., 2006)
		symptomatic	brainstem and cortex	WB and IHC		(Bataveljic et al., 2012)
	$SOD1^{G93A}$	presymptomatic	lumbar spinal cord	transcriptomics, lactate level in spinal cord and astrocyte-conditioned medium and qPCR of LMN	lactate release ↓	(Ferraiuolo et al., 2011)
		neonatal (P2-3)	spinal cord	LC-HRMS metabolomics of astrocyte mono-cultures and astrocyte-LMN (WT) co-cultures upon glutamate treatment		(Madji Hounoum et al., 2017)
	$SOD1^{G93A}$	end-stage	motor cortex and spinal cord	IF,WB, Fura-2 indicated Ca^{2+} imaging combined with GAP26 treatment	Cx43 ↑	(Almad et al., 2016)
	$SOD1^{G93A}$	neonatal (P1-2)	brain and spinal cord	IHC astrocyte-MN co-culture, RCR indicating oxygen consumption measured before and after NOS inhibitor	NOS ↑	(Cassina et al., 2008)
	$SOD1^{G93A}$	presymptomatic and symptomatic	lumbar spinal cord	2D-HPLC	D-Serine ↑	(Sasabe et al., 2012)
		presymptomatic, symptomatic and end-stage	lumbar spinal cord	IF, D-Serine level measured by chemiluminescence, viability assay of LMN/UMN culture upon treatment of D-Serine or antagonist to the glycine-binding site of NMDARs		(Sasabe et al., 2007)

	SOD1^{G93A}	disease onset and presymptomatic	spinal cord	WB, Fura-4 indicated Ca^{2+} imaging and luciferase assay	ER Ca^{2+} release↑ ER Ca^{2+} storage ↑ ATP secretion ↑ Ca^{2+} influx dysregulation	(Kawamata et al., 2014)
		neonatal (P2)	cortex			
	SOD1^{G93A}	symptomatic	motor cortex	*in vivo* awakening two-photo Ca^{2+} imaging and Ca^{2+} imagining with mPTP-I treatment to acute cortical slices	Ca^{2+} activity ↑	(Agarwal et al., 2017)
	SOD1^{G93A}	symptomatic and end-stage	spinal cord	IF and WB	TGF-β1 ↑	(Endo et al., 2015)
	SOD1^{G85R} and SOD1^{G37R}	end-stage				
	SOD1^{G93A}	neonatal (P1-3)	n.s.	IF of human ESC-derived MNs co-cultured with astrocyte and viability assay of MNs with PDG2 receptor antagonist MK0524 treatment	PDG2 ↑	(Di Giorgio et al., 2008)
	SOD1^{G93A}	disease onset and symptomatic	spinal cord	WB, ELISA and IF	IFN- γ ↑	(Aebischer et al., 2011)
		neonatal (P1-2)		WB, ELISA, viability assay of LMN (wt)-astrocyte co-culture and IFN-γ antagonist treatment		
	SOD1^{G93A}	presymptomatic	lumbar spinal cord	RNA-seq, qPCR, ESC-derived (E15) MNs treated with the potent ER stress inducer	IFN-α ↑ ISG ↑	(Wang et al., 2011)
	SOD1^{G93A}	disease onset and symptomatic	spinal cord	RT RT-qRCR of GDNF, TNF and TNFR1, reduction and increase of TNFR1 expression, IHC	GDNF ↑ TNF ↑ TNFR1 ↑	(Brambilla et al., 2016)
human-derived astrocytes	fALS (*SOD1*^{D90A} mutation)	n.a.	IPSC-derived astrocytes	qPCR and WB	Kir 4.1 ↓	(Kelley et al., 2018)
	fALS (*SOD1 or C9orf72*) and sALS	n.a.	IPSC-derived astrocytes	IF, WB, Fura-2 indicated Ca^{2+} imaging rescued with Cx43 blocker GAP26 treatment	Cx43 ↑	(Almad et al., 2016)
	SOD1^{G37R}	fetal	cerebral cortex obtained from fetal human brain culture	WB, IHC, NOX2 inhibitor or antioxidant treatment	ROS↑ NOX2↑ iNOS ↑	(Marchetto et al., 2008)
ALS patients	fALS and sALS	post-mortem (mean: 61 yrs)	motor cortex and lumbar spinal cord	WB	EAAT2 ↓	(Rothstein et al., 1995)
	fALS (*SOD1*^{A4V} mutation) and sALS	post-mortem	lumbar spinal cord	IHC	D-Serine ↑	(Sasabe et al., 2007)
	fALS and sALS	post-mortem	lumbar spinal cord	WB and IF	IFN-α ↑ ISG ↑	(Wang et al., 2011)
	sALS	post-mortem	spinal cord	RT-qPCR	GDNF ↑ TNF ↑ TNFR1 ↑	(Brambilla et al., 2016)

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