



References on the Amyotrophic Lateral Sclerosis (ALS) Research Using ALZET® Osmotic Pumps

Q10963: S. Minamiyama, *et al.* Efficacy of oligodendrocyte precursor cells as delivery vehicles for single-chain variable fragment to misfolded SOD1 in ALS rat model. *Molecular Therapy: Methods and Clinical Development* 2023;28(312-329

Agents: D3-1 antibody, mouse **Vehicle:** PBS; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Strain:** SOD1H46R; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Dose (1 mg/mL); Controls received mp w/ vehicle; animal info: 1- to 2-day-old Sprague-Dawley rats; behavioral testing (Hindfoot reflex test; Inclined plate test; Grip test); functionality of mp verified by D3-1 concentrations with ELISA; neurodegenerative: Amyotrophic lateral sclerosis; good methods p. 14

Q8270: M. Luisetto*, *et al.* Role of plants, environmental toxins and physical neurotoxicological factors in Amyotrophic lateral sclerosis, Alzheimer Disease and other Neurodegenerative Diseases. *Journal of Neuroscience and Neurological Disorders* 2019;3(1):001-086

Agents: Rotenone **Vehicle:** Not stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not stated; **Duration:** 6 days;

ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; Rotenone aka Rot; neurodegenerative (Alzheimer's Disease, Parkinson's Disease, Lou Gehrig's Disease);

Q9161: E. Blacher, *et al.* Potential roles of gut microbiome and metabolites in modulating ALS in mice. *Nature* 2019;572(7770):474-480

Agents: Nicotinamide; Phenol Sulfate **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 months;

ALZET Comments: Dose (NAM- 30.8 mg/kg/week or 49.28 mg/kg/week); Controls received mp w/ vehicle; animal info (40-180 days old); pumps replaced every 4 weeks; Nicotinamide aka NAM ; neurodegenerative (Amyotrophic Lateral Sclerosis);

Q7540: S. Watanabe, *et al.* Intracerebroventricular administration of Cystatin C ameliorates disease in SOD1-linked amyotrophic lateral sclerosis mice. *J Neurochem* 2018;145(1):80-89

Agents: Cystatin C, Recombinant human **Vehicle:** PBS; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: Dose (66 ng/day); Controls received mp w/ vehicle; animal info (100-day-old, transgenic SOD1G93A, male \geq 30g and female \geq 20g); stability verified by (influenza hemagglutinin (HA)-tagged CysC administration for 1 week); CysC is an endogenous protease inhibitor; enzyme inhibitor (cathepsin); ALZET brain infusion kit used; neurodegenerative (ALS); "After 1 week of continuous HA-tagged CysC administration using an osmotic pump, the CysC was successfully delivered to the lumbar spinal cord and was predominantly distributed in the ventral horn neurons (Fig. 1b and c), whereas CysC was rarely found in neurons of the dorsal horn. These data indicate that intracerebroventricular administration was sufficient to deliver CysC to lower motor neurons in the lumbar spinal cord." pg.82; implanted pump remained on the back of mice until end-stage; "the disease end-stage was determined as the time when animals in a lateral position were unable to right themselves within 20s" p.81; Therapeutic indication (Bunina body formation and regulation of AMPK/PGC-1 α pathway);

Q7312: N. Tsuburaya, *et al.* A small-molecule inhibitor of SOD1-Derlin-1 interaction ameliorates pathology in an ALS mouse model. *Nat Commun* 2018;9(1):2668

Agents: SOD1-Derlin-1 inhibitor #56-40, SOD1-Derlin-1 inhibitor #56-59 **Vehicle:** DMSO; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 2006; **Duration:** 36 weeks;

ALZET Comments: Dose (1 mM #56-40 or 3 mM #56-59); Controls received mp w/ vehicle; animal info (22 weeks, male, C57BL/6); behavioral testing (rotarod performance); behavioral testing (rotarod performance); pumps replaced every 6 weeks until mouse showed paralysis onset; long-term study; stability verified by (in-vitro immunoprecipitation assay); 3-Amino-N-(4-pyridyl)-6-(3-pyridyl)thieno[2,3-b]pyridine-2-carboxamide aka #56-40; N-Allyl-3-amino-N-phenyl-6-(pyridin-3-yl)thieno[2,3-b]pyridine-2-carboxamide aka #56-59; enzyme inhibitor (SOD1-Derlin-1 interaction); ALZET brain infusion kit 3 used; neurodegenerative (Amyotrophic lateral sclerosis);



Q7208: J. J. Riehm, *et al.* Poloxamer 188 decreases membrane toxicity of mutant SOD1 and ameliorates pathology observed in SOD1 mouse model for ALS. *Neurobiol Dis* 2018;115(115-126

Agents: Poloxamer 188 **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 2006, 1004; **Duration:** 42 days;

ALZET Comments: Dose (1.5 pM/h); Controls received mp w/ vehicle; animal info (40-55 day old male B6SJL-Tg(SOD1*G93A)1Gur/J mice); neurodegenerative (amyotrophic lateral sclerosis);

Q7210: M. Maier, *et al.* A human-derived antibody targets misfolded SOD1 and ameliorates motor symptoms in mouse models of amyotrophic lateral sclerosis. *Sci Transl Med* 2018;10(470):

Agents: miSOD1, alpha- **Vehicle:** PBS; **Route:** CSF/CNS (left ventricle); **Species:** Mice; **Pump:** 1004; **Duration:** 20, 30, 40, 55, 70, 80 days;

ALZET Comments: Dose (0.1 mg/kg/day); Controls received mp w/ vehicle; animal info (Mice, 60 days of age); pumps replaced every 28 days; ALZET brain infusion kit used; neurodegenerative (amyotrophic lateral sclerosis); Therapeutic indication (amyotrophic lateral sclerosis);

Q7189: A. U. Joshi, *et al.* Inhibition of Drp1/Fis1 interaction slows progression of amyotrophic lateral sclerosis. *EMBO Molecular Medicine* 2018;10(3):

Agents: P110-TAT (47-57) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 28 day pump; **Duration:** 60 days;

ALZET Comments: Dose (3 mg/kg/day); animal info (4–6 weeks old AdultB6SJL Tg (SOD1G93A) 1 Gur/J male mice); behavioral testing (Activity chamber); pumps replaced after 30 days; long-term study; P110 is a selective peptide inhibitor of Drp1/Fis1; neurodegenerative (amyotrophic lateral sclerosis); neurodegenerative (amyotrophic lateral sclerosis); stress/adverse reaction: (see pg. 14);

Q7904: U. Gomez-Pinedo, *et al.* Histological changes in the rat brain and spinal cord following prolonged intracerebroventricular infusion of cerebrospinal fluid from amyotrophic lateral sclerosis patients are similar to those caused by the disease. *Neurologia* 2018;33(4):211-223

Agents: Cerebrospinal fluid, cytotoxic ALS **Vehicle:** Saline, physiological; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2006; **Duration:** 20, 43 days;

ALZET Comments: Dose (0.15 l/h); Controls received sham surgery w/ inert tube; animal info (1-5 months, male, Wistar); behavioral testing (inclined plane test); Cytotoxic CSF obtained from ALS patients; ALZET brain infusion kit used; Brain coordinates (-0.5 mm anteroposterior, -1.4 mm lateral and -3.3 mm dorsoventral); neurodegenerative (amyotrophic lateral sclerosis); no stress ("none of them showed signs of infection (abscess, edema or discharge in the implant)" see pg.215); main article written in Spanish. Alzet infusion cannula used but model not stated.;

Q5704: W. Wang, *et al.* Motor-Coordination and Cognitive Dysfunction Caused by Mutant TDP-43 Could Be Reversed by Inhibiting Its Mitochondrial Localization. *Mol Ther* 2017;25(1):127-139

Agents: Peptide, PM1 **Vehicle:** PBS; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2006; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ control peptide; animal info (C57BL/6-Tg); neurodegenerative (amyotrophic lateral sclerosis); behavioral testing (Rotarod; grip strength; open field; y maze; t maze; object recognition, fear conditioning); Pumps primed in 37C PBS overnight; Dose (1.5 or 0.5 mg/kg/day);

Q5884: U. N. Ramirez-Jarquín, *et al.* Chronic infusion of SOD1(G93A) astrocyte-secreted factors induces spinal motoneuron degeneration and neuromuscular dysfunction in healthy rats. *J Cell Physiol* 2017;232(10):2610-2615

Agents: ACM-hG93A **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2004; **Duration:** 16 days;

ALZET Comments: animal info (male, Wistar, 270-300g, adult); neurodegenerative (amyotrophic lateral sclerosis); post op. care (IM penicillin); behavioral testing (rotarod test; paw grip endurance); Pumps primed in 37C saline for 28 hours; used wound clips;



Q5882: L. Pasetto, *et al.* Targeting Extracellular Cyclophilin A Reduces Neuroinflammation and Extends Survival in a Mouse Model of Amyotrophic Lateral Sclerosis. *J Neurosci* 2017;37(6):1413-1427

Agents: MM218 Inhibitor **Vehicle:** PBS; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2004; **Duration:** 56 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (SOD1 mice; 98 days old); pumps replaced after 28 days; ALZET brain infusion kit 3 used; post op. care (0.15 mg/kg buprenorphine as analgesic immediately before and 12 h after the surgery); behavioral testing (Rotarod test); "MM218 does not pass the blood-brain barrier (BBB), so the drug was administered intracerebroventricularly by continuous infusion using minipumps" p. 1421; MM218 is a specific inhibitor of extracellular PPIA ; Therapeutic indication (Amyotrophic Lateral Sclerosis); Dose (1 or 10 μ M);

Q5207: Y. Solomonov, *et al.* Reduction of cytosolic phospholipase A2alpha upregulation delays the onset of symptoms in SOD1G93A mouse model of amyotrophic lateral sclerosis. *J Neuroinflammation* 2016;13(1):134

Agents: Oligonucleotide, antisense anti-Cytosolic phospholipase A2 alpha **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 4 weeks; 6 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, B6.Cg-Tg(SOD1G93A)1Gur/J hemizygous transgenic, 10 weeks old, 25 g); ALZET brain infusion kit 3 used; antisense (oligonucleotide anti-Cytosolic phospholipase A2 alpha); neurodegenerative (amyotrophic lateral sclerosis); behavioral testing (rotarod test; ladder testing); pumps primed overnight in 37C saline; Dose (10 μ g/day); Brain coordinates (right lateral cerebral ventricle (-1.0 mm mediolateral and -0.5 mm anteroposterior from Bregma));

Q5186: U. N. Ramirez-Jarquín, *et al.* Neuropathological characterization of spinal motor neuron degeneration processes induced by acute and chronic excitotoxic stimulus in vivo. *Neuroscience* 2016;331(78-90)

Agents: AMPA **Vehicle:** Phosphate buffer; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2004; **Duration:** 5 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 270-300g); neurodegenerative (amyotrophic lateral sclerosis); post op. care (IM penicillin); behavioral testing (rotarod, paw grip endurance; stride analysis); AMPA aka a-amino-3- hydroxy-5- methyl-4- isoxazoleacetic acid; pumps primed for 48 hours in 37C saline; used surgical clips;

Q4859: D. Matusica, *et al.* Inhibition of motor neuron death in vitro and in vivo by a p75 neurotrophin receptor intracellular domain fragment. *Journal of Cell Science* 2016;129(517-530)

Agents: Peptide, c29 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (SOD G93A, 9 weeks old); pumps replaced every month until death; neurodegenerative (amyotrophic lateral sclerosis); neurodegenerative (amyotrophic lateral sclerosis); long-term study; peptides; Dose (5 mg/kg/day);

Q4830: M. Gravel, *et al.* IL-10 Controls Early Microglial Phenotypes and Disease Onset in ALS Caused by Misfolded Superoxide Dismutase 1. *The Journal of Neuroscience* 2016;36(3):1031-1048

Agents: Antibody, Interleukin-10 receptor **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2006; **Duration:** 42 days;

ALZET Comments: Controls received mp w/ saline; animal info (SOD1 G93A, 60 days old); neurodegenerative (amyotrophic lateral sclerosis); behavioral testing (hindlimb reflex); pumps primed overnight in 37C saline; used dental cement; Dose (3.6 μ g/day);

Q4951: F. G. Vieira, *et al.* Guanabenz Treatment Accelerates Disease in a Mutant SOD1 Mouse Model of ALS. *PLoS One* 2015;10(8):e0135570

Agents: Guanabenz acetate **Vehicle:** Ethanol; water; propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 2004;

ALZET Comments: Controls received mp w/ vehicle; animal info (SOD1-G93A); pumps replaced every 28 days; dose-response (pg 4); neurodegenerative (amyotrophic lateral sclerosis); post op. care (antibiotic ointment; buprenorphine 0.1 mg/kg); used lot#10284-12; Dose (0.45, 1.5, or 4.5 mg/kg/day);



Q4930: A. Ruban, *et al.* Combined Treatment of an Amyotrophic Lateral Sclerosis Rat Model with Recombinant GOT1 and Oxaloacetic Acid: A Novel Neuroprotective Treatment. *Neurodegener Dis* 2015;15(4):233-42

Agents: Kanic acid; cyclothiazide **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 14 days; 36 days;

ALZET Comments: animal info (male, Wistar, 8-9 weeks old, 240-250g); pumps replaced every week; neurodegenerative (ALS amyotrophic lateral sclerosis); behavioral testing (rotarod testing); pumps primed in 37C sterile saline overnight; catheter placement verified by visual examination;

Q5255: P. Rabinovich-Toidman, *et al.* Mutant SOD1 Increases APP Expression and Phosphorylation in Cellular and Animal Models of ALS. *PLoS One* 2015;10(11):e0143420

Agents: Antibody, monoclonal, BBS; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice; **Pump:** 2006; **Duration:** 42 days;

ALZET Comments: Controls received mp w/ isotype-matched non relevant MAb; animal info (male Hemizygous B6SJLTgN (SOD1G93A) 1 Gur mice); brain infusion cannula used; neurodegenerative (ALS); immunology; antibodies infused; MAb aka Monoclonal antibody; Ketamine and Xylazine anesthesia; Dose (1.5 mg/mL); Brain coordinates; l-2mm [Bregma] in the antero-posterior direction, 2.8mm in mediolateral direction and 3mm depth

Q3981: Y. J. Liu, *et al.* Activation of AMP-activated protein kinase alpha1 mediates mislocalization of TDP-43 in amyotrophic lateral sclerosis. *Human Molecular Genetics* 2015;24(787-801

Agents: JMF1907 **Vehicle:** Saline; **Route:** SC; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 18 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (B6SJL-Tg, 6 weeks old); pumps replaced every 4 weeks; neurodegenerative (Amyotrophic lateral sclerosis); no stress (see pg. 792); behavioral testing (rotarod, forelimb grip); long-term study;

Q4324: G. Battaglia, *et al.* Activation of mGlu3 metabotropic glutamate receptors enhances GDNF and GLT-1 formation in the spinal cord and rescues motor neurons in the SOD-1 mouse model of amyotrophic lateral sclerosis. *NEUROBIOLOGY OF DISEASE* 2015;74(126-136

Agents: LY379268 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 40 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6J or SOD1G93A, 8 weeks old, 20-22g); pumps replaced every 28 days; neurodegenerative (amyotrophic lateral sclerosis); behavioral testing (rotarod testing); immunology;

Q4207: H. Z. Yin, *et al.* Intrathecal infusion of BMAA induces selective motor neuron damage and astrogliosis in the ventral horn of the spinal cord. *Experimental Neurology* 2014;261(1-9

Agents: Propanoic acid, amino-beta-methyl **Route:** CSF/CNS (intrathecal); **Species:** Rat (transgenic); **Pump:** 2004; **Duration:** 30 days;

ALZET Comments: Controls received mp w/ saline; animal info (male, hemizygous SOD1 G93A, 80 days old); neurodegenerative (amyotrophic lateral sclerosis); toxicology; amino-beta-methylaminopropanoic acid aka beta-N-methylamino-L-alanine aka BMAA; BMAA is a neurotoxin; used PE5 catheter for IT cannulation;

Q5465: B. Otsmane, *et al.* Cerebrospinal fluid-targeted delivery of neutralizing anti-IFNgamma antibody delays motor decline in an ALS mouse model. *Neuroreport* 2014;25(1):49-54

Agents: Antibody, Rat monoclonal antagonistic anti-IFN γ ; Antibody, irrelevant rat IgG1 monoclonal **Vehicle:** PBS; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: Animal info (Hb9::GFP mice, 13-week); ALZET brain infusion kit 3 used; neurodegenerative (Amyotrophic lateral sclerosis); Glue and dental cement used to secure cannula to skull; Dose (300 ug/mL); Brain coordinates (0.3mm anterior and 1mm lateral relative to bregma; 2.6mm below the surface of the skull);

Q3554: M. Oono, *et al.* Transglutaminase 2 accelerates neuroinflammation in amyotrophic lateral sclerosis through interaction with misfolded superoxide dismutase 1. *Journal of Neurochemistry* 2014;128(3):403-418

Agents: Cystamine **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Mice; **Pump:** 2006; **Duration:** 42 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (WT C57BL6 or mSOD1, 30 weeks old); neurodegenerative (amyotrophic lateral sclerosis); immunology; stability "Cystamine hydrochloride has previously been shown to be very stable for long time use in the osmotic minipump" pg 417;



Q4777: J. D. P. Ghanashyam D. Ghadge, *et al.* Single chain variable fragment antibodies block aggregation and toxicity induced by familial ALS-linked mutant forms of SOD1. *NEUROBIOLOGY OF DISEASE* 2013;56(74-78

Agents: anti-SOD1 monoclonal antibodies (mAbs) **Vehicle:** Not Stated; **Route:** CSF/CNS (lateral ventricle); **Species:** mice; **ALZET Comments:** FALS transgenic mice; anti SOD1 monoclonal antibody; neurodegenerative (Amyotrophic Lateral Sclerosis); paper does not mention ALZET much, or pump model.

Q5045: G. D. Ghadge, *et al.* Single chain variable fragment antibodies block aggregation and toxicity induced by familial ALS-linked mutant forms of SOD1. *Neurobiol Dis* 2013;56(74-8

Agents: antibody, monoclonal anti-SOD1 **Route:** CSF/CNS (ventricles); **Species:** mice; **ALZET Comments:** animal info: FALS transgenic mice; anti SOD1 monoclonal antibody; neurodegenerative (Amyotrophic Lateral Sclerosis); paper does not mention ALZET much, or pump model;

Q2404: A. Van Hoecke, *et al.* EPHA4 is a disease modifier of amyotrophic lateral sclerosis in animal models and in humans. *Nature Medicine* 2012;18(9):1418-U168

Agents: KYLPYWPVLSSL **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** Not Stated; **ALZET Comments:** Animal info (60 days old, female); KYLPYWPVLSSL is an Epha4 blocking peptide; peptides;

Q2019: Y. Z. Li, *et al.* Exendin-4 Ameliorates Motor Neuron Degeneration in Cellular and Animal Models of Amyotrophic Lateral Sclerosis. *PLoS One* 2012;7(2):U436-U448

Agents: Exendin-4 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 12 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (SOD1, G93A, 6 wks old); pumps replaced every 3 weeks; long-term study; neurodegenerative (amyotrophic lateral sclerosis);

P8852: H. Y. Wang, *et al.* Therapeutic gene silencing delivered by a chemically modified small interfering RNA against mutant SOD1 slows amyotrophic lateral sclerosis progression. *Journal of Biological Chemistry* 2008;283(23):15845-15852

Agents: RNA, small interfering, modified; RNA, small interfering **Vehicle:** PBS; **Route:** CSF/CNS (intrathecal, subarachnoid space); **Species:** Mice (transgenic); **Pump:** 1007D; 2004; **Duration:** 7, 28 days; 72 hours; **ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by residual volume; dose-response (Fig. 3); no stress (see pg. 15846, 15849); stability verified by 28 days in vivo (see Fig. 2); half-life (p. 15846) "short"; gene therapy; brain tissue distribution; animal info (SOD1G93A Tg); neurodegenerative (ALS); mp + catheter positioning confirmed; Target (SOD1); "when infused at disease onset at the therapeutic dose for 4 weeks, this siRNA slows disease progression without detectable adverse effects." The catheter was implanted between the L5 and L6 vertebra and connected to a primed Alzet osmotic pump with the PE50 tube. The catheter was stitched to the surface muscle, and the Alzet osmotic pumps were placed under the skin on the back of the mouse.

P9435: C. Pitzer, *et al.* Granulocyte-colony stimulating factor improves outcome in a mouse model of amyotrophic lateral sclerosis. *Brain* 2008;131(3335-3347

Agents: Granulocyte-colony stimulating factor **Vehicle:** Sorbitol; sodium acetate buffer; tween 80; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 4, 8 weeks; 4 days; **ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by G-CSF serum concentration; replacement therapy (sciatic nerve axotomy); pumps replaced after 4 weeks; half-life (p. 5) 4 hours in humans and rodents; brain tissue distribution; peptide; animal info (female, C57BL/6, wt, SOD1(G93A)Tg, 11 wks old); neurodegenerative (ALS); behavioral testing (rotarod test, motor performance); 0.004% Tween 80 used

P9209: Y. Ohta, *et al.* Therapeutic benefits of intrathecal protein therapy in a mouse model of amyotrophic lateral sclerosis. *Journal of Neuroscience Research* 2008;86(13):3028-3037

Agents: TAT-GFP; TAT-Bcl-X_L **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intrathecal); **Species:** Mice; Mice (transgenic); **Pump:** 2001; 2004; **Duration:** 7, 28 days; **ALZET Comments:** Controls received mp w/ vehicle; stability verified by antiapoptotic effect at 7, 14, and 28 days at 37 degree Celsius (p. 3031); peptides; animal info (male, B6SJL, wt, G93A SOD1 Tg, 91 days old); neurodegenerative (ALS); behavioral testing (Rotarod test, wheel running test); "intrathecal infusion of TAT-infused proteins using an osmotic minipump is a better method of delivering therapeutic proteins into the spinal cord." (p. 3035)



P9379: G. Gowing, *et al.* Ablation of Proliferating Microglia Does Not Affect Motor Neuron Degeneration in Amyotrophic Lateral Sclerosis Caused by Mutant Superoxide Dismutase. *Journal of Neuroscience* 2008;28(41):10234-10244

Agents: Ganciclovir **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 30 days;

ALZET Comments: Controls received mp w/ saline; animal info (CD11b-Tkmt-30-SOD1G93A Tg, 85 days old); neurodegenerative (ALS); IP injection of ganciclovir given 24 hours before and during mp implantation surgery; behavioral testing (hindlimb reflex); "chronic and systemic injection of the nucleoside analog ganciclovir is lethal for CD11b-Tkmt30 transgenic mice, and ganciclovir is not highly diffusible within CNS tissue... To overcome this constraint, we proceeded with direct delivery of ganciclovir to the spinal cord via an osmotic pump connected to a cannula located in the intrathecal space." (p. 10240)

P8266: M. Urushitani, *et al.* Therapeutic effects of immunization with mutant superoxide dismutase in mice models of amyotrophic lateral sclerosis. *Proceedings of the National Academy of Sciences* 2007;104(7):2495-2500

Agents: Antibody, mouse anti hSOD1; Antibody, rabbit polyclonal anti-hSOD1-FITC **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2004; **Duration:** 16, 28 days;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by residual volume; stability verified by Western Blot w/ residual volume AB after 18 days infusion; brain tissue distribution; animal info (G93A SOD1, 85 days old); neurodegenerative (ALS)

P8481: F. Locatelli, *et al.* Fas small interfering RNA reduces motoneuron death in amyotrophic lateral sclerosis mice. *Annals of Neurology* 2007;62(1):81-92

Agents: RNA, small interfering **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: Neurodegenerative (Amyotrophic Lateral Sclerosis); siRNA was used to silence the Fas receptor; animal info (C57BL/6, 90 days old); "Our study demonstrated that Fas silencing is able to interfere with motoneuron degeneration...providing new insights into the ALS pathogenesis and suggesting new possible strategies of molecular therapy...of ALS." p.91

P8908: A. Ishigaki, *et al.* Intrathecal delivery of hepatocyte growth factor from amyotrophic lateral sclerosis onset suppresses disease progression in rat amyotrophic lateral sclerosis model. *Journal of Neuropathology and Experimental Neurology* 2007;66(11):1037-1044

Agents: Hepatocyte growth factor, recomb. human **Vehicle:** PBS, sulfoxide; **Route:** CSF/CNS (intrathecal, subarachnoid space); **Species:** Rat (transgenic); **Pump:** 2002; 2004; **Duration:** 2, 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; dose-response (fig. 2); peptides; animal info (G93A Tg, 100 and 115 days old); neurodegenerative (ALS); "we examined the effects of continuous intrathecal delivery of human recombinant HGF (hrHGF) into Tg rats using implanted infusion pumps for selective and less invasive supply of HGF to the spinal cord." (p.1038)

P9501: R. A. Smith. Antisense oligonucleotide therapy for neurodegenerative disease. *Journal of Clinical Investigation* 2006;116(8):2290-2296

Agents: Oligonucleotide, phosphorothioate antisense; oligonucleotide, phosphorothioate missense **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; Rat (transgenic); **Pump:** Not Stated; **Duration:** 14, 28 days;

ALZET Comments: Controls received mp w/ missense oligo; antisense (SOD1); brain tissue distribution; animal info (Sprague Dawley, SOD1G93A Tg, 65-75 days old); neurodegenerative (ALS)

P8274: V. Sava, *et al.* Can low level exposure to ochratoxin-A cause parkinsonism? *Journal of the Neurological Sciences* 2006;249(1):68-75

Agents: Ochratoxin-A **Vehicle:** Sodium bicarbonate; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; dose-response (fig. 3); comparison of IP injections vs. mp; no stress (see pg. 71); half-life (p. 71) 20-224 hours in various brain tissue; animal info (male, Swiss ICR, 22 grams); neurodegenerative (Amyotrophic Lateral Sclerosis, Parkinson's disease); mycotoxin; "Notably chronic exposure did not alter behavior or spontaneous locomotor activity, nor did it result in abnormal clasping or posturing of the limbs when handled by the tail." (p. 71)



P6730: E. Storkebaum, *et al.* Treatment of motoneuron degeneration by intracerebroventricular delivery of VEGF in a rat model of ALS. *Nature Neuroscience* 2005;8(1):85-92

Agents: Vascular endothelial growth factor, recomb. rat **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 100 days; **ALZET Comments:** Long-term study; pumps replaced every 28 days; ALZET brain infusion kit used; VEGF was cleared from CSF within 3h; "70-80% of VEGF in pumps remained active after 4 weeks."; neurodegenerative (Amyotrophic Lateral Sclerosis)

P7621: H. Narai, *et al.* Prevention of spinal motor neuron death by insulin-like growth factor-1 associating with the signal transduction systems in SOD(G93A) transgenic mice. *Journal of Neuroscience Research* 2005;82(4):452-457

Agents: Insulin-like growth factor I, recomb. human **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intrathecal, subarachnoid space, lumbar); **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 5,10 weeks; **ALZET Comments:** Controls received mp w/ vehicle; dose-response (fig 1); pumps replaced every 4 weeks; neurodegenerative (Amyotrophic Lateral Sclerosis); animal info (C57BL/6J, female); cannula used for IT placement

Q5957: A. Witting, *et al.* Endocannabinoids accumulate in spinal cord of SOD1 G93A transgenic mice. *J Neurochem* 2004;89(6):1555-7

Agents: Cannabinol **Vehicle:** PEG 400; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 12 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (SOD1 transgenic; 6 week old; 25 grams); Dose (5 mg/kg/day); long-term study; pumps replaced every 4 weeks up to 2 times; neurodegenerative (ALS); no stress (see pg. 183): dose and the repeated pump replacements were well tolerated; cannabinol (CBN) is a nonpsychotropic cannabinoid; Therapeutic indication (amyotrophic lateral sclerosis);

P6100: S. J. Feeney, *et al.* The effect of leukaemia inhibitory factor on SOD1 G93A murine amyotrophic lateral sclerosis. *Cytokine* 2003;23(4-5):108-118

Agents: Leukemia inhibitory factor **Route:** CSF/CNS (intrathecal); **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 13 weeks; **ALZET Comments:** Comparison of SC injections vs. IT mp; long-term study; pumps replaced every 4 weeks; ALZET brain infusion kit 1 used (per Dr. Feeney); used the BIK for the IT infusion; glued and sutured the cannula in place; "All mice that entered the study recovered from the surgical procedure and appeared to have no adverse effects." (p. 111); neurodegenerative (Amyotrophic Lateral Sclerosis)

Q7334: O. A. Andreassen, *et al.* Effects of an inhibitor of poly(ADP-ribose) polymerase, desmethylselegiline, trientine, and lipoic acid in transgenic ALS mice. *Experimental Neurology* 2001;168(2):419-24

Agents: Desmethylselegiline **Vehicle:** vehicle not stated; **Route:** SC; **Species:** Mice; **Pump:** pump model not stated; **Duration:** pump model not stated; **ALZET Comments:** Dose (10 mg/kg/day); Controls received sham surgery w/ plastic tubes; animal info (6SJL-TgN (SOD1-G93A), 4 weeks); behavioral testing (rotarod test); pumps replaced every 1 month; long-term study; Desmethylselegiline (DMS) is a metabolite of selegiline; neurodegenerative (ALS); "The minipumps with DMS were replaced at 1-month intervals except that the first pump was a 15-day version which allowed us to make dose adjustments at the period when they grew relatively faster." p.420

P4452: M. Li, *et al.* Functional role of caspase-1 and caspase-3 in an ALS transgenic mouse model. *Science* 2000;288(14):335-339

Agents: zVAD-fmk **Vehicle:** DMSO; Pipes; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 56 days; **ALZET Comments:** Controls received mp w/vehicle; pumps replaced after 28 days; zVAD-fmk is a broad caspase inhibitor; also called N-benzyloxycarbonyl-Val-Asp- fluoromethylketone; neurodegenerative (Amyotrophic Lateral Sclerosis); long-term study

Q0041: L. L. Dugan, *et al.* Carboxyfullerenes as neuroprotective agents. *Proceedings of the National Academy of Sciences* 1997;94(9434-9439)

Agents: Carboxyfullerene, C3 **Vehicle:** Saline, physiological; **Route:** IP; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 2 months; **ALZET Comments:** Controls received mp w/ vehicle; neurodegenerative (amyotrophic lateral sclerosis); animal info (G93A SOD1 G1, 10 weeks old); functionality of mp verified by residual volume; pumps replaced after 4 weeks; behavioral testing (motor performance)