References on Neurodegenerative Studies
Using ALZET® Osmotic Pumps

1. ALS


**Agents:** CLR01  **Vehicle:** Saline;  **Route:** SC;  **Species:** Mice;  **Pump:** 1004;  **Duration:** 6 weeks;
**ALZET Comments:** Dose (0, 0.5, or 5.0 mg/kg); 0.9% saline used; Controls received mp w/ vehicle; animal info (Transgenic B6SJL-Tg mice); behavioral testing (grip-strength test, rotarod test); half-life: 1-2 hours (p.5); CLR01 is a broad-spectrum inhibitor of the self-assembly and toxicity of amyloid proteins; enzyme inhibitor (superoxide dismutase 1 (SOD1); neurodegenerative (amyotrophic lateral sclerosis);


**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≥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);


**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:** 58 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  **Vehicle:** Not Stated;  **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); pumps replaced every 28 days; ALZET brain infusion kit used; neurodegenerative (amyotrophic lateral sclerosis);


**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);
2. Alzheimer’s


**Agents:** Reboxetine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

**ALZET Comments:** Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (7 month old male WT and heterozygous 5xFAD mice); half-life (p. 2; 12.5 hr); neurodegenerative (Alzheimer’s);


**Agents:** Interleukin-6 **Vehicle:** Saline; **Route:** CNS/CSF; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

**ALZET Comments:** Dose (100 ng/day); Controls received mp w/ vehicle; animal info (Male, C57BL/6N); neurodegenerative (Alzheimer’s Disease);


**Agents:** PAI-039 **Vehicle:** Not stated; **Route:** CNS/CSF; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

**ALZET Comments:** Dose (42 ng/kg/min); Controls received mp w/ vehicle; animal info (10-11 months old); behavioral testing (Maze Test, Novel Object Recognition Test); enzyme inhibitor (PAI-1 inhibitor); Brain coordinates (-0.22 mm lateral, 0.8 mm, dorsal 2 mm); neurodegenerative (Alzheimer’s Disease);


**Agents:** Zymosan; CU-CPT22 **Vehicle:** Not stated; **Route:** CSF/CNS (intracerebral); IV; **Species:** Mice; **Pump:** 1007D; 1004; 1002; **Duration:** 1 week; 28 days; 2 weeks;

**ALZET Comments:** Dose (25 ug zymosan; 10 ug/day CU-CPT22); animal info (male and female 5xFAD mice); CU-CPT22 aka Toll-like receptor 2 antagonist; Brain coordinates (A = 0, L = 1, H = 2.5); neurodegenerative (Alzheimer’s Disease);

Q8611: M. Krishnan, et al. beta-hydroxybutyrate Impedes the Progression of Alzheimer’s Disease and Atherosclerosis in ApoE-Deficient Mice. Nutrients 2020;12(2)

**Agents:** Beta-hydroxybutyrate **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 8 weeks;

**ALZET Comments:** Dose (1.5 mmol/kg/day); Controls received mp w/ vehicle; animal info (Six-week-old male ApoE−/− and C57BL/6J mice); pumps replaced every 4 weeks; Beta-hydroxybutyrate aka B-OHB; neurodegenerative (Alzheimer’s Disease);

3. Ataxia


**ALZET Comments:** Isoproterenol, I-; SC; Mice; 7 days; Animal info (4 mo old, male, female, wt, hKO).


**ALZET Comments:** EUK-189; Mannitol; SC; Mice; 2004; 56, 84 days; Controls received mp w/ vehicle; long-term study; pumps replaced every 28 days; no stress (see pg.941); cancer (thymoma); EUK-189 is a synthetic catalytic antioxidant w/ both catalase & superoxide dismutase activities; neurodegenerative (ataxia telangiectasia).

4. Huntington’s
Agents: MK-28 Vehicle: DMSO; PEG-400; Route: SC; Species: Mice; Pump: 1004; Duration: 2 weeks; 28 days;
ALZET Comments: Dose (6 mg/kg; 1 mg/kg); Controls received mp w/ vehicle; animal info (B6 wild type mice; four-week-old mice); behavioral testing (Rotarod test); MK-28 aka small molecule PERK activator; neurodegenerative (Huntington's disease);

Agents: cyclodextrin, methyl-b Vehicle: CSF, Artificial; Route: CSF/CNS (corpus striatum); Species: Mice; Pump: 1004; Duration: 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (wild-type mice, 5 weeks old); behavioral testing (Rotarod, Activity Cage, Novel object recognition (NOR) test); methyl-b-cyclodextrin aka MBCD; ALZET brain infusion kit 3 used; Brain coordinates (stereotaxic coordinates 1.75 mm mediolateral, 0.5 mm anteroposterior, 3 mm dorsoventral);

Agents: neurotrophic factor, Recombinant brain derived Vehicle: Saline; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Dose (4 ug/d); Controls received mp w/ vehicle; animal info (4 week old, Male); neurodegenerative (Huntington's Disease);

Q6969: A. U. Joshi, et al. Drp1/Fis1-mediated mitochondrial fragmentation leads to lysosomal dysfunction in cardiac models of Huntington's disease. J Mol Cell Cardiol 2019;127(125-133
Agents: P110 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 8 weeks;
ALZET Comments: Dose ((3 mg/Kg/day); animal info (5-week old Hemizygous R6/2 HD mice); P110 is a Drp1/Fis1 interaction peptide inhibitor; neurodegenerative (Huntington's);

Agents: XPro1595 Vehicle: Saline; Route: CSF/CNS (lateral ventricle); Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: "Dose (0.08 mg/kg/day); Controls received mp w/ vehicle; animal info (6.5 weeks, Transgenic R6/2); XPro1595 is a dominant-negative inhibitor of soluble TNF-alpha; ALZET brain infusion kit 3 used; neurodegenerative (Huntington's); Therapeutic indication (disease progression in HD due to inflammation); "

S. Neimann

ALZET Comments: MARCKS peptide; Saline, sterile; CSF/CNS; Mice; 1004; Control animals received mp w/ vehicle; animal info (ASMko, 4 mo old); peptides; ALZET brain infusion kit 3 used; cyanoacrylate used; behavioral testing (accelerating rotarod); MARCKS is a protein required for PI(4,5)P2 membrane clustering and hydrolysis.

ALZET Comments: Cyclodextrin, 2-hydroxypropyl-B; CSF/CNS; Mice; Animal info (NPC); pumps mentioned in introduction.

ALZET Comments: Nerve growth factor; CSF, artificial; CSF/CNS; Mice; 1002; 7 days; Controls received mp w/ vehicle; animal info (BALB/c, NPC/1 -/-); aCSF recipe; brain infusion kit used.

ALZET Comments: PD-98059; DMSO; saline; dye, Evan’s blue; CSF/CNS; Mice; 1002; 2 weeks; Controls received mp w/ vehicle; functionality of mp verified by dye infusion; dose-response (fig. 1); enzyme inhibitor (MAPK/ERK 1); brain tissue distribution; animal info (female, BALB/c, Nctr-Npc, 5 wks old); 50% DMSO used; behavioral testing (limb motor activity/coat hanger test).


ALZET Comments: Roscovitine; olomoucine; iso-olomoucine; DMSO; CSF/CNS; Mice; 1002; 2, 4 weeks; Pumps replaced every 2 weeks for 4 week infusions; enzyme inhibitor (CDK); neurodegenerative (Alzheimer’s disease, Amyotrophic Lateral Sclerosis, Niemann-Pick Type C disease); lynch coil used to accommodate 75% DMSO.

6. Parkinson


Agents: 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine Vehicle: Saline; Route: SC; Species: Monkey; Pump: Not stated; Duration: 2 weeks;

ALZET Comments: Dose (0.5 mg/day); animal info (adult female monkeys, 4 to 11 years old, 2.4 to 4.6 kg); 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine aka MPTP; neurodegenerative (Parkinson’s Disease);


Agents: Oligonucleotides, antisense Vehicle: CSF, Artificial; Route: CNS/CSF (lateral ventricle); Species: Mice; Primate; Pump: 1004; 2ML4; Duration: 28 days;

ALZET Comments: Dose (30 ug/day; 100 ug/day; 1 mg/day); Controls received mp w/ vehicle; animal info (Eight-week-old male C57BL/6J mice; male and female hesus macaques, 20 years or older); antisense oligonucleotides aka IND-ASO; ALZET brain infusion kit 3 used; Brain coordinates (antero-posterior -0.34, medial-lateral -1.0 and dorsal-ventral -2.2 in mm); neurodegenerative (Parkinson’s Disease);


Agents: pyridine, 1-methyl-4-phenyl-1,2,3,6-tetrahydro Vehicle: Saline; Route: IP; Species: Mice; Pump: 2002; Duration: 14 days;

ALZET Comments: Dose (30 mg/kg/day); Controls received mp w/ vehicle; animal info (Male C57BL/6 mice 6-8 weeks old); MPTP aka 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; neurodegenerative (Parkinson’s);


Agents: Diphenyleneiodonium Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 3 months;

ALZET Comments: Dose (10 ng/kg/day); Controls received mp w/ vehicle; animal info (C57/BL, 3 months old, Male); DPI aka Diphenyleneiodonium ; enzyme inhibitor (NOX2 inhibitor); neurodegenerative (Parkinson’s Disease);


Agents: Rotenone Vehicle: DMSO, PEG; Route: SC; Species: Mice; Pump: 2004; Duration: 4 weeks;
**ALZET Comments:** Dose (2.5 mg/kg/day); 50 DMSO: 50 PEG used; Controls received mp w/ vehicle; animal info (male C57BL/6J mice nine weeks old; approximately 25 g); enzyme inhibitor (Rotenone is a mitochondrial complex I inhibitor); neurodegenerative (Parkinson’s disease);