References on the Administration of Leupeptin
Using ALZET® Osmotic Pumps

Q8244: J. H. Lee*, et al.* Transgenic expression of a ratiometric autophagy probe specifically in neurons enables the interrogation of brain autophagy in vivo. Autophagy 2019;15(3):543-557
Agents: Chloroquine, Pan-MTOR inhibitor-21 mg/ml, or leupeptin **Vehicle:** DMSO; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 5 days (Pan-MTOR inhibitor) or 7 days (leupeptin);
ALZET Comments: Dose (Chloroquine-5 mg/kg/day, Pan-MTOR inhibitor-50 mg/kg/day, or leupeptin-4 mg/kg/day); 4% DMSO used; animal info (TRGL6, 4 months old); Pan-MTOR inhibitor aka AZD8055, leupeptin aka cysteine protease inhibior ; enzyme inhibitor (Cysteine protease inhibitor); Brain coordinates (lateral ventricle: AP – 0.3mmto bregma,ML 1.0mmto bregma, and DV 2.5 mm to cranium); neurodegenerative (Autophagy-Lysosome Pathway);

Q3854: M. R. Deshotels*, et al.* Angiotensin II Mediates Angiotensin Converting Enzyme Type 2 Internalization and Degradation Through an Angiotensin II Type I Receptor-Dependent Mechanism. Hypertension 2014;64(1368-U438
Agents: Angiotensin II; leupeptin **Vehicle:** Saline; CSF, artificial; **Route:** SC; CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57Bl6 or ACE2 KO, 25-30g, 14-16 weeks old); cardiovascular; peptides; bp measured using radiotelemetry; Ang II infused SC; leupeptin infused ICV;

Q0954: L. Abaamrane*, et al.* Intracochlear perfusion of leupeptin and z-VAD-FMK: influence of antiapoptotic agents on gunshot-induced hearing loss. European Archives of Oto-Rhino-Laryngology 2011;268(7):987-993
Agents: Leupeptin; z-VAD-FMK **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received no treatment; animal info (albino, 400-600 g); enzyme inhibitor (caspase); artificial perilymph solution recipe; "A miniature glass pipette with a ring of glue placed next to the tip to provide a leak-proof seal protecting the cochlea from contamination was connected to the catheter." pg 988; tissue perfusion

Q0252: M. Shinohara*, et al.* Reduction of Brain beta-Amyloid (A-beta) by Fluvastatin, a Hydroxymethylglutaryl-CoA Reductase Inhibitor, through Increase in Degradation of Amyloid Precursor Protein C-terminal Fragments (APP-CTFs) and A-beta Clearance. Journal of Biological Chemistry 2010;285(29):22091-22102
Agents: Leupeptin; E-64a **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 1 week;
ALZET Comments: Controls received mp w/ vehicle; peptides; ALZET brain infusion kit 3 used; no stress (see pg 22092); neurodegenerative (Alzheimer's Disease); animal info (male, C57BL/6, APP23 Tg, 8 wks old); lysosomal inhibitor; aCSF recipe

P9059: D. S. Yang*, et al.* Neuronal apoptosis and autophagy cross talk in aging PS/APP mice, a model of Alzheimer's disease. American Journal of Pathology 2008;173(3):665-681
Agents: Leupeptin **Vehicle:** HEPES, buffer; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 2 weeks;
ALZET Comments: Enzyme inhibitor (cysteine protease); cyanoacrylate adhesive; animal info (6 months old, PS/APP, or wt); neurodegenerative (Alzheimer's Disease); pumps primed in sterile saline at 37 degree Celsius for 48 hours

P7214: T. Nakajima*, et al.* Alpha-Synuclein-positive structures induced in leupeptin-infused rats. Brain Research 2005;1040(1-2):73-80
Agents: Leupeptin **Vehicle:** PBS; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (protease); peptides; "The leupeptin infusion rat model is thought to be a useful material for studying several neuronal changes resembling the aging or degeneration of the central nervous tissue." (p. 79)

P7091: C. yala-Grosso*, et al.* Effects of fimbria-fornix transection on calpain and choline acetyl transferase activities in the septohippocampal pathway. Neuroscience 2004;126(4):927-940
Agents: Leupeptin; MDL 28170 **Vehicle:** Saline, sterile; DMSO; cyclodextrin; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ vehicle; replacement therapy (axotomy); enzyme inhibitor (calpain); 2% DMSO; mp primed overnight at 37 degree Celsius; 10% cyclodextrin used

P4742: W. Tang, *et al.* The effects of leupeptin on cochlear blood flow, auditory sensitivity, and histology. International Tinnitus Journal 2001;7(1):4-12
Agents: Leupeptin; **Vehicle:** Hank's solution;; **Route:** ear (round window);; **Species:** Guinea pig;; **Pump:** 2002;; **Duration:** 8 weeks;;
ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (bulla); long-term study, pumps replaced every 13 days; IntraEAR catheter used; Leupeptin is a potent calpain inhibitor; neuroprotection; buprenorphine given as postoperative analgesic; chloramphenicol given as prophlactic antibiotic;

P4270: S. A. Frautschy, *et al.* Protease inhibitor coinfusion with amyloid beta-protein results in enhanced deposition and toxicity in rat brain. Journal of Neuroscience 1998;18(20):8311-8321
Agents: Amyloid protein, beta; Aprotinin; Leupeptin; **Vehicle:** HEPES;; **Route:** CSF/CNS;; **Species:** Rat; **Pump:** 2004;; **Duration:** 4 weeks;
ALZET Comments: controls received mp w/ vehicle; peptides; ALZET brain infusion kit used; beta-amyloid protein infused alone, or concomitantly with aprotinin or leupeptin; enzyme inhibitors

P3822: T. Arai, *et al.* Memory disturbance and hippocampal degeneration induced by continuous intraventricular infusion of a protease inhibitor, leupeptin. Brain Research 1997;754(157-162
Agents: Leupeptin **Vehicle:** CSF, artificial;; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received mp w/aCSF; ALZET brain infusion kit used

P3263: E. H. Karran, *et al.* A simple in vivo model of collagen degradation using collagen-gelled cotton buds: the effects of collagenase inhibitors and other agents. Inflamm. Res 1995;44(36-46
Agents: Collagenase inhibitor A; Collagenase inhibitor B; Collagenase inhibitor C; tempol; Superoxide dismutase-PEG; Cytochalasin B; Pepstatin; APMSF; TLCK; SBTI; Leupeptin; E-64; Methylamine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2ML1; **Duration:** 7 days;
ALZET Comments: controls received mp w/vehicle; no stress (see pg. 39); immunology; pumps connected with catheter tubing to 14C-collagen-gelled cotton buds

P2002: K. Kitani, *et al.* Effect of leupeptin on the lateral mobility of proteins in the plasma membrane of hepatocytes of C57BL/6 mice: FRAP studies on liver smears. Archives of Biochemistry and Biophysics 1992;14(27-45
Agents: Leupeptin **Vehicle:** Not Stated; **Route:** IP; **Species:** mice; **Pump:** Not Stated; **Duration:** 2,5,8,11,14 days;
ALZET Comments: stress/adverse reaction: states IP mp may have had adverse effect on results, however, mp size used was too large for animal/implant site per manufacturer; thiol-protease inhibitor

P1987: G. O. Ivy. Protease inhibitors as a model for NCL disease, with special emphasis on the infantile and adult forms. American Journal of Medical Genetics Part A 1992;42(555-560
Agents: E-64C; Aprotinin; Chloroquine; Leupeptin **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: no comment posted

P1916: K. S. Lee, *et al.* Inhibition of proteolysis protects hippocampal neurons from ischemia. Proc. Natl. Acad. Sci 1991;88(7233-7237
Agents: Leupeptin **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** gerbil; **Pump:** Not Stated; **Duration:** 3 days;
ALZET Comments: Ischemia (cerebral); peptides

P1897: G. O. Ivy, *et al.* Leupeptin causes an accumulation of lipofuscin-like substances in liver cells of young rats. Mech. Ageing Dev 1991;57(213-231
Agents: Leupeptin **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: peptides; thiol protease inhibitor

P3762: E. A. Porta, *et al.* Effects of lovastatin and leupeptin on ceroidogenesis of vitamin E-deficient and-supplemented young rats. In 'Lipofuscin and ceroid pigments', E. A. Porta (ed.), Plenum Press, N. Y 1990;169-190
Agents: Leupeptin **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 2002; **Duration:** 45 days;

ALZET Comments: long-term study, pumps replaced every 15 days; no stress (see pgs. 178, 180)

P1243: U. Staubli, *et al.* Chronic administration of a thiol-proteinase inhibitor blocks long-term potentiation of synaptic responses. Brain Research 1988;444(1):153-158
Agents: Leupeptin **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 3 days;
ALZET Comments: controls received mp w/ saline; mp connected to cannula in left ventricle; peptides

P0935: R. Siman, *et al.* Ontogeny, compartmentation, and turnover of spectrin isoforms in rat central neurons. J. Neurosci 1987;7(1):55-64
Agents: Leupeptin **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 10 days;
ALZET Comments: mp model not stated; controls received mp w/saline; peptides; see p.534 for methods

P1100: R. G. M. Morris, *et al.* Spatial learning in the rat: Impairment induced by the thiol-proteinase inhibitor, leupeptin, and an analysis of [3H] glutamate receptor binding in relation to learning. Behavior Genetics 1987;47(333-345
Agents: Leupeptin **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 5 days;
ALZET Comments: controls received mp w/saline; mp connected to catheter in lateral ventricle; 2 experiments were conducted, only 1 used the mp; peptides

P0884: L. E. Ostrowski, *et al.* Selective inhibition of proteolytic enzymes in an in vivo mouse model for experimental metastasis. Cancer Research 1986;46(4121-4128
Agents: Arginal, H-D-Phe-Pro-; EP-453; Leupeptin **Vehicle:** DMSO; PBS; Propylene glycol; **Route:** SC; **Species:** mice; **Pump:** 2001; **Duration:** 5-7 days;
ALZET Comments: controls received mp w/vehicle; mice injected w/melanoma cells; comparison of ip injections vs. mp infusion; cancer; no stress (see p. 4123); peptides

P0633: U. Staubli, *et al.* Olfactory discrimination learning is blocked by leupeptin, a thiol protease inhibitor. Brain Research 1985;337(333-336
Agents: Leupeptin **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: 2 doses leupeptin given; dose-response data; infusion into lateral ventricle; peptides

P0456: G. Lynch, *et al.* The biochemistry of memory: a new and specific hypothesis. Science 1984;224(4653):1057-1063
Agents: Leupeptin **Vehicle:** Aprotinin; Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: comparison of agents effects; 3 different drug concentrations used in mp: 4 mg Leu./ml saline, 8 mg/ml, 20 mg/ml; aprotinin and saline used separately as controls; peptides

P0534: G. O. Ivy, *et al.* Inhibitors of lysosomal enzymes: accumulation of lipofuscin-like dense bodies in the brain. Science 1984;226(4677):985-987
Agents: Chloroquine; Leupeptin **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: mp model not stated; comparison of icv injection vs. mp infusion; comparison of agents effects; 3 doses of leupeptin used; peptides

P0362: M. J. Kuranda, *et al.* Tissue locations for the turnover of radioactively labeled rat orosomucoid in vivo. Archives Italiennes de Biologie 1983;224(2):526-533
Agents: Leupeptin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1 1/2 days;
ALZET Comments: 125I-orosomucoid admin. 12 hours after pump implant; peptides