



### References on the Administration of Leupeptin Using ALZET® Osmotic Pumps

**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

**ALZET Comments:** Angiotensin II; leupeptin; Saline; CSF, artificial; SC; CSF/CNS; Mice; 14 days; 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. Abamrane, *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

**ALZET Comments:** Leupeptin; z-VAD-FMK; Ear (cochlea); Guinea pig; 2001; 7 days; 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

**ALZET Comments:** Leupeptin; E-64a; CSF, artificial; CSF/CNS; Mice (transgenic); 2002; 1 week; 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

**ALZET Comments:** Leupeptin; HEPES, buffer; CSF/CNS; Mice (transgenic); 2004; 2 weeks; 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

**ALZET Comments:** Leupeptin; PBS; CSF/CNS; Rat; 2002; 14 days; 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

**ALZET Comments:** Leupeptin; MDL 28170; Saline, sterile; DMSO; cyclodextrin; CSF/CNS; Rat; 5 days; 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

**ALZET Comments:** Leupeptin;; Hank's solution;; ear (round window);; Guinea pig;; 2002;; 8 weeks;; Controls received mp w/ vehicle; tissue perfusion (bullae); 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 prophylactic 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



**ALZET Comments:** Amyloid protein, beta; Aprotinin; Leupeptin;; HEPES;; CSF/CNS;; Rat; 2004;; 4 weeks; 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)

**ALZET Comments:** Leupeptin; CSF, artificial;; CSF/CNS; Rat; 2002; 14 days; 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)

**ALZET Comments:** Collagenase inhibitor A; Collagenase inhibitor B; Collagenase inhibitor C; tempol; Superoxide dismutase-PEG; Cytochalasin B; Pepstatin; APMSF; TLCK; SBTI; Leupeptin; E-64; Methylamine; SC; Rat; 2001; 2ML1; 7 days; 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. *Arch. Gerontol. Geriatr* 1992;14(27-45)

**ALZET Comments:** Leupeptin; IP; mice; 2,5,8,11,14 days; 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. *Am. J. Med. Genet* 1992;42(555-560)

**ALZET Comments:** E-64C; Aprotinin; Chloroquine; Leupeptin; CSF/CNS; Rat; 2002; 2 weeks; 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)

**ALZET Comments:** Leupeptin; CSF/CNS; gerbil; 3 days; 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)

**ALZET Comments:** Leupeptin; Saline; IP; Rat; 2 weeks; 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

**ALZET Comments:** Leupeptin; Saline; IP; Rat; 2002; 45 days; 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

**ALZET Comments:** Leupeptin; Saline; CSF/CNS; Rat; 2002; 3 days; 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

**ALZET Comments:** Leupeptin; Saline; CSF/CNS; Rat; 10 days; 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. *Behav. Neural. Biol* 1987;47(333-345)

**ALZET Comments:** Leupeptin; Saline; CSF/CNS; Rat; 2002; 5 days; 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 Res* 1986;46(4121-4128)

**ALZET Comments:** Arginal, H-D-Phe-Pro-; EP-453; Leupeptin; DMSO; PBS; Propylene glycol; SC; mice; 2001; 5-7 days; 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)

**ALZET Comments:** Leupeptin; Saline; CSF/CNS; Rat; 2002; 2 weeks; 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

**ALZET Comments:** Leupeptin; Aprotinin; Saline; CSF/CNS; Rat; 2002; 2 weeks; 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

**ALZET Comments:** Chloroquine; Leupeptin; Saline; CSF/CNS; Rat; 2 weeks; 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 orosomuroid in vivo. *Arch. Biochem. Biophys* 1983;224(2):526-533

**ALZET Comments:** Leupeptin; Saline; SC; Rat; 2ML1; 1 1/2 days; 125I-orosomuroid admin. 12 hours after pump implant; peptides.