References on the Administration of Leupeptin Using ALZET® Osmotic Pumps


**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 inhibitor; enzyme inhibitor (Cysteine protease inhibitor); Brain coordinates (lateral ventricle: AP – 0.3mm to bregma, ML 1.0mm to 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; **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;


**Agents:** Leupeptin; z-VAD-FMK **Vehicle:** Not Stated; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** Not Stated; **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


**Agents:** Leupeptin; E-64a **Vehicle:** CSF, artificial; **Route:** SCF/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


**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


**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)


**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
    **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 prophylactic antibiotic;

    **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 aprotnin or leupeptin; enzyme inhibitors

    **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

    **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

    **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

    **Agents:** E-64C; Aprotinin; Chloroquine; Leupeptin **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
    **ALZET Comments:** no comment posted

    **Agents:** Leupeptin **Vehicle:** Not Stated; **Route:** IP; **Species:** gerbil; **Pump:** Not Stated; **Duration:** 3 days;
    **ALZET Comments:** Ischemia (cerebral); peptides

    **Agents:** Leupeptin **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 weeks;
    **ALZET Comments:** peptides; thiol protease inhibitor

    **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)

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

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

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

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

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

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

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

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