**References on the Administration of Metalloproteinase Inhibitors Using ALZET® Osmotic Pumps**


**Agents:** 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid  
**Vehicle:** Not Stated  
**Route:** IV (inferior mesenteric vein); IP  
**Species:** Rat (transgenic)  
**Pump:** 2ML1; 2001; **Duration:** 7 days  
**ALZET Comments:** Dose (100 μg/h); animal info (Male Lew-Tg(CAG-EGFP)y); (Matrix metalloproteinases 2/9);

**Q8973:** H. Yu, et al. FOXO3a (Forkhead Transcription Factor O Subfamily Member 3a) Links Vascular Smooth Muscle Cell Apoptosis, Matrix Breakdown, Atherosclerosis, and Vascular Remodeling Through a Novel Pathway Involving MMP13 (Matrix Metalloproteinase 13). Arteriosclerosis, Thrombosis, and Vascular Biology 2018;38(3):555-565

**Agents:** WAY-170523  
**Vehicle:** DMSO, PEG 400 buffered  
**Route:** SC  
**Species:** Mice  
**Pump:** 1007D; **Duration:** 3, 7 days  
**ALZET Comments:** Dose (7.5mg/kg/day); 50% DMSO with PEG400 used; Controls received mp w/ vehicle; animal info (5-6 months, male, ApoE(−/−) and SM22alphaFOXO3aA3ER); WAY170523 is a MMP13-selective inhibitor; enzyme inhibitor (matrix metalloproteinase 13); cardiovascular; results section states mp implanted days 0-7 while materials and methods states mp implanted days 7-10;


**Agents:** Angiotensin II  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Mice  
**Pump:** 2004; **Duration:** 30 days  
**ALZET Comments:** Dose (2.2 mg/kg/day or 4.4 mg/kg/day); animal info (male apolipoprotein E and tissue inhibitor of metalloproteinases-1 knockout mice); cardiovascular;

**Q4464:** R. P. Iyer, et al. Early matrix metalloproteinase-12 inhibition worsens post-myocardial infarction cardiac dysfunction by delaying inflammation resolution. INTERNATIONAL JOURNAL OF CARDIOLOGY 2015;185(198-208

**Agents:** RXP 470.1  
**Vehicle:** Saline; sodium acetate; DMSO  
**Route:** CSF/CNS (medial prefrontal cortex);  
**Species:** Rat  
**Pump:** 2006; **Duration:** Not Stated;  
**ALZET Comments:** Control animals received mp w/ artificial CSF; animal info (Wistar, adult, male); enzyme inhibitor (matrix metalloproteinase); cannula placement verified via histology with 0.6% cresyl violet, 2 ul over 60 s
Agents: Marimastat Vehicle: DMSO; water; Route: SC; Species: Rat; Pump: 2ML2; Duration: 15-17 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 180-370); wound clips used; enzyme inhibitor (matrix metalloproteinase, MMP-13)

Agents: Nerve growth factor, beta, recomb.; GM6001 Vehicle: CSF, artificial; albumin, rat serum; Route: CSF/CNS (intrathecal, subarachnoid space); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague-Dawley, male, 250-300 g); enzyme inhibitor (metalloproteinase); PE10 connected to PE60 tubing

Agents: GM6001; AG3340 Vehicle: DMSO; Route: SC; Species: Rat; Pump: 2ML1; Duration: Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (male Sprague-Dawley, 205-360 g); enzyme inhibitor (matrix metalloproteinase, MMP); 50% DMSO used

Agents: Insulin-like growth factor-1, human, recomb. Vehicle: HCl; saline, isotonic, sterile; Route: SC; Species: Mice (transgenic); Pump: 1004; Duration: 56 days;
ALZET Comments: Animal info (transgenic, Zmpste24 metalloproteinase deficient); pumps replaced after 28 days

Agents: MMP-3 Vehicle: Not Stated; Route: IP; Species: Mice (SCID); Pump: Not Stated; Duration: Not Stated;
ALZET Comments: Controls received mp w/ PBS; peptides; enzyme inhibitor (metalloproteinase); cancer; Loop 6, anti-angiogenic peptide, is a smaller domain C-terminal portion of TIMP-2

Agents: MMI270 Vehicle: DMSO; PEG 300; Route: SC; Species: Mice; Pump: 2004; 2004; Duration: 14; 21 days;
ALZET Comments: Comparison of SC injections vs. mp; enzyme inhibitor (matrix metalloproteinase); cancer (melanoma); animal info (7 wks old, BDF1, male, lymphadrectomy; 50% DMSO used; 50% PEG 300 used

Agents: GM6001 Vehicle: DMSO; Route: CSF/CNS; Species: Mice; Pump: 1007D; Duration: 4 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (metalloproteinase); ALZET brain infusion kit 3 used; dental cement and stay screws used; animal info (male, C57BL/6, wt, Ptprz -/-, adult); 50% DMSO used
**Agents**: RNA, small interfering **Vehicle**: Not Stated; **Route**: Not Stated; **Species**: Mice (nude); **Pump**: Not Stated; **Duration**: 3-4 weeks;
**ALZET Comments**: Controls received no treatment; cancer (meningioma); animal info (athymic, nude); siRNA plasmid vectors targeting cathepsin B and matrix metalloproteinase MMP9

**Agents**: Neuroserpin; GM6001 **Vehicle**: CSF, artificial, PBS; **Route**: CSF/CNS (parietal cortex); **Species**: Rat; **Pump**: 2001; **Duration**: 72 hours;
**ALZET Comments**: Controls received mp w/ vehicle into contralateral side; enzyme inhibitor (tpa, metalloproteinase); multiple pumps per animal (2); animal info (Fischer 344, 6 month old); Lynch coil with air-oil spacer at mp end of tubing; bilateral infusion cannulae; tissue perfusion (parietal cortex)

**Agents**: MMI270 **Vehicle**: DMSO; PEG 300; **Route**: IP; **Species**: Mice; **Pump**: 2004; **Duration**: 15 days;
**ALZET Comments**: Controls received mp w/ vehicle; no stress (see pg.27); enzyme inhibitor (matrix metalloproteinase); cancer (lung); MMI270 was formerly termed CGS27023A; 50% DMSO used; 50% PEG 300 used; “The continuous administration of MMI270 for 15 days using an osmotic pump led to a significant decrease in the weight of tumor-metastasized lymph nodes” (p. 29)

**Agents**: BB-3644 **Vehicle**: PBS; **Route**: SC; **Species**: Mice (SCID); **Pump**: 2001; **Duration**: 8 days;
**ALZET Comments**: Controls received mp w/ vehicle; comparison of IV injections vs. mp; enzyme inhibitor (metalloproteinases); cancer (lymphoma); “when BB-3644 was continuously applied via a small osmotic pump, the antitumor activity of a single dose of Ki-3(scFv)-ETA' was further enchanced with a tumor-free survival of all animals treated for more than 200 days.” (p. 572)

**Agents**: MMI270 **Vehicle**: DMSO; PEG 300; **Route**: SC; **Species**: Mice; **Pump**: Not Stated; **Duration**: 6 days;
**ALZET Comments**: Controls received mp w/ vehicle; functionality of mp verified by serum MMI270 levels; enzyme inhibitor (metalloproteinase)

**Agents**: CIMP **Vehicle**: Not Stated; **Route**: IP; **Species**: Mice; **Pump**: 1002; **Duration**: 4 weeks;
**ALZET Comments**: Controls received no treatment/sham AVF surgery; enzyme inhibitor (metalloproteinase); cardiovascular; peptides; agent also known as (metalloproteinase, cardiac inhibitor)

**Agents**: Marimastat **Vehicle**: DMSO; water; **Route**: SC; **Species**: Mice (SCID); **Pump**: 2002; **Duration**: 2 weeks;
**ALZET Comments**: controls received mp w/ vehicle; enzyme inhibitor (matrix metalloprotease); marimastat, the broad-spectrum matrix metalloproteinase inhibitor was dissolved in 50% DMSO; angiogenesis inhibitor
ALZET Bibliography


Agents: MMI270 Vehicle: DMSO; PEG 300; Route: IP; Species: Rat; Pump: 2001D; 2ML1; Duration: 7 days; 24 hours;
ALZET Comments: Controls received mp/ vehicle; no stress (see pg. 652); enzyme inhibitor (matrix metalloproteinase);


Agents: Marimastat Vehicle: DMSO; Route: SC; Species: Mice (nude); Pump: Not Stated; Duration: 28 days;
ALZET Comments: Controls received mp/ vehicle; pumps replaced after 14 days; matrix metalloproteinase inhibitor;


Agents: Marimastat Vehicle: DMSO; Water, sterile; Route: SC; Species: Mice; Pump: 2002; Duration: 17 days;
ALZET Comments: Controls received mp w/vehicle; cancer; enzyme inhibitor (matrix metalloproteinase);


Agents: BE16627B Vehicle: DMSO; ethylene glycol; Route: SC; Species: Rat; Pump: 1003D; Duration: 3 days;
ALZET Comments: Controls received mp w/ vehicle; vehicle mix was 50:50 ratio; BE16627B matrix metalloproteinase inhibitor;


Agents: CGS 27023A Vehicle: DMSO; Route: SC; Species: Rat; Pump: 2ML2; 2ML4; Duration: 9,47 days;
ALZET Comments: Cardiovascular; enzyme Inhibitor; CGS 27023A hydroxamic acid matrix metalloproteinase inhibitor


Agents: E-64; GI168; GI173; GI179; GI184 Vehicle: DMSO; Saline; Ethanol; Buffer, sodium citrate; Tappsol HPB-20; Route: SC; Species: Mice; Pump: 2001; 2002; Duration: 2, 7, 14 days;
ALZET Comments: Controls received mp w/vehicle; cancer; matrix metalloproteinase inhibitors; mice received 2 pumps each;


Agents: MI-1; MI-2 Vehicle: Propylene glycol; Route: Cartilage, femoral head; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Tissue perfusion (femoral head cartilage); good methods (p. 663); MI-1 and MI-2 are matrix metalloproteinase inhibitors; enzyme inhibitors


Agents: GI168 Vehicle: DMSO; Sodium citrate buffer; Route: SC; Species: Rat; Pump: 2ML2; Duration: 2 weeks;
ALZET Comments: controls received mp/w/vehicle; dose-response (see p. 451); immunology; multiple pumps per animal (2); “GI168 had poor oral bioavailability and a short plasma t 1/2 after subcutaneous injection... so minipump delivery was evaluated.” p. 451; enzyme inhibitor (matrix metalloproteinase)


Agents: BE16627B; Doxorubicin HCl Vehicle: DMSO; Ethylene glycol; Route: SC; Species: Mice (nude); Pump: 2001; 2002; Duration: 3 weeks, 18 days;
ALZET Comments: controls received vehicle or no treatment; pumps replaced; stress/ adverse reaction: skin inflammation and necrosis around delivery site in mice treated with Adriamycin (pg. 733); BE16627B animals were fine; stability verified for 18 days by assay; cancer; enzyme inhibitor; BE16627B is a metalloproteinase inhibitor; 2002 replaced w/ 2001 after 20 days; adriamycin is doxorubicin HCl