Recent References on the Administration of AIDS or HIV Treatments Using ALZET® Osmotic Pumps
(Note: Please see CYTO bibliography for additional cytokines)

Aprotinin
Agents: Aprotinin; HOE-140 Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 3 days;
ALZET Comments: Animal info (Wistar, male, female, 150 days old)

Agents: FR-190997; aprotinin; SBTI Vehicle: Saline; water; HCL; Route: IV (vena cava, cervical vein); Species: Rat; Pump: 2001D; Duration: 24 hours;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular; FR-190997 (a nonpeptide mimic of bradykinin beta 2 agonist) was infused into the vena cava; aprotinin infused into the cervical vein; SBTI & aprotinin are plasma kallikrein inhibitors from soybeans

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

Agents: Aprotinin; Hoe 140; Losartan Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 5,7 days;
ALZET Comments: controls received mp w/saline

P3035: N. J. Morin, et al. Potentiation of gentamicin nephrotoxicity in the rat by infusion of aprotinin. Experimental and Molecular Pathology 1994;60(197-213
Agents: Aprotinin Vehicle: Not Stated; Route: IV; Species: Rat; Pump: 2ML1; Duration: 8 days;
ALZET Comments: controls received mp w/saline; immunology; toxicology

Agents: Kininogen, bovine; Hoe 140; Aprotinin Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: controls received mp w/saline

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: Aprotinin Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: no comment posted
P1673: R. Pakzad. Influence of the trypsin inhibitors aprotinin (Trasylol) and TLCK, administered locally by osmotic minipumps, on the gelatinolytic activity of acrosin and the transport of spermatozoa in the female reproductive tract of rabbits. Z. Mikrosk.-Anat. Forsch 1989;103(6):957-966

**Agents:** Lysine chloromethyl ketone, N-a-tosyl-L-; **Route:** Intrauterine; **Species:** Rabbit; **Duration:** 6 days;

**ALZET Comments:** German with English summary (p. 957); trypsin inhibitors; tissue perfusion (uterus)

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**Azidothymidine**


**Agents:** Azidothymidine **Vehicle:** Sodium hydroxide; **Route:** SC; **Species:** Monkey (pregnant); **Pump:** 2ML4; **Duration:** 28 days;

**ALZET Comments:** Controls received mp w/vehicle; functionality of mp verified by plasma levels of AZT; teratology; AZT is azidothymidine, also known as zidovudine; multiple pumps per animal (3-4); "Circulating levels of AZT remained constant during the course of treatment and were achieved by the first (24 hr.) sample (p. 11); antiretroviral drug

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**Agents:** Azidothymidine **Vehicle:** Propylene glycol; Water; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 5 days;

**ALZET Comments:** Functionality of mp verified by plasma AZT levels; comparison of b.i.d. s.c. injections vs. mp; good methods; also called zidovudine; pK; half-life (p.577); continuous infusion significantly more effective than bolus injection; antiretroviral drug

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**Agents:** Azidothymidine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (pregnant); **Pump:** 2001; **Duration:** 21 days;

**ALZET Comments:** Pumps replaced after each week to achieve 3 weeks duration; immunology; teratology; oral delivery of AZT resulted in highly variable plasma levels; antiretroviral drug

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**Agents:** Azidothymidine **Vehicle:** Not Stated; **Route:** IA (carotid); **Species:** Rat; **Pump:** 2001; **Duration:** 3, 7 days;

**ALZET Comments:** Dose-response; blood levels; comparison of IV injections vs. mp; alkaline pH of 11 inc solubility, stability

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**Clindamycin**


**Agents:** Acyclovir; cimetidine; clindamycin; metformin; terbutaline; verapamil; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** 72 hours;

**ALZET Comments:** Animal info (female, lactating, Bcrp KO or WT FVB); functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer.

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**Agents:** acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopyramide phosphate salt, labeltalol hydrochloride, nitrofurantoin + -propranolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cephapirin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, praziquantel, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide. **Vehicle:** DMSO; water; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** Not Stated;

**ALZET Comments:** animal info: lactating mice, postnatal age of 14 days; functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer.
**Agents:** Clindamycin HCl; Penicillin G  **Vehicle:** Sodium hydroxide; Water;  **Route:** SC;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 72 hours;

**ALZET Comments:** Pump model not stated; controls received mp w/water; dose-response; mp primed overnight in PSB; 2 doses of agent infused; agent infused separately; antibiotic

**Agents:** Clindamycin; Methylprednisolone; Gentamicin; Naloxone  **Vehicle:** Saline;  **Route:** SC;  **Species:** Rat;  **Pump:** 2001;  **Duration:** 7 days;

**ALZET Comments:** controls received mp w/saline; toxicology; multiple pumps per animal (3); comparison of bolus injections vs. mp infusion; antibiotic

Interferons (2010-Present)

**Agents:** Interferon, alpha  **Vehicle:** PBS;  **Route:** CSF/CNS (left ventricle);  **Species:** Mice;  **Pump:** 1002;  **Duration:** 14 days;

**ALZET Comments:** Dose (250 IU/day); Controls received mp w/ vehicle; animal info (male 8–12-week-old mice); post op. care (buprenorphine); Interferon, alpha aka IFN-α; ALZET brain infusion kit 3 used; Brain coordinates (0.2 mm anterior and 0.9 mm lateral to bregma); dependence;

**Agents:** Interferon, alpha  **Vehicle:** PBS;  **Route:** SC;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 14 days;

**ALZET Comments:** Dose (0.25 ul/h); Controls received mp w/ vehicle; animal info (NZB/W F1 female mice, 20 weeks old); behavioral testing (Forced Swim Test, Rotarod Test, Locomotor Activity Monitoring Test, Elevated Plus Maze Test); Interferon, alpha aka IFNa; immunology;

**Agents:** Interferon, gamma; Albumin, porcine serum  **Vehicle:** Not stated;  **Route:** Intrauterine (uterine horn);  **Species:** Pig;  **Pump:** 2ML1;  **Duration:** 5 days;

**ALZET Comments:** Dose (240 ul/day); animal info (Sexually mature gilts); Interferon, gamma aka IFNG; Porcine serum albumin aka PSA; dependence;

**Agents:** Interleukin-1 beta; Interleukin-6; Interleukin-10; Interleukin-12; Interleukin-23; Interferon, gamma; Tumor Necrosis Factor, alpha; Interleukin-1 beta, anti; Transforming Growth Factor-B1, anti  **Vehicle:** PBS;  **Route:** SC;  **Species:** Mice;  **Pump:** 1007D;  **Duration:** 10 Days;

**ALZET Comments:** Dose (IL-1b (83μg/ml); IL-6 (83μg/ml); IL-10 (166μg/ml); IL-12 (83μg/ml); IL-17 (125μg/ml); IFNγ (83μg/ml); TNFα (166μg/ml); anti-TGF-b1 (166μg/ml); anti-IL-1b (150μg/ml); Controls received mp w/ vehicle; animal info (Eight- to twelve-week-old female C57BL/6 mice); Immunology (“evaluate the suitability of osmotic pumps as a model for biofilms in implant associated infections, we implanted osmotic pumps pre-colonized with bioluminescent Staphylococcus aureus”);

Q7192: A. Kimura, et al. Protective Roles of Interferon-gamma in Cardiac Hypertrophy Induced by Sustained Pressure Overload. J Am Heart Assoc 2018;7(6);
**Agents:** Interferon, gamma  **Vehicle:** Not Stated;  **Route:** SC;  **Species:** Mice;  **Pump:** 1007D;  **Duration:** 7 days;

**ALZET Comments:** Dose (15 uM/d); animal info (8-10 week old, male, BALB/c); cardiovascular;
Q4560: L. Pereira, et al. IFN gamma regulates proliferation and neuronal differentiation by STAT1 in adult SVZ niche. Frontiers in Cellular Neuroscience 2015;9(U1-U10
Agents: Interferon, gamma Vehicle: Saline; Route: CSF/CNS (third ventricle); Species: Mice; Pump: 1007D; Duration: 7 days; ALZET Comments: Controls received mp w/ vehicle; animal info (male, STAT2 KO or 12956/Svev); immunochemistry; cross-reactivity.

Agents: Interferon-a, murine; polyinosinic/polycytidylic acid Vehicle: PBS; Route: CSF/CNS; Species: Mice; Pump: 1002; Duration: 14 days; ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6J); behavioral testing (open field test; tail suspension test; behavioral testing); polyinosinic/polycytidylic acid is a toll-like receptor-3 agonist; Dose (mIFN-a 250 IU/day; poly(I:C) 1 ug/day);

Agents: U0126; serum protein, ovine; interferon tau, recombinant ovine Vehicle: DMSO; Route: Intrauterine (uterine horn); Species: Sheep (ewe); Pump: 2ML1; Duration: 6 days; ALZET Comments: Controls received mp w/ vehicle; animal info (female, Suffolk Ovis aries); 3% DMSO used; tissue perfusion (uterine horn); cyanoacrylate adhesive; used cyanoacrylate glue to anchor pump; interferon tau aka IFNT;

Agents: Interferon, gamma Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days; ALZET Comments: Controls received mp w/ vehicle; animal info (prf -/- or WT, lymphocytic choriomeningitis virus infected); functionality of mp verified by serum levels; immunology; murine model of hemophagocytic lymphohistiocytosis;

Agents: Cortisol; PF915275; meloxicam; interferon, tau, recomb. ovine Vehicle: Ethanol; Route: Intrauterine (uterine horn); Species: Sheep (ewe); Pump: Not Stated; ALZET Comments: Controls received mp w/ vehicle; animal info (mature, rambouillet, female, ewe); 2% ethanol used; vinyl catheter used (0007760); “Our previous studies found that infusion of that amount of IFNT in the uterine lumen each day mimics effects of the conceptus on endometrial expression of hormone receptors and IFNT-stimulated genes during early pregnancy in ewes” pg 932

Agents: interferon-tau, recombinant ovine Vehicle: BSA; Route: IV (jugular, intrauterine); Species: ewe; Pump: 2001D, 1003D; Duration: 1 day, 3 day; ALZET Comments: controls received mp w/ vehicle; functionality of mp verified by serum antiviral activity; pumps were anchored in the s.c. space with cyanoacrylate glue; 200 ug/day (uterine vein); 200 ug/day (jugular vein)

Agents: Interferon, alpha; interferon, gamma Vehicle: PBS; BSA; Route: SC; Species: Mice; Pump: 2006; Duration: 16 weeks; ALZET Comments: Animal info (13 wks old, female, B/W); pumps replaced after 8 weeks; long-term study; stability verified after 8 weeks; “residue IFNs from the pumps at the end of treatment were tested on IFN and IFN responsive cell lines and demonstrated that the in vivo conditions in the pump did not affect bioactivity of both IFNs (data not shown)” pg 63

Agents: Interferon, gamma Vehicle: PBS; BSA; Route: Not Stated; Species: Rat; Pump: 1002; Duration: 2 weeks; ALZET Comments: Controls received mp w/ vehicle; animal info (Sprague Dawley)

**Agents:** Interferon, gamma, recomb. mouse  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1007D;  
**Duration:** 7 days;  
**ALZET Comments:** Animal info (BALB/c, male, 8-10 wks old)


**Agents:** Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2a, ovine serum; PGI2, ovine serum  
**Vehicle:** Ethanol; saline;  
**Route:** Intrauterine (uterine horn);  
**Species:** Sheep (ewe);  
**Pump:** 2ML1;  
**Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Mature Rambouillet); good methods (pg 2); vinyl tubing used (0007760); 2% ethanol used; enzyme inhibitor (prostaglandin synthase two); tissue perfusion (intrauterine)


**Agents:** Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2a, ovine serum; PGI2, ovine serum  
**Vehicle:** Ethanol; saline;  
**Route:** Intrauterine (uterine horn);  
**Species:** Sheep (ewe);  
**Pump:** 2ML1;  
**Duration:** 5 days;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Mature Rambouillet); tissue perfusion (intrauterine); multiple pumps used (2); enzyme inhibitor (prostaglandin synthase two)


**Agents:** Interferon-gamma  
**Vehicle:** PBS; BSA;  
**Route:** Not Stated;  
**Species:** Mice (transgenic);  
**Pump:** Not Stated;  
**Duration:** 4 weeks;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (wt B6, IFN-gamma transgenic, 2 mo old)


**Agents:** Interferon, gamma  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 12 days;  
**ALZET Comments:** Animal info (F1, Tbet -/-)


**Agents:** Meloxicam; interferon, recomb. ovina, tau  
**Vehicle:** Ethanol; Saline;  
**Route:** Intrauterine (uterine horn);  
**Species:** Sheep (ewe);  
**Pump:** 2ML1;  
**Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (ewе, mature, Rambouillet); cyanoacrylate adhesive; enzyme inhibitor (prostaglandin synthase (PTGS)); vinyl catheter used (0007760); "The Alzet pump was then affixed to the mesometrial ligament between the uterine horn and oviduct by using cyanoacrylate glue... and then secured by sewing the oviduct to the perimetrium of the uterine horn, using 0 coated polyglactin suture." pg 1120; 2% ethanol used; photo of pump and catheter placement, fig. 1; "Intrauterine infusion of that amount of IFNT mimics effects of the conceptus on endometrial expression of hormone receptors and IFNT-stimulated genes during early pregnancy in ewes." pg 1120


**Agents:** Interferon, gamma  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 12 days;  
**ALZET Comments:** Animal info (F1, Tbet -/-)


**Agents:** Antibody, anti IL-18; IL-18, recomb. rat; interferon, gamma, recomb. rat; antibody, anti interferon, gamma; IL-18 receptor antagonist; interferon, gamma, receptor antagonist  
**Vehicle:** Saline;  
**Route:** CSF/CNS;  
**Species:** Rat;  
**Pump:** 1007D;  
**Duration:** 1 week;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Sprague Dawley, 7 wks old); ALZET brain infusion kit 1 used
Interleukin-2 (2001-Present)


**Agents**: Interleukin-2  
**Vehicle**: Not Stated  
**Route**: IP  
**Species**: Rat  
**Pump**: 2002  
**Duration**: 5 days

**ALZET Comments**: Dose (0.05, 0.10, or 0.20 ng/ml); dose-response (p. 3); animal info (Timed-pregnant Sprague Dawley rats); 98 mmHg - 111 mmHg; Interleukin-2 aka IL-2; dependence;

Q10183: S. Hirose, et al. Type 2 Innate Lymphoid Cells Induce CNS Demyelination in an HSV-IL-2 Mouse Model of Multiple Sclerosis. iScience 2020;23(10):101549

**Agents**: Interleukin-2  
**Vehicle**: Not Stated  
**Route**: CSF/CNS  
**Species**: Mice  
**Pump**: Not Stated  
**Duration**: Not Stated

**ALZET Comments**: animal info: wild-type (WT) HSV-1 Interleukin -2 aka (IL-2) peptides; immunology;


**Agents**: Interleukin-1 beta; Interleukin-6; Interleukin-10; Interleukin-12; Interleukin-23; Interferon, gamma; Tumor Necrosis Factor, alpha; Interleukin-1 beta, anti; Transforming Growth Factor-B1, anti  
**Vehicle**: PBS  
**Route**: SC  
**Species**: Mice  
**Pump**: 1007D  
**Duration**: 10 Days

**ALZET Comments**: Dose (IL-1b (83μg/ml); IL-6 (83μg/ml); IL-10 (166μg/ml); IL-12 (83μg/ml); IL-17 (125μg/ml); IL-23 (166μg/ml); IFNγ (83μg/ml); TNFa (166μg/ml); anti-TGF-b1 (166μg/ml); anti-IL-1b (150μg/ml)); Controls received mp w/ vehicle; animal info (Eight- to twelve-week-old female C57BL/6 mice); Immunology ("evaluate the suitability of osmotic pumps as a model for biofilms in implant associated infections, we implanted osmotic pumps pre-colonized with bioluminescent Staphylococcus aureus");


**Agents**: Interleukin-25, recombinant mouse  
**Vehicle**: Not Stated  
**Route**: SC  
**Species**: Mice (transgenic)  
**Pump**: Not Stated  
**Duration**: 4 weeks

**ALZET Comments**: Controls received mp w/ control medium; animal info (Apoe -/-, 9-10 or 21 weeks old); cardiovascular; brain tissue distribution; pumps removed after 4 weeks in young mice;


**Agents**: Interleukin-2, murine; antibody, anti-interleukin-2  
**Vehicle**: PBS  
**Route**: SC  
**Species**: Mice (transgenic)  
**Pump**: Not Stated  
**Duration**: 10 days

**ALZET Comments**: Controls received mp w/ vehicle; animal info (HLA-DR3); comparison of injection vs mp; immunology;


**Agents**: Interleukin-2  
**Vehicle**: PBS  
**Route**: CSF/CNS  
**Species**: Mice  
**Pump**: Not Stated  
**Duration**: 2 weeks

**ALZET Comments**: Controls received mp w/ Interleukin 2 without HSV-1 infection; animal info (6 weeks) ; ALZET brain infusion kit 1 used; neurodegenerative (demyelination); Therapeutic indication (CNS demyelination; Herpes simplex virus 1; HSV); Dose (1 ug/24 h);


**Agents**: Interleukin-2, human  
**Vehicle**: Not Stated  
**Route**: SC  
**Species**: Mice (nude)  
**Pump**: Not Stated  
**Duration**: Not Stated

**ALZET Comments**: Animal info (6 wks old, male, Nu/J); 7-day pumps used

Agents: Interleukin-2; Interleukin-7; Interleukin-15 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2001; Duration: 7 days;

ALZET Comments: Controls received mp w/ PBS; animal info (6-12 wks old, gender, age matched); immunology


Agents: Interleukin-2, recomb. Vehicle: PBS; Albumin, human; Route: SC; Species: Mice (nude); Pump: Not Stated; Duration: 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (8 wks old, female, Balb/C, nu/nu); cancer (melanoma); "These pumps are easily loaded and then placed s.c., minimizing discomfort and handling of the mice as needed for repeated IL2 administration by injection." pg 2777


Agents: Interleukin-2 Vehicle: Saline; Route: CSF/CNS (striatum); Species: Rat; Pump: 2002; Duration: 12 days;

ALZET Comments: Controls received mp w/ no treatment; cancer (neuroblastoma); peptides; animal info (female, Sprague Dawley); neurodegenerative (Parkinson’s Disease); behavioral testing (rotational behavior and locomotor; axial, limb, and orolingual movements)


Agents: Interleukin-2, recomb. human Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2001; Duration: 4 days;

ALZET Comments: Controls received mp w/ no treatment; cancer (neuroblastoma); peptides; animal info (female, A/J, ICR, 6-8 weeks old); gene therapy


Agents: Interleukin-15, recomb. human; Interleukin-2, recomb. human Vehicle: PBS; albumin, human; Route: SC; Species: Mice (SCID); Pump: 1007D; Duration: 10 days;

ALZET Comments: Controls received mp w/ vehicle; immunology; animal info (female, CB17, hu-PBL-SCID, 8-12 weeks old)


Agents: Interleukin-2, recomb. human Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2001; Duration: 7 days;

ALZET Comments: Controls received mp w/ PBS; no stress (see pg.4841); cancer (neuroblastoma); peptides


Agents: Colony-stimulating factor, GM; Interleukin-2; Interleukin-12 Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2004; Duration: 4 weeks;

ALZET Comments: Cancer (gliosarcoma); GM-CSF was infused alone or with cytokines


Agents: Interleukin-2 Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: Not Stated; Duration: 7 days;

ALZET Comments: Controls received mp w/ saline; peptides; examined anhedonic effects of IL-2


Agents: Interleukin-2 Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: 1007D; Duration: 7 days;

ALZET Comments: controls received no IL-2 treatment; immunology; peptides
Muramyl Dipeptide


ALZET Comments: Endotoxin, LPS; muramyl dipeptide; Saline, sterile; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; functionality of mp verified by weight; peptides; animal info (male, Sprague-Dawley, 250-350 grams).


ALZET Comments: Muramyl dipeptide; Saline; SC; mice; 7 days; comparison of ip injec. vs sc infusion; immunotherapy; peptides.

PMEA


ALZET Comments: PMEA; Mice; no duration posted; comparison of ip injections vs. mp; teratology; antiviral agent.

R-95288


ALZET Comments: R-95288; Saline; IP; SC; mice (SCID); 2002; no duration posted; controls received mp w/saline; antisense; mice were transplanted w/human peripheral blood leukocytes; R-95288 protects human chimeric mice against HIV-1 infection; AIDS.

SID 791


ALZET Comments: SID 791; Saline, sterile; SC; Mice (SCID); mice; 2002; no duration posted; functionality of mp verified by plasma levels; dose-response; comparison of sc injections vs. mp; immunology; SID 791 is a bicyclam which inhibits HIV replication in vivo; human fetal liver & thymus transplanted into SCID mice.