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

1. 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 (veina 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 veina cava; aprotinin infused into the cervical vein; SBTI & aprotinin are plasma kallikrein inhibitors from soybeans

Agents: Amyloid protein, beta; Aprotinin; Leupeptin; Vehicle: HEPES; 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

2. Azidothymidine

ALZET Comments: Azidothymidine; Sodium hydroxide; SC; monkey (pregnant); 2ML4; 28 days; 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.

ALZET Comments: Azidothymidine; Propylene glycol; Water; SC; mice; 2001; 5 days; 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.

**ALZET Comments:** Azidothymidine; mice (pregnant); 2001; 21 days; Pumps replaced after each week to achieve 3 weeks duration; immunology; teratology; oral delivery of AZT resulted in highly variable plasma levels; antiretroviral drug.


**ALZET Comments:** Azidothymidine; IA (carotid); Rat; 2001; 3-7 days; Dose-response; blood levels; comparison of IV injections vs. mp; good methods; antiviral; alkaline pH of 11 increased solubility and stability of AZT; antiretroviral drug.

### 3. Clindamycin


**ALZET Comments:** Acyclovir; cimetidine; clindamycin; metformin; terbutaline; verapamil; IP; Mice; 1003D; 72 hours; Animal info (female, lactating, Bcrp KO or WT FVB); functionality of mp verified by plasma and milk concentrations; no stress "All mice survived the surgical procedure and appeared to be lactating normally, and all pups thrived throughout the course of the experiment." (see pg. 3343);


**ALZET Comments:** acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopropyldiamine phosphate salt, labetalol hydrochloride, nitrofurantoin +propanolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cephepin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chromaphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide.; DMSO; water; IP; mice; 1003D; 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.


**ALZET Comments:** Clindamycin HCl; Penicillin G; Sodium hydroxide; Water; SC; mice; 72 hours; 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.


**ALZET Comments:** Clindamycin; Methylprednisolone; Gentamicin; Naloxone; Saline; SC; Rat; 2001; 7 days; controls received mp w/saline; toxicology; multiple pumps per animal (3); comparison of bolus injections vs. mp infusion; antibiotic.

### 4. Interferons


**Agents:** Interleukin-1 beta; Interleukin-6; Interleukin-10; Interleukin-12; Interleukin-17; Interleukin-23; Interferon, gamma; Tumor Necrosis Factor, alpha; Interleukin-1 beta, anti; Transforming Growth Factor-B1, anti **Vehicle:** Saline; **Route:** SC

**Species:** Mice; **Pump:** 1007D; **Duration:** Not stated;
### ALZET Comments

Dose (IL-1β- 83 μg/ml, IL-6-83 μg/ml, IL-10-166 μg/ml, IL-12-83 μg/ml, IL-17-125 μg/ml, IL-23- 126 μg/ml, IFN-γ-83 μg/ml, TNFα-166 μg/ml, anti-TGF-B1-166 μg/ml, or anti-IL-1β-150 μg/ml); Controls received mp w/ vehicle; animal info (8-12 weeks old, Female, C57BL/6); immunology;


**Agents:** Interleukin-1 beta; Interleukin-6; Interleukin-10; Interleukin-12; Interleukin-17; 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); 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”);


**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 129S6/SvEv); immunology;


**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; forced swimming test); polyinosinic/polycytidylic acid is a toll-like receptor-3 agonist; Dose (mIFN-a 250 IU/day; poly(I:C) 1 ug/day);

**5. Interleukin-2**

### Q8018: R. Gutierrez Jauregui, et al. IL-1beta Promotes Staphylococcus aureus Biofilms on Implants in vivo. Front Immunol 2019;10(1082)

**Agents:** Interleukin-1 beta; Interleukin-6; Interleukin-10; Interleukin-12; Interleukin-17; Interleukin-23; Interferon, gamma; Tumor Necrosis Factor, alpha; Interleukin-1 beta, anti; Transforming Growth Factor-B1, anti

**Vehicle:** Saline; **Route:** SC;

**Species:** Mice; **Pump:** 1007D; **Duration:** Not stated;

**ALZET Comments:** Dose (IL-1B- 83 ug/ml, IL-6-83 ug/ml, IL-10-166 ug/ml, IL-12-83 ug/ml, IL-17-125 ug/ml, IL-23- 126 ug/ml, IFNγ-83 ug/ml, TNFα-166 ug/ml, anti-TGF-B1-166 ug/ml, or anti-IL-1B-150 ug/ml); Controls received mp w/ vehicle; animal info (8-12 weeks old, Female, C57BL/6); immunology;


**Agents:** Interleukin-1 beta; Interleukin-6; Interleukin-10; Interleukin-12; Interleukin-17; 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); TNFα (166μg/ml); anti-TGF-β1 (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; Pump: 1004; 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; SC; 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);

6. 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.

7. PMEA


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

8. 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.

9. 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.