References on the Administration of Cytokines
Using ALZET® Osmotic Pumps

1. Granulocyte-Macrophage Colony Stimulating Factor

Q3634: F. Zhu, et al. MINOCYCLINE ALLEVIATES BEHAVIORAL DEFICITS AND INHIBITS MICROGIAL ACTIVATION INDUCED BY INTRAHIPPOCAMPAL ADMINISTRATION OF GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR IN ADULT RATS. Neuroscience 2014;266(275-281
ALZET Comments: Colony stimulating factor, GM, recombinant rat; Saline; CSF/CNS (hippocampus); Rat; 1007D; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 280-320g); ALZET brain infusion kit 3 used; Multiple pumps per animal (2); behavioral testing (locomotor activity; social interaction test; PPI); used dental acrylic resin; schizophrenia;

ALZET Comments: Colony-stimulating factor, GM; SC; Rat; 2004; 28 days; Animal info (male, inbred, Fischer 344, 10-12 wks old); comparison of "all in-vivo therapy" vs mp; cancer.

ALZET Comments: Colony-stimulating factor, GM, murine; interleukin-12; PBS; SC; Rat; 28 days; Controls received mp w/ vehicle; dose-response (fig 1); no stress (see pg. 1209); cancer (upper aerodigestive tract carcinoma); peptides; animal info (Fischer 344, 125-150 g); good methods; "This latter method (mp) has several advantages. First, the use of minipumps obviates the cumbersome need to transfect tumor cells and completely characterize their cytokine repertoires. Second, it allows for independent and rigorous control over the kinetics of administration of cytokine and antigen dosages. Third, it may generate less controversy than those techniques requiring "gene therapy" IRB approval." (p. 1213).

ALZET Comments: Colony-stimulating factor, GM, murine; interleukin-12; PBS; SC; Rat; 14 days; Controls received mp w/ vehicle or no treatment; cancer (RT-2 glioma); peptides; animal info (Fischer, 200-350 grams, SC and ICV tumors); "continuously infused cytokine using an osmotic mini pump to...avoid the side effects of a single large dose of cytokine and one with a concept similar to that of gene-therapy." (p. 874).

ALZET Comments: Colony-stimulating factor, GM; interleukin-2; interleukin-12; SC; Rat; 2004; 4 weeks; Cancer (gliosarcoma); GM-CSF was infused alone or with cytokines.

ALZET Comments: Colony-stimulating factor, GM, recomb. mouse; SC; Rat; 2004; 4 weeks; Cancer; animal info (male, Fischer 344, 10-12 wks old).

ALZET Comments: Colony-stimulating factor, GM; PBS; BSA; SC (tumor vaccine injection site); Mice; 1002; 14 days; Controls received mp w/ PBS; immunology; GM-CSF is recombinant murine; tissue perfusion.
ALZET®
Bibliography

ALZET Comments: Interleukin-4; Colony-stimulating factor, GM; Saline; SC; mice; 1007D; 7 days; controls received mp w/ vehicle; functionality of mp verified by serum levels via ELISA; immunology; peptides; recombinant cytokines; agents administered singly or concomitantly.

ALZET Comments: Colony-stimulating factor, GM;; Saline, isotonic;; SC;; Rat;; 2004;; 28 days;; Controls received mp w/ saline; does-response; cancer; immunology; peptides; recomb. murine colony-stimulating factor, GM used.

P4130: M. Roelofs, et al. Transforming growth factor b1 involvement in the conversion of fibroblasts to smooth muscle cells in the rabbit bladder serosa. Histochemical J 1998;30(393-404
ALZET Comments: Transforming growth factor-B1; Epidermal growth factor; Fibroblast growth factor, basic; Granulocyte-colony stimulating factor; Platelet-derived growth factor; Colony-stimulating factor, GM; PBS; bladder wall; rabbit; 2ML2; 2ML4; no duration posted; controls received mp w/PBS; no stress (see pg. 395); "a minipump filled with Evans Blue solution was used to determine area of growth factor delivery"; peptides; tissue perfusion (bladder wall).

ALZET Comments: MegaKaryocyte growth development factor, PEG-recomb. human; colony-stimulating factor, GM, recomb. murine; PBS; BSA; SC; Mice; 2002; 18 days; Controls received mp w/ vehicle; dose-response (fig.1); immunology; "To avoid potential scheduling problems in these experiments we have delivered rmGM-CSF by continuous s.c. infusion" (p.44).

ALZET Comments: Colony-stimulating factor, GM; Antibody, monoclonal anti-TNFa;; Saline, isotonic;; IP;; Mice (nude);; 4 weeks;; controls received mp w/vehicle; functionality of mp verified by plasma levels; immunology; peptides;.

ALZET Comments: HP5b; Interleukin-1; Colony-stimulating factor, GM; PBS; Mercaptoethanol, 2-; NaN3; SC; mice; 1007D; 3, 7, 14 days; cancer; immunology; peptides; HP5b is a hemoregulatory peptide.

ALZET Comments: Megakaryocyte growth development factor, PEG-recomb. human; colony-stimulating factor, G, recomb. human; colony-stimulating factor, GM, recomb. mouse; PBS; BSA; SC; Mice; 1007D; 2002; 7, 9, 16-18 days; Controls received mp w/ vehicle; replacement therapy (splenectomy); no stress (see pg. 367); cardiovascular; immunology; animal info (female, BDNF1, 8-12 wks; male, C57BL x DBA2BDNF1, 12-20 wks old); transplantation; "mice were healthy and had pumps still in position and in good condition at the end of the mobilization protocol." (p. 367).

ALZET Comments: Colony-stimulating factor, GM; Interleukin-1, alpha; PBS; SC; mice; no duration posted; comparison of injections vs. mp; cancer; immunology.

ALZET Comments: Colony-stimulating factor, GM; Tumor necrosis factor; Platelet-derived growth factor; Saline; SC; Rat; 2001; 2-7 days; controls received mp w/ TNF, PDGF or carrier solution; functionality of mp verified upon removal; pump infused GM-CSF to study formation of granulation tissue at infusion site; recomb. murine TNF used.

ALZET Comments: Colony-stimulating factor, GM, murine; tumor necrosis factor-a, recomb. mouse; interleukin-1a, recomb. human; PBS; IP; Mice (nude); 2002; 10 days; Controls received mp w/ normal saline; immunology; peptides; animal info (BALB/c, athymic, nu/nu, euthymic, 2-4 wks old).

ALZET Comments: Interleukin-1, alpha; Colony-stimulating factor, GM; PBS; SC; mice; 2002; 14 days; controls received mp w/PBS; immunology; peptides; agents given singly, together, or sequentially; "...for a 14-day administration schedule, continuous subcutaneous administration is favorable." (pg. 1618).

ALZET Comments: Erythropoietin; Interleukin-3; Colony-stimulating factor, GM; PBS; Glycerol; SC; mice; 2002; 14 days; immunology; peptides.

ALZET Comments: Interleukin-3; Colony-stimulating factor, GM; Erythropoietin; PBS; Glycerol; LPS, e. coli; SC; mice; 2002; no duration posted; controls received mp with vehicles +/- LPS; immunology; peptides; recomb. mouse GM-CSF & IL-3 used; recomb. human EPO used.

ALZET Comments: Colony-stimulating factor, GM; SC; monkey; 2001; 7 days; dose-response; cancer/immunology; no stress; peptides.

ALZET Comments: Interleukin-3, human; colony-stimulating factor, GM, human; SC; Mice; mice (SCID); 4-5 weeks; 15 days; Controls received mp w/ saline; peptides; immunology.

ALZET Comments: Colony-stimulating factor, GM; Endotoxin, E. coli; Saline; IP; mice; 2001; 6 days; controls received mp w/ LPS free isotonic saline; 2 exp.; comparison of ip injections vs. mp infusion; functionality of mp verified.

ALZET Comments: Colony-stimulating factor, GM; Dextrose; SC; monkey; 2ML1; 1 week; half-life; 1 of 3 experiments using mp.
2. Macrophage Colony Stimulating Factor


**ALZET Comments:** Colony-stimulating factor, M; SC; Mice; 28 days; Animal info (male, C57BL/6 J, 7 wks old); comparison of SC injections vs mp; lack of cortical response in both daily injection and pump studies, pg 550.


**ALZET Comments:** Colony-stimulating factor, M; Interleukin-2; Granulocyte-colony stimulating factor; SC; mice; no duration posted; controls received mp with PBS; cancer; immunology; peptides; M-CSF + IL-2 given concomitantly provided best antitumor protection; recomb. IL-2 used; human G-CSF used.

3. Erythropoietin

**Q4880:** E. H. Sanchez-Mendoza, *et al.* Implantation of Miniosmotic Pumps and Delivery of Tract Tracers to Study Brain Reorganization in Pathophysiological Conditions. *Journal of Visualized Experiments* 2016;107(1-9)

**ALZET Comments:** Erythropoietin, recombinant human; CSF/CNS; Mice; 30 days; Controls received mp w/ vehicle; animal info (C57BL6); good methods (Jove Video; picture of pump and implantation pg. 4); ischemia (cerebral); post op. care (Carprofen 4 mg/kg); behavioral testing (rotarod test; hand grip strength); cyanoacrylate adhesive; “In this work we have shown the method of implantation of minipumps with a cannula connected to the skull in order to deliver the plasticity promoting protein rhEpo directly into the ventricle, thus circumventing the BBB.” pg 8; Cannula placement verified via histologic analysis “The are no evident severe tissue alterations based on Nissl staining as compared to the corresponding contralateral area”;

**Q6648:** M. Rauner, *et al.* Increased EPO Levels Are Associated With Bone Loss in Mice Lacking PHD2 in EPO-Producing Cells. *J Bone Miner Res* 2016;31(10):1877-1887

**ALZET Comments:** Erythropoietin, recombinant human; SC; Mice (knockout); Mice (transgenic); 30 days; Dose (3 U EPO/day or 10 U EPO/day); Controls received mp w/ vehicle; animal info (8-12 week old WT and Osx:cre-PHD2f/f and Vav:cre-PHD2f/f mice);

**Q3130:** G. B. Wang, *et al.* The AKT/mTOR pathway mediates neuronal protective effects of erythropoietin in sepsis. *MOLECULAR AND CELLULAR BIOCHEMISTRY* 2014;385(1-2):125-132

**ALZET Comments:** Erythropoietin, human recombinant; PBS; BSA; SC; Rat; 1 week; Controls received mp w/ vehicle or sham surgery; animal info (Sprague Dawley, 120 days old, 240-280g); behavioral testing (open field exploration, inhibitory avoidance, Morris water maze);

**Q3518:** M. S. Jeffers, *et al.* Epidermal Growth Factor and Erythropoietin Infusion Accelerate Functional Recovery in Combination With Rehabilitation. *Stroke* 2014;45(185-+

**ALZET Comments:** Epidermal Growth Factor; erythropoietin; CSF, artificial; CSF/CNS; Rat; 2001; 14 days; Animal info (male, Sprague Dawley); pumps replaced every 7 days; ischemia (cerebral); behavioral testing (staircase test); pumps removed 7 days after serial implantation;


**ALZET Comments:** Epidermal growth factor; erythropoietin; CSF, artificial; CSF/CNS; Mice; 1007D; 14 days; Animal info (male, C57BL6, 9-11 weeks old); EGF-PGF pumps replaced after 7 days with pump filled with ETO; ALZET brain infusion kit 3 used; comparison of epicortical composite vs mp; stress/adverse reaction: ”Unlike the ICV catheter/minipump, which causes significant tissue damage, the epicortical composite provides a minimal invasiveness and no tissue damage.”(see pg.9); immunology; Pumps implanted 4 days after stroke; BIK implanted same day as stroke;
Q2546: J. Unden, et al. Post-ischemic continuous infusion of erythropoietin enhances recovery of lost memory function after global cerebral ischemia in the rat. BMC NEUROSCIENCE 2013;14():U1-U8
ALZET Comments: Erythropoietin; saline; IV (jugular); rat; 2001D; 1003D; 72 hours; control animals received mp w/ vehicle; animal info (Wistar, male, 300-350 g); silastic tubing used.

ALZET Comments: Erythropoietin; saline; IV; rat; 2ML4; animal info (athymic, male, 10-15 wks old); pump functionality measured via residual volume.

ALZET Comments: Erythropoietin; NaCl; CSF/CNS; mice; 4 weeks; controls received mp w/ vehicle; animal info (C57Bl6/j, male, 23-25 g, 8-10 wks old); ALZET brain infusion kit 3 used; ischemia (focal cerebral).

ALZET Comments: Epidermal growth factor, recomb. human; erythropoietin; cyclosporine A; CSF/CNS; SC; mice (NOD/SCID); 1007D; animal info (male, C57/BL6, 8-10 wks old); pumps replaced after 7 days; ALZET brain infusion kit 3 used.

ALZET Comments: Erythropoietin, asialo-; saline, sterile; SC; rat; 2001; 4 days; controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-275 g).

ALZET Comments: Erythropoietin, human, recomb.; antibody, anti-EPO; saline; CSF/CNS; rat; 6 days; 24 hours; controls received mp w/ rat serum albumin, or control mouse IgG; animal info (male, Fischer 344, 10-12 wks old, 200-250 g, SLC).

ALZET Comments: Erythropoietin; albumin, rat serum; saline; CSF/CNS; rat; 2001; 1 week; controls received mp w/ vehicle; animal info (Sprague Dawley, 220-225 g).

ALZET Comments: Granulocyte-colony stimulating factor, human, recomb.; erythropoietin, human, recomb.; IP; rat; 2ML1; 48 hours; controls received mp w/ saline; animal info (male, CD, 250 g, splenectomy).

ALZET Comments: Erythropoietin, human, recomb.; saline; albumin, rat serum; CSF/CNS; rat; 2001; 7 days; controls received mp w/ vehicle; animal info (male, 190-210 g).
**ALZET Comments:** Erythropoietin; Saline; IV (femoral); Rat; 2ML1; 3 days; Controls received mp w/ vehicle; animal info (male, Long-Evans, 280-330 g., MCAO).

**ALZET Comments:** Epidermal growth factor, recomb. human; fibroblast growth factor-2, recomb. human; insulin-like growth factor I, recomb. human; erythropoietin, recomb. rat; brain-derived neurotrophic factor, recomb. human; DDL4, recomb. mouse; CSF/CNS; Rat; 1003D; 3 days; Ischemia; animal info (male, Wistar, 8wks old, 280-300 g.); bilateral infusion.

**ALZET Comments:** Granulocyte-colony stimulating factor-, recomb. human; erythropoietin; IP; Rat; 2ML1; 7 days; Controls received mp w/ saline; peptides; animal info (male, Sprague Dawley, 300 -350 g., splenectomy); "We used implantable osmotic minipumps to guarantee continuous systemic delivery of the tested cytokines over the first even days upon intraperitoneal deposition." pg. 353.

**ALZET Comments:** Erythropoietin receptor, soluble; Phosphate buffer; CSF/CNS; Mice; 1003D; 3 days; Controls received mp w/ vehicle; ALZET brain infusion kit used; animal info (male C57/BL6, 3 months old, hypoxia).

**ALZET Comments:** Erythropoietin; epidermal growth factor; CSF, artificial; CSF/CNS; Rat; 2001; 7, 14 days; Controls received mp w/ vehicle; peptides; animal info (male, Long-Evans, 90-110 days old); ischemia (cerebral); behavioral testing (forelimb asymmetry, forelimb inhibition (swimming), reaching); some animals received 7 days EGF.

**ALZET Comments:** Erythropoietin; Ear (round window); Guinea pig; 1007D; 1 week; Controls received mp w/ saline; replacement therapy (noise-induced hearing impairment); comparison of acute admin. vs. mp; peptides; animal info (male, Dunkin-Hartley); tissue perfusion (round window); mp primed 6 hours in 37 Celsius saline; correct catheter placement confirmed.

4. Interferon

**ALZET Comments:** Interferon, gamma; SC; Mice; 1007D; 7 days; 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
**ALZET Comments:** Interferon, gamma; Saline; CSF/CNS (third ventricle); Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, STAT2 KO or 129S6/SvEv); immunology;
ALZET Comments: Interferon-a, murine; polyinosinic/polyctydlylic acid; PBS; CSF/CNS; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (C57BL6J); behavioral testing (open field test; tail suspension test; forced swimming test); polyinosinic/polyctydlylic acid is a toll-like receptor-3 agonist; Dose (mIFN-a 250 IU/day; poly(I:C) 1 ug/day));

ALZET Comments: U0126; serum protein, ovine; interferon tau, recombinant ovine; DMSO; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 6 days; 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;

ALZET Comments: Interferon, gamma; Saline; SC; Mice; 7 days; 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;

ALZET Comments: Cortisol; PF915275; meloxicam; interferon, tau, recombin. ovine; Ethanol; Intrauterine (uterine horn); Sheep (ewe); 2ML1; Control animals 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.

ALZET Comments: interferon-tau, recombinant ovine; BSA; IV (jugular, intrauterine); ewe; 2001D, 1003D; 1 day, 3 day; 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).

ALZET Comments: interferon, alpha; interferon, gamma; PBS; BSA; SC; Mice; 2006; 16 weeks; 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.

ALZET Comments: Interferon, gamma; PBS; BSA; Rat; 1002; 2 weeks; Controls received mp w/ vehicle; animal info (Sprague Dawley).

ALZET Comments: Interferon, gamma, recomb. mouse; SC; Mice; 1007D; 7 days; Animal info (BALB/c, male, 8-10 wks old).

ALZET Comments: Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2a, ovine serum; PGI2, ovine serum; Ethanol; saline; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 7 days; Controls received mp w/ vehicle; animal info
**ALZET Comments:** Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2a, ovine serum; PG12, ovine serum; Ethanol; saline; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 5 days; Controls received mp w/ vehicle; animal info (Mature Rambouillet); tissue perfusion (intrauterine); multiple pumps used (2); enzyme inhibitor (prostaglandin synthase two).

**ALZET Comments:** Interferon-gamma; PBS; BSA; Mice (transgenic); 4 weeks; Controls received mp w/ vehicle; animal info (wt B6, IFN-gamma transgenic, 2 mo old).

**ALZET Comments:** Interferon, gamma; SC; Mice; 2001; 7 days; Animal info (C57BL6/J).

**ALZET Comments:** Meloxicam; interferon, recomb. ovina, tau; Ethanol; saline; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 7 days; Controls received mp w/ vehicle; animal info (ewe, 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.

**ALZET Comments:** Interferon, gamma; SC; Mice; 12 days; Animal info (F1, Tbet -/-).

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

**ALZET Comments:** Interferon-tau, recomb, ovine; IV (uterine vein); Sheep (ewe); 2001D; 2ML1; 7 days; 24 hours; Controls received mp w/BSA or sham surgeries; animal info (white-faced, western range ewe); cyanoacrylate adhesive.

**ALZET Comments:** Interferon-beta, recomb. human; Mice; 2002; 14 days; Animal info (Hmox1 KO).
ALZET®
Bibliography

**ALZET Comments:** Interferon-alpha, recomb. human; Saline; SC; Mice; 2001; 6 days; Controls received mp w/ vehicle; comparison of SC injections vs. mp; half-life (p. 579) "relatively short"; peptides; animal info (male, ICR, 5 wks old); behavioral testing (locomotor activity).

**ALZET Comments:** Interferon-gamma, recomb. murine; SC; Mice; 7 days; Controls received mp w/ vehicle; cancer (tumorigenic hepatitis, liver); peptides; animal info (male, female, A/JCr).

**ALZET Comments:** Interferon-gamma; PBS; BSA; IP; Mice (transgenic); 2, 8, 12 weeks; Controls received mp w/ vehicle; comparison of IP injections vs. mp; peptides; animal info (12.4 KVI/EGFP tg; C57BL/6J; 4 months old); long-term study.

**ALZET Comments:** Interferon-gamma, mouse; PBS; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; no stress (see pg. 4286); immunology; peptides; animal info (C57BL/6).

**ALZET Comments:** Interferon-a A/D, recomb. human; Saline; SC; Mice; 8 days; Controls received mp w/ vehicle; animal info (C57BL/6, diet-induced obese).

**ALZET Comments:** Interferon, mouse; PBS; BSA; SC; Mice; 1002; 8-10 weeks; Controls received mp w/ vehicle; pumps replaced every 2 weeks; immunology.

**ALZET Comments:** Interferon-gamma, recomb. mouse; IP; Mice; 1002; 14 days; Controls received PBS; animal info (c57BL/6).

**ALZET Comments:** Interferon-gamma, recomb. mouse; SC; Mice; 4-6 days; Controls received mp w/ saline; replacement therapy (hepatectomy).

**ALZET Comments:** Interferon-gamma, murine; PBS; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; dose-response (fig. 7); no stress (pg. 1209); stress/adverse reaction: (see pg. 1205) "modest though not significant rise in peripheral white blood cell count" (pg. 1205); "IFN-gamma was overall well tolerated by both WT and Fancc -/- mice." (pg. 1208); hematology.

**ALZET Comments:** Interleukin-1, beta recombinant rat; Interferon-gamma, recombinant rat; Saline, physiological; albumin, human serum; CSF/CNS (intratumoral); Rat; 1003D; 48 hours; Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioma).


**ALZET Comments:** Interleukin-4; interferon-gamma; PBS; IP; Mice; 1007D; 7 days; Controls received mp w/ vehicle; comparison of IP injections vs. IP mp.


**ALZET Comments:** Interferon-gamma; Abdominal wall; mice; 2004; tissue perfusion (abdominal wall); immunology; peptides; pump implanted SC, catheter tube perfused matrigel plug in abdominal wall.


**ALZET Comments:** Interferon-alpha; Saline, sterile; SC; Mice; 2001; 7 days; Controls received mp w/ vehicle; immunology; peptides.


**ALZET Comments:** Influenza virus nucleoprotein-derived peptide; interferon, gamma; PBS; SC; Mice; 1003D; 3 days; animal info (C57BL/6 mice; 8–12 week old); comparison of SC injections vs mp; Flu peptide administered continuously by osmotic pump with IFN injection elicited CTL response, whereas Flu peptide administered by injection with IFN did not (Figs 3 and 4); Therapeutic indication (antigen immunization);.

### 5. Interleukin-1


**ALZET Comments:** Interleukin-1 beta; Saline, pyrogen-free; CSF/CNS (lateral ventricle); Rat; 1002; 14 days; Dose (10 ng/7uL/rat/day); Controls received mp w/ vehicle; animal info (Male Sprague Dawley rats (220–260 g)); behavioral testing (open field, elevated plus maze and sucrose preference); ALZET brain infusion kit used; Brain coordinates (AP=−1 mm, ML=+1.4 mm, DV=−1 mm); Therapeutic indication (depression);


**ALZET Comments:** Interleukin-1 beta; Saline; CSF/CNS (lateral ventricle); Rat; 1002; 14 days; Dose (10 ng/7uL/rat/day); animal info (Male Sprague Dawley rats (220–260 g)); behavioral testing (open field, elevated plus maze and sucrose preference); functionality of mp verified by residual volume; ALZET brain infusion kit used; Brain coordinates (AP=−1 mm, ML=+1.4 mm, DV=−1 mm.); Cannula placement verified via sectioning the brains coronally;


**ALZET Comments:** Interleukin-1 beta, mouse recombinant; PBS; SC; Mice; 1002; 14 days; Dose (10 ng/h); 0.1% bovine serum albumin used; animal info (12-week-old male C57Bl/6 mice);
**ALZET Comments:** Placenta growth factor, recombinant human; antibody, interleukin-1B; PBS; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle or control antibody; animal info (male, C57BL6, 8 weeks old, STZ); immunology; diabetes; Dose (PlGF 10 ug/mouse; anti-IL-1B 1 ug/day).

Q6636: C. S. Nunemaker. Considerations for Defining Cytokine Dose, Duration, and Milieu That Are Appropriate for Modeling Chronic Low-Grade Inflammation in Type 2 Diabetes. J Diabetes Res 2016;2016(2846570
**ALZET Comments:** Interleukin-1beta; Interleukin-6; Saline; SC; Mice; 1007D; 7 days; Dose (32.

**ALZET Comments:** Antibody, anti-interleukin-1a; antibody, anti-interleukin-6; antibody, tumor necrosis factor-alpha; antibody, macrophage inflammatory protein-1 alpha; CSF/CNS (intrathecal); Rat; 1002; 2 weeks; Controls received mp w/ control antibody; animal info (female, Sprague Dawley, adult); functionality of mp verified by decreased activity of targets; used silicone tubing 0.3 mm ID for catheter; catheter was fixed to surrounding muscle with 8-0 sutures; pumps removed after 2 weeks;

**ALZET Comments:** Losartan; interleukin-1, beta; CSF, artificial; CSF/CNS; rats; 2004; 4 weeks; Controls: sham rats w/ no treatment; rats given artificial CSF; animal info (Male Sprague–Dawley rats, 200–250 g); functionality of mp verified by echocardiography and plasma levels; bilateral cannula used; Plastics One double cannula; cardiovascular; heart failure; brain tissue distribution; Cannula placement verified via brain coordinates; LOS aka losartan; IL-1B aka interleukin-1B; Dose: LOS 200ug/day, IL-1B 1ug/day; Resultant plasma level (pg 872-874); Brain coordinates; pg. 871 (2.0mm posterior to the bregma and 8.5mm ventral from the skull surface).

Q3976: W. Liang, et al. Metabolically induced liver inflammation leads to NASH and differs from LPS- or IL-1 beta-induced chronic inflammation. LABORATORY INVESTIGATION 2014;94(491-502
**ALZET Comments:** Endotoxin, LPS; interleukin-1B, recombinant murine; SC; Mice; 1004; 10 weeks; Controls received mp w/ PBS; animal info (male, APOE3L.CETP, 10-14 weeks old); immunology;.

Q3178: C. M. O’Neill, et al. Circulating Levels of IL-1B+IL-6 Cause ER Stress and Dysfunction in Islets From Prediabetic Male Mice. Endocrinology 2013;154(9):3077-3088
**ALZET Comments:** Interleukin-1, beta; Interleukin-6; Saline; SC; Mice; 1007D; 7 days; Controls received mp w/ sham surgery; animal info [male, CD1 5 weeks old, C57BL6J 11 weeks old]; functionality of mp verified by measurement of serum levels; no stress (see pg. 3084); immunology; diabetes; Pumps primed 18-22 h at 37C.

**ALZET Comments:** Antibody, interleukin-1 beta; CSF/CNS; Rat; 1003D; Animal info (Sprague Dawley, male, 260-270 g); ischemia.

**ALZET Comments:** Interleukin-1, beta, recomb. rat; PBS; SC; Rat; 2ML4; 4 weeks; Control animals received mp w/ vehicle; animal info (SHR, SHRSP. male, 10 wks old).

**ALZET Comments:** Interleukin-1 beta; CSF, artificial; CSF/CNS; IP; Rat; 2001; 1003D; 3 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, 250-350 g); ALZET brain infusion kit 2 used.
Q0621: H. Kimura, et al. The Chondroprotective Agent ITZ-1 Inhibits Interleukin-1 beta-Induced Matrix Metalloproteinase-13 Production and Suppresses Nitric Oxide-Induced Chondrocyte Death. JOURNAL OF PHARMACOLOGICAL SCIENCES 2009;110(2):201-211
**ALZET Comments:** Interleukin-1, beta; BSA; saline, sterile; Knee (articular cavity); Rat; 1007D; 7 days; Animal info (8 wks old, male, Sprague-Dawley, CRJ:IGS).

**ALZET Comments:** Interleukin-1, beta; CSF/CNS (sciatic nerve); Rat; 2002; 2 weeks; Controls received mp w/ PBS; animal info (female, Wistar, 180-220 g., sciatic nerve injury); behavioral testing (motor function, toe spreading test, sensory function).

**ALZET Comments:** Interleukin-1, beta; Saline; BSA; SC; Mice; 3, 7 days; Controls received mp w/ vehicle; animal info (male, CD-1, 6-7 wks old); behavioral testing (motor activity).

P7971: I. R. S. Sosenko, et al. IL-1 alpha causes lung inflammation and maturation by direct effects on preterm fetal lamb lungs. PEDIATRIC RESEARCH 2006;60(3):294-298
**ALZET Comments:** Interleukin-1, alpha, recomb. ovine; Intratracheal; Sheep (fetus); 2001D; Controls received mp w/ saline; animal info (merino, ewes + fetuses); silicone tubing used to collect lung fluid; vinyl tubing for intratracheal infusion; tissue perfusion (trachea).

**ALZET Comments:** Interleukin-1 beta; tumor necrosis factor-alpha; Saline; IP; Rat (pregnant); 2001D; Controls received mp w/ vehicle; functionality of mp verified by residual volume.

**ALZET Comments:** Interleukin-1, beta; tumor necrosis factor-alpha; Saline; IP; Rat (pregnant); 1003D; 72 hours; Controls received mp w/ vehicle.

**ALZET Comments:** Interleukin-1, beta recomb. rat; Interferon-gamma, recomb. rat; Saline, physiological; albumin, human serum; CSF/CNS (intratumoral); Rat; 1003D; 48 hours; Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioma).

**ALZET Comments:** Ornithine decarboxylase-inducing factor; Interleukin-1, alpha; tumor necrosis factor-µ; Interleukin-6; SC; IP; Mice; 1007D; 6 days; Controls received mp w/ PBS vehicle; cancer; IL-1µ (human recomb) & ornithine decarboxylase-inducing factor (ODC factor) were infused via IP route; IL-6 was infused (SC).

**ALZET Comments:** Tumor necrosis factor-alpha; transforming growth factor-beta; interleukin-1; Saline, normal; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; no stress (see pg. 17); cancer (lung).


**ALZET Comments:** Interleukin-1, beta; Interleukin-6; Tumor necrosis factor-a; Albumin, human serum; CSF/CNS (hypothalamus, lateral ventricle); Rat; 1003D; 4,8,24,48 hours; Controls received mp w/ vehicle; functionality of mp verified by CSF cell infiltration; dose-response (p. 213); ALZET brain infusion kit used; IL-1ß was rat recomb; cannula position verified histologically; cytokine levels in CSF were assayed.


**ALZET Comments:** Interleukin-1, beta; Rat; 1 week; Peptides; p. 360.

6. Interleukin-2


**ALZET Comments:** Interleukin-25, recombinant mouse; SC; Mice; 1004; 4 weeks; Controls received mp w/ control medium; animal info (Apoel-/-, 9-10 or 21 weeks old); cardiovascular; brain tissue distribution; pumps removed after 4 weeks in young mice;


**ALZET Comments:** Interleukin-2, murine; antibody, anti-interleukin-2; PBS; SC; Mice (transgenic); 10 days; Controls received mp w/ vehicle; animal info (HLA-DR3); comparison of injection vs mp; immunology;

Q5597: K. R. Mott, et al. Role of interleukin-2 and herpes simplex virus 1 in central nervous system demyelination in mice. JViro 2013;87(22):12102-9

**ALZET Comments:** Interleukin-2; PBS; CSF/CNS; SC; Mice; 2 weeks; 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);


**ALZET Comments:** Interleukin-2, human; SC; Mice (nude); Animal info (6 wks old, male, Nu/J); 7-day pumps used.


**ALZET Comments:** Interleukin-2; interleukin-7; interleukin-15; SC; Mice; 2001; 7 days; Controls received mp w/ PBS; animal info (6-12 wks old, gender, age matched); immunology.


**ALZET Comments:** Interleukin-2, recomb.; PBS; albumin, human; SC; Mice (nude); 7 days; 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.
**ALZET Comments:** Interleukin-2; Saline; CSF/CNS (striatum); Rat; 2002; 12 days; Controls received mp w/ vehicle; animal info (female, Sprague Dawley); neurodegenerative (Parkinson's Disease); behavioral testing (rotational behavior and locomotor; axial, limb, and orolingual movements).

**ALZET Comments:** Interleukin-2, recomb. human; SC; Mice; 2001; 4 days; Controls received mp w/ no treatment; cancer (neuroblastoma); peptides; animal info (female, A/J, ICR, 6-8 weeks old); gene therapy.

**ALZET Comments:** Interleukin-15, recomb. human; interleukin-2, recomb. human; PBS; albumin, human; SC; Mice (SCID); 1007D; 10 days; Controls received mp w/ vehicle; immunology; animal info (female, CB17, hu-PBL-SCID, 8-12 weeks old).

**ALZET Comments:** Interleukin-2, recomb. human; SC; Mice; 2001; 7 days; Controls received mp w/ PBS; no stress (see pg.4841); cancer (neuroblastoma); peptides.

**ALZET Comments:** Colony-stimulating factor, GM; interleukin-2; interleukin-12; SC; Rat; 2004; 4 weeks; Cancer (gliosarcoma); GM-CSF was infused alone or with cytokines.

**ALZET Comments:** Interleukin-2; Mice; 7 days; Controls received mp w/ saline; peptides; examined anhedonic effects of IL-2.

**ALZET Comments:** Interleukin-2; mouse; 1007D; 7 days; controls received no IL-2 treatment; immunology; peptides.

**ALZET Comments:** Interleukin-2; Albumin, human; SC; Peritumoral (orthotopic); Rat; 2002; Controls received mp w/ vehicle; functionality of mp verified by in vitro assay; no stress (see p. 4496); good methods pumps weighed p. 4496; cancer (prostate); immunology; peptides; rats had a prostatic adenocarcinoma tumor implanted; Albumin vehicle was 20% concentration; SC & peritumoral orthotopic implantation; Note: these pumps were left in for 28 days.

P4630: M. Ueno. Lymphokine-activated killer cells induced in vivo in mice showing IL-2 toxicity have cytoplasmic granules containing perforin and its hemolytic activity. Immunopharmacology 1998;39(75-82
**ALZET Comments:** Interleukin-2; SC; mice; 2001; 8 days; immunology; peptides; recomb. human IL-2 was used.

**ALZET Comments:** Interleukin-2, recomb. human; PEG; mice; 2002; 12 days; controls received mp w/vehicle; comparison of IP injections of PEG-IL-2 vs. IL-2 infusion via mp; cancer; immunology; peptides.
**ALZET Comments:** Interleukin-2; SC; Rat; 2002; 6 weeks; pumps replaced every 2 weeks; cancer; immunology; peptides.

**ALZET Comments:** Interleukin-2; Albumin; intratumoral; Rat; no duration posted; controls received mp w/albumin; tissue perfusion (intratumoral); cancer (prostate); immunology; peptides.

**ALZET Comments:** Interleukin-12; Interleukin-2; Lysozyme, hen egg white; Ovalbumin; Interferon-gamma; PBS; Albumin, mouse serum; SC; mice; 2001; 9 days; controls received mp w/ PBS; comparison of ip injections vs. mp; immunology; peptides; agents infused singly or in combination in the same pump; recomb. human IL-2 used; recomb. mouse IFN-gamma used.

P6325: M. Isobe, et al. Regulation by Differential Development of Th1 and Th2 Cells in Peripheral Tolerance to Cardiac Allograft Induced by Blocking ICAM-1/LFA-1 Adhesion. Circulation 1997;96(2247-2253)  
**ALZET Comments:** Interleukin-2, recomb.; Culture medium, RPMI 1640; fetal calf serum; Mice; 1007D; 7 days; Cardiovascular.

**ALZET Comments:** Interleukin-2; PBS; Serum, syngenic mouse; SC; Mice; 8 weeks; Controls received mp w/vehicle; functionality of mp verified by plasma levels; long-term study, pump replaced every 10 days; immunology; peptides.

**ALZET Comments:** Interleukin-2; SC; mice; 2001; no duration posted; immunology; peptides; penicillin g given prophylactically; recomb. human IL-2 used.

**ALZET Comments:** Interleukin-2 receptor-alpha;; 131I tracer;; SC;; mice;; 7 days;; functionality of mp verified by plasma levels; comparison of IP injections vs. mp; IL-2 receptor-alpha also called CD25 or Tac; pumps were used to infuse radiolabeled receptor;.

**ALZET Comments:** Interleukin-2; CSF/CNS; Rat; 1007D; 2002; 7,14 days; controls received mp with vehicle; IL-2 receptor-alpha also called CD25 or Tac; pumps were used to infuse radiolabeled receptor;.

**ALZET Comments:** Interleukin-2; mice; 3 days; no comment posted.

**ALZET Comments:** Interleukin-2; Rat; 2002; 14 days; controls received mp with vehicle; immunology; peptides; normal and incisors absent osteopetrotic rats used; recomb. human IL-2 used.
ALZET Comments: Interleukin-2; Saline; Serum; intrasplenic; mice; 14 days; tissue perfusion (spleen); dose-response (graph, p.156); cancer; immunology; peptides.

ALZET Comments: Interleukin-2; Interleukin-2, inactivated; PBS; Albumin, bovine serum; CSF/CNS; Rat; 2002; 14 days; controls received mp w/ inactivated IL-2 or only cannula implantation; functionality of mp verified by opening pump body after infusion; no stress (see pg. 2466); stability verified for up to 7 days at 37°C in cat CSF w/o any decrease in biological activity; peptides; ALZET brain infusion kit used; minimal tissue damage confined to cannula tract; recomb. human IL-2 used.

ALZET Comments: Interleukin-2-PEG; Interleukin-2; IP; mice; no duration posted; cancer; half-life prolonged by complexing IL-2 to polyethylene glycol.

7. Interleukin-3

ALZET Comments: Interleukin-31, recombinant mouse; SC; Mice; 14 days; animal info (6 – 8 week old, C57BL/6 and Trpv1 knockout mice); functionality of mp verified by observation of skin phenotype; dose-response (pg. 508.e5); Dose (20 mg/day).

ALZET Comments: Interleukin-3- SC; Mice; Animal info (C57BL/6:SV129 IK-/-).

P9822: T. Yoshimoto, et al. Basophils contribute to Th2-IgE responses in vivo via IL-4 production and presentation of peptide-MHC class II complexes to CD4+ T cells. NATURE IMMUNOLOGY 2009;10(7):706-U54
ALZET Comments: Interleukin-3; PBS; SC; Mice; Animal info (DO11.10, IL-4 deficient).

Q0809: S. Kim, et al. Basophils Can Directly Present or Cross-Present Antigen to CD8 Lymphocytes and Alter CD8 T Cell Differentiation into IL-10-Producing Phenotypes. Journal of Immunology 2009;183(5):3033-3039
ALZET Comments: Interleukin-3; Mice (transgenic); 7 days; Animal info (C57BL/6, OT-I TCR-transgenic, IL-4KO B6); immunology.

ALZET Comments: Interleukin-3; Mice; Animal info (BALB/c, IL-3 deficient).

ALZET Comments: Interleukin-3; SC; Mice; mice (transgenic); 7 days; Controls received mp w/ PBS or no treatment; immunology; peptides; animal info (C57BL/6, BIO.A Rag -/-); "Sought an alternative strategy to generate basophils in vivo by administering IL-3 into mice via a miniosmotic pump." (p. 2923).
**ALZET Comments:** Interleukin-31, mouse; PBS; BSA; SC; Mice; 7-14 days; Controls received mp w/ vehicle; immunology.

**ALZET Comments:** Interferon-gamma; Interleukin-3; Albumin, mouse serum; PBS; SC; mice; 1007D; 7 days; controls received mp w/ vehicle; stability verified after 7 day storage; immunology; peptides; cytokines given singly and together.

**ALZET Comments:** Erythropoietin; Interleukin-3; Colony-stimulating factor, GM; PBS; Glycerol; SC; mice; 2002; 14 days; immunology; peptides.

**ALZET Comments:** Interleukin-3; Colony-stimulating factor, GM; Erythropoietin; PBS; Glycerol; LPS, e. coli; SC; mice; 2002; no duration posted; controls received mp with vehicles +/- LPS; immunology; peptides; recomb. mouse GM-CSF & IL-3 used; recomb. human EPO used.

**ALZET Comments:** Interleukin-3; Nerve growth factor; Albumin, bovine serum; PBS; CSF/CNS; 2002; 14 days; two doses of hIL-3 infused; B-NGF used; human IL-3 used.

**ALZET Comments:** Atrial natriuretic factor; cholecystokinin; Granulocyte-colony stimulating factor; glucagon; insulin; interleukin-2; interleukin-3; melatonin; nerve growth factor; neurotensin; prolactin; theophylline; CSF/CNS; IA (femoral); intrasplenic; IP; SC; no duration posted; peptides; ALZA-authored, review of peptide delivery issues and applications; tissue perfusion (spleen).

**ALZET Comments:** Interleukin-3, recomb. mouse; Penicillin; Streptomycin; Glycerol; PBS; IP; SC; mice; 2001; 2002; 7 days, 2 weeks; controls received mp w/vehicle; 2002 mp infused IL-3 ip for 2 weeks, additional mps implanted sc; peptides; antibiotics; IL-3 infused simultaneously with penicillin and streptomycin.

**ALZET Comments:** Interleukin-3, human; colony-stimulating factor, GM, human; SC; Mice; mice (SCID); 4-5 weeks; 15 days; Controls received mp w/ saline; peptides; immunology.

**ALZET Comments:** Interleukin-2; Interleukin-3; SC; mice; 2001; 8, 16 days; controls received mp w/ unspecified vehicle or sham op; 2 experiments using mp, IL-2 infused for 8 days, IL-3 infused for 16 days; comparison of agents effects; pump replaced after eight days; peptides.

ALZET Comments: Endotoxin, E. coli; Interleukin-3, recomb. mouse; Penicillin; Streptomycin; Glycerol; PBS; SC; mice; 3 and 7 days; infusion supplemented w/ip injections; interleukin activity in blood variable - aggregation in pump? (see p. 1004); mp infusion in normal and irradiated mice; half-life; peptides; antibiotic.

8. Interleukin-4


ALZET Comments: Interleukin-4; IP; Rat (pregnant); 19 days; Dose (600 ng/day); animal info (pregnant Sprague-Dawley rats; pumps implanted on gestational day 14); ischemia (placental).


ALZET Comments: Ultra-high molecular weight polyethylene particles; interleukin-4, mouse recombinant; BSA; PBS; Bone (femur); Mice; 2006; 4 weeks; Controls received mp w/ vehicle; animal info (male, BALB/cByJ, 10-12 weeks old); 1% BSA used; post op. care (buprenorphine injection SC); used vinyl tubing to connect pumps to titanium rods.


ALZET Comments: Interleukin-4; Saline; CSF/CNS (ventricle); Mice (knockout); 2001; 7 days; Controls received mp w/ vehicle; animal info (C57/BL6 mice; 8-10 weeks, 25-30 g); ischemia (cerebral; stroke model); behavioral testing (Rotarod, corner, foot fault, and Morris water maze tests); healing, recovery; learning, memory; Therapeutic indication (Cerebral ischemia); Dose (60 ng/day); Brain coordinates: −0.20 mm anterior and 1.00 mm lateral to bregma.


ALZET Comments: Interleukin-4, mouse recombinant; BSA; PBS; In vitro (cell culture); Cell culture; 2006; 4 weeks; 1% BSA used; immunology; "Osmotic pumps delivered IL-4 at a rate that closely followed the expected delivery rate." pg 1343; used vinyl tubing; pumps lead into mouse bone marrow macrophage augmented media; incubated at 37C.


ALZET Comments: Antibody, interleukin-4Ra; CSF/CNS (hippocampus); Mice; 1004; 28 days; Controls received mp w/ control antibody; animal info (APPswe/SP1dE9, 7-5 months old); ALZET brain infusion kit 3 used; neurodegenerative (Alzheimer's disease); immunology; pumps primed 48 hours in 37C saline.

Q0583: J. D. Milner, et al. Sustained IL-4 exposure leads to a novel pathway for hemophagocytosis, inflammation, and tissue macrophage accumulation. Blood 2010;116(14):2476-2483

ALZET Comments: Interleukin-4, recomb. mouse; interleukin-13 recomb. mouse; SC; Mice; 3 days; Controls received mp w/ PBS; animal info (C57BL6, b6 Rag2 -/-, b6 Stat6 -/-); 100 ul sized pump used; immunology.

P9263: L. Wang, et al. Blimp-1 induced by IL-4 plays a critical role in suppressing IL-2 production in activated CD4 T cells. Journal of Immunology 2008;181(8):5249-5256

ALZET Comments: Interleukin-4; ovalbumin; SC; Mice; 7 days; Immunology, animal info (CD45.1, C57BL/6).


ALZET Comments: Interleukin-4; IP; Mice; 3 weeks; Controls received mp w/ PBS; IL-4 knockout; animal info (C57BL/6, 9 weeks old).
**P6048**: Y. Zavros, et al. Treatment of Helicobacter gastritis with IL-4 requires somatostatin. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2003;100(22):12944-12949

**ALZET Comments**: Interleukin-4; interferon-gamma; PBS; IP; Mice; 1007D; 7 days; Controls received mp w/ vehicle; comparison of IP injections vs. IP mp.


**ALZET Comments**: Interleukin-4; Colony-stimulating factor, GM; Saline; SC; mice; 1007D; 7 days; controls received mp w/ vehicle; functionality of mp verified by serum levels via ELISA; immunology; peptides; recombinant cytokines; agents administered singly or concomitantly.


**ALZET Comments**: Interleukin-1; Interleukin-4; Interleukin-6; Fibroblast growth factor, basic; Nerve growth factor; Ciliary neurotrophic factor; Water; PBS; BSA; CHAPS; CSF/CNS (intrathecal); Rat; 2001; 7 days; controls received mp w/ vehicle; tissue perfusion (injury site); good methods; peptides; 1:10 dilutional effect of CSF confirmed by dye study; PE10/50 tubing used with pump and 30 gauge needle to deliver drugs through small dural plial opening.

**P4119**: A. Mathur, et al. Effect of IL-7 or IL-4 on reconstitution of donor lymphoid cells in congenic murine bone marrow transplantation. Bone Marrow Transplantation 1995;16(119-124

**ALZET Comments**: Interleukin-7; Interleukin-4; PBS; IP; mice; 14 days; controls received mp w/vehicle; immunology; peptides; recomb. mouse IL-4 and IL-7 used.


**ALZET Comments**: Interleukin-4; Interleukin-10; IA (brachiocephalic); Rat; 14 days; immunology; peptides; pump infused the brachiocephalic artery of a harvested heart, which was then implanted into a recipient; recomb. mouse IL-4 & IL-10 used.


**ALZET Comments**: Interleukin-4; PBS; SC; mice (SCID); 2002; no duration posted; long-term study, pumps replaced; immunology; human IL-4 used.

### 9. Interleukin-5


**ALZET Comments**: Interleukin-5, recombinant rat; Rat (pregnant); 2002; 5 days; Controls received mp w/ vehicle; animal info (pregnant, 14-19 days gestation); cardiovascular; bp measured using catheter; preeclampsia.


**ALZET Comments**: Interleukin-5; PBS; BSA; IP; Mice (transgenic); 2001; 8 days; Controls received mp w/ vehicle; Immunology; peptides; human IL-5 used.
10. Interleukin-6

ALZET Comments: Interleukin-6; SC; Mice; 15 days; Dose (1.0 mg/ml); Dose (1.0 mg/ml); Interleukin-6 aka IL-6; spinal cord injury;

ALZET Comments: Interleukin-6, human; NaCl; BSA; Mice; 14 days; animal info (male, mINDY KO); 0.1% BSA used; immunology;

ALZET Comments: Transforming growth factor-β1; SJN2511; Interleukin-6; Bovine serum albumin; CSF; artificial; dextran; CSF/CNS; Mice; 7 days; Dose (0.4mM BSA, 100 ng/ml (TGF- β1, 300μM SJN2511)); Controls received mp w/ vehicle; animal info (2- to 3-month-old FVB/N and C57BL/6 mice); SJN2511 is a selective blocker of the TGF- B type I receptor/ALK5; Brain coordinates (0.5 mm posterior, 1 mm lateral to bregma);

ALZET Comments: Interleukin-6, recomb. mouse; Saline; SC; Mice; 1007D; 1 week; Dose (16 mg/ml); Controls received mp w/ vehicle; animal info (12- to 15-wk-old male C57BL6J mice);

ALZET Comments: Interleukin-6; Mice; 7 days; animal info (male, C57Bl6J, 12 weeks old); diabetes;

Q6636: C. S. Nunemaker. Considerations for Defining Cytokine Dose, Duration, and Milieu That Are Appropriate for Modeling Chronic Low-Grade Inflammation in Type 2 Diabetes. J Diabetes Res 2016;2016(2846570
ALZET Comments: Interleukin-1beta; Interleukin-6; Saline; SC; Mice; 2001; 7 days; Dose (32.

Q4828: N. Gomez-Lopez, et al. Interleukin-6 controls uterine Th9 cells and CD8+ T regulatory cells to accelerate parturition in mice. immunology and Cell Biology 2016;94(79-89
ALZET Comments: Interleukin-6, recomb. human; PBS; BSA; SC; Mice (pregnant); 1007D; 7 days; Controls received mp w/ vehicle; animal info (female, pregnant, Il6 +/- or Il6 -/-, 11.5 dpc, 8-12 weeks old); 0.1% BSA used; immunology; Dose (5 ng/h);

Q3865: L. Dou, et al. MiR-301a Mediates the Effect of IL-6 on the AKT/GSK Pathway and Hepatic Glycogenesis by Regulating PTEN Expression. CELLULAR PHYSIOLOGY AND BIOCHEMISTRY 2015;35(1413-1424
ALZET Comments: Interleukin-6; NaCl; BSA; SC; Mice; 2001; 7 days; Animal info (male, C57BL6J, 12 weeks old); 0.1% BSA used; immunology; diabetes;

Q4408: L. Dou, et al. MiR-19a regulates PTEN expression to mediate glycogen synthesis in hepatocytes. SCIENTIFIC REPORTS 2015;5(U1-U11
ALZET Comments: Interleukin-6; NaCl; BSA; SC; Mice; 2001; 7 days; Animal info (male, C57BL6J, 12 weeks old); 0.1% BSA used; immunology;

ALZET Comments: Interleukin-6, murine recombinant; SC; Mice; 1007D; 7 days; Controls received mp w/ saline; animal info (male, IL-6 -/- or C57BL6J, 8-12 weeks old); functionality of mp verified by plasma levels; cardiovascular; immunology;
Q3178: C. M. O'Neill, et al. Circulating Levels of IL-1B+IL-6 Cause ER Stress and Dysfunction in Islets From Prediabetic Male Mice. Endocrinology 2013;154(9):3077-3088
**ALZET Comments:** Interleukin-1, beta; Interleukin-6; Saline; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle or sham surgery; animal info (male, CD1 5 weeks old, C57BL6J 11 weeks old); functionality of mp verified by measurement of serum levels; no stress (see pg. 3084); immunology; diabetes; Pumps primed 18-22 h at 37C.

**ALZET Comments:** Interleukin-6; NaCl; BSA; SC; Mice; 2001; 7 days; Animal info (C57BL/6J).

**ALZET Comments:** Interleukin-6, recomb. murine; endotoxin, LPS; SC; Mice; 7 days; Animal info (C57BL/6J, male, IL-6 null); functionality of mp verified via blood IL-6 levels.

**ALZET Comments:** Interleukin-6; Mice; 1, 3, 5 days; Controls received mp w/ saline; animal info (10 wks old, male, CDF1); pump infused at a rate of 1 ul/hr.

**ALZET Comments:** Interleukin-6; Albumin, rat; IP; Rat; 2001; 7 days; Controls received mp w/ vehicle; cardiovascular; no stress (pg 227); animal info (male, Sprague-Dawley, 250-300 g); post op. care (buprenorphine HCl).

**ALZET Comments:** Interleukin-6, recomb. murine; SC; IP; Mice; 7 days; Animal info (6-8 wks old, male, C57BL/6J).

**ALZET Comments:** Interleukin-1 receptor antagonist, recomb. human; interleukin-6 recomb. mouse; Sodium citrate; sodium chloride; EDTA; Tween 80; PBS; SC; wound site; Mice; 1003D; 2002; 3, 14 days; Controls received mp w/ vehicle; animal info (male, B6D2F1, 8-12 wks, 27-30 g., IL-1R KO); mp was fitted with a polypropylene mesh collar containing a PVA sponge; agent also known as Anakinra; deep tissue wounds; 0.1% Tween 80 used; 0.5 mM EDTA;.

**ALZET Comments:** Interleukin-6, recomb. human; Saline; SC; Mice; 2001; 7 days; Controls received mp w/ saline; animal info (Apoe-/-, ob/ob, 11 wks old).

**ALZET Comments:** Interleukin-6, recomb. rat; Intramuscular (gastrocnemius); Rat; 2002; 14 days; Controls received mp w/vehicle; functionality of mp verified by residual volume; animal info (Sprague Dawley, 5.5 wks old, 118g); fenestrated catheter used.

ALZET Comments: Interleukin-6, recombinant human; SC; Mice (transgenic); mice; 2001; 7 days; Controls received sham surgery; immunology; peptides; animal info (BALB/c, wt, GM-CSF -/-, DO11.10 TG, 8-12 wks old); “To ensure a continuous supply, we implanted osmotic minipump containing IL-6 in mice.” (p. 2289).


ALZET Comments: Interleukin-6, recombinant human; Saline; BSA; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; no stress (see pg. 369); peptides; animal info (male, Wistar, 220 g.); endocrinology.


ALZET Comments: Interleukin-6, recombinant mouse; NaCl; PBS; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; peptides; animal info (C57BL/6).


ALZET Comments: Interleukin-6, recombinant mouse; PBS; BSA; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; functionality of mp verified by plasma IL-6 concentrations; peptides; cardiovascular; animal info (C57BL/6, male).


ALZET Comments: Interleukin-6, recombinant mouse; Saline, sterile; IP; Mice; 7 days; Controls received mp w/ vehicle; functionality of mp verified by serum IL-6 levels; peptides; animal info (male, C57BL6/J).

P7821: Z. X. Cao, et al. The cytokine interleukin-6 is sufficient but not necessary to mimic the peripheral conditioning lesion effect on axonal growth. Journal of Neuroscience 2006;26(20):5565-5573

ALZET Comments: Interleukin-6, recombinant rat; Saline; CSF/CNS (intrathecal); Rat; 1002; 2 weeks; 24 hours; Controls received mp w/ vehicle; functionality of mp verified by residual volume; dose-response (fig. 7); no stress (see pg. 5571); peptides; animal info (female, Long-Evans, pg. 21-pg. 23; bilateral dorsal column lesion, 8wk old); mp primed at least 4 hours at 37 celsius.


ALZET Comments: Interleukin-6, recombinant human; PBS; serum, rat; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle plus human albumin; functionality of mp verified by serum rh IL-6 levels; dose-response; cardiovascular; peptides.


ALZET Comments: Interleukin-6; Saline; Intramuscular (tibialis anterior); Rat; 2002; 3,14 days; Controls received mp w/ vehicle or had contralateral muscle w/ no treatment; functionality of mp verified by residual volume; no stress (see pg. 912,913); good methods p. 912; peptides; mp primed in sterile saline at 37 degrees celsius.


ALZET Comments: Interleukin-6, recombinant human; SC; Rat; 1003D, 2001; 3, 7 days; Controls received mp w/ PBS, no stress (see pg. 646), peptides.

**ALZET Comments:** Tumor necrosis factor-α, recomb. rat; interleukin-1 beta, recomb. rat; interleukin-10, recomb. rat; interleukin-6, recomb. rat; Albumin, human serum; CSF/CNS; Rat; 1003D; 48 hours; Controls received mp w/ vehicle; dose-response (fig 1); ALZET brain infusion kit used; correct localization of cannula confirmed histologically.


**ALZET Comments:** Interleukin-6; SC; Mice (nude); 3 weeks; Controls received SC saline injections; comparison of SC injections vs. mp; no stress (see pg. 511); cancer (prostate).


**ALZET Comments:** Interleukin-6, recomb. human; PBS; serum, mouse; SC; Mice; 1007D; 6 days; Controls received mp w/ vehicle; functionality of mp verified by serum rhIL-6 levels; dose-response (table 1); toxicology; peptides; animal info (female, 20 wks old).


**ALZET Comments:** Ornithine decarboxylase-inducing factor; Interleukin-1, alpha; tumor necrosis factor-µ; Interleukin-6; SC; IP; Mice; 1007D; 6 days; Controls received mp w/ PBS vehicle; cancer; IL-1µ (human recomb) & ornithine decarboxylase-inducing factor (ODC factor) were infused via IP route; IL-6 was infused (SC).


**ALZET Comments:** Interleukin-6; Saline; BSA; SC; Mice; 2001; 5 days; IL-6 plasma levels taken; 0.1% BSA used.


**ALZET Comments:** Interleukin-6; SC; Mice; 1003D; 3 days; Controls received mp w/ mouse serum; functionality of mp verified by IL-6 serum levels; peptides; IL-6 is human recombinant.


**ALZET Comments:** Interleukin-1, beta; Interleukin-6; Tumor necrosis factor-α; Albumin, human serum; CSF/CNS (hypothalamus, lateral ventricle); Rat; 1003D; 4,8,24,48 hours; Controls received mp w/ vehicle; functionality of mp verified by CSF cell infiltration; dose-response (p. 213); ALZET brain infusion kit used; IL-1β was rat recombinant; cannula position verified histologically; cytokine levels in CSF were assayed.

### 11. Interleukin-7


**ALZET Comments:** Interleukin-7; PBS; SC; Mice; 5 days; Controls received mp w/ vehicle; immunology; “we utilized osmotic pumps to administer recombinant IL-7 and increase IL-7 bioavailability in vivo... T-cell proliferation was dramatically increased in IL-7 pump installed mice compared to control PBS pump installed mice” pg 1671; Therapeutic indication (T-cell homeostasis); Dose (5 ug).
ALZET Comments: Interleukin-2; interleukin-7; interleukin-15; SC; Mice; 2001; 7 days; Controls received mp w/ PBS; animal info (6-12 wks old, gender, age matched); immunology.

ALZET Comments: Interleukin-7; SC; Mice; 1007D; 7 days; Controls received mp w/ PBS; animal info (C57BL/6, 6-16 wks old); wound clips used; post op. care (betadine).

P9932: J. H. Park, et al. Signaling by intrathymic cytokines, not T cell antigen receptors, specifies CD8 lineage choice and promotes the differentiation of cytotoxic-lineage T cells. NATURE IMMUNOLOGY 2010;11(3):257-U10
ALZET Comments: Interleukin-7, recomb. mouse; SC; Mice; 2 weeks; Animal info (79Z); immunology.

ALZET Comments: Interleukin-7, recomb. mouse; SC; Mice; 7 days; Controls received mp w/ PBS; animal info (C57BL/6).

ALZET Comments: Interleukin-7, recomb. mouse; SC; Mice (transgenic); 7-14 days; Controls received mp w/ PBS; animal info (C57BL/6, 8-10 wk old).

P7263: B. Min, et al. Spontaneous and homeostatic proliferation of CD4 T cells are regulated by different mechanisms. Journal of Immunology 2005;174(10):6039-6044
ALZET Comments: Interleukin-7, recomb. mouse; Mice; mice (transgenic); 7, 28 days; Controls received mp w/ PBS; immunology; peptides.

ALZET Comments: Interleukin-7, recomb. mouse; PBS; sucrose; serum, normal mouse; SC; Mice; 1007D; 1002; 7,14 days; Controls received mp w/ vehicle; replacement therapy (thymectomy); immunology.

ALZET Comments: Interleukin-7; SC; Mice; 1002; 14 days; animal info (8-12 weeks); cancer (Lung cancer); Immunology (dendritic cells); Therapeutic indication (Lung cancer); Dose (5 ng/mL);.

ALZET Comments: Interleukin-7; PBS; SC; Mice (transgenic); 2002; 14 days; Dose (1 µg/d,); Controls received mp w/ vehicle; animal info (Female C57BL/6J (B6, H-2b), C3FeB6F1/J([B6 3 C3H]F1; H-2b/k), B10.BR (H-2k), and CBA/J (H-2k) mice), between 8 and 10 weeks of age or 9 months old; immunology;.

ALZET Comments: Interleukin-7; Water; Saline; Albumin, mouse serum; SC; mice; 1007D; no duration posted; controls received mp w/vehicle; functionality of mp verified by residual protein in reservoir; comparison of ip injections vs. mp; no stress (see p. 406); immunology; recomb. murine & human IL-7 used; peptides.
P4119: A. Mathur, et al. Effect of IL-7 or IL-4 on reconstitution of donor lymphoid cells in congenic murine bone marrow transplantation. Bone Marrow Transplantation 1995;16(119-124)
**ALZET Comments:** Interleukin-7; Interleukin-4; PBS; IP; mice; 14 days; controls received mp w/vehicle; immunology; peptides; recomb. mouse IL-4 and IL-7 used.

12. Interleukin-8

**ALZET Comments:** Interleukin-8; BSA; IA (renal); Rat; 2ML1; 5 days; controls received mp w/BSA; good methods (pg. 275); peptides; used PE-10 catheter stretched to further reduce its diameter.

**ALZET Comments:** Interleukin-1 receptor antagonist; Interleukin-6; Interleukin-1, beta heat inactivated; Interleukin-8; Interleukin-1, beta; Tumor necrosis factor-a; Saline, sterile physiological; BSA; CSF/CNS; Rat; 2001; 7 days; controls received mp w/vehicle; guide cannula was used, and a sterile 29 g stainless steel obturator was used to ensure cannula patency during at least a 10 day recovery period after surgery; BSA added as stabilizing agent and carrier protein for cytokines; recomb. human IL-6 & 8 used.

13. Interleukin-10

**ALZET Comments:** Angiotensin II; Interleukin-10, recomb. human; PBS; SC; Mice; 1002; 14 days; Dose (Angiotensin II (1000 ng/kg/min); IL-10 (60ng/day)); Controls received mp w/ vehicle; animal info (Eight - to 10-week-old C57BL/6 male mice); cardiovascular;

**ALZET Comments:** Angiotensin II; Interleukin-10, recombinant mouse;; Saline; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (male, IL-10 -/- or WT, 10-12 weeks old); functionality of mp verified by plasma levels; immunology; bp measured using catheter; Dose (Ang II 90 ng/min; IL-10 0.5 ng/min);

**ALZET Comments:** Interleukin-10; PBS; SC; Mice; 2001; 9 days; Controls received mp w/ vehicle; animal info (male, female C57BL/6 mice, 8 – 12 weeks old); functionality of mp verified by hind limb muscle withdrawal; behavioral testing (running wheel); “Mice treated with systemic IL-10 had significantly less hyperalgesia compared with mice that received vehicle” pg. 75; analgesia produced by regular physical activity; Dose (2 ug/day);

**ALZET Comments:** Interleukin-10; U0126; Saline; SC; Mice; 1007D; 4 days; 7 days; Controls received mp w/ vehicle; animal info (IL-10 KO); immunology;

**ALZET Comments:** Albumin, mouse; interleukin-10, recomb.; SC; Mice; 4 weeks; Animal info (C57BL/6, 22-25 g, KBT, IL-10 KO).
ALZET Comments: Interleukin-10, recomb.; SC; Rat; mice; 4 weeks; Controls received mp w/ mouse serum albumin; animal info (C57Bl/6J, IL-10KO; Sprague Dawley, male).

ALZET Comments: Interleukin-10; Mice; 3 days; Controls received mp w/saline; animal info (male, C57BL/6, 10 wks old); diabetes.

ALZET Comments: Interleukin-10; interleukin-1 receptor antagonist; Saline; DMSO; SC; Mice (SCID); 2004; 40 days; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; good methods (p.125); peptides; animal info (female, SCID, 4-5 wks old); Rheumatoid arthritis; pump and technique schematics p. 125; stability (with an excellent description of methods) was verified for 40 days @ 37C; 50% DMSO used; "... the application of proteins via osmotic pumps is an affective tool to evaluate the effects of cytokines and inhibitors in vitro." p. 128.

ALZET Comments: Interleukin-10; Saline; SC; 3 days; Peptides; animal info (male, C57BL/6, 6 weeks old).

ALZET Comments: Interleukin-10, recomb.mouse; Saline; SC; Mice; 72 hours; Controls received mp w/ vehicle; dose-response (Fig. 4); peptides.

ALZET Comments: Tumor necrosis factor-a, recomb. rat; interleukin-1 beta, recomb. rat; interleukin-10, recomb. rat; interleukin-6, recomb. rat; Albumin, human serum; CSF/CNS; Rat; 1003D; 48 hours; Controls received mp w/ vehicle; dose-response (fig 1); ALZET brain infusion kit used; correct localization of cannula confirmed histologically.

ALZET Comments: Interleukin-10; PBS; BSA; Bone; Rabbit; 2004; 3 or 6 weeks; Controls received mp w/ vehicle; immunology; peptides; diagram of pump and bone chamber (p. 44).

ALZET Comments: Interleukin-10; Saline; IP; Rat; 2002; 14 days; functionality of mp verified by IL-10 plasma levels; immunology; peptides.

ALZET Comments: Interleukin-10; PBS, sterile; SC; Rat; 2ML2; 14 days; controls received mp w/ PBS; comparison of footpad injections vs. mp; immunology; peptides.
14. Interleukin-11

Q4341: J. N. Buzzelli, et al. IL-1RT1 signaling antagonizes IL-11 induced STAT3 dependent cardiac and antral stomach tumor development through myeloid cell enrichment. ONCOTARGET 2015;6(679-695
ALZET Comments: Interleukin-11, recombinant human; SC; Mice; 1007D; 7 days; Controls received mp w/ saline; animal info (WT or IL-1RT1, 12-14 weeks old); immunology.

ALZET Comments: Interleukin-11; Saline; IV (jugular); Rat; 1003D; 48 hours; Controls received mp w/ vehicle; peptides; IL-11 was human recombinant; ischemia (intestinal).

ALZET Comments: Interleukin-11; Saline; IV (jugular); Rat; 1003D; 3 days; controls received mp w/ vehicle; peptides; ischemia (bowel).

ALZET Comments: Interleukin-11; Stem cell factor; Granulocyte-colony stimulating factor, PEGylated; Erythropoietin;; SC;; mice;; 2002; 1007D;; 7 days;; controls received mp w/ saline; functionality of mp verified by pilot studies; no stress (see pg. 3223); peptides; recombinant human interleukin-11, EPO, & G-CSF used; recombinant rat stem cell factor used (PEGylated); agents were given in every combination;.

ALZET Comments: Interleukin-11; Antibody, anti-interleukin-1 receptor; Serum, mouse; Saline, sterile; SC; mice; 3, 7, 10, 13 days; controls received mp w/ vehicle; comparison of sc injections vs. mp; immunology; peptides; cardiovascular;
"Compared to SC injection, both the magnitude and duration of the platelet increase were significantly enhanced following continuous SC infusion." (pg. 270).

15. Interleukin-12

ALZET Comments: Interleukin-12, recombinant human; Saline; SC; Mice (SCID; NOD/SCID); 2004; 28 days; Animal info (female, SCID and NOD/SCID, 8-10 weeks old); cancer (Lymphoma);.

ALZET Comments: Interleukin-12, murine; PBS; CSF/CNS (intratumoral); Mice; 1004; 2004; 28 days; Controls received mp w/ vehicle; animal info (C57BL6); cancer (glioma); tissue perfusion (tumor; glioma); immunology; pumps primed at 37C; pumps explanted after 28 days;

ALZET Comments: Colony-stimulating factor, GM, murine; interleukin-12; PBS; SC; Rat; 28 days; Controls received mp w/ vehicle; dose-response (fig 1); no stress (see pg. 1209); cancer (upper aerodigestive tract carcinoma); peptides; animal info (Fisher 344, 125-150 g); good methods; "This latter method (mp) has several advantages. First, the use of minipumps obviates the cumbersome need to transfect tumor cells and completely characterize their cytokine repertoires. Second, it allows for independent and rigorous control over the kinetics of administration of cytokine and antigen dosages. Third, it may generate less controversy than those techniques requiring "gene therapy" IRB approval." (p. 1213).


ALZET Comments: Colony-stimulating factor, GM, recomb. mouse; interleukin-12, recomb. mouse; BSA; PBS; SC; Rat; 2002; 14 days; Controls received mp w/ vehicle or no treatment; cancer (RT-2 glioma); peptides; animal info (Fischer, 200-350 grams, SC and ICV tumors); "continuously infused cytokine using an osmotic mini pump to...avoid the side effects of a single large dose of cytokine and one with a concept similar to that of gene-therapy." (p. 874).


ALZET Comments: Interleukin-12; recomb.; PBS; SC; Mice; 1007D; 21 days; Controls received mp w/ vehicle; pumps replaced at day 7 & day 14.


ALZET Comments: Interleukin-12; PBS; SC; Mice; 2001; 7 days; Immunology.


ALZET Comments: Colony-stimulating factor, GM; interleukin-2; interleukin-12; SC; Rat; 2004; 4 weeks; Cancer (gliosarcoma); GM-CSF was infused alone or with cytokines.


ALZET Comments: Interleukin-12; PBS; SC; Mice (SCID); 2004; 1 week; Controls received mp w/ vehicle; functionality of mp verified by pump explantation, examination and tumor reduction; cancer (Hemangiosarcoma); peptides; pump model not listed; tumor cells from a canine.


ALZET Comments: Interleukin-12; PBS; Albumin, bovine serum; SC; Rat; 2004; 20 days; controls received mp w/vehicle; dose-response (p. 851); "an immunotherapeutic approach using cytokine-infusing minipumps and irradiated tumor cells can circumvent many of the problems associated with most popular methods..." (p. 854); cancer; immunology; peptides; recomb. mouse IL-12 used.


ALZET Comments: Interleukin-12; Interleukin-2; Lysozyme, hen egg white; Ovalbumin; Interferon-gamma; PBS; Albumin, mouse serum; SC; mice; 2001; 9 days; controls received mp w/ PBS; comparison of ip injections vs. mp; immunology; peptides; agents infused singly or in combination in the same pump; recomb. human IL-2 used; recomb. mouse IFN-gamma used.
16. Interleukin-13


**ALZET Comments:** Etoposide, Bevacizumab, IMCA12, Interleukin-13-PE38, Tetrakis Chlorin; CSF/CNS (intratumoral); Mice, Rat; 2001D, 1003D, 1007D, 1004, 2004; 24 hours, 3, 7, 21, 28 days; ALZET brain infusion kit 1, 2, and 3 used; cancer (Glioblastoma);


**ALZET Comments:** Interleukin-13 Pseudomonas exotoxin; PBS; HSA; CSF/CNS (intracranial); Mice; 1003D; 3 days; Controls received mp w/ vehicle; animal info (tumor-bearing mice); cancer (glioblastoma multiforme); brain tissue distribution; HSA aka human serum albumin; CED model, convection-enhanced delivery; orthotopic mouse model of human glioma; Dose (3,700 kBq);


**ALZET Comments:** Interleukin-13-Pseudomonas exotoxin, recomb.; IP; Mice (nu/nu, 5-6 wks old); comparison of IP injections vs IP mp; IL-13-PE is a recombinant immunotoxin; "Mice receiving continuous IL-13-PE exhibited better tumor response compared to bolus administration" pg 1224.

**Q1342:** T. Shimamura, *et al.* Interleukin 13 Mediates Signal Transduction through Interleukin 13 Receptor alpha 2 in Pancreatic Ductal Adenocarcinoma: Role of IL-13 Pseudomonas Exotoxin in Pancreatic Cancer Therapy. *Clinical Cancer Research* 2010;16(2):S77-S86

**ALZET Comments:** Interleukin-13; PBS; albumin, human serum; IP; Mice (SCID); 1007D; 7 days; Controls received vehicle injections; animal info (nu/nu, 5-6 wks old, male, SCID); comparison of ip injections vs ip mp; cancer (pancreatic); "Compared with (bolus IP) administration of 50 ug/kg IL-13 cytotoxin daily for 7 consecutive days, (ALZET pumps) (infused over 7 days) significantly suppressed tumor growth (P = 0.022) from the beginning of the treatment until the end of the experiment... Compared with the (bolus IP) 50 ug/kg group, a significant prolonged survival time was observed in the (ALZET pump) 50 ug/kg group", pg 581.

**Q0583:** J. D. Milner, *et al.* Sustained IL-4 exposure leads to a novel pathway for hemophagocytosis, inflammation, and tissue macrophage accumulation. *Blood* 2010;116(14):2476-2483

**ALZET Comments:** Interleukin-4, recomb. mouse; Interleukin-13 recomb. mouse; SC; Mice; 3 days; Controls received mp w/ PBS; animal info (C57BL6, b6 Rag2 -/-, b6 Stat6 -/-); 100 ul sized pump used; immunology.


**ALZET Comments:** Interleukin-13-PE38; Interleukin-13Ra2, pME18S; CSF/CNS (intratumoral); Mice (nude); 1003D; 1007D; 7 days; Controls received mp w/ vehicle or antisense IL-13Ra2 plasmid vector; pumps replaced after 3 days; cancer (glioblastoma); cyanoacrylate adhesive; convection enhanced delivery; IL-13Ra2 cDNA encoding plasmid vector; "the upregulated IL-13 Ra2 chain was successfully targeted with a continuous infusion of IL-13 cytotoxin." (p. 199).


**ALZET Comments:** Interleukin-13,PE38QQR; Saline; serum albumin; CSF/CNS (brain stem); Rat; 2001D; 24 hours; Tissue perfusion (brain stem); stability verified (7 days at 37 degrees Celsius); good methods p. 288; cancer; pump incorrectly labeled as a 2001; IL13-PE38QQR is a tumor specific, chimeric cytotoxin; 30 g Plastics One Cannula used; vinyl catheter tubing from DURECT used.
**ALZET Comments:** Interleukin-13, PE38; Albumin, human serum; PBS; CSF/CNS; Mice (nude); 1007D; 7 days; Comparison of CNS injections vs. mp; cancer (glioma); ALZET brain infusion kit; cyanoacrylate adhesive.

**ALZET Comments:** Interleukin-13 endotoxin; PBS; IP; Mice (nude); 7 days; Comparison of IV injections vs mp; cancer (head and neck); IL-13 endotoxin, also called IL13-PE38QQR, is composed of IL-13 and a mutated form of a Pseudomonas endotoxin; compared to IV injections, continuous infusion decreased the toxicity and increased the efficacy of IL-13 cytotoxin.

P4522: Y. H. Lai, et al. Mouse IL-13 enhances antibody production in vivo and acts directly on B cells in vitro to increase survival and hence antibody production. The Journal of Immunology 1999;162(78-87
**ALZET Comments:** Interleukin-13; PBS; IP; mice; 7 days; controls received mp w/vehicle; functionality of mp verified by plasma levels; Immunology; peptides; Recomb. mouse interleukin-13 used;

**ALZET Comments:** Interleukin-13; IP; mice; 7 days; controls received phosphate buffered saline infusion; peptides.

17. Interleukin-15

**ALZET Comments:** Interleukin-15; brain-derived neurotrophic factor; PBS; CSF/CNS (striatum); Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, C57BL6, 3 weeks or 2 months old); ALZET brain infusion kit 3 used; cancer (glioma, U87MG human); tissue perfusion (right striatum); immunology; pumps primed in 37C saline overnight;

**ALZET Comments:** Interleukin-2; interleukin-7; interleukin-15; SC; Mice; 2001; 7 days; Controls received mp w/ PBS; animal info (6-12 wks old, gender, age matched); immunology.

**ALZET Comments:** Interleukin-15, murine; Mice; 14 days; Animal info (Thy 1.1 C57BL/6).

**ALZET Comments:** Interleukin-15, recomb. human; SC; Rat; 2002; 14 days; Peptides; animal info (Fischer Brown Norway).

**ALZET Comments:** Interleukin-15, recomb. human; interleukin-2, recomb. human; PBS; albumin, human; SC; Mice (SCID); 1007D; 10 days; Controls received mp w/ vehicle; immunology; animal info (female, CB17, hu-PBL-SCID, 8-12 weeks old).

**ALZET Comments:** Interleukin-15; Saline; SC; Mice; 1002; 4 weeks; Pump modified to a 4 week infusion by partially dipping the pump in paraffin wax to reduce infusion rate to ~0.125 ul/hr.
18. Interleukin-31

**ALZET Comments:** Interleukin-31, recombinant mouse; SC; Mice; 14 days; animal info (6 – 8 week old, C57BL/6 and Trpv1 knockout mice); functionality of mp verified by observation of skin phenotype; dose-response (pg. 508.e5); Dose (20 mg/day).

**P7009:** S. R. Dillon, et al. Interleukin 31, a cytokine produced by activated T cells, induces dermatitis in mice. NATURE IMMUNOLOGY 2004;5(7):752-760  
**ALZET Comments:** Interleukin-31, mouse; PBS; BSA; SC; Mice; 7-14 days; Controls received mp w/ vehicle; immunology.

19. Leukemia inhibitory factor

**ALZET Comments:** Leukemia inhibitory factor; Cytochrome C; Saline; CSF/CNS (secondary visual cortex); Rat; 1007D; 7 days; Dose (0.083 μg/μl); Controls received mp w/ vehicle; To control for unspecific effects of the infusion protocol, 2 animals were infused with cytochrome C (cytC, 8.3 μg/μl).animal info (Pigmented Long Evans); Brain coordinates (1 mm lateral to lambda into medial area 18).

**Q5190:** Y. H. Rhee, et al. Neural stem cells secrete factors facilitating brain regeneration upon constitutive Raf-Erk activation. Sci Rep 2016;6(32025  
**ALZET Comments:** Raf-Transducer cells, conditioned media; leukemia inhibitory factor; fibroblast growth factor 2; vascular endothelial growth factor; CSF, artificial; CSF/CNS; Mice; 1007D; 6 days; Controls received mp w/ vehicle or control media; animal info (male, C57Bl6, 50-100g); ALZET brain infusion kit 2 used; immunology; cyanoacrylate adhesive; Brain coordinates.

**ALZET Comments:** Leukemia inhibitory factor; Saline; CSF/CNS (intrathecal); Mice; 2002; 3 weeks; Controls received mp w/ vehicle or sham surgery; animal info (C57BL, 8 weeks old); neurodegenerative (Parkinson’s disease); no stress (see pg. 368); behavioral testing (rotarod, bar grabbing, tremor analysis).

**Q6718:** C. Laterza, et al. iPSC-derived neural precursors exert a neuroprotective role in immune-mediated demyelination via the secretion of LIF. Nat Commun 2013;4(2597  
**ALZET Comments:** Antibody, leukemia inhibitory factor neutralizing; PBS; CSF/CNS (lateral ventricle); Mice; 1007D; 7 days; Dose (2 micrograms per day); Controls received mp w/ vehicle; animal info (E2.5 pseudo-pregnant CD1 females,); ALZET brain infusion kit 3 used; Brain coordinates ((from bregma, 0.3mm anterior, 0.8 lateral)).

**ALZET Comments:** Leukemia inhibitory factor; fibroblast growth factor, basic; Saline, normal; Mice; 21 days; Animal info (C57BL/6, male, 8 wks old).
ALZET Comments: Nerve growth factor, recomb. human; glial-derived neurotrophic factor, recomb. human; leukemia inhibitory factor, recomb. human; Saline; albumin, rat serum; CSF/CNS (intrathecal); Rat; 2002; 14 days; Controls received mp w/ vehicle; peptides, animal info (male, Wistar, 220-400 g.).

ALZET Comments: Leukemia inhibitory factor, antagonist; PBS; IP; Mice; Functionality of mp verified by plasma levels taken; comparison of SC/IP injections vs. mp; animal info (8-10 wk old, female, C57BL/6J).

ALZET Comments: Ara-C; leukemia inhibitory factor, recomb. mouse; epidermal growth factor, recomb. human; Saline; PBS; BSA; CSF/CNS; Mice; 1003D; 1007D; 1, 3, 6, 7, days; Controls received mp w/ vehicle; ALZET brain infusion kit 2 or 3 used; peptides; animal info (adult, male, C57BL/6J, 2-6 months old).

ALZET Comments: Nerve growth factor; NT-4/5; brain-derived neurotrophic factor; leukemia inhibitory factor; CSF/CNS (visual cortex); Rat; 1007D; 7 days; Controls received mp w/ cytochrome C; peptides.

ALZET Comments: Leukemia inhibitory factor; Saline; IP; Rabbit; 2ML4; 4 weeks; Controls received mp w/ vehicle; peptides; atherosclerosis.

ALZET Comments: Leukemia inhibitory factor; CSF/CNS (intrathecal); Mice (transgenic); 2004; 13 weeks; Comparison of SC injections vs. IT mp; long-term study; pumps replaced every 4 weeks; ALZET brain infusion kit 1 used (per Dr. Feeney); used the BIK for the IT infusion; glued and sutured the cannula in place; "All mice that entered the study recovered from the surgical procedure and appeared to have no adverse effects." (p. 111); neurodegenerative (Amyotrophic Lateral Sclerosis).

ALZET Comments: Leukemia inhibitory factor; Saline; CSF/CNS (intrathecal, Dorsal Root Ganglia); Rat; 2002; 2 weeks; controls received mp w/ vehicle; peptides; brain tissue distribution; recombinant human LIF used; some animals had undergone nerve injury axotomy on either the tibial or sciatic nerves, other remained uninjured.

ALZET Comments: Leukemia inhibitory factor;; Serum, rat; Saline; Radio-isotopes, 125I tracer;; CSF/CNS (gastrocnemius nerve);; Rat;; 2004;; 28 days;; controls received mp with vehicle; tissue perfusion (nerve repair site); functionality of mp verified by cross-section; peptides; recomb. mouse LIF used; rat serum reduced binding to pump reservoir; bioavailability of LIF was 50%; diagram of experimental model (p. 40).
**ALZET Comments:** Leukemia inhibitory factor; Interleukin-6; Transforming growth factor-a;; PBS;; Intramuscular; mice;; 7 days;; controls received mp w/vehicle; tissue perfusion (vastus lateralis muscle); peptides; targeted delivery of growth factors to the site of muscle injury via a cannula; "drug delivery targeted to a discrete tissue or organ offers significant advantages over systemic administration". (p. 355).

**ALZET Comments:** Leukemia inhibitory factor; CSF/CNS; Rat; 2002; 14 days; controls received mp w/PBS; peptides; ALZET brain infusion kit used.

**ALZET Comments:** Leukemia inhibitory factor; PBS; IP; rabbit; 2ML4; 4 weeks; controls received mp w/vehicle; functionality of mp verified by plasma levels and residual volume; peptides; recomb. human leukemia inhibitory factor used; wrong pump model number described in methods section as 4ML2; graph of pump functionality shown on page 1270; "The present study showed that the osmotic minipumps delivered the prescribed volume throughout the entire 4-week treatment." (p. 1271).

**ALZET Comments:** Leukemia inhibitory factor; Saline; IP; Rat; 1003D; 24 hours; controls received mp w/ saline; peptides; "Continuous infusion of rhLIF was chosen due to the short half-life of this peptide" (p.1926); recomb. human LIF used.

**ALZET Comments:** Leukemia inhibitory factor; Serum, mouse; Intramuscular; mice; 2001; 7 days; controls received mp w/ vehicle; tissue perfusion (muscle); peptides; recomb. murine LIF used.

**ALZET Comments:** Leukemia inhibitory factor; SC; mice; 1007D; 5 days; controls received PBS infusion; peptides; mice had disrupted LIF gene; recomb. human LIF used.

**ALZET Comments:** Leukemia inhibitory factor; PBS; IP; rabbit; 2ML4; 28 days; controls received mp w/ saline; functionality of mp verified by checking residual termination volume; peptides.

**ALZET Comments:** Leukemia inhibitory factor; PBS; Serum, mouse; Radio-isotopes; $^{125}$I tracer; Intramuscular (muscle crush); mice; 2001; 7 days; 24 hours; controls received mp with serum and PBS; peptides; tissue perfusion (muscle crush); mouse serum lessened adsorption to pump reservoir; narrowed catheter sutured to adjacent muscles; iodinated LIF used to confirm targeted delivery.
20. Tumor Necrosis Factor

ALZET Comments: Tumor necrosis factor, alpha human recombinant; PBS; SC; Mice; 1003D; 24 hours; Controls received mp w/ vehicle; animal info (female, C57BL6, 5-6 months old); Dose (1 ug/kg/day).

ALZET Comments: Tumor necrosis factor-a; Saline; SC; Mice; 1007D; Controls received mp w/ vehicle; animal info (C57BL/6JArc); MRI; Therapeutic indication (Hypertension, pre-eclampsia, pregnancy); Dose (500 ng/kg/day).

ALZET Comments: Tumor necrosis factor, murine; PBS; BSA; SC; Mice; 1007D; 7 days; Dose (20 ng/g/day); 0.5% BSA used; animal info (10-12 week old Male C57BL/6J mice weighing 25-30g); comparison of injection vs mp.

Q5999: G. Brower. Gender Differences In Cardiomyocyte Adhesion Cause Heart Failure. FASEB J 2016;
ALZET Comments: Tumor necrosis factor-a; SC; Rat; 2002; 3 days; animal info (Sprague Dawley); cardiovascular; Dose (17 pg/mL).

ALZET Comments: Tumor necrosis factor, alpha, recombin.; CSF/CNS; Mice; 1007D; Controls received mp w/ saline; animal info (female, C57BL6J, 1 year old); ALZET brain infusion kit 3 used; ischemia (cerebral); Dose (1 ug/day); brain coordinates.

ALZET Comments: Tumor necrosis factor-a receptor 1, soluble; CSF/CNS; Mice; 1007D; 1 weeks; Controls received mp w/ saline; animal info (female, C57BL6J, 1 year old); ALZET brain infusion kit 3 used; ischemia (cerebral); Dose (1 ug/day); brain coordinates.

Q4388: M. J. Cunningham, et al. Pregnant rats treated with a high-fat/prooxidant Western diet with ANG II and TNF-alpha are resistant to elevations in blood pressure and renal oxidative stress. AMERICAN JOURNAL OF PHYSIOLOGY-REGULATORY INTEGRATIVE AND COMPARATIVE PHYSIOLOGY 2015;308(R945-R956
ALZET Comments: Angiotensin II; tumor necrosis factor, alpha; SC; Rat (pregnant); 2ML2; 14 days; Controls received mp w/ saline; animal info (female, Sprague Dawley, 15-21 weeks, day 6 of pregnancy); cardiovascular; peptides.

ALZET Comments: Tumor necrosis factor receptor 1; CSF/CNS (cortex); Mice; 1002; Control animals received mp w/ vehicle; animal info (C57BL/6, male).

ALZET Comments: Tumor necrosis factor alpha; Saline; SC; Cattle (lactating); 2ML1; 7 days; Controls received mp w/ vehicle; animal info (female, Holstein, late lactation); Multiple pumps per animal (2); immunology.

ALZET Comments: Tumor necrosis factor, alpha; NaCl; BSA; SC; Mice; 7 days; Animal info (C57BL/6J, male, 12 wks old); 1.0 ul/hr rate of infusion.
ALZET Comments: Tumor necrosis factor, alpha; SC; Mice; 1007D; Controls received mp w/ saline; animal info (C57BL/6IArc, pregnant, gestation day 13.5); mp used to infuse TNF-a to induce hypertension in pregnant mice.

ALZET Comments: Tumor necrosis factor related protein 3, C1q, recomb.; IP; Mice; 2 weeks; Control animals received mp w/ vehicle; animal info (C57BL/6, male, adult); functionality of mp verified via plasma drug levels.

ALZET Comments: Tumor necrosis factor, alpha; Saline; CSF/CNS; Mice; 1002; 14 days; Control animals received mp w/ vehicle; animal info (C57BL/6, 20 g); ALZET brain infusion kit 3 used.

ALZET Comments: Leptin; tumor necrosis factor, alpha, recomb. murine; Mice; 2002; Controls received mp w/ PBS; animal info (male, MF1).

ALZET Comments: Tumor necrosis factor-alpha; PBS; IV (femoral); Monkey (pregnant, baboon); 2ML4; Controls received mp w/ vehicle; animal info (female, baboon, Papio hamadryas).

ALZET Comments: Tumor necrosis factor, alpha, p55 receptor; Saline; CSF/CNS; Rat; 1007D; 2 weeks; Controls received mp w/ vehicle; animal info (Sprague-Dawley); ALZET brain infusion kit 1 used.

Q1381: E. C. Wahl, et al. Direct bone formation during distraction osteogenesis does not require TNF alpha receptors and elevated serum TNF alpha fails to inhibit bone formation in TNFR1 deficient mice. Bone 2010;46(2):410-417
ALZET Comments: Tumor necrosis factor-alpha, recomb. murine; PBS; BSA; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (male, C57BL/6, R1KO, R2KO).

ALZET Comments: Tumor necrosis factor, recomb. mouse; PBS; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (male, C57BL/6 wt, p21 KO, 3 months old, distraction osteogenesis); functionality of mp verified by TNF serum levels.

ALZET Comments: Tumor necrosis factor-alpha, recomb. Periadventitial; Mice; 4 weeks; Controls received mp w/ PBS.

ALZET Comments: Tumor necrosis factor, recomb. mouse; SC; Mice; 2001; 7 days; Controls received mp w/ saline; animal info (db/+ , gd11.5).
**ALZET Comments:** Angiotensin II; tumor necrosis factor-alpha; DMEM; water, sterile; SC; Mice; 1 week; Animal info (9 wks old, C57/BL6); peptides.

**ALZET Comments:** Tumor necrosis factor-a; PBS; albumin, mouse serum; SC; Mice; 1007D; 5, 6 days; Controls received mp w/ vehicle; animal info (young Balb/cby, adult); immunology.

**ALZET Comments:** Tumor necrosis factor-a; Saline; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; functionality of mp verified by serum TNFa levels; cardiovascular; animal info (male, C57BL/6, wt, IL-1D -/-, 10 wks old).

**ALZET Comments:** Tumor necrosis factor, recomb. rat; CSF, artificial; CSF/CNS; Rat; 2002; 5 days; Functionality of mp verified by serum TNFa levels; peptides; animal info (male, Sprague Dawley, 200-300 g.); gentamycin was added to the aCSF to prevent bacterial growth; rat albumin was added to stabilize the infused compound.

**ALZET Comments:** Tumor necrosis factor-a; Saline; albumin, rat; chlorbutanol; CSF/CNS; Rat; 1007D; 4 days; Controls received mp w/ vehicle; peptides; animal info (male, Sprague Dawley, 175-200 g.).

P9211: B. LaMarca, et al. Autoantibodies to the Angiotensin Type I Receptor in Response to Placental Ischemia and Tumor Necrosis Factor-alpha in Pregnant Rats. Hypertension 2008;52(6):1168-1172
**ALZET Comments:** Tumor necrosis factor-a; Rat (pregnant); 2002; 5 days; Functionality of mp verified by serum TNFa levels; cardiovascular; peptides; ischemia (placental); animal info (female, Sprague Dawley, gd 14-19).

**ALZET Comments:** Tumor necrosis factor-alpha; Ear (cochlea); Guinea pig; 2001; 2-4 days; Controls received mp w/vehicle; animal info (Hartley albino); tissue perfusion.

**ALZET Comments:** Tumor necrosis Factor-a, recomb. rat; tumor necrosis factor-a, recomb. rat, heat-inactivated; amitriptyline; CSF, artificial; CSF/CNS; Rat; 8 days; Controls received mp w/ vehicle, or heat-inactivated rr-TNFa; comparison of ip injections vs. mp; peptides; animal info (male, Sprague-Dawley, 300-350g); chronic constriction injury to the right sciatic nerve; neuropathic pain.

**ALZET Comments:** Tumor necrosis factor; Saline; heparin; IV; Rat; 2001; 5 days; Controls received mp w/ vehicle; replacement therapy (ovariectomy); cardiovascular; animal info (female, Sprague-Dawley, 15 weeks old).

**ALZET Comments:** Tumor necrosis factor-alpha; BSA; PBS; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (7 wks old, C57BL/6).


**ALZET Comments:** Tumor necrosis factor receptor peptide WP9QY; PBS; DMSO; SC; Mice; 2001; 7 days; Controls received mp w/ vehicle; dose-response (fig. 4); no stress (see pg. 85, 89-90); peptides; animal info (Balb/c, male, 4 wk. old); 10% DMSO; “the WP9QY peptide degrades very fast, which is the reason why we use osmotic mini pump in this study” (pg. 90).


**ALZET Comments:** Tumor necrosis factor-a; Saline; Mice; 1003D; 24 hours; Controls received mp w/ vehicle; no stress (see pg. 468); animal info (C57BL/6, wt, TNFR1 -/-).


**ALZET Comments:** Tumor necrosis factor-a, recomb. mouse; Saline, physiological; albumin, mouse serum; SC; Mice; 2001; 7 days; Controls received mp w/ vehicle; functionality of mp verified by residual volume; no stress (see pg. 1396); peptides; animal info (male, C57BL/6J, 27-30g.).


**ALZET Comments:** Tumor necrosis factor-alpha, recomb. mouse; SC; Mice (pregnant); 2001; 7 days; Controls received mp w/ saline; dose-response (fig. 1); no stress (see pg. 560); teratology; peptides; animal info (female, C57BL/6, gd 11.5-18.5); endocrinology.


**ALZET Comments:** Tumor necrosis factor receptor peptide WP9QY; peptides, synthetic; PBS; DMSO; SC; Mice; 2002; 4 weeks; 3 days; Controls received mp w/ vehicle, or control peptide; dose-response (pg. 1530); pumps replaced after 2 weeks; no stress (see pg. 1529); peptides; animal info (female, C57BL/6j, 12 wk old); 10% DMSO; inhibits osteoclastogenesis and bone resorption.