



References on the Administration of Interferons Using ALZET® Osmotic Pumps

1. Alpha

Q1983: Y. Yuan, *et al.* Role of microRNA-15a in autoantibody production in interferon-augmented murine model of lupus. MOLECULAR IMMUNOLOGY 2012;52(2):61-70

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.

P9300: A. Shinohara, *et al.* Dosing schedule-dependent change in the disruptive effects of interferon-alpha on the circadian clock function. LIFE SCIENCES 2008;83(15-16):574-580

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).

P6142: S. Koyanagi, *et al.* Alteration of intrinsic biological rhythms during interferon treatment and its possible mechanism. MOLECULAR PHARMACOLOGY 2002;62(6):1393-1399

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

P3986: P. K. Henke, *et al.* Bacterial products primarily mediate fibroblast inhibition in biomaterial infection. J. Surg. Res 1998;74(17-22)

ALZET Comments: Antibody, anti-interferon gamma; Antibody, indomethacin; Antibody, anti-TNFa; Antibody, interleukin 1 alpha; PBS, sterile; ETHANOL; Indomethacin; SC; mice; 1007D; 7 days; immunology; pump implanted next to Dacron graft; peptides.

2. Beta

P9580: S. Tzima, *et al.* Myeloid heme oxygenase-1 regulates innate immunity and autoimmunity by modulating IFN-beta production. Journal of Experimental Medicine 2009;206(5):1167-1179

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

P6764: S. Frewert, *et al.* Intratumoral infusion of interleukin-1 beta and interferon-gamma; induces tumor invasion with macrophages and lymphocytes in a rat glioma model. Neuroscience Letters 2004;364(3):145-148

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).

P1845: M. Denis. Recombinant murine beta interferon enhances resistance of mice to systemic mycobacterium avium infection. Infect. Immun 1991;59(5):1857-1859

ALZET Comments: Interferon-beta; mice; 2002; no duration posted; controls received pumps with heat-inactivated cytokines; peptides.

3. Gamma

Q1327: J. A. B. Strickertsson, *et al.* Interferon-gamma inhibits ghrelin expression and secretion via a somatostatin-mediated mechanism. WORLD JOURNAL OF GASTROENTEROLOGY 2011;17(26):3117-3125



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

Q1352: Y. Tang, *et al.* The role of the Th1 transcription factor T-bet in a mouse model of immune-mediated bone-marrow failure. *Blood* 2010;115(3):541-548

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

Q0408: H. J. Ryu, *et al.* THE PROTECTIVE EFFECTS OF INTERLEUKIN-18 AND INTERFERON-gamma ON NEURONAL DAMAGES IN THE RAT HIPPOCAMPUS FOLLOWING STATUS EPILEPTICUS. *Neuroscience* 2010;170(3):711-721

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.

P8835: A. B. Rogers, *et al.* Hepatocellular carcinoma associated with liver-gender disruption in male mice. *Cancer Research* 2007;67(24):11536-11546

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).

P8739: X. T. Qiao, *et al.* Prospective identification of a multilineage progenitor in murine stomach epithelium. *Gastroenterology* 2007;133(6):1989-1998

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 Kvil-EGFP tg; C57BL/6J; 4 months old); long-term study.

P8261: Y. Si, *et al.* Continuous in vivo infusion of interferon-gamma (IFN-gamma) enhances engraftment of syngeneic wild-type cells in Fanca^{-/-} and Fancg^{-/-} mice. *Blood* 2006;108(13):4283-4287

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).

P7447: W. Q. Kang, *et al.* Interferon gamma induction of gastric mucous neck cell hypertrophy. *LABORATORY INVESTIGATION* 2005;85(5):702-715

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

P7132: J. T. Brooling, *et al.* Differential regulation of rodent hepatocyte and oval cell proliferation by interferon gamma. *Hepatology* 2005;41(4):906-915

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

P7042: X. X. Li, *et al.* Continuous in vivo infusion of interferon-gamma (IFN-gamma) preferentially reduces myeloid progenitor numbers and enhances engraftment of syngeneic wild-type cells in Fancc^{-/-} mice. *Blood* 2004;104(4):1204-1209

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.

P6764: S. Frewert, *et al.* Intratumoral infusion of interleukin-1 beta and interferon-gamma; induces tumor invasion with macrophages and lymphocytes in a rat glioma model. *Neuroscience Letters* 2004;364(3):145-148

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).



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.

P5102: D. K. Skovseth, *et al.* Vascular morphogenesis and differentiation after adoptive transfer of human endothelial cells to immunodeficient mice. American Journal of Pathology 2002;160(5):1629-1637

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.

Q3035: Interferon-alpha: an effective adjuvant for peptide-based cytotoxic T-cell vaccines. Kurume Med J. 2001;48(2):171-4

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);.

P4675: S. Jander, *et al.* Differential regulation of microglial keratan sulfate immunoreactivity by proinflammatory cytokines and colony-stimulating factors. Glia 2000;30(4):401-410

ALZET Comments: Interferon-gamma; Tumor necrosis factor- α ; PBS, sterile;; CSF/CNS;; Rat;; 1007D;; 6 days;; Controls received mp w/ vehicle; immunology; peptides; ALZET brain infusion kit used; proinflammatory cytokines;

4. Tau

Q3963: J. Lee, *et al.* Intrauterine Coadministration of ERK1/2 Inhibitor U0126 Inhibits Interferon TAU Action in the Endometrium and Restores Luteolytic PGF(2alpha) Pulses in Sheep. Biology of Reproduction 2014;91(U177-U185

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;.

Q2583: P. Dorniak, *et al.* Cortisol and Interferon Tau Regulation of Endometrial Function and Conceptus Development in Female Sheep. Endocrinology 2013;154(2):931-941

ALZET Comments: Cortisol; PF915275; meloxicam; interferon, tau, recomb. 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.

Q4759: A. Q. Antoniazzi. Endocrine Delivery of Interferon Tau Protects the Corpus Luteum from Prostaglandin F2 Alpha-Induced Luteolysis in Ewes. Biology of Reproduction 2013;88(6):1-12

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).

Q2056: P. Dorniak, *et al.* Endometrial HSD11B1 and Cortisol Regeneration in the Ovine Uterus: Effects of Pregnancy, Interferon Tau, and Prostaglandins. Biology of Reproduction 2012;86(4):U106-U115

ALZET Comments: Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2 α , ovine serum; PGI2, ovine serum; Ethanol; saline; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 7 days; Controls received mp w/ vehicle; animal info (Mature Rambouillet); good methods (pg 2); vinyl tubing used (0007760); 2% ethanol used; enzyme inhibitor (prostaglandin synthase two); tissue perfusion (intrauterine).



Q2057: P. Dorniak, *et al.* Conceptus-Derived Prostaglandins Regulate Endometrial Function in Sheep. *Biology of Reproduction* 2012;87(1):U80-U86

ALZET Comments: Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2a, ovine serum; PGI2, 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).

Q1040: P. Dorniak, *et al.* Prostaglandins Regulate Conceptus Elongation and Mediate Effects of Interferon Tau on the Ovine Uterine Endometrium. *Biology of Reproduction* 2011;84(6):1119-1127

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.

P9920: R. C. Bott, *et al.* Uterine Vein Infusion of Interferon Tau (IFNT) Extends Luteal Life Span in Ewes. *Biology of Reproduction* 2010;82(4):725-735

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.