



## References on the Administration of Interferons Using ALZET® Osmotic Pumps

### 1. Alpha

**Q7344:** R. Gutierrez Jauregui, *et al.* IL-1beta Promotes Staphylococcus aureus Biofilms on Implants in vivo. *Front Immunol* 2019;10(1082)

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

**Species:** Mice; **Pump:** 1007D; **Duration:** 10 Days;

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

**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

**Agents:** Interferon, alpha; interferon, gamma **Vehicle:** PBS; BSA; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 16 weeks;

**ALZET Comments:** Animal info (13 wks old, female, B/W); pumps replaced after 8 weeks; long-term study; stability verified after 8 weeks; "residue IFNs from the pumps at the end of treatment were tested on IFN and IFN responsive cell lines and demonstrated that the in vivo conditions in the pump did not affect bioactivity of both IFNs (data not shown)" pg 63

**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

**Agents:** Interferon-alpha, recomb. human **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 6 days;

**ALZET Comments:** 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

**Agents:** Interferon-alpha **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

**ALZET Comments:** 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)

**Agents:** Antibody, anti-interferon gamma; Antibody, indomethacin; Antibody, anti-TNFa; Antibody, interleukin 1 alpha

**Vehicle:** PBS, sterile; ETHANOL; Indomethacin; **Route:** SC; **Species:** mice; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** immunology; pump implanted next to Dacron graft; peptides

### 2. Beta

**Q7344:** R. Gutierrez Jauregui, *et al.* IL-1beta Promotes Staphylococcus aureus Biofilms on Implants in vivo. *Front Immunol* 2019;10(1082)

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

**Species:** Mice; **Pump:** 1007D; **Duration:** 10 Days;

**ALZET Comments:** Dose (IL-1b (83µg/ml); IL-6 (83µg/ml); IL-10 (166µg/ml);



IL-12 (83µg/ml); IL-17 (125µg/ml); IL-23 (166µg/ml); IFNγ (83µg/ml); TNFα (166µg/ml); anti-TGF-β1 (166µg/ml); anti-IL-1β (150µg/ml)); Controls received mp w/ vehicle; animal info (Eight- to twelve-week-old female C57BL/6 mice); Immunology (“evaluate the suitability of osmotic pumps as a model for biofilms in implant associated infections, we implanted osmotic pumps pre-colonized with bioluminescent *Staphylococcus aureus*”);

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

**Agents:** Interferon-β, recomb. human **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

**ALZET Comments:** Animal info (Hmox1 KO)

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

**Agents:** Interleukin-1, β recomb. rat; Interferon-γ, recomb. rat **Vehicle:** Saline, physiological; albumin, human serum; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 1003D; **Duration:** 48 hours;

**ALZET Comments:** Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioma)

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

**Agents:** Interferon-β **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** mice; **Pump:** 2002; **Duration:** no duration posted;

**ALZET Comments:** controls received pumps with heat-inactivated cytokines; peptides

### 3. Gamma

**Q7344:** R. Gutierrez Jauregui, *et al.* IL-1β Promotes *Staphylococcus aureus* Biofilms on Implants in vivo. *Front Immunol* 2019;10(1082)

**Agents:** Interleukin-1 β; Interleukin-6; Interleukin-10; Interleukin-12; Interleukin-17; Interleukin-23; Interferon, γ; Tumor Necrosis Factor, α; Interleukin-1 β, anti; Transforming Growth Factor-β1, anti **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 10 Days;

**ALZET Comments:** Dose (IL-1β (83µg/ml); IL-6 (83µg/ml); IL-10 (166µg/ml); IL-12 (83µg/ml); IL-17 (125µg/ml); IL-23 (166µg/ml); IFNγ (83µg/ml); TNFα (166µg/ml); anti-TGF-β1 (166µg/ml); anti-IL-1β (150µg/ml)); Controls received mp w/ vehicle; animal info (Eight- to twelve-week-old female C57BL/6 mice); Immunology (“evaluate the suitability of osmotic pumps as a model for biofilms in implant associated infections, we implanted osmotic pumps pre-colonized with bioluminescent *Staphylococcus aureus*”);

**Q7192:** A. Kimura, *et al.* Protective Roles of Interferon-γ in Cardiac Hypertrophy Induced by Sustained Pressure Overload. *J Am Heart Assoc* 2018;7(6):

**Agents:** Interferon, γ **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Dose (15 µM/d); animal info (8-10 week old, male, BALB/c); cardiovascular;

**Q4560:** L. Pereira, *et al.* IFN γ regulates proliferation and neuronal differentiation by STAT1 in adult SVZ niche. *Frontiers in Cellular Neuroscience* 2015;9(U1-U10)

**Agents:** Interferon, γ **Vehicle:** Saline; **Route:** CSF/CNS (third ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, STAT2 KO or 129S6/SvEv); immunology;

**Q3523:** T. S. Johnson, *et al.* Etoposide Selectively Ablates Activated T Cells To Control the Immunoregulatory Disorder Hemophagocytic Lymphohistiocytosis. *Journal of Immunology* 2014;192(1):84-91



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

**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

**Agents:** Interferon, alpha; interferon, gamma **Vehicle:** PBS; BSA; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 16 weeks;

**ALZET Comments:** Animal info (13 wks old, female, B/W); pumps replaced after 8 weeks; long-term study; stability verified after 8 weeks; "residue IFNs from the pumps at the end of treatment were tested on IFN and IFN responsive cell lines and demonstrated that the in vivo conditions in the pump did not affect bioactivity of both IFNs (data not shown)" pg 63

#### 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; PGF2a, 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.