



### References on Arthritis Research Using ALZET® Osmotic Pumps

- Q5917:** D. J. Wilkinson, *et al.* Matriptase Induction of Metalloproteinase-Dependent Aggrecanolytic In Vitro and In Vivo: Promotion of Osteoarthritic Cartilage Damage by Multiple Mechanisms. *Arthritis Rheumatol* 2017;69(8):1601-1611  
**ALZET Comments:** Antibody A11; compound 59; Saline; IP, SC; Mice; 1004, 2004; 4 weeks, 8 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 25-30g); pumps replaced every 4 weeks; Dose (Antibody: 1.5 ug/day; Compound 59: 5, 25, or 50 mg/kg/day);.
- Q6532:** K. Wang, *et al.* T140 blocks the SDF-1/CXCR4 signaling pathway and prevents cartilage degeneration in an osteoarthritis disease model. *PLoS One* 2017;12(4):e0176048  
**ALZET Comments:** T140; PBS; SC; Guinea pig; 2006; Dose (180 ug/d); Controls received mp w/ vehicle; animal info (9 month old male Hartley guinea pigs weighing about 600g); pumps replaced every 6 weeks; Therapeutic indication (osteoarthritis);.
- Q6522:** S. C. van Dalen, *et al.* Interleukin-1 is not involved in synovial inflammation and cartilage destruction in collagenase-induced osteoarthritis. *Osteoarthritis Cartilage* 2017;25(3):385-396  
**ALZET Comments:** Interleukin-1 receptor antagonist; Saline; IP; Mice; 1007D; 2 weeks; Dose (37.5 ug/hr); Controls received empty mp; animal info (12 week old female C57BL/6 mice);.
- Q5974:** H. Shimaoka, *et al.* A cytokine signal inhibitor for rheumatoid arthritis enhances cancer metastasis via depletion of NK cells in an experimental lung metastasis mouse model of colon cancer. *Oncol Lett* 2017;14(3):3019-3027  
**ALZET Comments:** Tofacitinib; PEG 300; CSF/CNS; Mice; 2002; 6 days; animal info (Wild-type CD1) ; Controls received mp w/vehicle; dose (15 mg/kg/day); cancer; enzyme inhibitor (JAK3).
- Q6216:** S. Liu, *et al.* Efficiency and Safety of CRAC Inhibitors in Human Rheumatoid Arthritis Xenograft Models. *J Immunol* 2017;199(5):1584-1595  
**ALZET Comments:** Antibody (hCRACM1-IgG); YM-58483; Saline; Intralipose; SC; Mice; 1004; 28 days; hCRACM1-IgG Dose (1 or 10 mg/kg), YM058483 Dose (1.5mg/kg); YM-58483 was mixed with 10% Intralipose, which is an i.v. lipid emulsion containing 10% soybean oil, 1.2% egg yolk phospholipids, and 2.2% glycerin; Controls received mp w/ vehicle; hCRACM1-IgG is a neutralizing monoclonal antibody targeting human CRACM1; YM-58483 is a small molecular CRAC blocker; Immunology (transplant);.
- Q6439:** J. Lee, *et al.* Nicotine drives neutrophil extracellular traps formation and accelerates collagen-induced arthritis. *Rheumatology (Oxford)* 2017;56(4):644-653  
**ALZET Comments:** Nicotine; PBS; SC; Mice; 2006; 42 days; Dose (15 mg/kg/day); Controls received mp w/ vehicle; animal info (male DBA/1J mice);.
- Q6440:** M. G. Ledesma-Colunga, *et al.* Prolactin blocks the expression of receptor activator of nuclear factor kappaB ligand and reduces osteoclastogenesis and bone loss in murine inflammatory arthritis. *Arthritis Res Ther* 2017;19(1):93  
**ALZET Comments:** Prolactin; SC; Rat; 28 days; animal info (Male Sprague-Dawley rats weighing 200–250 g);.
- Q6304:** A. Kaneguchi, *et al.* Nociception contributes to the formation of myogenic contracture in the early phase of adjuvant-induced arthritis in a rat knee. *J Orthop Res* 2017;35(7):1404-1413  
**ALZET Comments:** Morphine hydrochloride; SC; Rat; 2ML1; 5 days; Dose (41–48 mg/kg/day); animal info (8-week-old male Wistar rats weighing 200–240 g); Therapeutic indication (Knee arthritis);.
- Q6456:** M. Ito, *et al.* A novel JAK inhibitor, peficitinib, demonstrates potent efficacy in a rat adjuvant-induced arthritis model. *J Pharmacol Sci* 2017;133(1):25-33  
**ALZET Comments:** Peficitinib; PEG, Acetic acid; IP; Rat; 2ML2; Dose (0.12, 0.24, and 0.48 mg/day per body); Controls received mp w/ vehicle; Resultant plasma level (7.0 ng/mL, 18 ng/mL, and 35 ng/mL on day 13, and 7.1 ng/mL, 13 ng/mL, and 30 ng/mL on day 16);.



**Q6010:** Y. Chen, *et al.* Attenuation of subchondral bone abnormal changes in osteoarthritis by inhibition of SDF-1 signaling. *Osteoarthritis Cartilage* 2017;25(6):986-994

**ALZET Comments:** AMD3100; PBS; SC; Rat; 2006; 6 weeks; Controls received mp w/ vehicle; animal info (16 weeks old, Sprague-Dawley; 400-500 g); Therapeutic indication (Osteoarthritis, subchondral bone); Dose (22.3 mg/ml);

**Q6608:** W. Lu, *et al.* CXCL12/CXCR4 Axis Regulates Aggrecanase Activation and Cartilage Degradation in a Post-Traumatic Osteoarthritis Rat Model. *Int J Mol Sci* 2016;17(10):

**ALZET Comments:** AMD3100; PBS; Rat; 2004; 8 weeks; Dose (3 mg/day); Controls received mp w/ vehicle; animal info (8 week old male Sprague-Dawley rats weighing 190-210g); pumps replaced every 4 weeks; Therapeutic indication (osteoarthritis);

**Q4897:** Gisela Segond von Banchet, *et al.* Long-Lasting Activation of the Transcription Factor CREB in Sensory Neurons by Interleukin-1b During Antigen-Induced Arthritis in Rats. *ARTHRITIS & RHEUMATOLOGY* 2016;68(2):532-541

**ALZET Comments:** Anakinra; SC; Rat; 2ML4; 26 days; Controls received mp w/ saline; animal info (female, Lewis, 6-8 weeks old, 160-180g); animal info (female, Lewis, 6-8 weeks old, 160-180g); immunology; delayed delivery for 5 days; Dose (53 mg/kg/day);

**Q5339:** Y. Dong, *et al.* Inhibition of SDF-1alpha/CXCR4 Signalling in Subchondral Bone Attenuates Post-Traumatic Osteoarthritis. *Int J Mol Sci* 2016;17(6):

**ALZET Comments:** AMD3100; PBS; SC; Mice; 1004; 30 days; Controls received mp w/ vehicle and sham operation; animal info (C57BL/6J mice (30 males, 2 months old)); immunology; (AMD3100 is an immunostimulant); inhibitor of CXCR4; transected the anterior cruciate ligament on the right knee; caused joint instability; Dose (180 ug/day);

**Q4613:** N. P. Thomas, *et al.* Attenuation of cartilage pathogenesis in post-traumatic osteoarthritis (PTOA) in mice by blocking the stromal derived factor 1 receptor (CXCR4) with the specific inhibitor, AMD3100. *JOURNAL OF ORTHOPAEDIC RESEARCH* 2015;33(1071-1078

**ALZET Comments:** AMD3100; SC; Mice; 1004; 2 months; Controls received mp w/ PBS or empty pumps; animal info (male, C57BL6J, 2 months old); pumps replaced every 4 weeks;

**Q4279:** M. Radwan, *et al.* Protection against murine osteoarthritis by inhibition of the 26S proteasome and lysine-48 linked ubiquitination. *ANNALS OF THE RHEUMATIC DISEASES* 2015;74(1580-1587

**ALZET Comments:** MG132; DMSO; PEG 300; SC; Mice; 1004; 8 weeks; Controls received mp w/ vehicle; animal info (C57BOL6J or mutant-Ub transgenic, 8 weeks old); pumps replaced every 4 weeks; 50% DMSO used; 50% PEG 300; enzyme inhibitor (proteasome, general);

**Q4547:** F. R. Nieto, *et al.* Calcitonin Gene-Related Peptide-Expressing Sensory Neurons and Spinal Microglial Reactivity Contribute to Pain States in Collagen-Induced Arthritis. *ARTHRITIS & RHEUMATOLOGY* 2015;67(1668-1677

**ALZET Comments:** Calcitonin gene-related peptide (8-37); CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (female, Lewis, 180-200g); behavioral testing (Von Frey filaments; Plantar test); immunology; peptides;

**Q3829:** G. Kato, *et al.* The inhibitory effects of a RANKL-binding peptide on articular and periarticular bone loss in a murine model of collagen-induced arthritis: a bone histomorphometric study. *ARTHRITIS RESEARCH & THERAPY* 2015;17(U2-U15

**ALZET Comments:** Peptide, OP3-4; PBS; DMSO; SC; Mice; 49 days; Controls received mp w/ vehicle; animal info (male, DBA/1J, 7 weeks old); pumps replaced after day 35 or 42; 20% DMSO used; peptides; "a sustained-release carrier for OP3-4 needs to be developed since peptide drugs are unstable and aggregate easily in vivo. The effects of OP3-4 in this study were achieved using infusion pumps" pg 13.

**Q4440:** C. B. Hamilton, *et al.* Weight-bearing asymmetry and vertical activity differences in a rat model of post-traumatic knee osteoarthritis. *OSTEOARTHRITIS AND CARTILAGE* 2015;23(1178-1185



**ALZET Comments:** Water, distilled; SC; Rat; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 301-325g); pumps replaced every 4 weeks; post op. care (buprenorphine 50 ug/kg SC); behavioral testing (static weight bearing, exploratory motor behavior); long-term study;.

**Q5121:** C. T. Appleton, *et al.* Reduction in disease progression by inhibition of transforming growth factor alpha-CCL2 signaling in experimental posttraumatic osteoarthritis. *Arthritis Rheumatol* 2015;67(10):2691-701

**ALZET Comments:** AG1478; RS504393; DMSO; water, deionized; SC; Rat; 2ML4; 10 weeks; Controls received mp w/ vehicle; functionality of mp verified by plasma levels and knee articular cartilage; pumps replaced every 4 weeks; %50 of DMSO; long-term study; enzyme inhibitor (EGFR and CCR2 inhibitors); EGFR inhibitor AG1478, CCR2 inhibitor RS504393; Dose: (AG1478) 21 nmoles/kg/hour; (RS504393) 200 nmoles/kg/hour.

**Q4022:** K. Nishimura, *et al.* Tofacitinib Facilitates the Expansion of Myeloid-Derived Suppressor Cells and Ameliorates Arthritis in SKG Mice. *ARTHRITIS & RHEUMATOLOGY* 2014;66(S1271-S1272)

**ALZET Comments:** Tofacitinib; DMSO; SC; Mice; 5 days; Controls received mp w/ vehicle; animal info (female, SKG mice, arthritis induction); immunology; enzyme inhibitor (JAK3).

**Q3980:** G. J. Litherland, *et al.* Glycogen Synthase Kinase 3 Inhibition Stimulates Human Cartilage Destruction and Exacerbates Murine Osteoarthritis. *ARTHRITIS & RHEUMATOLOGY* 2014;66(2175-2187)

**ALZET Comments:** CT99021; DMSO; PEG 400; SC; Mice; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 10 weeks old); 50% PEG 400 used; 50% DMSO used; CT99021 is a GSK-3 inhibitor;.

**Q3906:** B. D. Furman, *et al.* Targeting pro-inflammatory cytokines following joint injury: acute intra-articular inhibition of interleukin-1 following knee injury prevents post-traumatic arthritis. *ARTHRITIS RESEARCH & THERAPY* 2014;16(U305-U319)

**ALZET Comments:** Interleukin-1 receptor antagonist; Saline; SC; Mice; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6, 8 weeks old); functionality of mp verified by serum levels; comparison of injection vs mp; stress/adverse reaction: (see pg. 4); post op. care (buprenorphine); "...no significant differences were detected for any of the outcome measures in mice receiving systemic saline via osmotic pump or IP injections.." pg 4; pumps removed after 28 days;.

**Q3460:** M. E. Dowty, *et al.* Preclinical to Clinical Translation of Tofacitinib, a Janus Kinase Inhibitor, in Rheumatoid Arthritis. *Journal of Pharmacology and Experimental Therapeutics* 2014;348(1):165-173

**ALZET Comments:** Tofacitinib; DMSO; PEG 300; SC; Mice; 36 days; Controls received mp w/ vehicle; animal info (male, DBA/1, 10-12 weeks old); functionality of mp verified by plasma levels; pumps replaced every 19 days; 33% DMSO used; dose-response (pg. 168); toxicology; immunology; Tofacitinib is a janus kinase inhibitor; enzyme inhibitor (JAK3).

**Q3045:** N. Adan, *et al.* Prolactin promotes cartilage survival and attenuates inflammation in inflammatory arthritis. *Journal of Clinical Investigation* 2013;123(9):3902-3913

**ALZET Comments:** Prolactin, ovine; SC; Rat; 6 days; 21 days; Animal info (male, Sprague Dawley, 200-250g); functionality of mp verified by serum levels at 21 days; behavioral testing (hind paw pain); immunology;.

**Q2910:** F. Y. Wei, *et al.* Attenuation of osteoarthritis via blockade of the SDF-1/CXCR4 signaling pathway. *ARTHRITIS RESEARCH & THERAPY* 2012;14(4):U233-U243

**ALZET Comments:** AMD 3100; PBS; SC; Guinea pig; 2006; 12 weeks; Controls received mp w/ PBS; animal info (0.88 kg+ 0.21 kg); pumps replaced once every 6 weeks; long-term study.

**Q2585:** E. Schurgers, *et al.* Pulmonary inflammation in mice with collagen-induced arthritis is conditioned by complete Freund's adjuvant and regulated by endogenous IFN- $\gamma$ . *European Journal of Immunology* 2012;42(12):3223-3234

**ALZET Comments:** Etanercept; PBS; Mice; 2004; Control animals received mp w/ vehicle; animal info (IFN gamma R KO, DBA/1).

**Q2259:** A. K. Clark, *et al.* Spinal cathepsin S and fractalkine contribute to chronic pain in the collagen-induced arthritis model. *Arthritis and Rheumatism* 2012;64(6):2038-2047



**ALZET Comments:** Cathepsin S; fractalkine; CSF/CNS (intrathecal); Rat; 2001; Animal info (adult, female, Lewis, 180-200 g); peptides.

**Q1778:** D. Y. Liu, *et al.* Population pharmacokinetic-pharmacodynamic-disease progression model for effects of anakinra in Lewis rats with collagen-induced arthritis. JOURNAL OF PHARMACOKINETICS AND PHARMACODYNAMICS 2011;38(6):769-786

**ALZET Comments:** Anakinra; SC; Rat; 1 week; Animal info (male, Lewis, 6-9 wks old); half-life "4-6 hours" pg 78; pharmacokinetic study; pk study.

**Q1059:** L. Evans, *et al.* Suppression of Leukocyte Infiltration and Cartilage Degradation by Selective Inhibition of Pre B-Cell Colony-Enhancing Factor/Visfatin/Nicotinamide Phosphoribosyltransferase APO866-Mediated Therapy in Human Fibroblasts and Murine Collagen-Induced Arthritis. Arthritis and Rheumatism 2011;63(7):1866-1877

**ALZET Comments:** APO866; Propylene glycol; saline; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (male, DBA/1, 7-8 wks old); half-life (~8 hours in humans pg 1876); APO866 is a small molecule inhibitor in human fibroblasts in vitro and in murine collagen arthritis; A maximum tolerated dose of APO866 of 0.126 mg/m<sup>2</sup>/hour in human clinical trials and 0.18 mg/m<sup>2</sup>/hour in rats has been reported" pg 1868.

**Q0010:** P. Ergang, *et al.* Local metabolism of glucocorticoids and its role in rat adjuvant arthritis. MOLECULAR AND CELLULAR ENDOCRINOLOGY 2010;323(2):155-160

**ALZET Comments:** Anakinra; Saline; sodium citrate; EDTA; tween 80; SC; Rat; 2ML1; 7 days; Controls received vehicle; animal info (male, Lewis, 7-9 weeks old; adjuvant-induced arthritis); IL-1B antagonist; 0.5mM EDTA; 0.1% Tween 80.

**P9904:** M. K. Boettger, *et al.* Spinal Tumor Necrosis Factor alpha-Neutralization Reduces Peripheral Inflammation and Hyperalgesia and Suppresses Autonomic Responses in Experimental Arthritis A Role for Spinal Tumor Necrosis Factor alpha-During Induction and Maintenance of Peripheral Inflammation. Arthritis and Rheumatism 2010;62(5):1308-1318

**ALZET Comments:** Etanercept; CSF/CNS (intrathecal); Rat; 2ML4; 3, 21 days; Controls received mp w/vehicle: animal info (Lewis, 6-8 wks, 160-180 g); ALZET intrathecal catheter used; schematic drawing with ALZET pump and catheter.

**Q0005:** M. K. Boettger, *et al.* Spinally applied ketamine or morphine attenuate peripheral inflammation and hyperalgesia in acute and chronic phases of experimental arthritis. BRAIN BEHAVIOR AND IMMUNITY 2010;24(3):474-485

**ALZET Comments:** Ketamine, Morphine; Saline; CSF/CNS (intrathecal); Rat; 2ML4; 21 days; Controls received mp w/ vehicle; tolerance; ALZET brain infusion kit used; half-life pg 477 (2.5 hrs in CSF (ketamine); 2.1 hrs (morphine)); animal info (Female, Lewis, 6-8 wks old, 160-180 g); dorsal laminectomy; behavioral testing (pain related behavior).

**P9905:** M. Stolina, *et al.* RANKL inhibition by osteoprotegerin prevents bone loss without affecting local or systemic inflammation parameters in two rat arthritis models: comparison with anti-TNF-alpha or anti-IL-1 therapies. ARTHRITIS RESEARCH & THERAPY 2009;11(6):U251-U265

**ALZET Comments:** Anakinra; SC; Rat; Animal info (Lewis, 7 to 8 wks old, AIA, CJA).

**P9023:** A. J. Milici, *et al.* Cartilage preservation by inhibition of Janus kinase 3 in two rodent models of rheumatoid arthritis. ARTHRITIS RESEARCH & THERAPY 2008;10(1):U175-U183

**ALZET Comments:** CP-690550; PEG 300; SC; Rat; mice; 2004; 2ML2; 2 weeks; 28 days; Controls received mp w/ vehicle or no pump; dose-response (fig. 1); enzyme inhibitor (JAK3, janus kinase 3); animal info (male, DBA/J1, male, Lewis); "it was necessary to administer CP-690550 via osmotic pumps due to the poor (PK) properties of this compound in rodents."

**P8953:** A. Knedla, *et al.* The therapeutic use of osmotic minipumps in the severe combined immunodeficiency (SCID) mouse model for rheumatoid arthritis. Annals of the Rheumatic Diseases 2008;68(1):124-129

**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.



- P9761:** E. Dahlen, *et al.* Development of interleukin-1 receptor antagonist mutants with enhanced antagonistic activity in vitro and improved therapeutic efficacy in collagen-induced arthritis. *Journal of Immunotoxicology* 2008;5(2):189-199  
**ALZET Comments:** Anakinra; NaCl; citric acid; EDTA; tween 80; IP; Mice; 1007D; 7 days; Anakinra is an interleukin-1 receptor antagonist; 0.35mM EDTA; 0.07% Tween 80;.
- P9287:** E. Brahn, *et al.* An Angiogenesis Inhibitor, 2-Methoxyestradiol, Involutes Rat Collagen-Induced Arthritis and Suppresses Gene Expression of Synovial Vascular Endothelial Growth Factor and Basic Fibroblast Growth Factor. *Journal of Rheumatology* 2008;35(11):2119-2128  
**ALZET Comments:** Estradiol, 2-methoxy-; SC; Rat; 2ML4; 18 days; Controls received mp w/ vehicle; comparison of oral gavage vs. mp; animal info (syngeneic LOU, 8-10 wks old, 100-150 g., Collagen-induced arthritis; "Delivery of 60 mg/kg by an osmotic pump, however, was similar in efficacy to 300 mg/kg oral gavage. This result suggests that a steady-state level of 2ME2 achieved equivalent arthritic inhibition at a lower total dose." (p. 2124).
- P8929:** N. Badlani, *et al.* The protective effect of OP-1 on articular cartilage in the development of osteoarthritis. *OSTEOARTHRITIS AND CARTILAGE* 2008;16(5):600-606  
**ALZET Comments:** Osteogenic protein-1; Lactose; Knee (articular cavity); Rabbit; 2004; 6 weeks; Controls received mp w/ vehicle; functionality of mp verified by separate in vivo test; peptides; post op. care ("appropriate"); animal info (New Zealand, White, 1 yr old); also known as BMP-7 or bone morphogenic protein-7; catheter was secured with polyethylene stents; "The efficacy of the (ALZET Pump) was tested in vivo before beginning the study with good results"; "constant infusion of OP-1 may be the most ideal form of delivery"; long-term study; good methods.
- P9324:** S. Averill, *et al.* Reg-2 expression in dorsal root ganglion neurons after adjuvant-induced monoarthritis. *Neuroscience* 2008;155(4):1227-1236  
**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.).
- R0248:** H. Tsutsumi, *et al.* Inhibitors of the chemokine receptor CXCR4: Chemotherapy of AIDS, metastatic cancer, leukemia and rheumatoid arthritis. *Letters in Drug Design & Discovery* 2007;4(1):20-26  
**ALZET Comments:** TN14003, 4F-benzoyl-; SC; Mice; Mice (SCID); Cancer (breast carcinoma); immunology; peptides; CXCR4 antagonist; review, see p. 21, 23.
- P8525:** H. Saito, *et al.* A tumor necrosis factor receptor loop peptide mimic inhibits bone destruction to the same extent as anti-tumor necrosis factor monoclonal antibody in murine collagen-induced arthritis. *Arthritis and Rheumatism* 2007;56(4):1164-1174  
**ALZET Comments:** Peptide, WP9QY; antibody, monoclonal, anti-TNF alpha; PBS; DMSO; SC; Mice; 2001; 19 days; Controls received mp w/ vehicle; dose-response (fig. 1); pumps replaced every 7 days; half-life (p. 1182) "short;" peptides; animal info (male, DBA/1J, 6 weeks old, collagen induced arthritis); 10% DMSO.
- P8965:** H. Matsuno, *et al.* Requirement of methotrexate in combination with anti-tumor necrosis factor alpha therapy for adequate suppression of osteoclastogenesis in rheumatoid arthritis. *Journal of Rheumatology* 2007;34(12):2326-2333  
**ALZET Comments:** Infliximab; immunoglobulin G, human; SC; Mice (SCID); 2 weeks; Controls received mp w/ human IgG; immunology; animal info (SCID-HuRAG-pit, 6-7 wks old; TNF-alpha inhibitor).
- P8793:** D. Kurosaka, *et al.* The effect of endostatin evaluated in an experimental animal model of collagen-induced arthritis. *SCANDINAVIAN JOURNAL OF RHEUMATOLOGY* 2007;36(6):434-441  
**ALZET Comments:** Endostatin; PBS; IP; Mice; 2 weeks; Controls received mp w/ vehicle; animal info (1J, 6 week); "compared with the once daily dosing regimen, the administration of endostatin by an osmotic pump achieved a similar arthritis-inhibiting effect at one-tenth of the dose...the administration method using osmotic pump is useful." pg. 434.



**P8454:** L. Geboes, *et al.* Freund's complete adjuvant induces arthritis in mice lacking a functional interferon-gamma receptor by triggering tumor necrosis factor alpha-driven osteoclastogenesis. *Arthritis and Rheumatism* 2007;56(8):2595-2607

**ALZET Comments:** Etanercept; Water, sterile; SC; Mice; 2004; 28 days; Controls received mp w/vehicle; animal info (male, DBA/1, wt, IFN $\gamma$ -KO, 8-12 weeks old).

**P7770:** C. M. Paulos, *et al.* Folate-targeted immunotherapy effectively treats established adjuvant and collagen-induced arthritis. *ARTHRITIS RESEARCH & THERAPY* 2006;8(3):U243-U252

**ALZET Comments:** Anakinra; SC; Rat; 4 weeks; Animal info (female, Lewis, 200g.).

**P7678:** G. Q. Guan, *et al.* Estrogenic effect on swelling and monocytic receptor expression in an arthritic temporomandibular joint model. *Journal of Steroid Biochemistry and Molecular Biology* 2005;97(3):241-250

**ALZET Comments:** Estradiol, 17 $\beta$ -; PEG; Rat; 2002; 14 days; Animal info (OVX, Sprague-Dawley, 200-225 g, female).

**P7446:** G. Gaitan, *et al.* Enhancement of fentanyl antinociception by subeffective doses of nitroparacetamol (NCX-701) in acute nociception and in carrageenan-induced monoarthritis. *LIFE SCIENCES* 2005;77(1):85-95

**ALZET Comments:** Fentanyl; Saline; SC; Rat; 2ML1; 5 days; Controls received mp w/ vehicle; tolerance; animal info (male, Wistar, 250-320 g).

**P7498:** B. De Klerck, *et al.* Pro-inflammatory properties of stromal cell-derived factor-1 (CXCL12) in collagen-induced arthritis. *ARTHRITIS RESEARCH & THERAPY* 2005;7(6):R1208-R1220

**ALZET Comments:** AMD 3100; SC; Mice; 2002; 14 days; Controls received mp w/ PBS; immunology; animal info (male, 8-12 weeks).

**P6677:** J. Zwerina, *et al.* Single and combined inhibition of tumor necrosis factor, interleukin-1, and RANKL pathways in tumor necrosis factor-induced arthritis - Effects on synovial inflammation, bone erosion, and cartilage destruction. *Arthritis and Rheumatism* 2004;50(1):277-290

**ALZET Comments:** Interleukin-1 receptor antagonist; SC; Mice (transgenic); 2004; 4 weeks;

**P6767:** H. Tamamura, *et al.* Identification of a CXCR4 antagonist, a T140 analog, as an anti-rheumatoid arthritis agent. *FEBS Letters* 2004;569(1-3):99-104

**ALZET Comments:** TN14003, 4F-benzoyl-; PBS; SC; Mice; 1007D; 2002; 7,14 days; Controls received mp w/ vehicle; dose-response (Fig.2); immunology; peptides.

**P7427:** S. U. Simjee, *et al.* Modulation of the gait deficit in arthritic rats by infusions of muscimol and bicuculline. *Pain* 2004;109(453-460)

**ALZET Comments:** Muscimol; bicuculline; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; dose-response; no stress (see pg. 455-6).

**R0219:** W. B. Van Den Berg. Is there a rationale for combined TNF and IL-1 blocking in arthritis? *Clinical and Experimental Rheumatology* 2002;20(Suppl. 28):S21-S25

**ALZET Comments:** Insulin-like growth factor I, receptor antagonist; Mice; "In mice full protection is only achieved with continued dosing in ALZET minipumps." (p. S-24).

**P5046:** A. Scharstuhl, *et al.* Inhibition of endogenous TGF-beta during experimental osteoarthritis prevents osteophyte formation and impairs cartilage repair. *Journal of Immunology* 2002;169(507-514)

**ALZET Comments:** Transforming Growth Factor-B2, soluble receptor; Polymyxin B; IP; mice; 1007D; 2002; 7,14 or 21 days; Arthritis; controls received empty pumps or mp w/ vehicle; functionality of mp verified by residual aspiration; pumps replaced after 14 days; stability verified by ELISA after infusion (p. 508, 510); soluble TGF-B RII selectively inhibits transforming growth factor-B; peptides; polymyxin B included as endotoxin inhibitor; 2002 pumps used for 7 and 14 day administration, 21-day group received a 1007D pump for final 7 days.



**P5094:** H. Matsuno, *et al.* The role of TNF-alpha in the pathogenesis of inflammation and joint destruction in rheumatoid arthritis (RA): a study using a human RA/SCID mouse chimera. *Rheumatology* 2002;41(329-337

**ALZET Comments:** Tumor necrosis factor-a; Interleukin-6; Serum, fetal bovine; Culture medium, RPMI 1640; SC; Mice (SCID); 1007D; 7 days; controls received mp w/ vehicle; functionality of mp verified by serum cytokine levels; immunology; peptides; cytokines were recombinant; pump incorrectly called an osmium pump (p. 331); agents administered singly.

**P5978:** A. Luttun, *et al.* Revascularization of ischemic tissues by PIGF treatment, and inhibition of tumor angiogenesis, arthritis and atherosclerosis by anti-Flt1. *Nature Medicine* 2002;8(8):831-840

**ALZET Comments:** Placental growth factor; vascular endothelial growth factor; SC; Mice; 2001; 7 days; Angiogenesis.

**P5458:** A. Coxon, *et al.* Inhibition of interleukin-1 but not tumor necrosis factor suppresses neovascularization in rat models of corneal angiogenesis and adjuvant arthritis. *Arthritis and Rheumatism* 2002;46(10):2604-2612

**ALZET Comments:** Interleukin-1 receptor antagonist; Saline; sodium citrate; EDTA; Tween 80; SC; Rat; 2ML1; 7 days; Controls received mp w/ BSA "to control for nonspecific anti-angiogenic effects of stress associated with implantation of the osmotic minipump." (p. 2605); implantation of pumps delivering BSA caused no angiogenesis; 0.5mM EDTA; 0.1% Tween 80;.

**R0169:** S. B. Abramson, *et al.* Blocking the effects of IL-1 in rheumatoid arthritis protects bone and cartilage. *Rheumatology* 2002;41(9):972-980

**ALZET Comments:** SC; Rabbit; 14 days; Peptides.

**Q6819:** J. Braz, *et al.* Therapeutic Efficacy in Experimental Polyarthritis of Viral-Driven Enkephalin Overproduction in Sensory Neurons. *The Journal of Neuroscience* 2001;21(20):7881-7888

**ALZET Comments:** Naloxone; Naloxone methiodide; Saline; SC; Rat; 2001; 3 days; Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (polyarthritic male sprawg dawley rats, 6 weeks old); behavioral testing (foot withdrawal (pain)); Therapeutic indication (Rheumatoid arthritis);.

**P4412:** R. E. Voll, *et al.* Amelioration of type II collagen induced arthritis in rats by treatment with sodium diethyldithiocarbamate. *The Journal of Rheumatology* 1999;26(6):1352-1358

**ALZET Comments:** Diethyldithiocarbamate, Sodium;; PBS, sterile;; SC;; Rat;; 2002; 2ML2;; 7, 9 days;; controls received mp w/vehicle; functionality of mp verified by plasma levels; comparison of IP injections vs. mp; agent also called Ditiocarb or DDTC; arthritis;.

**P4417:** J. Dawson, *et al.* Effects of soluble interleukin-1 type II receptor on rabbit antigen-induced arthritis: clinical, biochemical and histological assessment. *Rheumatology* 1999;38(401-406

**ALZET Comments:** Interleukin-1 receptor;; Saline;; SC;; rabbit;; 14 days;; controls received mp w/vehicle; functionality of mp verified by plasma levels; immunology; peptides; arthritis; soluble interleukin-1 type II receptor used;.

**P3724:** C. J. Blais, *et al.* Involvement of endogenous kinins in the pathogenesis of peptidoglycan-induced arthritis in the lewis rat. *Arthritis Rheum* 1997;40(7):1327-1333

**ALZET Comments:** Hoe 140; Bradykinin, Lys-Leu8-des-Arg9; Saline, sterile; SC; Rat; 1007D; 6 days; controls received mp w/ vehicle; peptides; agents administered singly and in combination.

**P3568:** S. Persson, *et al.* Interleukin-10 suppresses the development of collagen type II-induced arthritis and ameliorates sustained arthritis in rats. *Scand. J. Immunol* 1996;44(607-614

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

**P6296:** L. A. B. Joosten, *et al.* Anticytokine Treatment Of Established Type II Collagen-Induced Arthritis in DBA/1 Mice. *Arthritis and Rheumatism* 1996;39(5):797-809

**ALZET Comments:** Interleukin-1 receptor antagonist, recomb. human; IP; Mice; 1007D; 7 days; Controls received mp w/ BSA; immunology.



**P3563:** P. L. E. M. Van Lent, *et al.* Major role for interleukin 1 but not for tumor necrosis factor in early cartilage damage in immune complex arthritis in mice. *J. Rheumatol* 1995;22(2250-2258

**ALZET Comments:** Interleukin-1 receptor antagonist; IP; mice; 1007D; no duration posted; controls received empty pumps or mp w/ vehicle; immunology.

**P4079:** A. A. J. van de Loo, *et al.* Role of interleukin-1 in antigen-induced exacerbations of murine arthritis. *Am. J. Pathol* 1995;146(1):239-249

**ALZET Comments:** Interleukin-1 receptor antagonist; IP; 7 days; brief mention of mp on p. 247; immunology.

**P3995:** S. J. Oliver, *et al.* Suppression of collagen-induced arthritis by an angiogenesis inhibitor, AGM-1470, in combination with cyclosporin: reduction of vascular endothelial growth factor (VEGF). *Cellular Immunol* 1995;166(196-206

**ALZET Comments:** Cyclosporin A; PEG 300; SC; Rat; 2ML4; no duration posted; photo of rat showing implanted pump (pg. 204); no stress (see pp. 199, 204, 205); immunology; controls received sham surgeries.

**P3379:** J. G. Conway, *et al.* Inhibition of cartilage and bone destruction in adjuvant arthritis in the rat by a matrix metalloproteinase inhibitor. *J. Exp. Med* 1995;182(449-457

**ALZET Comments:** GI168; DMSO; Sodium citrate buffer; SC; Rat; 2ML2; 2 weeks; controls received mp w/vehicle; dose-response (see p. 451); immunology; multiple pumps per animal (2); "GI168 had poor oral bioavailability and a short plasma t 1/2 after subcutaneous injection... so minipump delivery was evaluated." p. 451; enzyme inhibitor (matrix metalloproteinase).

**P2940:** J. R. Earl, *et al.* Proinflammatory effects of morphine in the rat adjuvant arthritis model. *Int. J. Tiss. React* 1994;XVI(4):163-170

**ALZET Comments:** Morphine sulfate; Naloxone HCl; Saline; SC; Rat; 2ML4; no duration posted; controls received mp with saline or were naive.

**P3096:** D. O. Willenborg, *et al.* Inhibition of adjuvant arthritis in the rat by phosphosugars and the a-glucosidase inhibitor castanospermine. *Immunol. Cell Biology* 1992;70(369-377

**ALZET Comments:** Castanospermine; Mannose, D-; Phosphate, mannose-6-; Phosphate, fructose-1-; Saline; SC; IP; Rat; 2002; 14 days; controls received mp with saline or sham operation; comparison of drinking water admin. of CS vs. mp; immunology.

**P2361:** F. J.-P. Miao, *et al.* Chronically administered nicotine attenuates bradykinin-induced plasma extravasation and aggravates arthritis-induced joint injury in the rat. *Neuroscience* 1992;51(3):649-655

**ALZET Comments:** Nicotine hydrogen tartrate; ICI-118,551 Hexamethonium chloride; Saline; Ethanol; SC; Rat; 2ML2; 2ML4; 16,30 days; comparison of sc injections vs. mp; immunology; ICI-118,551 is a b2-adrenoceptor antagonist; antihypertensive.

**P2020:** E. Brahn, *et al.* Effects of tumor necrosis factor alpha (TNF-a) on collagen arthritis. *Lymphokine Cytokine Res* 1992;11(5):253-256

**ALZET Comments:** Tumor necrosis factor-a; Albumin, bovine serum; Water; Rat; 2ML4; 28 days; peptides.

**P1956:** M. Mihara, *et al.* Interleukin 6 inhibits delayed-type hypersensitivity and the development of adjuvant arthritis. *Eur. J. Immunol* 1991;21(2327-2331

**ALZET Comments:** Interleukin-6; PBS; Serum, mouse; SC; mice; 2ML2; 2ML4; 2, 4 weeks; immunology; peptides.

**P1837:** H. Lorberboum-Galski, *et al.* Administration of IL-2-PE40 via osmotic pumps prevents adjuvant induced arthritis in rats. Improved therapeutic index of IL-2-PE40 administered by continuous infusion. *Int. J. Immunopharmac* 1991;13(2/3):305-315

**ALZET Comments:** Interleukin-2, PE40; NAD; IP; Rat; 2001; no duration posted; functionality of mp verified by serum levels of IL-2-PE40; comparison of of bid ip injections vs. mp; no stress (see pg. 314); stability achieved for 6 days by adding NAD (p. 308); multiple pumps per animal (2); half-life of 1-2 hours when given ip.





**P1958:** E. Brahn, *et al.* Suppression of collagen-induced arthritis by combination cyclosporin A and methotrexate therapy. *Arthritis Rheum* 1991;34(10):1282-1288

**ALZET Comments:** Cyclosporin A; PEG 300; Rat; 2ML4; 28 days; dose response (graph, p. 1284); immunology.

**P1957:** L. Borella, *et al.* Rapid induction of early osteoarthritic-like lesions in the rabbit knee by continuous intra-articular infusion of mammalian collagenase or interleukin-1. *Agents Actions* 1991;34(1/2):220-222

**ALZET Comments:** Interleukin-1; Collagenase, APMA-activated; Albumin; Saline; knee (articular cavity); rabbit; 2ML1; 7 days; stability verified in vitro for 7 days at 37 degrees C; collagenase was aminophenyl mercuric acetate-activated.

**P1453:** K. Fogh, *et al.* 15-Hydroxy-eicosatetraenoic acid (15-HETE) inhibits carrageenan-induced experimental arthritis and reduces synovial fluid leukotriene B4 (LTB4). *Prostaglandins* 1989;37(2):213-228

**ALZET Comments:** HETE, 15-; Saline; knee (articular cavity); dog; 2ML2; 2ML4; 10 days; tissue perfusion (knee joint).

**P1400:** J. T. Hom, *et al.* In vivo administration with IL-1 accelerates the development of collagen-induced arthritis in mice. *J. Immunol* 1988;141(3):834-841

**ALZET Comments:** Interleukin-1, alpha recomb. human; Interleukin-1, beta recomb. human; PBS; SC; mice; 2002; 7-14 days; dose-response; cancer/immunology; peptides.