



References on the Administration of Calcitonin and Calcitriol Using ALZET® Osmotic Pumps

1. Calcitonin

Q6507: E. Tavares, *et al.* Potential Role of Aminoprocalcitonin in the Pathogenesis of Alzheimer Disease. *Am J Pathol* 2016;186(10):2723-35

ALZET Comments: Neuroendocrine peptide aminoprocalcitonin, anti-; PBS; Mice (transgenic); 1004; 28 days; Dose (500 ug/kg/day); animal info (Adult male C57BL/6 and APP/PS1 mice); neurodegenerative (Alzheimer Disease);.

Q4655: J. G. Yan, *et al.* CALCITONIN PUMP IMPROVES NERVE REGENERATION AFTER TRANSECTION INJURY AND REPAIR. *MUSCLE & NERVE* 2015;51(229-234

ALZET Comments: Calcitonin; Water, distilled sterile; CSF/CNS (sciatic nerve); Rat; 2006; 12 weeks; Animal info (Sprague Dawley, 250-300g, 3 months old); half-life (p.233); long-term study; "To achieve a continuous and gradual mode of delivery, a mini-osmotic pump was implanted to deliver medication at a constant 0.15 ul/h" pg 233; "Calcitonin has short absorption and elimination half-lives of 10–15 minutes and 50–80 minutes, respectively; however, using an osmotic pump allows for gradual and prolonged release." pg233; pg230 diagram of pump implantation;.

Q4065: C. E. Riera, *et al.* TRPV1 Pain Receptors Regulate Longevity and Metabolism by Neuropeptide Signaling. *Cell* 2014;157(1023-1036

ALZET Comments: Calcitonin gene related peptide (8-37); Mice; 6 weeks; Animal info (male, C57BL6J, 22 months old); functionality of mp verified by serum levels; peptides; diabetes;.

Q4016: D. Navarro, *et al.* Late Maternal Hypothyroidism Alters the Expression of Camk4 in Neocortical Subplate Neurons: A Comparison with Nurr1 Labeling. *Cerebral Cortex* 2014;24(2694-2706

ALZET Comments: Parathormone (1-84), rat; calcitonin, rat; Acetate buffer; SC; Rat; 2001; 22 days; Animal info (female, Wistar, E0); replacement therapy (thyroidectomy); teratology;.

Q3125: J. G. Yan, *et al.* The effect of calcium modulating agents on peripheral nerve recovery after crush. *Journal of Neuroscience Methods* 2013;217(1-2):54-62

ALZET Comments: Nifedipine; calcitonin; CSF/CNS (sciatic nerve); Rat; 2006; 4 weeks; Controls received mp w/ saline or sham only; animal info (3 month old, male, Sprague-Dawley 250-300g); functionality of mp verified by decrease in calcium levels; peptides; Picture of MP p56, Fig1A. MP Pump setup p56, Fig1B;.

Q2997: D. Brown, *et al.* New insights into the dynamic regulation of water and acid-base balance by renal epithelial cells. *AMERICAN JOURNAL OF PHYSIOLOGY-CELL PHYSIOLOGY* 2012;302(10):C1421-C1433

ALZET Comments: Calcitonin; Rat; 4, 12, 24 hours; Animal info (Brattleboro rats); functionality of mp verified by measuring urine output and concentration; ALZET osmotic pumps used to infuse calcitonin to increase trafficking of aquaporin 2 vesicles in collecting duct. Effect is short lived, despite continued calcitonin delivery; might need dose adjustment; diabetes;.

Q1310: S. J. Sample, *et al.* Role of Calcitonin Gene-Related Peptide in Bone Repair after Cyclic Fatigue Loading. *PLoS One* 2011;6(6):U98-U107

ALZET Comments: Calcitonin gene related peptide; calcitonin gene related peptide (8-37); SC; Rat; 10 days; Controls received mp w/ saline; animal info (Sprague Dawley, male, 292-305 g, 67 days); CGRP (8-37) is a CGRP1 receptor antagonist; peptides.

Q1449: R. Bouley, *et al.* Calcitonin Has a Vasopressin-like Effect on Aquaporin-2 Trafficking and Urinary Concentration. *Journal of the American Society of Nephrology* 2011;22(1):59-72

ALZET Comments: Calcitonin; Saline; SC; Rat; 7 days; Controls received mp w/ vehicle; pumps removed and new pump implanted after 10 days; animal info (Brattleboro, VP-deficient, adult, male).



Q0079: B. Morte, *et al.* Thyroid Hormone Regulation of Gene Expression in the Developing Rat Fetal Cerebral Cortex: Prominent Role of the Ca²⁺/Calmodulin-Dependent Protein Kinase IV Pathway. *Endocrinology* 2010;151(2):810-820

ALZET Comments: Parathyroid hormone (1-84); calcitonin, rat; Acetate buffer; SC; Rat; 2001; Controls received mp w/ vehicle; animal info (female, Wistar, adult, 250-300 g); replacement therapy (parathyroidectomy).

Q0003: P. Berbel, *et al.* Role of Late Maternal Thyroid Hormones in Cerebral Cortex Development: An Experimental Model for Human Prematurity. *Cerebral Cortex* 2010;20(6):1462-1475

ALZET Comments: Parathyroid hormone, rat (1-84); calcitonin, rat; thyroxine; Acetate buffer; SC; Rat (pregnant); 2001; 4-8 days; Teratology; peptides; animal info (Female, Wistar, 250-300 g); replacement therapy (parathyroidectomy).

P9799: B. R. Becklund, *et al.* Enhancement of 1,25-dihydroxyvitamin D₃-mediated suppression of experimental autoimmune encephalomyelitis by calcitonin. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2009;106(13):5276-5281

ALZET Comments: Calcitonin, salmon; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; functionality of mp verified by residual volume; dose-response (Fig. 2); animal info (female, C57BL/6, 6 wks old).

P6828: B. Z. Yuan, *et al.* Evidence for abnormal translational regulation of renal 25-hydroxyvitamin D-1 α -hydroxylase activity in the Hyp-mouse. *Endocrinology* 2004;145(8):3804-3812

ALZET Comments: Parathyroid hormone, bovine 1-34; calcitonin, salmon; Saline, physiological; cysteine hydrochloride; SC; Mice; 1003D; 2001; 12 hours; Controls received mp w/ vehicle.

P5359: W. Wang, *et al.* Role of calcitonin in the rapid minute-to-minute regulation of plasma Ca²⁺ homeostasis in the rat. *European Journal of Clinical Investigation* 2002;32(9):674-681

ALZET Comments: Calcitonin, salmon; Acetic acid; Sodium acetic; Sodium chloride; water, distilled; SC; Rat; 2ML1; 7 days; 24 hours; Functionality of mp verified by calcitonin plasma levels.

P6319: B. A. Dani, *et al.* Skeletal Effects of Parathyroid Hormone (1-34) in Ovariectomized Rats With or Without Concurrent Administration of Salmon Calcitonin. *Pharmsci* 2001;3(4):1-7

ALZET Comments: Parathyroid hormone, human 1-34; calcitonin, salmon; Acetate buffer; saline; SC; Rat; 2004; 28 days; Controls received mp w/ vehicle or sham ovx + mp w/ vehicle; functionality of mp verified by serum levels; replacement therapy (ovariectomy); comparison of daily PTH sc injections vs. mp; peptides.

P3929: M. G. Tordoff, *et al.* Calcium intake by rats: influence of parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D. *Am. J. Physiol* 1998;274(43):R214-R231

ALZET Comments: Parathyroid hormone; Calcitonin; Vitamin D, 1,25-dihydroxy-; NaCl; HCl; Cysteine; Saline, isotonic; SC; Rat; 2002; 13 days; controls received sham tubing; functionality of mp verified by hormone assays; replacement therapy (thyroidectomy, thyroparathyroidectomy); dose-response; stress/adverse reaction: high doses led to animal death; peptides; agents given singly and in combination.

P4223: M. Li, *et al.* A comparison of the skeletal effects of intermittent and continuous administration of calcitonin in ovariectomized rats. *Bone* 1996;18(4):375-380

ALZET Comments: Calcitonin, salmon; Saline; Benzyl alcohol; Gelatin; Rat; 6 weeks; controls received mp w/vehicle; functionality of mp verified by calcitonin plasma levels by radioimmunoassay; comparison of s.c. injections vs. mp; pumps replaced after 3 weeks; peptides.

P3194: C. Hemmingsen, *et al.* Regulation of renal calbindin-D28K: the role of calcitonin. *Calcif. Tissue Int* 1995;56(372-375)

ALZET Comments: Calcitonin, salmon; Aminocaproic acid; HCl; Rat; 2ML1; 4 days; controls received mp with vehicle.

P2283: G. Golomb, *et al.* A new route of drug administration: intrauterine delivery of insulin and calcitonin. *Pharmaceut. Res* 1993;10(6):828-833

ALZET Comments: Calcitonin, human; intrauterine; SC; Rat; 2001; 14 days; tissue perfusion (uterus); dose-response (graph, p.832); comparison of polyurethane matrices vs mp.



P1714: A. J. Yates, *et al.* A noncyclical analog of salmon calcitonin (N-a-propionyl di-Ala1,7,des-Leu19 sCT) retains full potency without inducing anorexia in rats. *Endocrinology* 1990;126(6):2845-2849

ALZET Comments: Calcitonin analog; Calcitonin, synthetic salmon; Gelatin; Saline; SC; mice; 2001; 48 hours; pumps were reimplanted in a second animal; analog is RG-12851.

Q5639: G. Davidai. Normal Regulation of Calcitriol Production in Gy Mice. *Journal of Clinical Investigation* 1990;85(2):334-9

ALZET Comments: Parathyroid hormone, bovine; calcitonin; Saline, cysteine hydrochloride; SC; mice; 2001; 7 days; Controls received mp w/ vehicle; animal info (4-5 wk old); Dose: calcitonin (2 IU/ul), PTH (1 IU/ul);.

Q5594: T. Nesbitt. Calcitonin Stimulation of Renal 25-Hydroxyvitamin D-1a-Hydroxylase Activity in Hypophosphatemic Mice. *Journal of Clinical Investigation* 1987;79(15-19)

ALZET Comments: Calcitonin, Parathyroid hormone; Saline, Physiologic; SC; Mice; 2001; 3, 6, 12, 18, 24, 48 and 72 hrs; Controls received mp w/ vehicle; dose-response (0.1, 0.375, 0.5, 0.75, 1.0, or 1.25 IU/h); Multiple pumps per animal (2): Animals receiving

both hormones were implanted through separate skin incisions with two pumps. "To control the uniformity of the applied stimulus, we used surgically implantable Alzet osmotic minipumps...

for continuous subcutaneous infusion of calcitonin." pg 15; Dose (0.5 IU/hr);.

P1087: Z. Bouizar, *et al.* Down-regulation of rat kidney calcitonin receptors by salmon calcitonin infusion evidenced by autoradiography. *Proc. Natl. Acad. Sci* 1987;84(5125-5128)

ALZET Comments: Calcitonin, salmon; Aminocaproic acid; SC; Rat; 2002; 1, 4, 7 days; controls received mp w/vehicle; dose-response; mp primed w/saline 12 hours before implantation; stability; peptides.

P0863: P. Jaeger, *et al.* Evidence that calcitonin stimulates 1,25-dihydroxyvitamin D production and intestinal absorption of calcium in vivo. *J. Clin. Invest* 1986;78(456-461)

ALZET Comments: Calcitonin; SC; Rat; 2002; 6-12 days; controls received sham implantation; replacement therapy (thyroparathyroidectomy); peptides.

P1252: C. Rebut-Bonneton, *et al.* Effect of calcitonin in pregnant rats on bone resorption in fetuses. *J. Endocrinol* 1983;99(3):347-353

ALZET Comments: Calcitonin, salmon; Albumin, bovine serum; PBS; SC; Rat (pregnant); 5 days; pump model not stated; replacement therapy (thyroparathyroidectomy); peptides.

P0031: J. F. Obie, *et al.* Loss of calcemic effects of calcitonin and parathyroid hormone infused continuously into rats using the ALZET osmotic minipump. *J. Pharmacol. Exp. Ther* 1979;209(3):422-428

ALZET Comments: Calcitonin; Parathyroid hormone, bovine; Cysteine HCl; HCl; Saline; SC; Rat; 7 days; organ replacement therapy (thyroparathyroidectomy); peptides.

P0272: J. W. Bastian, *et al.* (Calcitonin: consideration of its dosage and other aspects). In 'Calcitonin: Nuove Acquisizioni e Prospettive,' G. De Bastiani, A. Pecile, V. Pietrogrande, and C. Sirtori (eds.), Fondazione Carlo Erba, Milano (Italian) 1979;

ALZET Comments: Calcitonin, salmon; SC; Rat; 1-14 days; comparison of human vs. animal data; intermittent vs. mp infusion; peptides.

2. Calcitriol

Q4377: C. L. Chou, *et al.* Beneficial Effects of Calcitriol on Hypertension, Glucose Intolerance, Impairment of Endothelium-Dependent Vascular Relaxation, and Visceral Adiposity in Fructose-Fed Hypertensive Rats. *PLoS One* 2015;10(U2028-U2046)



ALZET Comments: Calcitriol; PEG; SC; Rat; 2002; 4 weeks; Animal info (male, Wistar-Kyoto, 200-230g); functionality of mp verified by residual volume; pumps replaced every 2 weeks; post op. care (penicillin SC injection 5000 U/kg); bp measured using tail cuff;

Q3664: T. Takenaka, *et al.* Calcitriol Supplementation Improves Endothelium-Dependent Vasodilation in Rat Hypertensive Renal Injury. *KIDNEY & BLOOD PRESSURE RESEARCH* 2014;39(17-27

ALZET Comments: Calcitriol; SC; Rat; 6 weeks; Controls received mp w/ vehicle; animal info (male, Spontaneously hypertensive rats, stroke-prone, 8 weeks old); cardiovascular; long-term study;

Q3219: R. Goyal, *et al.* Characterization of an animal model of pregnancy-induced vitamin D deficiency due to metabolic gene dysregulation. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2014;306(3):E256-E266

ALZET Comments: Calcitriol; Ethanol; propylene glycol; SC; Rat; 2004; Control animals received mp w/ vehicle; animal info (Sprague Dawley, P9); 50% ethanol used; 50% propylene glycol used.

Q5540: G. Duque, *et al.* Pharmacological inhibition of PPARgamma increases osteoblastogenesis and bone mass in male C57BL/6 mice. *J Bone Miner Res* 2013;28(3):639-48

ALZET Comments: Calcitriol; DMSO; SC; Mice; 6 weeks; Controls received mp w/ vehicle; animal info (9 month old); 15% DMSO used; Dose (18pm/d); Therapeutic indication (osteoporosis);

P8449: K. D. Goodwin, *et al.* Preventing oxidative stress in rats with aldosteronism by calcitriol and dietary calcium and magnesium supplements. *American Journal of the Medical Sciences* 2006;332(2):73-78

ALZET Comments: Aldosterone; calcitriol; SC; Rat; 2004; 2ML4; 4 weeks; Controls received no treatment; replacement therapy (uninephrectomy); cardiovascular; animal info (male, Sprague-Dawley, 8 wks old).

P4473: A. Szabo, *et al.* Physiological doses of calcium regulatory hormones do not normalize bone cells in uraemic rats. *European Journal of Clinical Investigation* 1999;29(529-535

ALZET Comments: Parathyroid hormone (1-34); Calcitriol;; Cysteine; Propylene glycol; Saline;; Rat;; 2002;; 14 days;; controls received mp w/vehicle; replacement therapy (parathyroidectomy; nephrectomy); peptides;

P3236: J. F. Long, *et al.* Comparative effects of calcitriol and parathyroid hormone on serum aluminum in vitamin D-depleted rabbits fed an aluminum-supplemented diet. *Res. Commun. Chem. Pathol. Pharmacol* 1994;83(1):3-14

ALZET Comments: Calcitriol; Parathyroid hormone (1-34); Cysteine; HCl; Saline; rabbit; 7 days; functionality of mp verified by serum levels; peptides.

P2142: T. Shimosawa, *et al.* Enhancement of vasoconstrictor response by a noncalcemic analogue of vitamin D3. *Hypertension* 1993;21(2):253-258

ALZET Comments: Oxacalcitriol, 22-; Vitamin D3, 24,25-dihydroxy-; Vitamin D3, 1,25-dihydroxy-; Propylene glycol; SC; Rat; 2002; 14 days; no comment posted.

P2664: A. J. Brown, *et al.* The mechanism for the disparate actions of calcitriol and 22-oxacalcitriol in the intestine. *Endocrinology* 1993;133(3):1158-1164

ALZET Comments: Oxacalcitriol, 22-; Vitamin D3, 1,25-dihydroxy-; Propylene glycol; SC; Rat; 2002; 3 days; controls received mp w/ vehicle; comparison of ip injections vs. mp; agent is 1,25-(OH)2D3.

P2356: J. F. Long, *et al.* Effect of calcitriol infusions on serum aluminum in vitamin D-depleted rabbits fed an aluminum-supplemented ration. *Res. Commun. Chem. Pathol. Pharmacol* 1991;74(1):89-104

ALZET Comments: Calcitriol; Propylene glycol; SC; rabbit; 7, 28 days; functionality of mp verified by plasma levels; toxicology.

P1502: S. N. Popoff, *et al.* Treatment of congenital osteopetrosis in the rabbit with high-dose 1,25-dihydroxyvitamin D. *J. Bone and Min. Res* 1989;4(1):57-67



ALZET Comments: Calcitriol; Propylene glycol; SC; rabbit; 2 weeks; dose-response; functionality of mp verified by serum levels.

P1656: S. Patel, *et al.* Effect of vitamin D metabolites on calcitriol metabolism in experimental renal failure. *Kidney Int* 1989;36(234-239)

ALZET Comments: Calcitriol; Vitamin D3, 1,25-dihydroxy-; Ethanol; Propylene glycol; SC; Rat; 2001; 1 week; functionality of mp verified by measuring residual volume.

P1654: J. F. Long, *et al.* Serum calcitriol and parathyroid hormone levels following prolonged infusion of calcitriol in vitamin D replete and depleted rabbits. *Res. Commun. Chem. Pathol. Pharmacol* 1989;64(2):273-286

ALZET Comments: Calcitriol; Propylene glycol; SC; rabbit; 2ML1; 2ML4; 7, 28 days; functionality of mp verified by serum calcitriol levels; dose-response (graphs); 3 doses of calcitriol infused.

P0508: A. M. Parfitt, *et al.* Calcitriol but no other metabolite of vitamin D is essential for normal bone growth and development in the rat. *J. Clin. Invest* 1984;73(576-586)

ALZET Comments: Calcitriol; Propylene glycol; SC; Rat; 2002; 40 days; comparison of calcitriol or OHD2 po 3x/wk vs. mp infusion; intermittent oral dosing; mp replaced every 2 weeks; no stress implied by the normal growth of the animals.