



Recent References on the Administration of Agents to Livestock
Using ALZET® Osmotic Pumps

Cattle (1995-Present)

Q4384: H. M. Crawford, *et al.* Evidence for a Role of Prolactin in Mediating Effects of Photoperiod during the Dry Period. *Animal Science Journal* 2015;5(803-820)

Agents: Prolactin **Vehicle:** Saline; **Route:** SC; **Species:** Cattle (pregnant); **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Controls received no mp; animal info (female, Holstein, multiparous); functionality of mp verified by blood samples; pumps removed after 28 days;

Q4316: J. H. Bae, *et al.* Continuous ophthalmic treatment using an osmotic pump in a bull calf following surgical removal of an ocular dermoid: a case report. *VETERINARNI MEDICINA* 2015;60(282-287)

Agents: Ciprofloxacin **Vehicle:** Not Stated; **Route:** Eye; **Species:** Cattle (bull); **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Animal info (male, Hanwoo bull calf, 6 months old); functionality of mp verified by drug levels in aqueous humor and residual volume; good methods (pg. 284); no stress (see pg. 285); "As the owner could not apply topical medications regularly, a drug-filled osmotic pump (Alzet; Alza, Palo Alto, CA) was implanted subconjunctivally under the upper eyelid and connected to a catheter at the lateral limbus." pg 282; "... it is clear that the osmotic infusion pump maintained the aqueous concentration of ciprofloxacin at a reasonable steady state until its removal four weeks after implantation. The amount of drug remaining in the pump was about 17 µg/ml after four weeks. This also demonstrates the reliability of the pump. " pg. 286; picture of pump pg 283; pumps primed for 40 hours in 37C saline; pumps removed after 4 weeks;

Q3560: C. A. Martel, *et al.* Continuous low-dose infusion of tumor necrosis factor alpha in adipose tissue elevates adipose tissue interleukin 10 abundance and fails to alter metabolism in lactating dairy cows. *Journal of Dairy Science* 2014;97(4897-4906)

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

Q2176: A. Contri, *et al.* Successful use of a gonadotropin-releasing hormone (GnRH) analog for the treatment of tertiary hypogonadism (GnRH deficiency) in a 5-year-old Belgian Blue bull. *VETERINARY QUARTERLY* 2012;32(1):51-54

Agents: Buserelin acetate **Vehicle:** NaCl; **Route:** SC; **Species:** Cattle (bull); **Pump:** 2ML4; **Duration:** 9 weeks;
ALZET Comments: Animal info (Belgian, blue, beef, 5 years old); pumps replaced every 28 days; long-term study; buserelin acetate is a gonadotrophin releasing hormone analog

P9771: J. R. Roche, *et al.* Long-Term Infusions of Ghrelin and Obestatin in Early Lactation Dairy Cows. *Journal of Dairy Science* 2008;91(12):4728-4740

Agents: Ghrelin, Dap³; obestatin **Vehicle:** DMSO; **Route:** SC; **Species:** Cattle (cow); **Pump:** 2ML4; **Duration:** 8 weeks;
ALZET Comments: Controls were untreated; functionality of mp verified by residual volume; long-term study; pumps replaced after 28 days; animal info (multiparous); 50% DMSO used; wound clips used; peptides

P6946: J. H. Hampton, *et al.* Gonadotropin requirements for dominant follicle selection in GnRH agonist-treated cows. *REPRODUCTION* 2004;127(6):695-703

Agents: Buserelin **Vehicle:** Not Stated; **Route:** SC; **Species:** Cattle; **Pump:** 2ML4; **Duration:** 2 months;
ALZET Comments: Long-term study

P7044: T. L. Auchtung, *et al.* Prolactin mediates photoperiodic immune enhancement: Effects of administration of exogenous prolactin on circulating concentrations, receptor expression, and immune function in steers. *Biology of Reproduction* 2004;71(6):1913-1918

Agents: Prolactin, recomb. bovine **Vehicle:** Saline; **Route:** SC; **Species:** Cattle; **Pump:** 2ML2; **Duration:** 10 days;
ALZET Comments: Comparison of IV injections vs mp; no stress (see pg. 1914); immunology; peptides; post op. care (prodine, excenel); each animal received 4 rounds of 10 day prolactin treatment (2 w/ mp, 2 IV injection) with 11 days of non treatment between each round; wound clips used



P5812: H. Jimenez-Severiano, *et al.* Effect of chronic treatment with the gonadotrophin-releasing hormone agonist azagly-nafarelin on basal concentrations of LH in prepubertal bulls. REPRODUCTION 2003;125(2):225-232

Agents: Azagly-Nafarelin; Gonadotrophin-releasing hormone agonist **Vehicle:** Mannitol; water, distilled; **Route:** SC; **Species:** Cattle (bull); **Pump:** 2ML4; **Duration:** 50 weeks;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by blood samples taken; dose-response (p.227); Azagly-Nafarelin (GnRH agonist) was dissolved in 5% mannitol in water

P6227: T. L. Davis, *et al.* Chronic treatment with an agonist of gonadotropin-releasing hormone enhances luteal function in cattle. Biology of Reproduction 2003;69(2):398-403

Agents: Azagly-Nafarelin **Vehicle:** Sodium Chloride; **Route:** SC; **Species:** Cattle; **Pump:** 2ML2; 2ML4; **Duration:** 9, 18 days;

ALZET Comments: Controls received no treatment; replacement therapy (ovariectomy); agent is a gonadotrophin-releasing hormone agonist

P5097: H. A. Garverick, *et al.* Regulation of expression of ovarian mRNA encoding steroidogenic enzymes and gonadotrophin receptors by FSH and GH in hypogonadotrophic cattle. REPRODUCTION 2002;123(651-661

Agents: Buserelin **Vehicle:** Not Stated; **Route:** SC; **Species:** cattle; **Pump:** 2ML4; **Duration:** 7.5 weeks;

ALZET Comments: long-term study, pmps replaced after 28 days; buserelin is a gonadotrophin-releasing hormone (GnRH) agonist; multiple pumps per animal (2)

P4752: G. E. Mann, *et al.* Effect of continuous infusion of a GnRH agonist (Buserelin™) on ovarian hormone secretion and estrous cycle length in cows. Theriogenology 2000;54(219-227

Agents: Buserelin; **Vehicle:** Not Stated; **Route:** SC;; **Species:** cattle (lactating);; **Pump:** 2ML2;; **Duration:** 30 days;;

ALZET Comments: Functionality of mp verified by residual volume; pumps replaced at Day 16; multiple pumps per animal (2) used at once; Buserelin is a GnRH (gonadotropin releasing hormone).

P4160: N. D. Turner, *et al.* Plasma kinetics of zeranol in steers receiving variable doses in implant or mini-osmotic pump form. Unknown 1999;71-75

Agents: Zeranol **Vehicle:** Water; **Route:** Not Stated; **Species:** cattle (steer); **Pump:** Not Stated; **Duration:** 56 days;

ALZET Comments: comparison of pellets vs. mp; long-term study, pumps replaced after 28 days

P3546: S.-G. Roh, *et al.* Characteristics of growth hormone secretion responsiveness to growth hormone-releasing peptide-2 (GHRP-2 or KP102) in calves. Endocrine Journal 1996;43(3):291-298

Agents: Growth hormone-rel. factor-2 **Vehicle:** DMSO; PEG 400; Tween 80; Saline; **Route:** SC; **Species:** cattle; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: controls received mp w/ vehicle; peptides; agent also called KP102; multiple pumps per animal (3 or 4); comparison between injections vs. mp

P3692: J. G. Gong, *et al.* Suppression in the secretion of follicle-stimulating hormone and luteinizing hormone, and ovarian follicle development in heifers continuously infused with a gonadotropin-releasing hormone agonist. Biology of Reproduction 1996;55(68-74

Agents: Buserelin **Vehicle:** Not Stated; **Route:** SC; **Species:** cattle; **Pump:** 2ML4; **Duration:** 48 days;

ALZET Comments: controls received no treatment; long-term study, pumps replaced after 28 days; agent is a GnRH agonist; pumps replaced in opposite shoulder than original placement; researchers compare mp w/ injections from previous study (p. 72)

P3799: N. D. Turner, *et al.* Metabolic and hormonal changes occurring in response to level and pattern of zeranol delivered to steers. J. Anim. Sci 1995;73(1):65-70

Agents: Zeranol **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** cattle; **Pump:** Not Stated; **Duration:** 1,2,4,8 days;

ALZET Comments: no comment posted



Horse

Q10444: V. N. Bailey, *et al.* Endocrine and ovarian responses to combined estradiol benzoate-sulpiride in seasonally anovulatory mares treated with kisspeptin. *Animal Reproduction Science* 2022;247(107087)

Agents: Kisspeptin-10 **Vehicle:** Saline; **Route:** SC; **Species:** Horse; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Dose (50 µg/h;); 0.9% saline used; Controls received mp w/ vehicle; animal info (18 total; Anestrous mares; Received 50 mg estradiol benzoate before pumps implanted); post op. care (Received 3 g sulpiride); peptides; replacement therapy (Estradiol infusion);

Q7612: M. M. O'Neil, *et al.* Differential Regulation of Gonadotropins in Response to Continuous Infusion of Native Gonadotropin-Releasing Hormone in the Winter Anovulatory Mare and Effects of Treatment With Estradiol-17beta. *J Equine Vet Sci* 2019;75(93-103)

Agents: Gonadotropin-releasing Hormone **Vehicle:** Saline; **Route:** SC; **Species:** Horse; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (20 mg/mL); 0.9% Saline used; animal info (Female,); Gonadotropin-releasing Hormone aka GnRH; dependence;

Q3671: J. F. Thorson, *et al.* Hypothalamic Distribution, Adenohypophyseal Receptor Expression, and Ligand Functionality of RFamide-Related Peptide 3 in the Mare During the Breeding and Nonbreeding Seasons. *Biology of Reproduction* 2014;90(2):U75-U83

Agents: Gonadotropin-releasing hormone **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Horse; **Pump:** Not Stated;

Duration: 7 days; 12-18 days;

ALZET Comments: Animal info (female, Quarter horse and mixed breed, 5-10 years old);

Q3670: J. F. Thorson, *et al.* Pharmacologic application of native GnRH in the winter anovulatory mare, II: Accelerating the timing of pregnancy. *Theriogenology* 2014;81(4):625-631

Agents: Gonadotropin-releasing hormone **Vehicle:** Saline; **Route:** SC; **Species:** Horse (mare); **Pump:** 2ML2; 2ML4; **Duration:** 8 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Quarter Horse grade); pumps replaced every 14 days (2ML2) or 28 days (2ML4); Multiple pumps per animal (4 2ML2 or 2 2ML4); used contralateral side for next pump implantation; pumps removed at end of study;

Q3669: J. F. Thorson, *et al.* Pharmacologic application of native GnRH in the winter anovulatory mare, I: Frequency of reversion to the anovulatory state following ovulation induction and cessation of treatment. *Theriogenology* 2014;81(4):579-586

Agents: Gonadotropin-releasing hormone **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Horse (mare); **Pump:** 2ML2; **Duration:** 28 days;

ALZET Comments: Controls received sham pumps (silastic tubing); animal info (female, American Quarter Horses, 409-522 kg); pumps replaced every 14 days; post op. care (wound cleaned, disinfected with povidone iodine, antibacterial ointment - PO); pumps primed for 16 hours in 37C saline; used contralateral location for next pump implantation;

P8916: S. M. Collins, *et al.* Continuous administration of low-dose GnRH in mares II. Pituitary and ovarian responses to uninterrupted treatment beginning near the autumnal equinox and continuing throughout the anovulatory season. *Theriogenology* 2007;68(4):673-681

Agents: Gonadotropin-releasing hormone **Vehicle:** Saline, physiological; **Route:** SC; **Species:** Horse; **Pump:** 2004; **Duration:** 120 days;

ALZET Comments: Controls received sham pumps; long-term study; pumps replaced every 30 days; animal info (mare, 18 mo to 24 years); pumps were disinfected using chlorhexidine gluconate, sham pumps were made from silicon tubing filled with medical grade silicone adhesive to approximate the size of the ALZET pumps, then cold-sterilized (similar to pumps) before surgical insertion

R0209: A. Rothen-Weinhold, *et al.* Formulation and technology aspects of controlled drug delivery in animals. *PSTT* 2000;3(7):222-231

Agents: Gonadotrophin-releasing hormone **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Cat; horse; **Pump:** Not Stated;

Duration: Not Stated;

ALZET Comments:



P3967: S. E. Wheeler, *et al.* Prolactin concentrations are not suppressed in mares administered constant exogenous melatonin. *J. Equine Vet. Sci* 1998;18(1):44-47

Agents: Melatonin **Vehicle:** Saline; DMSO; **Route:** SC; **Species:** horse; **Pump:** Not Stated; **Duration:** 12 weeks;
ALZET Comments: controls received mp w/vehicle; functionality of mp verified by serum assays on days 5, 26 and 59; long-term study, pumps replaced every 28 days

P3029: D. K. Vanderwall, *et al.* Corpus luteal function in nonpregnant mares following intrauterine administration of prostaglandin E2 or estradiol-17B. *Theriogenology* 1994;42(1069-1083

Agents: Prostaglandin E2; Estradiol, 17B- **Vehicle:** Ethanol; PBS; **Route:** intrauterine; **Species:** horse; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received no treatment or mp with vehicle; tissue perfusion (uterine horn lumen); no stress (see pg. 1078); benzathine penicillin-G given prophylactically

P2503: J. H. Hyland. Uses of gonadotrophin releasing hormone (GnRH) and its analogues for advancing the breeding season in the mare. *Animal Reproduction Science* 1993;33(195-207

Agents: Luteinizing HRH **Vehicle:** Not Stated; **Route:** SC; **Species:** horse; **Pump:** 2ML2; 2ML4; **Duration:** 14 or 28 days;
ALZET Comments: comprehensive review of other GnRH induced estrous studies (pp. 198-199)

P3241: S. E. Becker, *et al.* Effects of gonadotropin-releasing hormone infused in a pulsatile or continuous fashion on serum gonadotropin concentrations and ovulation in the mare. *J. Anim. Sci* 1992;70(1208-1215

Agents: Luteinizing HRH **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** horse; **Pump:** 2ML1; **Duration:** 7-16 days;
ALZET Comments: controls received no treatment; functionality of mp verified by LH plasma levels; comparison of iv pulsatile infusion vs. mp; peptides

P2042: T. C. Lewis, *et al.* The effect of an extended artificial photoperiod and gonadotrophin-releasing hormone infusions in inducing fertile oestrus in anoestrous mares. *Australian Veterinary Journal* 1991;68(12):400-402

Agents: Luteinizing HRH **Vehicle:** Saline; **Route:** SC; **Species:** horse; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: peptides

P2350: T. V. Little, *et al.* Ovarian and hormonal responses in anoestrous mares to a GnRH agonist: a comparison of injections with osmotic minipump delivery. *J. Reprod. Fertil* 1991;44(680-682

Agents: Wy-40972 **Vehicle:** Saline; **Route:** SC; **Species:** horse; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received saline injections; functionality of mp verified by LH RIA; comparison of i.m. injections vs mp; pumps inserted via trochar; Wy-40972 is lutrelin

P2223: M. S. Boyle, *et al.* The effects of continuous treatment of stallions with high levels of a potent GnRH analogue. *J. Reprod. Fertil. , Suppl* 1991;44(169-182

Agents: Buserelin **Vehicle:** Not Stated; **Route:** SC; **Species:** horse; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: functionality of mp verified by dissection; animals received 1-2 pumps

P1984: C. G. V. Ainsworth, *et al.* Continuous infusion of gonadotrophin-releasing hormone (GnRH) advances the onset of oestrous cycles in thoroughbred mares on Australian studfarms. *J. Reprod. Fertil* 1991;44(235-240

Agents: Luteinizing HRH **Vehicle:** Saline; **Route:** SC; **Species:** horse; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: peptides

P1491: D. J. Kesler, *et al.* The effect of constant delivery of GnRH on the episodic secretion of equine LH. *J. Controlled Release* 1988;8(55-61

Agents: Luteinizing HRH **Vehicle:** Not Stated; **Route:** SC; **Species:** horse; **Pump:** 2001; **Duration:** 6 days;
ALZET Comments: functionality of mp verified in vitro; peptides



P1322: J. H. Hyland, *et al.* Control of transitional anestrus in mares by infusion of gonadotropin releasing hormone. *Theriogenology* 1988;29(6):1383-1391

Agents: Luteinizing HRH **Vehicle:** Saline; **Route:** SC; **Species:** horse; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: peptides

P1131: D. J. Kesler, *et al.* Constant delivery of GnRH to infertile or subfertile females with hypothalamic-pituitary axes that release hormones in episodic bursts. *Proc. 14th Int'l Symp. on Controlled Release of Bioactive Materials* 1987;47-48

Agents: Luteinizing HRH **Vehicle:** Potassium phosphate; **Route:** SC; **Species:** horse; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls receive mp w/ vehicle; dose-response; mp primed 4 hours before implant; 2 experiments using mp; progesterin silastic implants used concomitantly with GnRH; peptides

P1134: J. H. Hyland, *et al.* Infusion of gonadotrophin-releasing hormone (GnRH) induces ovulation and fertile oestrus in mares during seasonal anoestrus. *J. Reprod. Fertil* 1987;35(211-220)

Agents: Luteinizing HRH **Vehicle:** Saline; **Route:** SC; **Species:** horse; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: controls remained untreated; dose-response; infusion of GnRH via mp did not produce linear plasma increase, possibly because of stability of GnRH in solution or pooling at implant site; peptides

Pig (2011-Present)

Q10994: D. Selvakumar, *et al.* Delivery of Cardioactive Therapeutics in a Porcine Myocardial Infarction Model. *Journal of Visual Experiment* 2023;192:

Agents: Platelet-derived growth factor-AB, human **Vehicle:** Saline; **Route:** IV (jugular); **Species:** Pig; **Pump:** 2ML1; 2ML2; 2ML4;
Duration: 7 days;

ALZET Comments: Dose: Controls received mp w/ vehicle; animal info: Pre-pubescent large white x landrace gilts, 18-20 kg, post op. care: 0.2 mg/kg of meloxicam SC; comparison of injections (thoracotomy, transepical, percutaneous transendocardial) vs mp; functionality of mp verified by recomb protein serum concentration (ELISA); cardiovascular (myocardial infarction); good methods p. 8, 13 fig. 2; no stress; "Jugular vein minipump insertion provides a safe and reliable method of PDGF delivery over a 7 day time period." p. 13

Q10516: V. Despotovski, *et al.* Early Postnatal Exposure to Intermittent Hypercapnic Hypoxia (IHH), but Not Nicotine, Decreases Reelin in the Young Piglet Hippocampus. *NEUROTOXICITY RESEARCH* 2022;40(6):1859-1868

Agents: Nicotine **Vehicle:** Water, sterile; **Route:** IP; **Species:** Piglet; **Pump:** 2ML2; **Duration:** 12 days;
ALZET Comments: Dose (2 mg/kg/day); Controls received mp w/ vehicle; animal info (Piglets; Hypercapnic hypoxia exposure; 10-13 days old);

Q10295: D. Olivari, *et al.* Searching for Preclinical Models of Acute Decompensated Heart Failure: a Concise Narrative Overview and a Novel Swine Model. *Cardiovascular Drugs and Therapy* 2022;36(4):727-738

Agents: Serelaxin **Vehicle:** Saline; **Route:** IV; **Species:** Pig; **Pump:** Not Stated; **Duration:** 48 hours;
ALZET Comments: Dose: (30 µg/kg/day); Controls received mp w/ vehicle; animal info: 17 male *Sus scrofa domestica* pig weighing 34 ± 4 kg; post op. care: Analgesia was performed with butorphanol; Cardiovascular "

Q9971: S. Thavapalachandran, *et al.* Platelet-derived growth factor-AB improves scar mechanics and vascularity after myocardial infarction. *Cardiology* 2020;

Agents: Recombinant human platelet-derived growth factor-AB; **Species:** Pig; **Duration:** 7 days;
ALZET Comments: Dose (65 µg/kg); animal info (Landrace, 2-4 months old, 25-30 kg; ischemia (Myocardial));

Q8658: B. A. McLendon, *et al.* Pig conceptuses secrete interferon gamma to recruit T cells to the endometrium during the peri-implantation period. *Biology of Reproduction* 2020;103(5):1018-1029

Agents: Interferon, gamma; Albumin, porcine serum **Route:** Intrauterine (uterine horn); **Species:** Pig; **Pump:** 2ML1; **Duration:** 5 days;
ALZET Comments: Dose (240 uL/day); animal info (Sexually mature gilts); Interferon, gamma aka IFNG; Porcine serum albumin aka PSA; dependence;



Q7681: Y. Wang, *et al.* C-X-C Motif Chemokine Receptor 4 Blockade Promotes Tissue Repair After Myocardial Infarction by Enhancing Regulatory T Cell Mobilization and Immune-Regulatory Function. *Circulation* 2019;139(15):1798-1812

Agents: POL5551; POL6326 **Vehicle:** Saline; **Route:** SC; **Species:** Mice; Pigs; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (8mg/kg/dose); Controls received mp w/ vehicle; animal info (female pigs; 8- to 10-week-old male mice); enzyme inhibitor (peptidic macrocycle CXCR4 antagonist); cardiovascular; Therapeutic indication (Acute myocardial infarction);

Q6526: A. Vivekanandarajah, *et al.* Intermittent hypercapnic hypoxia effects on the nicotinic acetylcholine receptors in the developing piglet hippocampus and brainstem. *Neurotoxicology* 2017;60(23-33)

Agents: Nicotine Hydrogen Tartrate Salt **Vehicle:** Water (sterile); **Route:** IP; **Species:** Pig (neonate); **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (2.0 mg/kg/day); animal info (mixed-breed miniature piglets); comparison of patch vs mp; Resultant plasma level (serum cotinine: 23.1 + 17.3 ng/mL); "The use of an osmotic minipump as opposed to a skin patch was chosen as the method of nicotine delivery given it provides a steady state, same dose, infusion over our 14 day study whereas patches result in sudden spikes in plasma levels and require replacement of patches every 1–2 days dependent on chosen patch " pg. 2

Q6137: J. Huang, *et al.* Hypoxia and nicotine effects on Pituitary adenylate cyclase activating polypeptide (PACAP) and its receptor 1 (PAC1) in the developing piglet brainstem. *Neurotoxicology* 2017;62(30-38)

Agents: Nicotine **Vehicle:** Water; **Route:** IP; **Species:** Pig; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (2 mg/kg/day); Controls received mp w/ vehicle; "The delivery of nicotine via the minipump provides a steady state infusion over our 14 day study whereas other methods result in sudden spikes in plasma levels (reviewed by Shiffman *et al.*, 2005) and require more animal handling and stress." pg. 31;

Q4908: MingWu, *et al.* Placental growth factor 2 — A potential therapeutic strategy for chronic myocardial ischemia. *International Journal of Cardiology* 2016;203(534-542)

Agents: Placental growth factor-2, recombinant human **Vehicle:** PBS; **Route:** IV; **Species:** Pig; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Sus Scrofa, 20-25kg); functionality of mp verified by plasma levels; ischemia (myocardial); cardiovascular; Dose (15 ug/kg/day);

Q5376: N. J. Hunt, *et al.* Changes in orexinergic immunoreactivity of the piglet hypothalamus and pons after exposure to chronic postnatal nicotine and intermittent hypercapnic hypoxia. *European Journal of Neuroscience* 2016;43(12):1612-22

Agents: Nicotine hydrogen tartrate salt **Vehicle:** Water; **Route:** SC; **Species:** Pig (mini); **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male mixed breed miniature piglets, postnatal day 2, 1.27 kg); functionality of mp verified by brain analysis; toxicology; Chronic postnatal nicotine and intermittent hypercapnic hypoxia (IHH); Dose (2 mg/kg/day);

Q5358: A. Garcia-Alvarez, *et al.* Beta-3 adrenergic agonists reduce pulmonary vascular resistance and improve right ventricular performance in a porcine model of chronic pulmonary hypertension. *Basic Research in Cardiology* 2016;111(4):49

Agents: BRL37344 **Vehicle:** Saline; **Route:** IV (right jugular vein); **Species:** Pigs; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (pig, 4 months old, 45 kg); functionality of mp verified by plasma levels; cardiovascular; antihypertensive; PE-60 catheter used for IV application; BRL37344 is a B3AR agonist; Dose (10 ug/kg/day BRL37344);

Q5289: A. Vivekanandarajah, *et al.* Postnatal nicotine effects on the expression of nicotinic acetylcholine receptors in the developing piglet hippocampus and brainstem. *Int J Dev Neurosci* 2015;47(Pt B):183-91

Agents: Nicotine Hydrogen Tartrate **Vehicle:** water; **Route:** IP; **Species:** Pig (mini); **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (piglets); functionality of mp verified by blood and urine samples; toxicology; Dose (2 mg/kg/d); Resultant plasma level (20.3 ± 2.5 ng/mL);



Q4474: K. D. Katleba, *et al.* Steroid regulation of early postnatal development in the corpus epididymidis of pigs. *JOURNAL OF ENDOCRINOLOGY* 2015;225(125-134

Agents: Fulvestrant **Vehicle:** DMSO; PBS; **Route:** Not Stated; **Species:** Pig; **Pump:** 2ML2; 2ML4; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (boar, 6-6.5 weeks old); 50% DMSO used; Fulvestrant is a nuclear estrogen receptor antagonist and G protein-coupled receptor agonist;

Q4442: J. C. Hardwick, *et al.* Angiotensin receptors alter myocardial infarction-induced remodeling of the guinea pig cardiac plexus. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2015;309(R179-R188

Agents: Captopril; losartan; CGP42112A **Vehicle:** Not Stated; **Route:** SC; **Species:** Guinea pig; **Pump:** 2ML4; **Duration:** 4 weeks; 6 weeks;

ALZET Comments: Animal info (male, Hartley, 9 weeks old, 500-650g); pumps replaced every 3 weeks; cardiovascular; long-term study;

Q3348: A. D. Lassaletta, *et al.* Microvascular Notch Signaling Is Upregulated in Response to Vascular Endothelial Growth Factor and Chronic Myocardial Ischemia. *Circulation Journal* 2014;78(3):743-751

Agents: Vascular endothelial growth factor, recombinant human **Vehicle:** Heparin; Saline; **Route:** Intrapericardial; **Species:** Pig; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Animal info (male, Yorkshire miniswine, 13-22kg); ischemia (cardiac, chronic); stress/adverse reaction: (see pg. 746); post op. care (Enrofloxacin 68mg PO daily for 5 days; aspirin 325 mg/day for 5 days; buprenorphine HCL 0.3 mg/kg, transdermal fentanyl patch 4mcg/kg for 72h); cardiovascular;

Q2769: N. J. Hunt, *et al.* Orexin receptors in the developing piglet hypothalamus, and effects of nicotine and intermittent hypercapnic hypoxia exposures. *Brain Research* 2013;1508(:):73-82

Agents: Nicotine **Vehicle:** Water, sterile; **Route:** IP; **Species:** Pig; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Control animals received mp w/ vehicle; animal info (piglet, mixed bred)

Q9157: T. Berger, *et al.* Increased testicular Sertoli cell population induced by an estrogen receptor antagonist. *Molecular and Cellular Endocrinology* 2013;366(1):53-8

Agents: ICI 182,780 **Vehicle:** Saline; **Route:** SC; **Species:** Pig; **Pump:** 2ML4, 2ML2; **Duration:** 4 weeks;

ALZET Comments: Dose (125 ug/kg); Controls received mp w/ vehicle; animal info (1-5 weeks old, Sygen); gene therapy;

Q2620: T. Berger, *et al.* Increased testicular Sertoli cell population induced by an estrogen receptor antagonist. *MOLECULAR AND CELLULAR ENDOCRINOLOGY* 2013;366(1):53-58

Agents: ICI 182,780 **Vehicle:** Saline; DMSO; **Route:** SC; **Species:** Pig; **Pump:** 2ML2; 2ML4; **Duration:** Not Stated;

ALZET Comments: Control animals received mp w/ vehicle; animal info (1 wk old, Sygen); 50% DMSO used; pumps replaced after 4 weeks

Q2846: A. A. Al Dayeh, *et al.* Real-time monitoring of the growth of the nasal septal cartilage and the nasofrontal suture. *American Journal of Orthodontics and Dentofacial Orthopedics* 2013;143(6):773-783

Agents: Amikacin; gentamicin **Vehicle:** Not Stated; **Route:** SC; **Species:** Pig (mini); **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Animal info (female, 3.5-4.5 mo old, 12-27 kg); 2ML sized pumps used; pump implanted in the back of the neck

Q1774: A. Bienemann, *et al.* The development of an implantable catheter system for chronic or intermittent convection-enhanced delivery. *Journal of Neuroscience Methods* 2012;203(2):284-291

Agents: CSF, artificial (agent) **Vehicle:** Not Stated; **Route:** CSF/CNS (patumen); **Species:** Pig; **Pump:** 2ML4; **Duration:** 1 month;

ALZET Comments: Animal info (Large White/Landrace); "due to concerns regarding the risk of blockage, catheters were modified to be connected to Alzet osmotic minipumps" pg 288

Q1664: L. M. Chu, *et al.* Resveratrol supplementation abrogates pro-arteriogenic effects of intramyocardial vascular endothelial growth factor in a hypercholesterolemic swine model of chronic ischemia. *Surgery* 2011;150(3):390-399

Agents: Vascular endothelial growth factor, recomb. human **Vehicle:** Not Stated; **Route:** Intrapericardial; **Species:** Pig;

ALZET Comments: Animal info (intact, male, Yorkshire); stress/adverse effects "sudden cardiac death", pg 393



Sheep (2014-Present)

Q10045: S. Z. McIntosh, *et al.* CXCR4 signaling at the fetal-maternal interface may drive inflammation and syncytia formation during ovine pregnancy. *Biology of Reproduction* 2021;104(2):468-478

Agents: AMD3100 **Vehicle:** PBS; Saline; **Route:** Intrauterine; **Species:** Sheep; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Dose (2060 ng); Controls received mp w/ vehicle; dependence;

Q9802: E. V. O'Neil, *et al.* Characterization and regulation of extracellular vesicles in the lumen of the ovine uterus. *Biology of Reproduction* 2020;102(5):1020-1032

Agents: Recombinant Ovine IFNT **Vehicle:** Saline; **Route:** SC; **Species:** Sheep; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Dose (10 ul/hr); Controls received mp w/ vehicle; dependence;

Q8845: C. L. Runyan, *et al.* CXCR4 signaling at the ovine fetal-maternal interface regulates vascularization, CD34+ cell presence, and autophagy in the endometrium. *Biology of Reproduction* 2019;101(1):102-111

Agents: AMD3100 **Vehicle:** Saline; **Route:** SC; **Species:** Sheep; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Dose (2060 ng); Controls received mp w/ vehicle; animal info (Female,); CXCR4 antagonist aka AMD3100; dependence;

Q7658: C. L. Runyan, *et al.* CXCR4 signaling at the ovine fetal-maternal interface regulates vascularization, CD34+ cell presence, and autophagy in the endometrium. *Biology of Reproduction* 2019;101(1):102-111

Agents: AMD3100 **Vehicle:** PBS; **Route:** Intrauterine; **Species:** Sheep (Pregnant); **Pump:** 2ML1; **Duration:** 8 days;

ALZET Comments: Dose (2060 ng at 10 µl/h); Controls received mp w/ vehicle; animal info (female, western white face); AMD3100 is a CXCR4 antagonist; cyanoacrylate adhesive; teratology;

Q8657: S. Z. McIntosh, *et al.* Intrauterine inhibition of chemokine receptor 4 signaling modulates local and systemic inflammation in ovine pregnancy. *Am J Reprod Immunol* 2019;82(5):e13181

Agents: CXCR4 inhibitor **Vehicle:** PBS; **Route:** Intrauterine; **Species:** Sheep; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Dose (4120 ng); Controls received mp w/ vehicle; animal info (Rambouillet-cross ewes); CXCR4 inhibitor aka AMD3100; toxicology;

Q7873: T. D. Tremaine, *et al.* Immunolocalization of angiogenic growth factors in the ovine uterus during the oestrus cycle and in response to Steroids. *Reprod Domest Anim* 2018;53(3):667-679

Agents: Buserelin acetate **Vehicle:** Saline; **Route:** SC; **Species:** Sheep; **Pump:** Not stated; **Duration:** 18 days;

ALZET Comments: Dose (1mg/ml at 2.5 µl/hr); Controls received mp w/ agent; animal info (female, Welsh mountain); Buserelin acetate is a gonadotrophin agonist; replacement therapy (oestradiol); Buserelin used to remove the effect of endogenous gonadotrophins, luteinizing hormone and follicle stimulating hormone;

Q7861: S. Ruoss, *et al.* Inhibition of calpain delays early muscle atrophy after rotator cuff tendon release in sheep. *Physiol Rep* 2018;6(21):e13833

Agents: calpeptin **Vehicle:** DMSO; **Route:** intramuscular (infraspinatus); **Species:** Sheep; **Pump:** 2ML4; **Duration:** 6 weeks;

ALZET Comments: Dose (0.75 mg/day); animal info (26.7+/-1.4 months, female, Swiss Alpine); pumps replaced at 2 weeks; calpeptin is a synthetic calpain inhibitor; enzyme inhibitor (calpain); tissue perfusion (m. infraspinatus); good methods (detailed pump implantation procedure on page 3.); Therapeutic indication (calpain inhibition prevented the early unloading adaptations, but not the subsequent initiation of rotator cuff disease); 75% DMSO used;

Q6917: K. J. McCarty, *et al.* Effect of chronic melatonin supplementation during mid to late gestation on maternal uterine artery blood flow and subsequent development of male offspring in beef cattle. *J Anim Sci* 2018;96(12):5100-5111

Agents: Melatonin **Vehicle:** Not Stated; **Route:** Intrauterine; **Species:** Sheep (pregnant);

ALZET Comments:



Q7745: R. Corona, *et al.* Disruption of adult olfactory neurogenesis induces deficits in maternal behavior in sheep. *Behavioural Brain Research* 2018;347(124-131

Agents: Ara-C **Vehicle:** Serum, Physiological; **Route:** CSF/CNS (lateral ventricle); **Species:** Sheep; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: 4% Physiological Serum used; Controls received mp w/ vehicle; animal info (primiparous parturient Ile de France ewes (2–3 years old)); post op. care (amoxicillin, diurizone, finadyne, morphine); functionality of mp verified; Brain coordinates (rostrocaudal plane, 36 mm; mediolateral plane, 4.3 ± 0.7mm from the middle of the third ventricle; and depth, 16.6 ± 1mm from the cortex surface); bilateral cannula used;

Q7174: M. Batailler, *et al.* Pineal-dependent increase of hypothalamic neurogenesis contributes to the timing of seasonal reproduction in sheep. *Sci Rep* 2018;8(1):6188

Agents: Ara-C **Vehicle:** Not Stated; **Route:** CSF/CNS (third ventricle); **Species:** Sheep; **Pump:** 2ML4; **Duration:** 4 Weeks;

ALZET Comments: Dose (500ug/day); animal info (Ewes, 58.8 ± 4.5 kg , 59.4 ± 4 kg)); Ara-C aka cytosine-b-D-arabinofuranoside; Ara-C aka cytosine-b-D-arabinofuranoside;

Q6226: A. J. Turner, *et al.* Tubuloglomerular feedback responses in offspring of dexamethasone-treated ewes. *American Journal of Physiology Renal Physiology* 2017;313(4):F864-F873

Agents: Dexamethasone 21-phosphate disodium salt **Vehicle:** Not Stated; **Route:** IV (lateral saphenous vein); **Species:** Sheep (pregnant); **Pump:** 2ML1; **Duration:** 48 hours;

ALZET Comments: Dose (0.48 mg/h);

Q5322: M. Bazargan, *et al.* Limited fetal metabolism of rosiglitazone: Elimination via the maternal compartment in the pregnant ewe. *Reprod Toxicol* 2016;61(162-8

Agents: Rosiglitazone Maleate **Vehicle:** Water, Ethanol; **Route:** SC; **Species:** Sheep (pregnant); **Pump:** 2ML1; **Duration:** 16 days;

ALZET Comments: animal info (Singleton pregnant sheep); functionality of mp verified by plasma level, amniotic fluid samples; 15% ethanol used; Multiple pumps per animal (4); stability verified by regular plasma level measurements (reached after day 5, tested through day 16; half life of 24-48 hours in sheep); Catheters flushed with heparinized saline; Dose (2.7 mg/fetus/d);

Q4800: K. B. a. T. E. Spencer. Biological Roles of Interferon Tau (IFNT) and Type I IFN Receptors in Elongation of the Ovine Conceptus1. *Biology of Reproduction* 2015;92(2)(47):1-10

Agents: oligonucleotides, antisense morpholino **Vehicle:** PBS; **Route:** Intrauterine; **Species:** Sheep (ewe, pregnant); **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ control oligonucleotides; animal info (female, Columbia Rambouillet); teratology; cyanoacrylate adhesive; used vinyl catheter tubing (0007760) to cannulate uterine lumen; pump affixed to mesosalpinx using cyanoacrylate glue;

Q4521: G. Maneenil, *et al.* Oral, Nasal and Pharyngeal Exposure to Lipopolysaccharide Causes a Fetal Inflammatory Response in Sheep. *PLoS One* 2015;10(U1091-U1101

Agents: Endotoxin, LPS **Vehicle:** Not Stated; **Route:** Oral cavity; **Species:** Sheep (ewe); **Pump:** Not Stated; **Duration:** 1 day; 6 days;

ALZET Comments: Controls received mp w/ saline; animal info (Merino); teratology; immunology;

Q3870: A. W. Eifert, *et al.* Effect of melatonin or maternal nutrient restriction on vascularity and cell proliferation in the ovine placenta. *Animal Science* 2015;153(13-21

Agents: Melatonin; luzindole **Vehicle:** DMSO; water; **Route:** Intrauterine; **Species:** Sheep (ewe; pregnant); **Pump:** 2ML4; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Western white face, GD62); functionality of mp verified by serum levels; 45% DMSO used; good methods (pg 15); no stress (see pg. 15); post op. care (BID IM injection flunixin meglumine; QD IP injection Penicillin G Procaine); teratology; cardiovascular; used 20 cm of PE 60 tubing; pumps primed overnight 37C saline with catheters;



Q4336: K. E. Brooks, *et al.* Peroxisome Proliferator Activator Receptor Gamma (PPARG) Regulates Conceptus Elongation in Sheep. *Biology of Reproduction* 2015;92(U102-U114)

Agents: Oligonucleotide, antisense morpholino PPARG; oligonucleotide, antisense morpholino PPARG **Vehicle:** PBS; **Route:** Intrauterine (uterine horn); **Species:** Sheep (ewe); **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ control morpholino; animal info (Ovis aries, 7 days after mating); cyanoacrylate adhesive; used vinyl catheter tubing; pump glued to mesosalpinx and sutures; pumps primed in 37C sterile PBS for 24 hours

Q4748: T. G. A. M. Wolfs, *et al.* Chorioamnionitis-induced fetal gut injury is mediated by direct gut exposure of inflammatory mediators or by lung inflammation. *American Journal of Physiology Gastrointestinal and Liver Physiology* 2014;306(5):G382-G393

Agents: Endotoxin, LPS **Vehicle:** Not Stated; **Route:** Intra-amniotic; **Species:** Sheep (fetus); **Pump:** Not Stated; **Duration:** 24 hours;

ALZET Comments: Controls received mp w/ saline; animal info (124 gestation day); immunology;

Q3583: I. Nitsos, *et al.* The Impact of Chronic Intrauterine Inflammation on the Physiologic and Neurodevelopmental Consequences of Intermittent Umbilical Cord Occlusion in Fetal Sheep. *Reproductive Sciences* 2014;21(658-670)

Agents: Endotoxin, LPS **Vehicle:** Not Stated; **Route:** Amniotic sac; **Species:** Sheep (fetus); **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ saline; animal info (female, pregnant, GD80); post op. care (benacillin); teratology; immunology; E.coli LPS 055:B5, 18 mg/ml;

Q3577: G. C. Musk, *et al.* Thermal and mechanical nociceptive threshold testing in pregnant sheep. *VETERINARY ANAESTHESIA AND ANALGESIA* 2014;41(305-311)

Agents: Medetomidine **Vehicle:** Saline; **Route:** IP; **Species:** Sheep (pregnant); **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Animal info (female, Merino singleton, pregnant at GD118-121); functionality of mp verified by plasma levels; comparison of transdermal patch vs mp; behavioral testing (mechanical nociceptive threshold; thermal nociceptive threshold); pumps primed at 37C overnight;

Q4730: S. Lie, *et al.* Exposure to rosiglitazone, a PPAR-gamma agonist, in late gestation reduces the abundance of factors regulating cardiac metabolism and cardiomyocyte size in the sheep fetus. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2014;306(6):R429-R437

Agents: Rosiglitazone **Vehicle:** Ethanol; **Route:** SC; **Species:** Sheep (fetus); **Pump:** 2ML4; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (fetus, 123-126 days gestation); 15% ethanol used; cardiovascular;

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)

Agents: U0126; serum protein, ovine; interferon tau, recombinant ovine **Vehicle:** DMSO; **Route:** Intrauterine (uterine horn); **Species:** Sheep (ewe); **Pump:** 2ML1; **Duration:** 6 days;

ALZET Comments: 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;

Q3925: M. L. Hyde, *et al.* In vivo measurement of the absorption of strontium in the rumen and small intestine of sheep as an index of calcium absorption capacity. *British Journal of Oral and Maxillofacial Surgery* 2014;112(718-724)

Agents: Hydroxyvitamin D3, 1a- **Vehicle:** Not Stated; **Route:** SC; **Species:** Sheep (ewe); **Pump:** 2002; **Duration:** 6 days;

ALZET Comments: Animal info (merino, mature); functionality of mp verified by plasma 1,25-dihydroxycholecalciferol levels;

Q3494: B. Guo, *et al.* A gene expression estimator of intramuscular fat percentage for use in both cattle and sheep. *JOURNAL OF ANIMAL SCIENCE AND BIOTECHNOLOGY* 2014;5(U1-U12)

Agents: Oxytocin **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Sheep; **Pump:** Not Stated; **Duration:** 90 days;

ALZET Comments: Pumps replaced every 30 days; long-term study;