



**Recent References (2017-2020) on the Administration of Leptin
Using ALZET® Osmotic Pumps**

Q8468: A. Fraga, *et al.* Temperature but not leptin prevents semi-starvation induced hyperactivity in rats: implications for anorexia nervosa treatment. *Sci Rep* 2020;10(1):5300

Agents: leptin, recomb. rat; **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 14 days;

ALZET Comments: Dose (1.29 mg/ml); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats (130–190 g)); dependence;

Q7682: Z. Wang, *et al.* Role of SOCS3 in POMC neurons in metabolic and cardiovascular regulation. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2019;316(4):R338-R351

Agents: Leptin **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 1007D; 1002; **Duration:** 7 days; 14 days;

ALZET Comments: Dose (4 ug/kg/min); animal info (6–17 wk of age, male and female mice); cardiovascular;

Q8364: S. Pereira, *et al.* Metabolic effects of leptin receptor knockdown or reconstitution in adipose tissues. *Sci Rep* 2019;9(1):3307

Agents: Recombinant Murine Leptin **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 8 days;

ALZET Comments: Dose (20 ug/day); Controls received mp w/ vehicle; animal info (8-12 weeks old); diabetes;

Q7524: R. B. S. Harris. Low-dose infusions of leptin into the nucleus of the solitary tract increase sensitivity to third ventricle leptin. *American Journal of Physiology Endocrinology and Metabolism* 2019;316(5):E719-E728

Agents: Leptin **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1004; **Duration:** 14 days;

ALZET Comments: Dose (5, 10 ng/day); 0.9% saline used; animal info (Male, Sprague-Dawley, 275-300 g); bilateral cannula used; dependence;

Q8021: M. T. Hackl, *et al.* Brain leptin reduces liver lipids by increasing hepatic triglyceride secretion and lowering lipogenesis. *Nat Commun* 2019;10(1):2717

Agents: Leptin; LpR **Vehicle:** Saline; CSF, artificial; **Route:** IP; CSF/CNS (third ventricle); **Species:** Rat; **Pump:** 2004; **Duration:** 2 weeks;

ALZET Comments: Dose (0.3 ug/day); 0.9% used; Controls received mp w/ vehicle; animal info (10 weeks old, Male, Sprague Dawley); dependence; LpR AKA Leptin Receptor Antagonist;

Q7976: O. S. Dallner, *et al.* Dysregulation of a long noncoding RNA reduces leptin leading to a leptin-responsive form of obesity. *Nat Med* 2019;25(3):507-516

Agents: Leptin **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 14 days;

ALZET Comments: Dose (0.5 µg/h); Controls received mp w/ vehicle; animal info (12 weeks, female, C57BL/J6 Lep(ob)/Lep(ob)); replacement therapy (leptin);

Q6983: C. Caballero-Eraso, *et al.* Leptin acts in the carotid bodies to increase minute ventilation during wakefulness and sleep and augment the hypoxic ventilatory response. *J Physiol* 2019;597(1):151-172

Agents: Leptin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 days;

ALZET Comments: Dose (120 µg/day); Controls received mp w/ vehicle;

Q6878: D. M. Arble, *et al.* Vertical sleeve gastrectomy improves ventilatory drive through a leptin-dependent mechanism. *JCI Insight* 2019;4(1):

Agents: Leptin **Vehicle:** Water; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 weeks;

ALZET Comments: Dose (10µg/day); Controls received mp w/ vehicle; animal info (C57BL6/J WT and ob/ob male mice, 6-8 weeks of age);

Q7849: Y. Ravussin, *et al.* Evidence for a Non-leptin System that Defends against Weight Gain in Overfeeding. *Cell Metabolism* 2018;28(2):289-299 e5

Agents: leptin, recomb. mouse **Vehicle:** Saline, buffered; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 33 days;



ALZET Comments: Dose (150 ng/hr); saline (pH 8) used; Controls were WT and received mp w/ agent; animal info (4 weeks, male, C57BL/6J(Lepob/ob)); Resultant plasma level (1.8 ± 1.4 ng/mL); replacement therapy (leptin); good methods (detailed pump placement on page e3);

Q7236: T. Murata, *et al.* Leptin Aggravates Reflux Esophagitis by Increasing Tissue Levels of Macrophage Migration Inhibitory Factor in Rats. *Tohoku J Exp Med* 2018;245(1):45-53

Agents: Leptin **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: Dose (0.6 mg/Kg-weight); 200 μ L of 10 mM used; Controls received mp w/ vehicle; Controls received mp w/ vehicle;

Q8123: T. H. Meek, *et al.* In Uncontrolled Diabetes, Hyperglucagonemia and Ketosis Result From Deficient Leptin Action in the Parabrachial Nucleus. *Endocrinology* 2018;159(4):1585-1594

Agents: Leptin **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** Not stated; **Duration:** Not stated;

ALZET Comments: Dose (1 μ g/day); animal info (Male, LepRbCCK KO); Brain coordinates (0.7mm posterior to bregma, 1.3 mm lateral, and 2.3 mm below the skull); bilateral cannula used; dependence;

R0365: L. Maletinska, *et al.* The impact of anorexigenic peptides in experimental models of Alzheimer's disease pathology. *J Endocrinol* 2018;

Agents: PrRP palmitoylated analogs, Leptin, Amylin, Cyclic AC253, Exendin 4 **Vehicle:** Not Stated; **Route:** SC, CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 months; 28 days; 5 weeks, 5 months, 16 weeks;

ALZET Comments: Dose: Palm11-PrRP (5 mg/kg/day), Leptin (2.4 nmol/day), Amylin (0.24 mg/kg/day), Exendin-4 (3.5 pmol/kg/min); animal info (7 month old THY-Tau22 mice; 5 month old APP/PS1 mice; 6 month old AMP8 mice); behavioral testing (Y-maze); neurodegenerative (Alzheimer's); This review summarizes current information on the potential neuroprotective properties of food intake-lowering (anorexigenic) peptides that have been tested in experimental models of AD-like pathology.

Q8099: V. Lopez, *et al.* Food Restriction is Required to Preserve the Antisteatotic Effects of Central Leptin in the Liver of Middle-Aged Rats. *Obesity (Silver Spring)* 2018;26(5):877-884

Agents: Leptin **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** Not stated; **Duration:** 7 days;

ALZET Comments: Dose (0.2 μ g/day); Controls received mp w/ vehicle; animal info (3 or 7 month old, Male, Wistar); bilateral cannula used; dependence;

Q8093: R. Liu, *et al.* Leptin upregulates smooth muscle cell expression of MMP-9 to promote plaque destabilization by activating AP-1 via the leptin receptor/MAPK/ERK signaling pathways. *Exp Ther Med* 2018;16(6):5327-5333

Agents: Recombinant Leptin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 4 weeks;

ALZET Comments: Dose (1 μ g/g/day); Controls received mp w/ vehicle; animal info (C57BL/6, 8 weeks old); cardiovascular;

Q8069: C. H. Lee, *et al.* Hypothalamic Macrophage Inducible Nitric Oxide Synthase Mediates Obesity-Associated Hypothalamic Inflammation. *Cell Rep* 2018;25(4):934-946 e5

Agents: Leptin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 4 weeks;

ALZET Comments: animal info (Male, 7 weeks old, C57BL/6J); ALZET brain infusion kit 1 used; Brain coordinates (0.6mm caudal to bregma, 1mm right to the sagittal sinus, and 2.0mm ventral to the sagittal sinus); bilateral cannula used; dependence;

Q8066: E. Lamy, *et al.* Effects of hyperleptinemia in rat saliva composition, histology and ultrastructure of the major salivary glands. *Arch Oral Biol* 2018;96(1-12)

Agents: Leptin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Dose (10 μ L/hr); Controls received mp w/ vehicle; animal info (Male, Wistar, 11-12 weeks old); Leptin aka recombinant rat leptin protein; dependence;

Q4806: M. Labyb, *et al.* Oxytocin Administration Alleviates Acute but Not Chronic Leptin Resistance of Diet-Induced Obese Mice. *Int J Mol Sci* 2018;20(1):



Agents: Oxytocin; leptin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: Dose (oxytocin (50 µg/day); leptin (20 or 40 µg/day)); Controls received mp w/ vehicle; animal info (Eight-week-old C57BL/6JRj male mice); “Osmotic pump content was verified postmortem in order to ensure complete drug delivery.”

Q7778: E. Burgos-Ramos, *et al.* The increase in fiber size in male rat gastrocnemius after chronic central leptin infusion is related to activation of insulin signaling. *Mol Cell Endocrinol* 2018;470(48-59

Agents: Leptin **Vehicle:** Saline; **Route:** CSF/CNS (right cerebral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Dose (12 µg/day); Controls received mp w/ vehicle; animal info (Male, Wistar, 240-260 g); Brain coordinates (0.3 mm anteroposterior, 1.1 mm lateral from Bregma); dependence;

Q5956: J. Tam, *et al.* Peripheral cannabinoid-1 receptor blockade restores hypothalamic leptin signaling. *Mol Metab* 2017;6(10):1113-1125

Agents: Leptin; SHU-9119 **Vehicle:** PBS; **Route:** SC; CSF/CNS; **Species:** Mice; **Pump:** 2004; **Duration:** 12 weeks, 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (leptin-deficient ob/ob mice); long-term study; pumps replaced every 28 days; SHU-9119 is a MC4R antagonist; Leptin dissolved in PBS and delivered SC for 12 weeks; SHU-9119 dissolved in saline and delivered ICV for 7 days; Pumps model incorrectly listed as Model 2001D. It should be Model 2004 based on description.

Q6797: Y. Shimizu, *et al.* Role of leptin in conditioned place preference to high-fat diet in leptin-deficient ob/ob mice. *Neurosci Lett* 2017;640(60-63

Agents: Leptin, recomb. mouse **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 1 week; 4 weeks;
ALZET Comments: Dose (4.8 µg/day); Controls received mp w/ vehicle; animal info (Animals Male C57BL/6J mice and ob/ob mice (5-week and 8-week old));

Q5797: M. Sakaguchi, *et al.* Adipocyte Dynamics and Reversible Metabolic Syndrome in Mice with an Inducible Adipocyte-Specific Deletion of the Insulin Receptor. *Cell Metabolism* 2017;25(2):448-462

Agents: Leptin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 12 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (8 weeks old); Therapeutic indication (Metabolic syndrome, Syndrome X);
Dose (10 µg/day);

Q6713: K. A. Philbrick, *et al.* Leptin stimulates bone formation in ob/ob mice at doses having minimal impact on energy metabolism. *J Endocrinol* 2017;232(3):461-474

Agents: Leptin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 12 days;
ALZET Comments: Dose (0, 4, 12, 40, 140, or 400 ng/h); dose-response (Fig 2; Page 16); animal info (6-week-old female ob/ob mice); Therapeutic indication (obesity);

Q5820: R. J. Perry, *et al.* Mechanism for leptin's acute insulin-independent effect to reverse diabetic ketoacidosis. *J Clin Invest* 2017;127(2):657-669

Agents: Leptin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 2 weeks, 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (8 weeks old); diabetes;
Therapeutic indication (diabetic ketoacidosis); Dose (0.624 µg/hr);

Q6701: P. Mota, *et al.* Mp17-14 Depletion of Peripheral Serotonin Synthesis Induces Benign Prostatic Growth in Mice: More Evidence for the New “Neuroendocrine Theory” in Bph Etiology. *The Journal of Urology* 2017;197(4):e216-e217

Agents: Leptin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 24 weeks;
ALZET Comments: Dose (5 mg/day; 10 mg/day); Controls received mp w/ vehicle; animal info (10-week-old male ObOb and strain-matched control mice); pumps replaced every 12 weeks; Multiple pumps per animal (2); long-term study;

Q5828: K. Matoba, *et al.* Leptin sustains spontaneous remyelination in the adult central nervous system. *Sci Rep* 2017;7(40397



Agents: Antibody, leptin neutralizing; leptin, recombinant mouse **Vehicle:** PBS; **Route:** CSF/CNS (intrathecal); **Species:** Mice; **Pump:** 1007D, 1002; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (7-8 weeks old) ; ALZET brain infusion kit used; neurodegenerative (Demyelination); Therapeutic indication (Demyelination); Dose ((12 μ g/kg body weight per day, 10 μ g/kg of body weight per day);

Q6248: R. B. S. Harris. Low-dose leptin infusion in the fourth ventricle of rats enhances the response to third-ventricle leptin injection. *American Journal of Physiology Endocrinology and Metabolism* 2017;313(2):E134-E147

Agents: Leptin **Vehicle:** Not Stated; **Route:** CSF/CNS (fourth ventricle); **Species:** Rat; **Pump:** 2004; **Duration:** 11 days; 13 days;

ALZET Comments: Dose (0.01, 0.1, 0.3, or 0.6 μ g/24 h); Controls received mp w/ vehicle; animal info (rats weighing ~280 g);

Q6091: A. Gupta, *et al.* Chronic hyper-leptinemia induces insulin signaling disruption in adipocytes: Implications of NOS2. *Free Radic Biol Med* 2017;112(93-108

Agents: Leptin, recomb. murine **Vehicle:** HCl; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments: Dose (2.5 mg/ml); animal info (6-8 week old C57BL/6 and NOS2-/- mice);

Q6257: N. Gomez-Hurtado, *et al.* Beneficial effects of leptin treatment in a setting of cardiac dysfunction induced by transverse aortic constriction in mouse. *J Physiol* 2017;595(13):4227-4243

Agents: Leptin **Vehicle:** Tris; Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 weeks;

ALZET Comments: Dose (0.36 mg/kg/day); 20 mmol L⁻¹ Tris, 150 nmol L⁻¹ NaCl used; Controls received mp w/ vehicle; animal info (Ten-week-old C57BL/6 male mice); cardiovascular;

Q6157: E. A. Flatow, *et al.* Elucidating the role of leptin in systemic inflammation: a study targeting physiological leptin levels in rats and their macrophages. *American Journal of Physiology Regulatory, Integrative, and Comparable Physiology* 2017;313(5):R572-R582

Agents: Leptin **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (Male Wistar rats weighing 180–250 g); post op. care (5 mg/kg ketoprofen); Brain coordinates (0.5 mm caudal to the bregma and 1.5 mm to the right of the midline);

Q6386: Dorfman MD, *et al.* Deletion of Protein Kinase C I in POMC Neurons Predisposes to Diet-Induced Obesity. *Diabetes* 2017;66(4):920-934

Agents: Leptin **Vehicle:** PBS; **Route:** CSF/CNS; **Species:** Rat; Mice; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: animal info (male Wistar rats; Eight-week-old male and female POMC-IKO and WT mice); Brain coordinates (0.8 mm posterior to bregma; 1.5 mm lateral to the sagittal suture, and 3.6 mm below the skull surface); diabetes;

Q6387: J. M. do Carmo, *et al.* Changes in ambient temperature elicit divergent control of metabolic and cardiovascular actions by leptin. *FASEB J* 2017;31(6):2418-2428

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

ALZET Comments: Dose (4 mg/kg/min); Controls received mp w/ vehicle; animal info (22 week old Male wild-type (WT) C57BL/6J mice); cardiovascular;

Q6021: A. A. da Silva, *et al.* Role of autonomic nervous system in chronic CNS-mediated antidiabetic action of leptin. *American Journal of Physiology Endocrinology and Metabolism* 2017;312(5):E420-E428

Agents: Leptin, Hexamethonium **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** 2002; **Duration:** 12 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (360-420g); diabetes; Therapeutic indication (Diabetes); Dose (Hexamethonium: 15 mg/kg);

Q6006: K. T. Chang, *et al.* Leptin is essential for microglial activation and neuropathic pain after preganglionic cervical root avulsion. *Life Sci* 2017;187(31-41



Agents: Leptin **Vehicle:** PBS; **Route:** CSF/CNS (Cervical); **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male and female, C57B/6 J (B6) and Ob); Therapeutic indication (Obesity, Neuropathic pain); Dose (1 ug/day);

Q6115: L. R. Beutler, *et al.* Dynamics of Gut-Brain Communication Underlying Hunger. *Neuron* 2017;96(2):461-475 e5
Agents: Leptin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 10 days;
ALZET Comments: Dose (450 ng/hr); Controls received mp w/ vehicle; animal info (ob/ob mice); Therapeutic indication (Obesity);