



References on the Administration of Estrogens Using ALZET® Osmotic Pumps

Q7244: R. Thakkar, *et al.* 17beta-Estradiol Regulates Microglia Activation and Polarization in the Hippocampus Following Global Cerebral Ischemia. *Oxid Med Cell Longev* 2018;2018(4248526)

ALZET Comments: Estradiol, 17b; Cyclodextrin, B-; SC; Rat; Pump model not stated; 14 days; Dose (0.0167 mg); 20% β -cyclodextrin used; animal info (3 month old, female, Sprague Dawley); ischemia (Cerebral);

Q7181: B. L. Hoh, *et al.* Estrogen Deficiency Promotes Cerebral Aneurysm Rupture by Upregulation of Th17 Cells and Interleukin-17A Which Downregulates E-Cadherin. *J Am Heart Assoc* 2018;7(8):

ALZET Comments: Angiotensin II, estradiol, 17beta-; PBS, Ethanol; SC; Mice; Ang-II (1000 ng/kg/min), Estradiol (0.25 ug/hr); Beta-estradiol reconstituted in a PBS-ethanol solution [9:1]; animal info (8- to 12-week-old female C57BL/6 mice);

Q5727: Y. Zhu, *et al.* Protective Effect of 17beta-Estradiol Upon Hippocampal Spine Density and Cognitive Function in an Animal Model of Vascular Dementia. *Sci Rep* 2017;7(42660)

ALZET Comments: Estradiol, 17b-; SC; Rat; 2006; Controls received mp w/ 20% cyclodextrin; animal info (male, Sprague Dawley, 250-300g, adult); functionality of mp verified by serum levels; behavioral testing (Morris water maze); replacement therapy (estradiol infusion); long-term study; cardiovascular; Dose (0.05 ug/h); "exogenous E2 replacement produced E2 levels of 25-33pg/ml" (pg 2);.

Q6521: S. Ucer, *et al.* The Effects of Aging and Sex Steroid Deficiency on the Murine Skeleton Are Independent and Mechanistically Distinct. *J Bone Miner Res* 2017;32(3):560-574

ALZET Comments: Estradiol; Mice; 2006; 6 weeks; Dose (6 μ g/d); animal info (5-month-old C57BL/6 male mice); replacement therapy (orchietomy);

Q6763: A. L. Russell, *et al.* The interaction of dietary isoflavones and estradiol replacement on behavior and brain-derived neurotrophic factor in the ovariectomized rat. *Neurosci Lett* 2017;640(53-59)

ALZET Comments: Estradiol, 17b-; Cyclodextrin, 2-hydroxypropyl- β -; water; SC; Rat; 2002; 14 days; Dose (0.25 mg/kg body weight); 27% hydroxypropyl- β -cyclodextrin used; animal info (ovariectomized (OVX) female Sprague Dawley rats, weighing between 200–225 g,); replacement therapy (estradiol);

Q6232: S. F. Rosen, *et al.* T-Cell Mediation of Pregnancy Analgesia Affecting Chronic Pain in Mice. *J Neurosci* 2017;37(41):9819-9827

ALZET Comments: Estradiol, 17b-; Progesterone sulfate; SC; Mice; 2002; 14 days; Dose (17b-estradiol : 0.1 mg/kg/d, progesterone sulfate: 0.25 mg/kg/d, 0.1 mg/kg/d estradiol + 0.25 mg/kg/d progesterone); Controls received mp w/ vehicle; animal info (7-12 week old female C57BL/6J mice); replacement therapy (estradiol, ovariectomy); Therapeutic indication.

Q6603: S. Menazza, *et al.* Non-nuclear estrogen receptor alpha activation in endothelium reduces cardiac ischemia-reperfusion injury in mice. *J Mol Cell Cardiol* 2017;107(41-51)

ALZET Comments: Estradiol; Dendrimer; Estrogen-dendrimer conjugate; ICI182,780; SC; Mice; 2 weeks; Dose (Estradiol (6 μ g/day); (Dendrimer 6 μ g/day), Estrogen-dendrimer conjugate (6 μ g/day); ICI182,780 (2mh/kg/day0); Controls received mp w/ vehicle; animal info (11 week old C57BL/6J female mice); Estrogen-dendrimer conjugate aka EDC; ischemia (Cardiac);

Q6143: S. Laouafa, *et al.* Estradiol Protects Against Cardiorespiratory Dysfunctions and Oxidative Stress in Intermittent Hypoxia. *Sleep* 2017;40(8):

ALZET Comments: Estradiol; SC; Rat; 2ML4; 28 days; Dose (0.5 mg/kg/d); Controls received mp w/ vehicle; animal info (Sprague-Dawley female rats weighing 230–250 g); post op. care (3.5 mg/kg bupivacaine and 7 mg/kg lidocaine SC injections for 48 hours after); functionality of mp verified by measuring residual volume at the end of the study; replacement therapy (estradiol);



Q6307: T. Jover-Mengual, *et al.* Molecular mechanisms mediating the neuroprotective role of the selective estrogen receptor modulator, bazedoxifene, in acute ischemic stroke: A comparative study with 17beta-estradiol. *J Steroid Biochem Mol Biol* 2017;171(296-304

ALZET Comments: Bazedoxifene; Estradiol, 17b-; DMSO; IP; Rat; 2ML1; Dose (Bazedoxifene: 3 mg/kg/day; Estradiol: 100 µg/kg/day); 100% DMSO used; Controls received mp w/ vehicle; animal info (male Wistar rats weighing 300–350g); Resultant plasma level (at 4 hours Bazedoxifene : 20.7 ± 2.1 ng/mL and Estradiol: 45.6 ± 7.8 pg/mL); Therapeutic indication (stroke);.

Q6325: H. Gao, *et al.* ESR1 and its antagonist fulvestrant in pituitary adenomas. *Mol Cell Endocrinol* 2017;443(32-41

ALZET Comments: Estradiol, 17 beta-; Glycerol, DMSO; SC; Rat; 2006; 8 weeks; Dose (10 mg); 50% (v/v) glycerol/50% (v/v) DMSO solution used; animal info (Female Fisher 344 rats);.

Q6373: A. L. Frump, *et al.* Estrogen receptor-dependent attenuation of hypoxia-induced changes in the lung genome of pulmonary hypertension rats. *Pulm Circ* 2017;7(1):232-243

ALZET Comments: Estradiol, 17b-; SC; Rat; 3 weeks; Dose (75 mg/kg/day); animal info (male Sprague-Dawley rats weighing 250–300g); cardiovascular; Therapeutic indication (Pulmonary arterial hypertension);.

Q5809: H. H. Farman, *et al.* Extra-nuclear effects of estrogen on cortical bone in males require ERalphaAF-1. *J Mol Endocrinol* 2017;58(2):105-111

ALZET Comments: Estradiol; DMSO, PBS, Ethanol; IP; mice; 1004; 3.5 weeks; Controls received mp w/ vehicle; animal info (5 months old) (15% EtOH, 43% DMSO, 42% PBS) replacement therapy (Estradiol); Therapeutic indication (Estrogen); Dose (6 ug/day);.

Q4911: J. Yang, *et al.* Inhibiting HIF-1alpha Decreases Expression of TNF-alpha and Caspase-3 in Specific Brain Regions Exposed Kainic Acid-Induced Status Epilepticus. *Cell Physiol Biochem* 2016;38(1):75-82

ALZET Comments: Estradiol, 2-methoxy; entanercept; CSF, artificial; CSF/CNS; Rat; 1003D; 3 days; Controls received mp w/ vehicle; animal info (male, Wistar, 200-250g); ALZET brain infusion kit used; Cannula placement verified via histologic analysis;.

Q5079: S. Uchida, *et al.* Sympathetic regulation of ovarian functions under chronic estradiol treatment in rats. *Auton Neurosci* 2016;197(19-24

ALZET Comments: Estradiol, 17B-; SC; Rat; 2004; 28 days; Controls received mp w/ saline; animal info (female, Wistar, 5-6 months old); functionality of mp verified by estrogen-mediated phenomena (cutaneous infusion of 17β-estradiol (5 µg/day) for 4 weeks demonstrated the well-known estrogen-mediated phenomena of acyclic conditions and uterine hypertrophy... This indicates that estradiol was definitely administered to our study rats) pg 23; Dose (5 ug/day);.

Q5081: A. E. Tschiffely, *et al.* A comparative evaluation of treatments with 17beta-estradiol and its brain-selective prodrug in a double-transgenic mouse model of Alzheimer's disease. *Horm Behav* 2016;83(39-44

ALZET Comments: DHED; estradiol, 17B-; Propylene glycol; SC; Mice (transgenic); 2004; 8 weeks; Controls received mp w/ vehicle; animal info (female, APPswe/PS1dE9, 6 months old); functionality of mp verified by plasma levels (see figure S1 - E2 only; no assay for DHED); pumps replaced every 4 weeks; neurodegenerative (Alzheimer's); replacement therapy (estradiol infusion); DHED aka 10β,17β-dihydroxyestra-1,4-dien-3-one; Dose (2 ug/day); Industry authored (AgyPharma LLC);.

Q5689: R. Thakkar, *et al.* NLRP3 Inflammasome Activation in the Brain after Global Cerebral Ischemia and Regulation by 17beta-Estradiol. *Oxid Med Cell Longev* 2016;2016(8309031

ALZET Comments: Estradiol, 17B-; Cyclodextrin, B-; SC; Rat; Mice; 2002; 14 days; animal info (Rats female, Sprague Dawley, 3 months old, OVX; Mice C27BL/6 PELP1, young adult, OVX); 20% Cyclodextrin used; ischemia (cerebral); replacement therapy (estradiol infusion); immunology; Resultant plasma level (10-15 pg/mL);.

Q4865: Osamu Nakagawasaia, *et al.* BE360, a new selective estrogen receptor modulator, produces antidepressant and antidementia effects through the enhancement of hippocampal cell proliferation in olfactory bulbectomized mice. *Behavioural Brain Research* 2016;297(315-322



ALZET Comments: BE360; estradiol, 17b-; tamoxifen; raloxifen hydrochloride; PEG 300; SC; Mice; 2002; 2 weeks; Controls received mp w/ vehicle; animal info (female, ddY, 10 weeks old, bulbectomized); dose-response (pg 317-318); neurodegenerative (dementia); behavioral testing (sucrose preference; y-maze); BE360 is a novel selective estrogen receptor modulator; Dose (100 ug/day);.

Q4860: E. Maggioli, *et al.* Estrogen protects the blood–brain barrier from inflammation-induced disruption and increased lymphocyte trafficking. *Brain Behav. Immun* 2016;51(212-222

ALZET Comments: Estradiol; Cyclodextrin, B-; SC; Mice; 2002; 14 days; Controls received mp w/ vehicle; animal info (C57BL6 or AnxA1 -/-, 2 months old, OVX); replacement therapy (estradiol infusion); immunology; dose: 100nM.

Q4788: Jeffrey A. Blair, *et al.* Luteinizing hormone downregulation but not estrogen replacement improves ovariectomy-associated cognition and spine density loss independently of treatment onset timing. *Horm. Behav* 2016;78(60-66

ALZET Comments: Estradiol, 17b; leuprolide acetate; Saline; SC; Mice; 1004; 2 months; Controls received mp w/ vehicle; animal info (C57BL6J, 9 months old, OVX); pumps replaced every month; behavioral testing (morris water maze); replacement therapy (estradiol infusion); Dose (E2 1.1 ng/day; leuprolide 3.6 ug/day);.

Q5377: A. Ichikawa, *et al.* Ketoconazole-induced estrogen deficiency causes transient decrease in placental blood flow associated with hypoxia and later placental weight gain in rats. *Reprod Toxicol* 2016;63(62-9

ALZET Comments: Estradiol, 17-beta-; Ethanol, Propylene Glycol; SC; Rat; 1003D; 3 days; animal info (Female Crl:CD (SD) rats, 11-12 weeks old); functionality of mp verified by plasma levels; 0.5% ethanol, 99.5% Propylene glycol used; dose-response (pg 63); E2 aka estradiol-17beta; hypoxia and later placental weight gain in rats; Dose (0, 0.1, or 1 ug/rat/day); Plasma Level: Lower limit of sensitivity (measured by double-antibody radioimmunoassay (RIA); 5 pg/mL);.

Q6040: B. Gerby, *et al.* High-throughput screening in niche-based assay identifies compounds to target preleukemic stem cells. *J Clin Invest* 2016;126(12):4569-4584

ALZET Comments: Methoxyestradiol, 2-; DMSO, PEG; SC; Mice; 2001; 7 days; Controls received mp w/ vehicle; animal info (C57BL6/J ; 50% DMSO; 50% PEG400 ; cancer (Leukemia); 2-methoxyestradiol (2-ME2) is an estrogen derivative ; Therapeutic indication (Cancer, chemotherapy); Dose (40 mg/kg/day);.

Q5763: K. L. Chambliss, *et al.* Nonnuclear Estrogen Receptor Activation Improves Hepatic Steatosis in Female Mice. *Endocrinology* 2016;157(10):3731-3741

ALZET Comments: Estradiol, estrogen dendrimer conjugate; IP; Mice; 2006; 12 weeks, 84 days; Controls received mp w/ vehicle; animal info (5 weeks old, ovariectomy); pumps replaced every 6 weeks; long-term study; Therapeutic indication (atherosclerosis); Dose (6 ug/day);.

Q4246: C. Weigt, *et al.* Effects of estradiol, estrogen receptor subtype-selective agonists and genistein on glucose metabolism in leptin resistant female Zucker diabetic fatty (ZDF) rats. *JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY* 2015;154(12-22

ALZET Comments: Estradiol; estrogen receptor selective agonist, alpha; estrogen receptor selective agonist, beta; DMSO; water; Rat; Animal info (juvenile, female, ZDF fa/fa, 6 wks old, 180-240 g).

P6007: M. Sarvari, *et al.* Hippocampal Gene Expression Is Highly Responsive to Estradiol Replacement in Middle-Aged Female Rats. *Endocrinology* 2015;156(7):2632-45

ALZET Comments: Estradiol, 17b-; Propylene glycol; SC; Rat; 2004; 29 days; Dose (0.33 mg/mL); animal info (Female Harlan-Wistar rats; 9 months old); replacement therapy (Estradiol);.

Q5257: L. Rigassi, *et al.* 2-Methoxyestradiol blocks the RhoA/ROCK1 pathway in human aortic smooth muscle cells. *Am J Physiol Endocrinol Metab* 2015;309(12):E995-1007

ALZET Comments: Estradiol, 2-methoxy; DMSO; IA (carotid artery); Rat; 8 days, 14 days; Controls received mp w/ vehicle; animal info (male Wistar Kyoto rats, 350 to 400 g); dose-response (E999); 0.1% DMSO; cardiovascular; cardiovascular; Balloon injury-induced neointima formation; Dose (350 ug/kg/day);.



- Q4669:** Z. pelletYu, *et al.* Role for HIF-1 α and Downstream Pathways in Regulating Neuronal Injury after Intracerebral Hemorrhage in Diabetes. *CELLULAR PHYSIOLOGY AND BIOCHEMISTRY* 2015;37(67-76)
ALZET Comments: Estradiol, 2-methoxy; ML228; CSF, artificial; Rat; 1003D; 3 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 200-300g, STZ); ALZET brain infusion kit used; diabetes; "This intervention allowed animals to receive continuous intracerebroventricular (ICV) infusion via the minipumps before brain tissues were removed." pg 69;.
- Q4536:** T. I. Montoya, *et al.* Effect of Vaginal or Systemic Estrogen on Dynamics of Collagen Assembly in the Rat Vaginal Wall. *BIOLOGY OF REPRODUCTION* 2015;92(U115-U123)
ALZET Comments: Estradiol; SC; Rat; 4 weeks; Animal info (female, Sprague Dawley, 12 weeks old); replacement therapy (estradiol infusion);.
- Q4530:** S. E. Mennenga, *et al.* Understanding the cognitive impact of the contraceptive estrogen Ethinyl Estradiol: Tonic and cyclic administration impairs memory, and performance correlates with basal forebrain cholinergic system integrity. *PSYCHONEUROENDOCRINOLOGY* 2015;54(1-13)
ALZET Comments: Estradiol, ethinyl; Propylene glycol; SC; Rat; 2006; 6 weeks; Controls received mp w/ vehicle; animal info (female, Fischer-344, OVX, 3 months old); functionality of mp verified by serum levels; dose-response (pg8); behavioral testing (water radial-arm maze, morris water maze, visible platform task); replacement therapy (estradiol infusion); long-term study;.
- Q4960:** Laszlo Prokai, *et al.* The prodrug DHED selectively delivers 17 β -estradiol to the brain for treating estrogen-responsive disorders. *Science Translational Medicine* 2015;7(297):1-11
ALZET Comments: DHED; estradiol, 17 β -; PEG; SC; Rat; 2ML4; 48 days; Controls received mp w/ vehicle; animal info (female, Fischer 344, middle aged, OVX); pumps replaced every 14 days; behavioral testing (plus maze); Dose (4 μ g/day);.
- Q4460:** T. Ikeda, *et al.* 17 α -Estradiol is generated locally in the male rat brain and can regulate GAD65 expression and anxiety. *NEUROPHARMACOLOGY* 2015;90(9-14)
ALZET Comments: Letrizole; estradiol, 17 β -; DMSO; saline; CSF/CNS; Rat; 3 days; Controls received mp w/ vehicle; animal info (male, Wistar/ST, 4 weeks old); 20% DMSO used; behavioral testing (open field test); "For the behavior test, to avoid stress from the daily handling, a tube from the subcutaneously-implanted osmotic pump was connected to the injection needle in the guide cannula for three days." pg 10; used guide cannula;.
- R0354:** D. Han, *et al.* Attenuation of mitochondrial and nuclear p38 α signaling: a novel mechanism of estrogen neuroprotection in cerebral ischemia. *Mol Cell Endocrinol* 2015;400(21-31)
ALZET Comments: Estradiol, 17 β -; Cyclodextrin, B-; SC; Rat; 1002; 14 days; Controls received mp w/ vehicle; animal info (3-month old female Sprague–Dawley rats); 20% beta cyclodextrin ; replacement therapy (estradiol); This dose of E2 (0.017 mg) was used to mimic low, physiological E2 levels produced during Diestrus I (10–15 pg/mL serum E2);.
- Q4406:** G. J. Dong, *et al.* 17 β -Estradiol enhances the activation of IFN- α signaling in B cells by down-regulating the expression of let-7e-5p, miR-98-5p and miR-145a-5p that target IKKepsilon. *BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR BASIS OF DISEASE* 2015;1852(1585-1598)
ALZET Comments: Estradiol, 17 β -; Ethanol; propylene glycol; SC; Mice; 1004; 4 weeks; Controls received mp w/ vehicle; animal info (female, C57BL6, 4 weeks old, OVX); 0.5% ethanol used; 99.5% polypropylene glycol used; replacement therapy (estradiol infusion);.
- Q4230:** J. Zhang, *et al.* Soy protein isolate down-regulates caveolin-1 expression to suppress osteoblastic cell senescence pathways. *FASEB Journal* 2014;28(3134-3145)
ALZET Comments: Estradiol, b-; PEG 400; SC; Rat (pregnant); 2004; 14 days; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, GD4); replacement therapy (ovarectomized);.



Q4192: B. J. Xue, *et al.* Estrogen regulation of the brain renin-angiotensin system in protection against angiotensin II-induced sensitization of hypertension. *American Journal of Physiology-Heart and Circulatory Physiology* 2014;307(H191-H198)

ALZET Comments: Angiotensin II; estradiol, 17 β -; angiotensin (1-7); A-779; Saline; DMSO; SC; CSF/CNS; Rat; 2001; 2002; 1 week; 2 weeks; Animal info (Sprague Dawley, 10-12 weeks old); ALZET brain infusion kit used; Multiple pumps per animal (2); replacement therapy (ovarectomized, estradiol infusion); cardiovascular; antihypertensive; peptides; bp measured using radiotelemetry (DSI);.

Q4138: A. L. B. Terzian, *et al.* Cannabinoid receptor type 1 receptors on GABAergic vs. glutamatergic neurons differentially gate sex-dependent social interest in mice. *European Journal of Neuroscience* 2014;40(2293-2298)

ALZET Comments: Estradiol, b-; Ethanol; propylene glycol; Mice; 1002; 1 week; Animal info (male, CB1 KO, 8-12 weeks old, OVX); 0.5% ethanol used; behavioral testing (social interaction test; three-chamber social investigation test); replacement therapy (ovariectomized, estradiol infusion);.

Q4091: E. L. Scott, *et al.* Surgical menopause enhances hippocampal amyloidogenesis following global cerebral ischemia. *JOURNAL OF SPORT AND HEALTH SCIENCE* 2014;3(206-216)

ALZET Comments: Estradiol, 17 β -; Cyclodextrin, B-; SC; Rat; 2002; 1 week; Controls received mp w/ vehicle; animal info (female, ovariectomized); 20% cyclodextrin used; ischemia (cerebral); replacement therapy (estradiol infusion); cardiovascular;.

Q3621: M. Sarvari, *et al.* Ovariectomy and Subsequent Treatment with Estrogen Receptor Agonists Tune the Innate Immune System of the Hippocampus in Middle-Aged Female Rats. *PLoS One* 2014;9(2):U411-U422

ALZET Comments: Estradiol, 17 β -; agonist, estrogen receptor 16- α -lactone; Propylene glycol; SC; Rat; 2004; 29 days; Controls received mp w/ vehicle or sham operation; animal info (female, Harlan-Wistar, OVX, 13 months old); replacement therapy (ovariectomized; estradiol infusion); immunology; 16- α -lactone estrogen agonist aka L2;.

Q4084: M. Sarvari, *et al.* Estradiol and isotype-selective estrogen receptor agonists modulate the mesocortical dopaminergic system in gonadectomized female rats. *Brain Research* 2014;1583(1-11)

ALZET Comments: Estradiol; Rat; 2004; Animal info (female, Harlan-Wistar 2 months old, ovariectomized); replacement therapy (estradiol infusion); mentions use of "silicone capsules", but only mentions pumps once;.

Q5464: R. Palm, *et al.* Down-regulation of serum gonadotropins but not estrogen replacement improves cognition in aged-ovariectomized 3xTg AD female mice. *J Neurochem* 2014;130(1):115-25

ALZET Comments: Leuprolide Acetate; Estradiol, 17 β ; Saline; SC; mice; 1004; 3 months; Controls received sham OVX surgery, mp w/ vehicle; animal info (female, 18 month old, triple-transgenic mice, OVX); functionality of mp verified by plasma levels; long-term study; pumps replaced every 4 weeks; neurodegenerative (Alzheimer's Disease); behavioral testing (morris water maze); LA aka Leuprolide Acetate; Cognition improvement study; learning and memory; Therapeutic indication (Alzheimer's Disease); Dose (3.6 μ g/day LA, 1.1 ng/day Estradiol);.

Q3744: P. R. Kramer, *et al.* INFUSION OF GABRA α 6 siRNA INTO THE TRIGEMINAL GANGLIA INCREASED THE MYOGENIC OROFACIAL NOCICEPTIVE RESPONSE OF OVARIECTOMIZED RATS TREATED WITH 17 β -ESTRADIOL. *Neuroscience* 2014;278(144-153)

ALZET Comments: Estradiol benzoate, 17 β -; SC; Rat; Animal info (Sprague Dawley, 250-300 g, female, ovariectomized); 28 day pump used; hormone replacement (ovariectomy).

Q3498: S. I. Han, *et al.* Estrogen Receptor Ligands Ameliorate Fatty Liver Through a Nonclassical Estrogen Receptor/Liver X Receptor Pathway in Mice. *Hepatology* 2014;59(1791-1802)

ALZET Comments: Estradiol, 17 β -; phloretin; Mice (transgenic); 2004; 4 weeks; Animal info (female, C57BL6 or ER α flox/flox, 5 weeks old); replacement therapy (ovariectomized); phloretin is a phytoestrogen;.

Q3432: M. Castello-Ruiz, *et al.* The selective estrogen receptor modulator, bazedoxifene, reduces ischemic brain damage in male rat. *Neuroscience Letters* 2014;575(53-57)



ALZET Comments: Estradiol, 17B-; bazedoxifene; DMSO; IP; Rat; 2ML1; Controls received mp w/ vehicle; animal info (male, Wistar, 300-350g); functionality of mp verified by plasma levels; 100% DMSO used; ischemia (cerebral, MCAO); cardiovascular;.

Q3225: L. Cao, *et al.* Effects of the estrogen receptor antagonist fulvestrant on F344 rat prolactinoma models. *Journal of Neuro-oncology* 2014;116(3):523-531

ALZET Comments: Estradiol, 17b-; Glycerol; DMSO; SC; Rat; 2006; 6 weeks; Controls received mp w/ vehicle; animal info (female, Fischer, 4 weeks old, 60-70g); functionality of mp verified by prolactinoma growth with PRL immunoreactive lactotrophs; 50% DMSO; 50% glycerol used; cancer (prolactinomas); long-term study;.

Q3228: Q. G. Zhang, *et al.* Hypersensitivity of the hippocampal CA3 region to stress-induced neurodegeneration and amyloidogenesis in a rat model of surgical menopause. *Brain* 2013;136(;):1432-1445

ALZET Comments: Estradiol, 17b-; SC; Rat; 21 days; Controls received mp w/ placebo; animal info (female, 3 months old, Sprague Dawley, ovariectomized); neurodegenerative (Alzheimer's disease); behavioral testing (Morris Water Maze); replacement therapy (17beta estradiol after ovariectomy);.

Q3227: C. Weigt, *et al.* Molecular effects of ER alpha- and beta-selective agonists on regulation of energy homeostasis in obese female Wistar rats. *MOLECULAR AND CELLULAR ENDOCRINOLOGY* 2013;377(1-2):147-158

ALZET Comments: Estradiol; agonist, estradiol receptor alpha-selective 16-alpha-VE2; agonist, estradiol receptor beta-selective 8-beta-VE2; DMSO; water; SC; Rat; 10 weeks; Controls received sham surgery; animal info (Female, Wistar, 120-150g, 6 weeks old); replacement therapy (ovariectomy, estradiol infusion); long-term study; immunology;.

Q4943: E. L. Scott, *et al.* Long-term estrogen deprivation leads to elevation of Dickkopf-1 and dysregulation of Wnt/beta-Catenin signaling in hippocampal CA1 neurons. *Steroids* 2013;78(6):624-32

ALZET Comments: Estradiol, 17 B-; Cyclodextrin, B-; SC; Rat; 14 days; 24- month old, female mice, ovariectomized; neurodegenerative (dementia); 20% cyclodextrin used; mp were used to infuse estradiol to mimic physiological levels during diestrus I (10-15 pg/mL); dose: 0.0167 mg.

Q6732: I. R. Miousse, *et al.* Feeding soy protein isolate and treatment with estradiol have different effects on mammary gland morphology and gene expression in weanling male and female rats. *Physiol Genomics* 2013;45(22):1072-83

ALZET Comments: Estradiol; PEG; SC; Rat; 2002; 14 days; Dose (10 µg/kg/day estradiol); animal info (Time-impregnated Sprague-Dawley rats);.

Q3226: I. R. Miousse, *et al.* Mammary gland morphology and gene expression signature of weanling male and female rats following exposure to exogenous estradiol. *EXPERIMENTAL BIOLOGY AND MEDICINE* 2013;238(9):1033-1046

ALZET Comments: Estradiol, 17b-; PEG; SC; Rat; 2002; 12 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, 21 days old); functionality of mp verified by serum measurement; dose-response (table 1 & 2); toxicology;.

Q2748: M. E. Basha, *et al.* Effect of Estrogen on Molecular and Functional Characteristics of the Rodent Vaginal Muscularis. *Journal of Sexual Medicine* 2013;10(5):1219-1230

ALZET Comments: Estradiol, 17-; Cyclodextrin; SC; Rat; 2002; 2 weeks; Control animals received mp w/ saline; animal info (Sprague Dawley, female, 3-4 mo old, 250-300 g); replacement therapy (ovariectomy).

Q2622: S. M. Bartell, *et al.* Non-Nuclear-Initiated Actions of the Estrogen Receptor Protect Cortical Bone Mass. *MOLECULAR ENDOCRINOLOGY* 2013;27(4):649-656

ALZET Comments: Estradiol; dendrimer, empty estradiol; IP; Mice; 2006; 6 weeks; Control animals received mp w/ vehicle; animal info (C57BL/6, female, 15 wks old); replacement therapy (ovariectomy);.

Q2817: S. Balgobin, *et al.* Estrogen Alters Remodeling of the Vaginal Wall after Surgical Injury in Guinea Pigs. *Biology of Reproduction* 2013;89(6):U91-U100

ALZET Comments: Estradiol; Polyethylene glycol; SC; Guinea pig; 2006; 21 days; Control animals received mp w/ vehicle; animal info (virginal, female, adult, Hartley, 12 wks old); replacement therapy (bilateral oophrectomy).



Q2606: R. K. Babbs, *et al.* 2-Hydroxyestradiol enhances binge onset in female rats and reduces prefrontal cortical dopamine in male rats. *Hormones and Behavior* 2013;63(1):88-96

ALZET Comments: Estradiol, hydroxy 2-; PEG 400; SC; Rat; 2ML4; 4 weeks; Control animals received mp w/ vehicle; animal info (Sprague Dawley, female); replacement therapy (ovariectomy); wound clips used; half-life (pg.89).

Q1979: N. Zoth, *et al.* Metabolic effects of estrogen substitution in combination with targeted exercise training on the therapy of obesity in ovariectomized Wistar rats. *Journal of Steroid Biochemistry and Molecular Biology* 2012;130(1-2):64-72

ALZET Comments: Estradiol, 17-beta; Rat; Animal info (Wistar, female, ovariectomized, obese, 400 g); replacement therapy (ovariectomy);

Q2141: J. Zhang, *et al.* Differential Effects of Short Term Feeding of a Soy Protein Isolate Diet and Estrogen Treatment on Bone in the Pre-Pubertal Rat. *PLoS One* 2012;7(4):U1022-U1030

ALZET Comments: Estradiol, 17-beta; SC; Rat; 2004; 14 days; Animal info (Sprague Dawley, female, pre-pubertal).

Q1795: C. Weigt, *et al.* Impact of estradiol, ER subtype specific agonists and genistein on energy homeostasis in a rat model of nutrition induced obesity. *MOLECULAR AND CELLULAR ENDOCRINOLOGY* 2012;351(2):227-238

ALZET Comments: Estradiol, 17-beta; estrogen receptor alpha specific agonist, 16-alpha-LE2; estrogen receptor beta specific agonist, 8-beta-VE2; DMSO; water; Rat; 10 weeks; Controls received mp w/ vehicle; animal info (Wistar, juvenile, 6 wks old, 120-150 g, female, ovariectomized); replacement therapy (ovariectomy).

Q2482: M. Sarvari, *et al.* Menopause leads to elevated expression of macrophage-associated genes in the aging frontal cortex: rat and human studies identify strikingly similar changes. *Journal of Neuroinflammation* 2012;9(1):U1-U13

ALZET Comments: Estradiol, 17b-; Rat; 2004; Control animals received sham operation; animal info (female, Wistar, young, middle-aged); replacement therapy (ovariectomy).

Q2367: M. J. J. Ronis, *et al.* Mammary Gland Morphology and Gene Expression Differ in Female Rats Treated with 17beta-Estradiol or Fed Soy Protein Isolate. *Endocrinology* 2012;153(12):6021-6032

ALZET Comments: Estradiol; Polyethylene glycol; SC; Rat; 2002; 14 days; Control animals received mp w/ vehicle; animal info (Sprague Dawley, female); replacement therapy (ovariectomy).

Q2328: M. B. Rabaglino, *et al.* Genomics of estradiol-3-sulfate action in the ovine fetal hypothalamus. *PHYSIOLOGICAL GENOMICS* 2012;44(13):669-677

ALZET Comments: Estradiol-3-sulfate; Water; CSF/CNS; Sheep (fetus); 2ML2; 7-12 days; Animal info (twin fetuses, 120-127 days of gestation); good methods, pg 669; functionality of mp verified via visual inspection at the time of death and tissue collection.

Q1851: K. E. Pelch, *et al.* Developmental Exposure to Xenoestrogens at Low Doses Alters Femur Length and Tensile Strength in Adult Mice. *Biology of Reproduction* 2012;86(3):U87-U95

ALZET Comments: Estradiol; Polyethylene glycol; DMSO; SC; Mice; 1002; 12 days; Controls received mp w/ vehicle; animal info (female, adult, C57BL/6J, ovariectomized); 20% DMSO used; 80% polyethylene glycol used; replacement therapy (ovariectomy); teratology.

Q6736: T. P. Nedungadi, *et al.* Site-specific effects of intracranial estradiol administration on recurrent insulin-induced hypoglycemia in the ovariectomized female rat. *Neuroendocrinology* 2012;96(4):311-23

ALZET Comments: Estradiol benzoate; PEG; CSF/CNS (left lateral ventricle); Rat; 1002; 4 days; Dose (1.0, 5.0, or 10.0 µg/6.0 µl/day); Controls received mp w/ vehicle; animal info (Adult female Sprague Dawley rats (220–300 g)); Brain coordinates (4.5 mm ventral to skull surface, 1.8 mm lateral to midline, and 1.1 mm posterior to bregma); diabetes;

Q2447: S. L. Kang, *et al.* Chronic Activation of the G Protein-Coupled Receptor 30 with Agonist G-1 Attenuates Heart Failure. *PLoS One* 2012;7(10):U552-U560



ALZET Comments: Estradiol; G protein-coupled receptor 30 agonist; SC; Rat; 2006; 2 weeks; Animal info (Sprague Dawley, female, 180-220 g); G protein-coupled receptor 30 agonist also known as G15.

Q2389: J. A. Johnson, *et al.* Testosterone interacts with the feedback mechanisms engaged by Tyr985 of the leptin receptor and diet-induced obesity. *Journal of Steroid Biochemistry and Molecular Biology* 2012;132(3-5):212-219

ALZET Comments: Estradiol; testosterone; Ethanol; propylene glycol; PBS; SC; Mice; 1002; 1004; 2, 4 weeks; Control animals received mp w/ vehicle; animal info (LEPR-B Tyr985Leu, male, female, OVX, castrated); 10% ethanol used; replacement therapy (ovariectomy); post op. care (analgesic, carprofen).

Q2684: W. F. Chen, *et al.* Estrogenic effects of ginsenoside Rg1 in endometrial cells in vitro were not observed in immature CD-1 mice or ovariectomized mice model. *MENOPAUSE-THE JOURNAL OF THE NORTH AMERICAN MENOPAUSE SOCIETY* 2012;19(9):1052-1061

ALZET Comments: Estradiol; Rg1; SC; Mice; 3 months; Control animals received mp w/ vehicle; animal info (C57BL/6J, female, OVX, 5 mo old); long-term study; replacement therapy (ovariectomy).

Q2375: F. L. Campos, *et al.* GDNF Contributes to Oestrogen-Mediated Protection of Midbrain Dopaminergic Neurons. *Journal of Neuroendocrinology* 2012;24(11):1386-1397

ALZET Comments: Oestradiol, 17b-; Ethanol; polypropylene glycol; SC; Rat; 1007D; 5, 8 days; Control animals received mp w/ vehicle; animal info (Wistar, male, adult, 200-400 g); 0.5% ethanol used; functionality of mp verified via serum drug levels.

Q1514: Q. G. Zhang, *et al.* C terminus of Hsc70-interacting protein (CHIP)-mediated degradation of hippocampal estrogen receptor-alpha and the critical period hypothesis of estrogen neuroprotection. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2011;108(35):E617-E624

ALZET Comments: Estradiol; SC; Rat; Animal info (male, Wistar, adult, 3 mo old, Sprague-Dawley, female, Harlan, adult, young, 3 mo old, middle-aged, 10 mo old, 24 mo old, Fischer 344); replacement therapy (ovariectomy).

Q1414: H. Yamashita, *et al.* Functional and morphological effects of beta-estradiol in eyes with N-methyl-D-Aspartate-induced retinal neurotoxicity in rats. *Experimental Eye Research* 2011;93(1):75-81

ALZET Comments: Estradiol; SC; Rat; 2ML4; 2 weeks; Controls received mp w/ vehicle; animal info (8 wks old, male, CRL, Sprague Dawley).

Q1405: S. Wu, *et al.* Jak2 Is Necessary for Neuroendocrine Control of Female Reproduction. *Journal of Neuroscience* 2011;31(1):184-192

ALZET Comments: Estradiol, beta-17; Ethanol; PBS; SC; Mice (transgenic); 1007D; Animal info (GnRH-Cr transgenic, Jak2 flox); replacement therapy (ovariectomized).

Q1487: C. E. Wood. Fetal Hypothalamus-Pituitary-Adrenal Responses to Estradiol Sulfate. *Endocrinology* 2011;152(12):4966-4973

ALZET Comments: Estradiol-3-sulfate; CSF/CNS; IV (femoral, saphenous); Sheep (ewe); 2ML4; Animal info (120-125 d gestation); post op. care (ampicillin); "metabolic clearance rates (MCR) were calculated for each hormone using infusion rates and changes in plasma concentration from this (for E2SO4) and one previous (for E2) study from this laboratory using the following formula: $MCR = \frac{\text{infusion rate}}{\text{change in plasma concentration at steady state}}$." pg 4968.

Q1399: J. Winikor, *et al.* Complex Actions of Estradiol-3-Sulfate in Late Gestation Fetal Brain. *REPRODUCTIVE SCIENCES* 2011;18(7):654-665

ALZET Comments: Estradiol-3-sulfate; Water; CSF/CNS; Sheep (pregnant); 2ML2; 7, 12 days; Controls received mp w/ vehicle; animal info (ewe); post op. care (ampicillin).

Q1955: Y. Touden, *et al.* Resistant starch promotes equol production and inhibits tibial bone loss in ovariectomized mice treated with daidzein. *METABOLISM-CLINICAL AND EXPERIMENTAL* 2011;60(10):1425-1432



ALZET Comments: Estradiol, 17-beta; SC; Mice; 40 days; Animal info (female, ddY, 8 wks old); replacement therapy (ovariectomy).

Q2227: H. Tagashira, *et al.* Distinct cardioprotective effects of 17 beta-estradiol and dehydroepiandrosterone on pressure overload-induced hypertrophy in ovariectomized female rats. *MENOPAUSE-THE JOURNAL OF THE NORTH AMERICAN MENOPAUSE SOCIETY* 2011;18(12):1317-1326

ALZET Comments: Estradiol; DMSO; SC; Rat; 14 Days; Animal info (Wistar, female); replacement therapy (ovariectomy).

Q1942: M. Sarvari, *et al.* Estrogens regulate neuroinflammatory genes via estrogen receptors alpha and beta in the frontal cortex of middle-aged female rats. *Journal of Neuroinflammation* 2011;8(;):U1-U10

ALZET Comments: Diarylpropionitrile; estradiol, 16-alpha-lactone; estradiol; Propylene glycol; SC; Rat; 2004; 29 days; Controls received mp w/ vehicle; animal info (Harlan Wistar, middle-aged, retired breeder, ovariectomized); replacement therapy (ovariectomy).

Q0892: A. Sakata, *et al.* Female type 2 diabetes mellitus mice exhibit severe ischemic brain damage. *Journal of the American Society of Hypertension* 2011;5(1):7-11

ALZET Comments: Estradiol, beta; Propylene glycol; IP; Mice; 1002; 2 weeks; Controls received mp w/ vehicle; animal info (C57BL/6, 10 wks old, KKAy, male, female, OVX); replacement therapy (ovariectomized).

Q1959: L. Raz, *et al.* Acetylation of the Pro-Apoptotic Factor, p53 in the Hippocampus following Cerebral Ischemia and Modulation by Estrogen. *PLoS One* 2011;6(10):U823-U832

ALZET Comments: Estradiol, 17-beta; Rat; Animal info (Sprague Dawley, female, adult, 3 mo old); replacement therapy (ovariectomy); wound clips used.

Q2233: J. Puri, *et al.* Estrogen in Cycling Rats Alters Gene Expression in the Temporomandibular Joint, Trigeminal Ganglia and Trigeminal Subnucleus Caudalis/Upper Cervical Cord Junction. *Journal of Cellular Physiology* 2011;226(12):3169-3180

ALZET Comments: Estradiol; Polyethylene glycol; Rat; Controls received mp w/ vehicle; animal info (Sprague Dawley, female, 250 g); replacement therapy (ovariectomy); 28-day pump used.

Q2279: J. O. Nyalala, *et al.* Estrogen Replacement Attenuates Exaggerated Neointimal Hyperplasia Following Carotid Endarterectomy in Rats. *Vascular and Endovascular Surgery* 2011;45(8):720-726

ALZET Comments: Estradiol; SC; Rat; Controls received placebo; animal info (Sprague Dawley, female, 6 mo old); replacement therapy (ovariectomy); infusion rate of 0.25 ul/hr.

Q1837: R. Hammond, *et al.* GPR30 co-localizes with cholinergic neurons in the basal forebrain and enhances potassium-stimulated acetylcholine release in the hippocampus. *Psychoneuroendocrinology* 2011;36(2):182-192

ALZET Comments: Estradiol; G-1; DMSO; Cyclodextrin, 2-hydroxypropyl-b-; SC; Rat; 2006; Controls received mp w/ vehicle; animal info (Sprague Dawley, female, young adult, ovariectomized); replacement therapy (ovariectomy); G-1 is a selective GPR30 agonist; 13.9% or 33.7% DMSO used.

Q5053: R. Hammond, *et al.* GPR30 is positioned to mediate estrogen effects on basal forebrain cholinergic neurons and cognitive performance. *Brain Res* 2011;1379(53-60)

ALZET Comments: estradiol, 17B; G-1; G Protein-couple receptor 30 antagonist; Rat; animal info (Ovx Rat); administration of estradiol to perimenopausal women, or women who have gone an ovariectomy, right after, will help with cognitive functions. There is a "window of opportunity to help with cognition. administration of estradiol to womem older than 69 might not be as useful, and even harmful; dose (5ug/day).