References on the Administration of Cholinergic Agents Using ALZET® Osmotic Pumps

1. Acetylcholine

P6643: A. E. Reyes*, et al.* Acetylcholinesterase-A beta complexes are more toxic than A beta fibrils in rat hippocampus - Effect on rat beta-amyloid aggregation, laminin expression, reactive astrocytosis, and neuronal cell loss. American Journal of Pathology 2004;164(6):2163-2174
ALZET Comments: Amyloid protein, beta (1-40); acetylcholinesterase; PBS; CSF/CNS (dorsal hippocampus); Rat; 2002; 4 weeks; 14 days; Comparison of acute injections vs. mp; brain tissue distribution; peptides; neurodegenerative (Alzheimer's disease).

P1926: C. Touvay*, et al.* Effect of long-term infusion of platelet-activating factor on pulmonary responsiveness and morphology in the guinea-pig. Pulmon. Pharm 1991;4(43-51
ALZET Comments: Acetylcholine; Platelet activating factor; Albumin, bovine serum; Saline; IV (jugular); Guinea pig; 2002; 15 days; Cholinergic agent; stability verified by measuring biological activity of residual solution from pumps after 12 days, no loss of activity observed.

P0812: T. Shimazu*, et al.* Chronic infusion of norepinephrine into the ventromedial hypothalmus induces obesity in rats. Brain Research 1986;369(1/2):215-223
ALZET Comments: Acetylcholine chloride; Cefalotin; Cholecystokinin tetrapeptide; Epinephrine HCl; Bombesin; Endorphin, B-; Enkephalin, methionine-; Norepinephrine HCl; Saline; Sodium bisulfite; CSF/CNS (hypothalamus); Rat; 2002; 5-20 weeks; Cholinergic agent; pumps replaced periodically; mp connected to perm. steel cannula in hypothalamus; cannula fitted w/removable protector; (see p.217); agents infused sep. (cefalotin infused w/each agent); long-term study; peptides.

P0439: B. Costall*, et al.* Locomotor hyperactivity caused by dopamine infusion into the nucleus accumbens of rat brain: specificity of action. Psychopharmacology 1984;82(174-180
ALZET Comments: Acetylcholine HCl; Aminobutyric acid, Y-; Serotonin bimaleinate; Dopamine HCl; Norepinephrine bitartrate; Nitrogen; Sodium metabisulfite; CSF/CNS (nucleus accumbens); Rat; 2002; 13 days; Cholinergic agent; comparison of agents effects; no stress p. 175; stability of substances remaining in pump after 13 days was verified.

2. Atropine

Q8110: I. Malaspinas*, et al.* Blockade of the cholinergic system during sensitization enhances lung responsiveness to allergen in rats. Clin Exp Pharmacol Physiol 2018;45(12):1293-1301
Agents: Atropine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML; **Duration:** Not stated;
ALZET Comments: Dose (10 mg/kg); Controls received mp w/ vehicle; animal info (13 weeks old, Brown Norway); dependence;

Q4725: T. Kashihara*, et al.* beta(2)-Adrenergic and M(2)-muscarinic receptors decrease basal t-tubular L-type Ca(2+) channel activity and suppress ventricular contractility in heart failure. European Journal of Pharmacology 2014;724(;):122-131
Agents: Atropine; ICI-118,551 **Vehicle:** Saline; DMSO; **Route:** Not Stated; **Species:** Mice; **Pump:** 1004; **Duration:** 21 days;
ALZET Comments: Animal info (male, C57BL6, 8-10 weeks old); cardiovascular;

Q4399: M. Demion*, et al.* Trpm4 Gene Invalidation Leads to Cardiac Hypertrophy and Electrophysiological Alterations. PLoS One 2014;9(U821-U848
Agents: Atropine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 2001; **Duration:** 6 hours;
ALZET Comments: Animal info (male, Trpm4 -/-, 12-32 weeks old); cardiovascular;

Q0436: G. Vrbova*, et al.* Chemical communication between regenerating motor axons and Schwann cells in the growth pathway. European Journal of Neuroscience 2009;30(3):366-375
Agents: Gallamine triethiodide; tubocurarine; atropine; suramin **Vehicle:** Not Stated; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2ML4; **Duration:** 2-4 weeks;
ALZET Comments: Controls received mp w/saline; animal info (female, adult, Sprague Dawley, 200-220 g); schematic illustration of pump with silastic catheter, Fig 1b

P8761: C. M. Hildreth*, et al.* Impaired serotonergic regulation of heart rate may underlie reduced baroreflex sensitivity in an animal model of depression. American Journal of Physiology Heart and Circulatory Physiology 2008;294(1):H474-H480
Agents: Metoprolol; atropine methylnitrate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3 days;
ALZET Comments: Cardiovascular; post op. care (carprofen, cephazolan); animal info (male, Sprague Dawley Flinders Resistive Line, Flinders Sensitive Line, 10-14 wks old)

3. Carbachol

Q4121: Y. Suzuki*, et al.* Vagal Hyperactivity Due to Ventromedial Hypothalamic Lesions Increases Adiponectin Production and Release. Diabetes 2014;63(1637-1648
ALZET Comments: Carbachol; Saline; SC; Rat; 5 days; Controls received mp w/ vehicle; animal info (female, Sprague-Dawley, 13 weeks old); carbachol is a parasympathetic stimulator; obesity;.

Q1999: A. Osaki*, et al.* Enhanced expression of nesfatin/nucleobindin-2 in white adipose tissue of ventromedial hypothalamus-lesioned rats. Neuroscience Letters 2012;521(1):46-51
ALZET Comments: Carbachol; Saline; SC; Rat; 5 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, female, 13 wks old).

Q0242: J. M. Van Kampen*, et al.* Agonist-induced restoration of hippocampal neurogenesis and cognitive improvement in a model of cholinergic denervation. Neuropharmacology 2010;58(6):921-929
ALZET Comments: Physostigmine; carbachol; nicotine; pirenzepine; oxotremorine; mecamylamine; Saline; CSF/CNS; Rat; 2002; 2004; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250 g.); neurodegenerative (Alzheimer's Disease).

P9643: K. Lorenz*, et al.* A new type of ERK1/2 autophosphorylation causes cardiac hypertrophy. Nature Medicine 2009;15(1):75-83
ALZET Comments: Angiotensin II; carbachol; SC; Mice (transgenic); 14 days; Animal info (wt, ERK2 ^{T188}); peptides.

P0998: P. J. Shiromani*, et al.* Continuous pontine cholinergic microinfusion via mini-pump induces sustained alterations in rapid eye movement (REM) sleep. Pharmacol. Biochem. Behav 1986;25(6):1253-1261
ALZET Comments: Carbachol; Scopolamine; Saline; CSF/CNS; CSF/CNS (medulla); CSF/CNS (pons); Rat; 2001; 7 days; Cholinergic agent; mp w/vehicle; mp connected to cann. in brain sites; MP failed to deliver drugs after 5 days possibly due to extended length of tubing.

4. Oxotremorin

Q0242: J. M. Van Kampen*, et al.* Agonist-induced restoration of hippocampal neurogenesis and cognitive improvement in a model of cholinergic denervation. Neuropharmacology 2010;58(6):921-929
ALZET Comments: Physostigmine; carbachol; nicotine; pirenzepine; oxotremorine; mecamylamine; Saline; CSF/CNS; Rat; 2002; 2004; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250 g.); neurodegenerative (Alzheimer's Disease).

P1408: M. Miyamoto*, et al.* Effects of continuous infusion of cholinergic drugs on memory impairment in rats with basal forebrain lesions. J. Pharmacol. Exp. Ther 1989;248(2):825-835
ALZET Comments: Oxotremorine; Physostigmine sulfate; Saline; SC; Rat; 2002; 3 weeks; no comment posted.

P0683: N. W. Pedigo Jr*, et al.* Reduced muscarinic receptor plasticity in frontal cortex of aged rats after chronic administration of cholinergic drugs. Life Sci 1985;37(15):1443-1449
ALZET Comments: Methylatropine; Oxotremorine; Saline; CSF/CNS; Rat; 2ML4; 3 weeks; comparison of agents effects in young and old rats; stability of drugs at 37C determined at weekly intervals for 5 wks by bioassay; delivery into lateral cerebroventricle.

P0663: J. C. R. Fernando*, et al.* Rapid induction of supersensitivity to muscarinic antagonists-induced motor excitation by continuous stimulation of cholinergic receptors. Life Sci 1985;37(9):883-892
ALZET Comments: Oxotremorine; Physostigmine sulfate; Saline; SC; Rat; 2002; 2 weeks; comparison of single sc injec vs. daily injec vs. mp infusion of agents effects.

5. Physostigmine

Q5056: D. P. Holschneider*, et al.* Remote brain network changes after unilateral cortical impact injury and their modulation by acetylcholinesterase inhibition. J Neurotrauma 2013;30(11):907-19
ALZET Comments: physostigmine; water; SC; Rat; 2ML4; 3 weeks; controls received mp w/ saline; animal info: sprague-dawley, male, 250-300g; functionality of mp verified by residual volume; enzyme inhibitor (Acetylcholine); neurodegenerative (Traumatic brain injury); except for model number, paper does not mention ALZET much; dose: 1.6 micromoles/kg/day.

Q2076: R. Miyazaki*, et al.* Acetyleholinesterase inhibitors attenuate angiogenesis. Clinical Science 2012;123(3-4):241-249
ALZET Comments: Physostigmine; Mice; 2 weeks; Animal info (C57BL/6, 9 wks old); enzyme inhibitor (acetylcholinesterase); hindlimb ischemia.

R0292: H. P. M. Van Helden*, et al.* Non-enzymatic pretreatment of nerve agent (soman) poisoning: A brief state-of-the-art review. TOXICOLOGY LETTERS 2011;206(1):35-40
ALZET Comments: Physostigmine; scopolamine; pyridostigmine bromide; SC; Guinea pig; 12 days;

Q0242: J. M. Van Kampen*, et al.* Agonist-induced restoration of hippocampal neurogenesis and cognitive improvement in a model of cholinergic denervation. Neuropharmacology 2010;58(6):921-929
ALZET Comments: Physostigmine; carbachol; nicotine; pirenzepine; oxotremorine; mecamylamine; Saline; CSF/CNS; Rat; 2002; 2004; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250 g.); neurodegenerative (Alzheimer's Disease).

Q0425: B. Mauck*, et al.* Cholinesterase inhibitors and stress: Effects on brain muscarinic receptor density in mice. Neurotoxicology 2010;31(5):461-467
ALZET Comments: Pyridostigmine bromide; physostigmine; SC; Mice; 30 days; Controls received mp w/saline; animal info (male, C57BL6, 25 g); enzyme inhibitor (cholinesterase).

6. Pyridostigmine

Q4881: B. C. Halil Sayin, Philippe Chevalier, Christian Barrès, Claude Julien. Assessment of cardiac autonomic tone in conscious rats. Autonomic Neuroscience-Basic & Clinical 2016;194(26-31
ALZET Comments: Pyridostigmine bromide; SC; Rat; 2ML4; 3 weeks; animal info (male, SHR, 46 weeks old); cardiovascular; bp measured using radiotelemetry; Dose (15 mg/kg/day);.

Q5005: R. M. Lataro*, et al.* Acetylcholinesterase Inhibition Attenuates the Development of Hypertension and Inflammation in Spontaneously Hypertensive Rats. Am J Hypertens 2015;28(10):1201-8
ALZET Comments: Pyridostigmine bromide; donepezil; SC; Rat; 2004; 16 weeks; animal info (male, Wistar-Kyoto or SHR); pumps replaced every 4 weeks; long-term study; cardiovascular; bp measured using tail cuff; Dose (Pyridostigmine bromide 1.5 mg/kg/day; donepezil 1.4 mg/kg/day);.

Q3860: M. T. Durand*, et al.* Pyridostigmine Restores Cardiac Autonomic Balance after Small Myocardial Infarction in Mice. PLoS One 2014;9(U327-U335
ALZET Comments: Pyridostigmine; Saline, sterile; SC; Mice; 1004; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6, 10-15 weeks old, 25-30g); ischemia (cardiac); cardiovascular; pyrostigmine is an acetylcholinesterase inhibitor; pyrostigmine aka PYR; bp measured using radiotelemetry; pumps primed at 37C saline for 48 hours;.

Q3265: M. Richtsfeld*, et al.* Prolonged Administration of Pyridostigmine Impairs Neuromuscular Function with and without Downregulation of Acetylcholine Receptors. Anesthesiology 2013;119(2):412-421
ALZET Comments: Pyridostigmine; Saline; SC; Rat; 2ML4; 14 days; 28 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-260g); dose-response (p.416, 418); post op. care (antibiotic ointment); incision closed with (4-0) suture;.

R0292: H. P. M. Van Helden*, et al.* Non-enzymatic pretreatment of nerve agent (soman) poisoning: A brief state-of-the-art review. TOXICOLOGY LETTERS 2011;206(1):35-40
ALZET Comments: Physostigmine; scopolamine; pyridostigmine bromide; SC; Guinea pig; 12 days;

7. Scopolamine

Q6743: H. Pierce*, et al.* Cholinergic Signals from the CNS Regulate G-CSF-Mediated HSC Mobilization from Bone Marrow via a Glucocorticoid Signaling Relay. Cell Stem Cell 2017;20(5):648-658 e4
ALZET Comments: Pirenzepine; Scopolamine hydrobromide; Metyrapone; luteinizing hormone; ACTH; PBS; CSF/CNS (Third ventricle); Mice (knockout); 1002; Dose (0.6 mg/kg/day Pirenzepine; 1.0 mg/kg Scopolamine hydrobromide; 100mg/kg/day Metyrapone; 2.8 mg/kg/day ACTH; 16ug/day LH); Controls received mp w/ vehicle; animal info (wild-type and Chrm1−/−); luteinizing hormone aka LH and adrenocorticotropic hormone aka ACTH; peptides; Brain coordinates (A/P −1.6 mm posterior to bregma, D/V −4.7 mm);.

Q6369: U. Gehlsen*, et al.* A semifluorinated alkane (F4H5) as novel carrier for cyclosporine A: a promising therapeutic and prophylactic option for topical treatment of dry eye. Graefes Arch Clin Exp Ophthalmol 2017;255(4):767-775
ALZET Comments: Scopolamine; SC; Mice; 1002; 2 weeks; Dose (0.1 mg/day); animal info (10–12-week-old female C57BL/6 mice); Therapeutic indication (experimental dry eye);.

Q4293: H. Saijo*, et al.* Microangiopathy triggers, and inducible nitric oxide synthase exacerbates dextran sulfate sodium-induced colitis. LABORATORY INVESTIGATION 2015;95(728-748
ALZET Comments: Butylscopolamine; PBS; SC; Mice; 1007D; 3 days; 5 days; 7 days;; Animal info (male, C57BL6J, 9-10 weeks old); ischemia (colitis);.

Q3274: W. W. Chen*, et al.* Lycium barbarum Polysaccharides Prevent Memory and Neurogenesis Impairments in Scopolamine-Treated Rats. PLoS One 2014;9(2):U1116-U1128
ALZET Comments: Scopolamine; SC; Rat; 2ML4; 28 days; Control animals received mp w/ saline; animal info (male, Sprague Dawley, 200-220 g, adult);.

Q5958: D. Y. Yoo*, et al.* Effects of luteolin on spatial memory, cell proliferation, and neuroblast differentiation in the hippocampal dentate gyrus in a scopolamine-induced amnesia model. Neurol Res 2013;35(8):813-20