



References on the Administration of Antidepressants Using ALZET® Osmotic Pumps

1. Acetylphenelzine

P2832: K. F. McKenna, *et al.* Chronic administration of the antidepressant phenelzine and its N-acetyl analogue: effects on GABAergic function. *J. Neural Transm* 1994;41(115-122)

ALZET Comments: Phenelzine sulfate; Acetylphenelzine, N2-; SC; Rat; 2ML2; 28 days; antidepressant; controls received mp with water.

P2971: R. L. Sherry-McKenna, *et al.* Monoamine oxidase inhibitors: effects on tryptophan concentrations in the rat brain. *J. Neural Transm* 1994;41(155-163)

ALZET Comments: Phenelzine; Tranylcypromine, 4-methoxy-; Acetylphenelzine, N2-; Tranylcypromine, 4-fluoro-; Tranylcypromine; Deprenyl; SC; IP; Rat; 28 days; antidepressant; controls received mp with vehicle; comparison of TCP and PLZ ip injections vs. mp.

2. Adinazolam

P0433: A. Turmel, *et al.* Sensitization of rat forebrain neurons to serotonin by adinazolam, an antidepressant triazolobenzodiazepine. *Eur. J. Pharmacol* 1984;99(241-244)

ALZET Comments: Adinazolam; Diazepam; Benzyl alcohol; Ethanol; Propylene glycol; Sodium benzoate; Water; IP; Rat; 2002; 5 and 14 days; comparison of adinazolam. iv injec vs. mp infusion; comparison of agents effects; adinazolam. used with water vehicle, Diaz. with combination vehicle.

3. Amitriptyline

Q6164: T. Jeanson, *et al.* Potentiation of Amitriptyline Anti-Hyperalgesic-Like Action By Astroglial Connexin 43 Inhibition in Neuropathic Rats. *Sci Rep* 2016;6(38766)

ALZET Comments: Amitriptyline; Saline; SC; Rat; 14 days; Dose (12 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats weighing 175–200 g); Resultant plasma level (brain AMIT levels reached $1350 \pm 210 \mu\text{g/g}$ (corresponding to $4.87 \pm 0.76 \mu\text{M}$), a value about 25 fold higher than that in serum: $55.3 \pm 5.4 \text{ ng/ml}$ (corresponding to $199.35 \pm 19.47 \text{ nM}$);.

Q0004: L. Bjartmar, *et al.* Long-term treatment with antidepressants, but not environmental stimulation, induces expression of NP2 mRNA in hippocampus and medial habenula. *Brain Research* 2010;1328(;):25-33

ALZET Comments: Amitriptyline; moclobemide; citalopram hydrobromide; maprotiline; SC; Rat; 3, 21 days; Controls received mp w/isotonic saline; enzyme inhibitor (monoamine oxidase-A); animal info (male, Sprague-Dawley, 200-250 g); "This method of delivery was chosen to avoid daily injections and thus manipulation of the animals." (p. 30); antidepressants.

P9075: Y. H. Tai, *et al.* Amitriptyline induces nuclear transcription factor-kappa B-dependent glutamate transporter upregulation in chronic morphine-infused rats. *Neuroscience* 2008;153(3):823-831

ALZET Comments: Morphine; amitriptyline; CSF/CNS (intrathecal); Rat; 2001; Controls received mp w/ saline; animal info (male, Wistar, 350-400 g.); intrathecal catheter constructed using polyethylene (0.008 in ID, 0.014 in OD) and silastic tube; behavioral testing (antinociception assay, hot water immersion, tail flick latency).

P8246: R. Sud, *et al.* Uncovering molecular elements of brain-body communication during development and treatment of neuropathic pain. *BRAIN BEHAVIOR AND IMMUNITY* 2007;21(1):112-124

ALZET Comments: Tumor necrosis Factor- α , recomb. rat: tumor necrosis factor- α , recomb. rat, heat-inactivated; amitriptyline; CSF, artificial; CSF/CNS; Rat; 8 days; Controls received mp w/ vehicle, or heat-inactivated rr-TNF α ; comparison



of ip injections vs. mp; peptides; animal info (male, Sprague-Dawley, 300-350g); chronic constriction injury to the right sciatic nerve; neuropathic pain.

P8011: Y. H. Tai, *et al.* Amitriptyline suppresses neuroinflammation and up-regulates glutamate transporters in morphine-tolerant rats. *Pain* 2006;124(1-2):77-86

ALZET Comments: Amitriptyline; morphine; Saline; CSF/CNS (intrathecal); SC; Rat; 2001; 5 days; Tolerance; animal info (male, Wistar, 350-400 grams); behavioral study.

P8973: D. V. Rossi, *et al.* Chronic administration of venlafaxine fails to attenuate 5-HT_{1A} receptor function at the level of receptor-G protein interaction. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2006;9(4):393-406

ALZET Comments: Amitriptyline HCl; sertraline HCl; venlafaxine HCl; Water, sterile; ethanol; SC; Rat; 2ML4; 21 days; Controls received mp w/ saline; functionality of mp verified by serum drug concentrations; dose- response (fig. 1); animal info (male, Sprague Dawley, 200-275 g.); 40% ethanol used; behavioral testing (hypothermic response).

P7726: G. G. Gould, *et al.* A comparison of the chronic treatment effects of venlafaxine and other antidepressants on serotonin and norepinephrine transporters. *Biological Psychiatry* 2006;59(5):408-414

ALZET Comments: Venlafaxine; sertraline; amitriptyline; paroxetine; desipramine; citalopram; Saline; water, deionized; ethanol; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug concentrations; dose-response (fig1); animal info (male, Sprague-Dawley, 150-200g); 50% EtoH in H₂O.

P7514: C. H. K. West, *et al.* A selective test for antidepressant treatments using rats bred for stress-induced reduction of motor activity in the swim test. *Psychopharmacology* 2005;182(1):9-23

ALZET Comments: Amitriptyline HCl; venlafaxine HCl; clordiazepoxide HCl; imipramine HCl; phenelzine sulfate; scopolamine HBr; desipramine HCl; bupropion HCl; chlorpheniramine maleate; fluoxetine HCl; sertraline; amphetamine sulfate, D-; Water, sterile distilled; PEG; SC; Rat; 2ML2; 6,14 days; Controls received mp w/ vehicle; functionality of mp verified by agent blood levels; dose-response (fig. 5); animal info (male, female, susceptible, selectively bred); some animals had saline-filled catheter attached to mp to delay drug infusion by 5 days; "The most notable advantage of minipump delivery is that it eliminates stress resulting from daily injection of drug....minipumps also provide constant infusion of drug" (pg. 22).

P7089: J. Andin, *et al.* Modulation of neuronal glutamate transporter rEAAC1 mRNA expression in rat brain by amitriptyline. *MOLECULAR BRAIN RESEARCH* 2004;126(1):74-77

ALZET Comments: Amitriptyline hydrochloride; Saline; SC; Rat; 3,7,21 days; Controls received mp w/ vehicle, or no treatment.

P5693: T. Pringsheim, *et al.* Selective decrease in serotonin synthesis rate in rat brainstem raphe nuclei following chronic administration of low doses of amitriptyline: an effect compatible with an anti-migraine effect. *Cephalalgia* 2003;23(5):367-375

ALZET Comments: Amitriptyline; Saline; IP; Rat; 2ML2; 21 days; Controls received the mp w/ vehicle; tricyclic antidepressant.

4. Befloxadone

P4052: N. Haddjeri, *et al.* Effect of the reversible monoamine oxidase-A inhibitor befloxadone on the rat 5-hydroxytryptamine neurotransmission. *Eur. J. Pharmacol* 1998;343(179-192)

ALZET Comments: Befloxadone; Pindolol; Water; Ethanol; SC; Rat; 2, 21 days; controls received mp w/vehicle; befloxadone is an antidepressant; agents infused separately or concomitantly; antihypertensive.

P2843: R. Mongeau, *et al.* Electrophysiologic evidence for desensitization of α_2 -adrenoceptors on serotonin terminals following long-term treatment with drugs increasing norepinephrine synaptic concentration. *Neuropsychopharm* 1994;10(1):41-51



ALZET Comments: Befloxatone; Nisoxetine; Paroxetine; SC; Rat; 3 weeks; antidepressant; controls received mp with saline; in vitro studies were also done (p49).

P2644: P. Blier, *et al.* Modulation of 5-HT release in the guinea-pig brain following long-term administration of antidepressant drugs. *Br. J. Pharmacol* 1994;113(485-495)

ALZET Comments: Paroxetine; Befloxatone; Ethanol; Water; Guinea pig; 2 or 21 days; antidepressant; controls received mp w/ vehicles; Paroxetine is a selective 5-HT reuptake inhibitor (SSRI) and Befloxatone is a Type A monoamine oxidase inhibitor (MAOI).

5. Bupropion

Q7076: A. Levy, *et al.* Bupropion and naltrexone combination alters high fructose corn syrup self-administration and gene expression in rats. *Neuropharmacology* 2018;135(547-554)

ALZET Comments: Bupropion hydrochloride, naltrexone hydrochloride; Saline; SC; Rat; 2ML2; 12 days; Dose (40 mg/kg/day BUP, 4 mg/kg/day NTX); Controls received sham surgery; animal info (Adult male Sprague-Dawley rats weighing 200-250 g); behavioral testing (locomotion tests); Drugs administered together or in separate pumps; Contrave® is an adjunct pharmacotherapy for obesity that contains bupropion and naltrexone.; Therapeutic indication (Obesity);

Q3871: M. El Mansari, *et al.* Restoration of Serotonin Neuronal Firing Following Long-Term Administration of Bupropion but Not Paroxetine in Olfactory Bulbectomized Rats. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2015;18(U87-U94)

ALZET Comments: Bupropion; paroxetine; Water; ethanol; SC; Rat; 2 days; 14 days; 28 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 300-500g, olfactory bulbectomized); 50% ethanol used; behavioral testing (open field);.

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;.

Q1534: R. Ghanbari, *et al.* Enhancement of serotonergic and noradrenergic neurotransmission in the rat hippocampus by sustained administration of bupropion. *Psychopharmacology* 2011;217(1):61-73

ALZET Comments: Bupropion; SC; Rat; 2, 14 days; Controls received mp w/ saline; animal info (Sprague Dawley, male, 270-320 g).

P9434: N. E. Paterson, *et al.* Chronic bupropion differentially alters the reinforcing, reward-enhancing and conditioned motivational properties of nicotine in rats. *NICOTINE & TOBACCO RESEARCH* 2008;10(6):995-1008

ALZET Comments: Bupropion HCl; Saline; SC; Rat; 2ML2; 14 days; Dose-response (fig 4); dependence; post op. care (antibacterial lotion); animal info (male, Wistar, 300-350 g.); "minipumps were used in the present study to deliver two bupropion doses... with the aim of establishing constantly high bupropion levels that may mitigate species differences in pharmacokinetics." (p. 1006).

P9318: M. El Mansari, *et al.* Sustained administration of bupropion alters the neuronal activity of serotonin, norepinephrine but not dopamine neurons in the rat brain. *Neuropharmacology* 2008;55(7):1191-1198



ALZET Comments: Bupropion HCl; Water, distilled; SC; Rat; 2, 7, 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-350 g.).

P9078: S. K. Billes, *et al.* Catecholamine reuptake inhibition causes weight loss by increasing locomotor activity and thermogenesis. *Neuropsychopharmacology* 2008;33(6):1287-1297

ALZET Comments: Nisoxetine; GBR12783; bupropion; DMSO; saline, nonpyrogenic; SC; Mice; 1007D; 2001; 7 days; Controls received mp w/vehicle; multiple pumps per animal (2); animal info (adult, male, C57BL/6J); 10% DMSO used; "we were limited to 7 days by drug solubility." pg. 1288; incision was closed with wound clips; nisoxetine is a norepinephrine reuptake inhibitor; GBR12783 is a dopamine reuptake inhibitor; "This study emphasizes that although acute studies may infer long-term drug effects, they do not necessarily predict a drug's chronic effects. Even though the chronic studies presented here were limited (by method of administration and drug solubility) to 1 week of treatment, they were sufficient to illustrate differences between the acute and subchronic effects of catecholamine reuptake inhibitors."

P8069: H. A. Mitchell, *et al.* The effects of norepinephrine transporter inactivation on locomotor activity in mice. *Biological Psychiatry* 2006;60(10):1046-1052

ALZET Comments: Reboxetine; bupropion; imipramine; desipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 18-20 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; no stress (see p.1049); post op. care (Buprenorphine); animal info (male, female, C57BL6/J, 3-7 months old); 50% ETOH vehicle for desipramine; mp primed 1 day in 37 celsius saline.

P7867: D. H. Malin, *et al.* Bupropion attenuates nicotine abstinence syndrome in the rat. *Psychopharmacology* 2006;184(3-4):494-503

ALZET Comments: Nicotine bitartrate; bupropion HCl; Saline; SC; Rat; 2ML1; 7, 14 days; Controls received mp w/ vehicle; comparison of acute SC injection vs. mp; pumps replaced after 7 days; dependence; animal info (male, Sprague-Dawley, 389-468g.).

P7901: T. H. Ahern, *et al.* The effects of chronic norepinephrine transporter inactivation on seizure susceptibility in mice. *Neuropsychopharmacology* 2006;31(4):730-738

ALZET Comments: Reboxetine; sertraline; desipramine; bupropion; imipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug levels; dose-response (fig. 4); comparison of IP injections vs. mp; stress/adverse reaction: (see pg. 731) Dbh -/- mice did not tolerate mp surgery well and showed signs of general malaise. All other mice strains showed no stress.; post op. care (buprenorphine); animal info (female, male, 3-7 month old; C57BL/6J NET -/- or wt; 257BL/6J 129SvEv Dbh -/-, +/-) 50% ethanol; mp primed 2 days in 37 celsius saline; "we achieved serum levels that fell within or very close to human therapeutic range for each drug with the exception of sertraline." (pg. 732).

P7514: C. H. K. West, *et al.* A selective test for antidepressant treatments using rats bred for stress-induced reduction of motor activity in the swim test. *Psychopharmacology* 2005;182(1):9-23

ALZET Comments: Amitriptyline HCl; venlafaxine HCl; clordiazepoxide HCl; imipramine HCl; phenelzine sulfate; scopolamine HBr; desipramine HCl; bupropion HCl; chlorpheniramine maleate; fluoxetine HCl; sertraline; amphetamine sulfate, D-; Water, sterile distilled; PEG; SC; Rat; 2ML2; 6,14 days; Controls received mp w/ vehicle; functionality of mp verified by agent blood levels; dose-response (fig. 5); animal info (male, female, susceptible, selectively bred); some animals had saline-filled catheter attached to mp to delay drug infusion by 5 days; "The most notable advantage of minipump delivery is that it eliminates stress resulting from daily injection of drug....minipumps also provide constant infusion of drug" (pg. 22).

P7421: S. J. Siegel, *et al.* Monoamine reuptake inhibition and nicotine receptor antagonism reduce amplitude and gating of auditory evoked potentials. *Neuroscience* 2005;133(3):729-738

ALZET Comments: Bupropion, HCl; haloperidol; Water; SC; Mice; 1002; 12 days; Controls received mp w/ vehicle; animal info (C57BL/6J, 10-16 weeks old).

6. Citalopram



Q6255: C. J. Greig, *et al.* Improved capacity to evaluate changes in intestinal mucosal surface area using mathematical modeling. *Microsc Res Tech* 2017;80(7):793-798

ALZET Comments: Citalopram hydrobromide; SC; Mice (knockout); 7 days; Dose (10 mg/kg/day); animal info (Wild type (WT) and SERT knockout (SERTKO) mice were bred on a C57BL/6 background);.

Q6046: Y. Ikawa, *et al.* Effects of citalopram on jaw-closing muscle activity during sleep and wakefulness in mice. *Neurosci Res* 2016;113(48-55)

ALZET Comments: Citalopram; Saline; SC; Mice; 2002; 6 days; Controls received mp w/ vehicle; animal info (C57BL/6J; 18-23 grams, 7-10 weeks); Dose (Citalopram (10 or 100 mg/kg/day));.

Q5857: C. J. Greig, *et al.* Enhanced serotonin signaling increases intestinal neuroplasticity. *J Surg Res* 2016;206(1):151-158

ALZET Comments: Citalopram hydrobromide; SC; Mice (knockout); 1007D; 7 days; Controls received mp w/ vehicle; animal info (8-10 weeks old) ; Dose (10 mg/kg/day);.

Q5814: A. Frey, *et al.* Early citalopram treatment increases mortality due to left ventricular rupture in mice after myocardial infarction. *J Mol Cell Cardiol* 2016;98(28-36)

ALZET Comments: Citalopram; Saline; Mice; 1002; 4 weeks, 6 weeks; Controls received mp w/ vehicle; animal info (6-9 weeks) cardiovascular; Therapeutic indication (MI, Myocardial Infarction); Dose (9.6 mg/kg/day);.

Q4832: Achikam Haima, *et al.* The effects of gestational stress and Selective Serotonin reuptake inhibitor antidepressant treatment on structural plasticity in the postpartum brain — A translational model for postpartum depression. *Hormones and Behavior* 2016;77(124-131)

ALZET Comments: Citalopram HBr; Saline; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; animal info (female, Sprague-Dawley, GD); functionality of mp verified by residual volume; post op. care (ibuprofen 15 mg/kg in drinking water for 7 days); post op. care (ibuprofen 15 mg/kg in drinking water for 7 days); teratology; Therapeutic indication (post partum stress); Dose (10 mg/kg/day);.

Q4628: A. K. D. Visser, *et al.* Serotonin-2C antagonism augments the effect of citalopram on serotonin and dopamine levels in the ventral tegmental area and nucleus accumbens. *NEUROCHEMISTRY INTERNATIONAL* 2015;81(10-15)

ALZET Comments: Citalopram HBr; Water, Ultra Pure; SC; Rat; 2 days; Controls received mp w/ vehicle; animal info (male, Wistar, 10 weeks old, 332+/-14g);.

Q4426: S. D. Geddes, *et al.* Time-dependent modulation of glutamate synapses onto 5-HT neurons by antidepressant treatment. *NEUROPHARMACOLOGY* 2015;95(130-143)

ALZET Comments: Citalopram; Cyclodextrin, 2-hydroxypropyl-b-; SC; Rat; 2 days; 7 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, 50-90g, 26-29 days old); 45% cyclodextrin used;.

Q3430: L. Cardamone, *et al.* Chronic antidepressant treatment accelerates kindling epileptogenesis in rats. *NEUROBIOLOGY OF DISEASE* 2014;63(:):194-200

ALZET Comments: Fluoxetine hydrochloride; citalopram hydrobromide; DMSO; water, saline; SC; Rat; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (male, Wistar, 9-11 weeks old); functionality of mp verified by blood plasma levels; pumps replaced every 4 weeks; 50% DMSO used; long-term study; "In addition, despite using a very high concentration of DMSO in the pumps, albeit at a very low release rate (60 ul/day), we noted no ill-effects of this with respect to the general health and well-being of the animals." pg 197; citalopram and fluoxetine are SSRI antidepressants;.

Q2402: O. Malkesman, *et al.* Targeting the BH3-interacting domain death agonist to develop mechanistically unique antidepressants. *Molecular Psychiatry* 2012;17(8):770-780

ALZET Comments: Citalopram; BI-2A7; BI-11A7; L447951; CSF/CNS (third ventricle); Mice; 1002; 14 days; Control animals received mp w/ saline; animal info (129S1/SVImJ, 20-25 g, male, 8 wks old); brain infusion kit 3 used.



P9901: O. Malkesman, *et al.* The Female Urine Sniffing Test: A Novel Approach for Assessing Reward-Seeking Behavior in Rodents. *Biological Psychiatry* 2010;67(9):864-871

ALZET Comments: Citalopram; CSF/CNS (third ventricle); Mice; 1002; 14 days; Controls received mp w/vehicle saline; ALZET brain infusion kit 3 used; animal info (129S1/SVImJ).

Q0087: G. Lucas, *et al.* Selective Serotonin Reuptake Inhibitors Potentiate the Rapid Antidepressant-Like Effects of Serotonin₄ Receptor Agonists in the Rat. *PLoS One* 2010;5(2):U300-U311

ALZET Comments: Prucalopride; RS 67333; citalopram; SC; Rat; Controls received mp w/ vehicle; multiple pumps per animal (2); animal info (Sprague Dawley, 250-300 g.).

Q1615: M. D. S. Lapiz-Bluhm, *et al.* A cognitive deficit induced in rats by chronic intermittent cold stress is reversed by chronic antidepressant treatment. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2010;13(8):997-1009

ALZET Comments: Citalopram hydrobromide; desipramine hydrochloride; Ethanol; saline; IP; Rat; 2ML4; Controls received mp w/ vehicle; 10% ethanol used; animal info (Sprague Dawley, male, 220-240 g, adult);.

Q0732: F. J. Bosker, *et al.* Biochemical and behavioral effects of long-term citalopram administration and discontinuation in rats Role of serotonin synthesis. *NEUROCHEMISTRY INTERNATIONAL* 2010;57(8):948-957

ALZET Comments: Citalopram hydrobromide; Saline; SC; Rat; 2ML2; 21 days; Controls received mp w/ vehicle; animal info (male, Wistar, 200-250 g); pumps replaced after 14 days; behavioral testing (Acoustic startle reflex).

Q0004: L. Bjartmar, *et al.* Long-term treatment with antidepressants, but not environmental stimulation, induces expression of NP2 mRNA in hippocampus and medial habenula. *Brain Research* 2010;1328(;):25-33

ALZET Comments: Amitriptyline; moclobemide; citalopram hydrobromide; maprotiline; SC; Rat; 3, 21 days; Controls received mp w/isotonic saline; enzyme inhibitor (monoamine oxidase-A); animal info (male, Sprague-Dawley, 200-250 g); "This method of delivery was chosen to avoid daily injections and thus manipulation of the animals." (p. 30); antidepressants.

7. Clomipramine

Q6771: S. Schreiber, *et al.* Interaction between methylphenidate, methadone and different antidepressant drugs on antinociception in mice, and possible clinical implications. *World J Biol Psychiatry* 2017;18(4):300-307

ALZET Comments: methadone; escitalopram; venlafaxine; desipramine; clomipramine; SC; Mice; 2002; 14 days; Dose: methadone (0.5 mg/kg) venlafaxine (2.5 mg/kg); escitalopram (20mg/kg); desipramine (1mg/kg); clomipramine (0.5 mg/kg); animal info (Male ICR mice, 25-35g); dependence.

Q5784: K. Deseure, *et al.* Differential drug effects on spontaneous and evoked pain behavior in a model of trigeminal neuropathic pain. *J Pain Res* 2017;10(279-286

ALZET Comments: Carbamazepine, baclofen, clomipramine; DMSO, PEG, Ethyl Alcohol, Acetone; SC; Rat; 2ML1; Controls received mp w/ vehicle; animal info (7 weeks old); dimethyl sulfoxide, propylene glycol, ethyl alcohol, and acetone at a ratio of 42:42:15:1; post op. care (morphine 5 mg/day); behavioral testing (Facial grooming); Therapeutic indication (Trigeminal neuralgia, neuropathic pain); Dose (30 mg/day carbamazepine (the first-line drug treatment for trigeminal neuralgia), 1.06 mg/day baclofen, 4.18 mg/day clomipramine, and 5 mg/day morphine);.

P5490: E. Dremencov, *et al.* Effects of chronic antidepressants and electroconvulsive shock on serotonergic neurotransmission in the rat hypothalamus. *PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY* 2002;26(6):1029-1034

ALZET Comments: Clomipramine; venlafaxine; Mice; 28 days; Antidepressants.



P3352: K. G. Todd, *et al.* Chronic administration of the antidepressants phenelzine, desipramine, clomipramine, or maprotiline decreases binding to 5-hydroxytryptamine_{2A} receptors without affecting benzodiazepine binding sites in rat brain. *Cell. Molec. Neuro* 1995;15(3):361-370

ALZET Comments: Clomipramine; Fluoxetine; Desipramine; Phenelzine; Maprotiline; SC; Rat; 2ML4; 21 days; antidepressant; no comment posted.

P3187: C. S. Aulakh, *et al.* Long-term antidepressant treatments alter 5-HT_{2A} and 5-HT_{2C} receptor-mediated hyperthermia in fawn-hooded rats. *Eur. J. Pharmacol* 1995;282(65-70)

ALZET Comments: Imipramine; Clomipramine; Clorgyline; SC; Rat; 2002; 21 days; antidepressant; controls received mp with saline.

P2800: K. Allison, *et al.* Behavioural response to SKF 38393 and quinpirole following chronic antidepressant treatment. *Eur. J. Pharmacol* 1995;277(139-144)

ALZET Comments: Desipramine HCl; Clomipramine HCl; Phenelzine sulfate; Clorgyline HCl; Water, distilled; SC; Rat; 2ML4; 28 days; controls received mp w/ vehicle; all agents are antidepressants.

P2654: K. Brodin, *et al.* Clomipramine and clonazepam increase cholecystokinin levels in rat ventral tegmental area and limbic regions. *Eur. J. Pharmacol* 1994;263(175-180)

ALZET Comments: Nortriptyline; Amitriptyline; Clomipramine; Alaproclate; Clonazepam; Alcohol; Saline; SC; Rat; 2ML2; 14 days; antidepressant; controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose-response (Table 1; pg. 177); enzyme inhibitor; clonazepam is a benzodiazepene; the others are monoamine uptake inhibitors.

P3067: D. D. Mousseau, *et al.* Effects of age and chronic antidepressant treatment on [3H]tryptamine and [3H]dihydroalprenolol binding to rat cortical membranes. *Cell. Molec. Neuro* 1993;13(1):3-13

ALZET Comments: Imipramine HCl; Desipramine HCl; Clomipramine HCl; Tranylcypromine HCl; Phenelzine sulfate; Clorgyline HCl; Deprenyl HCl; SC; Rat; 2002; 2ML4; 14,28 days; antidepressant; controls received mp with vehicle; drug concentrations determined from Greenshaw program.

P3668: K. P. Lesch, *et al.* Regional brain expression of serotonin transporter mRNA and its regulation by reuptake inhibiting antidepressants. *Mol. Brain Research* 1993;17(31-35)

ALZET Comments: Imipramine; Clomipramine; Desipramine; Fluoxetine; Clorgyline; 8-OH-DPAT; MCPP; DOI; Saline; SC; Rat; 21 days; controls received mp w/ saline; pumps replaced after 2 weeks; agents are antidepressants; DOI is l-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane.

P2596: K. Allison, *et al.* Chronic antidepressant drug treatment attenuates motor-suppressant effects of apomorphine without changing [3H]GBR 12935 binding. *Eur. J. Pharmacol* 1993;249(125-131)

ALZET Comments: Desipramine HCl; Phenelzine sulfate; Clomipramine HCl; SC; Rat; 2ML4; 28 days; antidepressant; controls received mp w/ distilled water; enzyme inhibitor; phenelzine sulfate is an MAO inhibitor.

P2005: J. Ortiz, *et al.* Effects of monoamine uptake inhibitors on extracellular and platelet 5-hydroxytryptamine in rat blood: different effects of clomipramine and fluoxetine. *Br. J. Pharmacol* 1992;105(941-946)

ALZET Comments: Clomipramine; Fluoxetine; DMSO; Tween; SC; Rat; 2002; 14 days; antidepressant; comparison of injections vs. mp; clomipramine dissolved in tween and fluoxetine dissolved in DMSO; short half-life of clomipramine discussed p. 943; serotonin uptake inhibitors.

P2365: P. J. Mitchell, *et al.* Chronic treatment with clomipramine and mianserin increases the hierarchical position of subdominant rats housed in triads. *Behav. Pharmacology* 1992;3(239-247)

ALZET Comments: Clomipramine; Mianserin; Water; SC; Rat; 2002; 7/14 days; antidepressant; controls received mp w/ water or sham op; no stress (see pg. 241).



8. Desipramine

Q6946: C. Alba-Delgado, *et al.* The onset of treatment with the antidepressant desipramine is critical for the emotional consequences of neuropathic pain. *Pain* 2018;159(12):2606-2619

ALZET Comments: Desipramine; Saline; SC; Rat; 2ML2; 2 weeks; Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (45-55 day old male Sprague–Dawley rats weighing 200-250 g); Therapeutic indication (neuropathy);

Q6771: S. Schreiber, *et al.* Interaction between methylphenidate, methadone and different antidepressant drugs on antinociception in mice, and possible clinical implications. *World J Biol Psychiatry* 2017;18(4):300-307

ALZET Comments: methadone; escitalopram; venlafaxine; desipramine; clomipramine; SC; Mice; 2002; 14 days; Dose: methadone (0.5 mg/kg) venlafaxine (2.5 mg/kg); escitalopram (20mg/kg); desipramine (1mg/kg); clomipramine (0.5 mg/kg); animal info (Male ICR mice, 25-35g); dependence.

Q6094: L. Deng, *et al.* Prophylactic treatment with the tricyclic antidepressant desipramine prevents development of paclitaxel-induced neuropathic pain through activation of endogenous analgesic systems. *Pharmacol Res* 2016;114(75-89)

ALZET Comments: Desipramine, naloxone, AM251, AM630; Water, saline, PEG400, DMSO; SC; Rat; 2ML4; 28 days; Dose: Desipramine (10 mg/kg/d), Naloxone (12 mg/kg/d), AM251 (3 mg/kg/d), AM630 (3 mg/kg/day); Desipramine dissolved distilled water, naloxone dissolved in saline, AM251 and AM630 dissolved in 50% PEG400 and 50% DMSO; Controls received mp w/ vehicle; animal info (Sprague-Dawley rats weighing 275–350 g); Multiple pumps per animal (2 when given the treatment of 2 different agents), Desipramine, vehicle, and all antagonists were delivered in separate osmotic pumps;

Q5315: L. Bravo, *et al.* Effect of DSP4 and desipramine in the sensorial and affective component of neuropathic pain in rats. *Prog Neuropsychopharmacol Biol Psychiatry* 2016;70(57-67)

ALZET Comments: Desipramine; Saline; SC; Rat; 2ML2; 2 weeks; Controls received mp w/ vehicle; animal info (Adult male Harlan Sprague-Dawley rats, 200-250 g); functionality of mp verified by pain level measurements; functionality of mp verified by pain level measurements; Noradrenaline reuptake inhibitor; Chronic Constriction Injury (CCI); Therapeutic indication (Pain); Dose (10 mg/kg/d);

Q4096: A. Shah, *et al.* Influence of acute or chronic administration of ovarian hormones on the effects of desipramine in the forced swim test in female rats. *Psychopharmacology* 2014;231(3685-3694)

ALZET Comments: Desipramine hydrochloride; Water, distilled; IP; Rat; 2ML4; 18 days; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250-350g, ovariectomized); functionality of mp verified by serum levels; comparison of injection vs mp; dose-response (pg 3690); post op. care (penicillin and saline injection; atipamezol 1 mg/kg); behavioral testing (forced swimming test; locomotor activity); replacement therapy (estradiol pellets); solutions filtered through 0.9 um nitrocellulose filters; pumps primed at room temperature saline; used sutures;

Q1811: M. L. Rovin, *et al.* Influence of chronic administration of antidepressant drugs on mRNA for galanin, galanin receptors, and tyrosine hydroxylase in catecholaminergic and serotonergic cell-body regions in rat brain. *Neuropeptides* 2012;46(2):81-91

ALZET Comments: Phenzelzine; desipramine; paroxetine; DMSO; PEG; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, adult, 5-7 mo old); Osmotic minipumps were chosen for AD delivery because they slowly release drug over 14 days, thus eliminating the stress animals would experience by daily injections of the AD" pg 83; IP catheter used; wound clips used; enzyme inhibitor (monoamine oxidase); 50% DMSO used; 25% PEG used.

Q1779: H. Furmaga, *et al.* Comparison of Delta FosB Immunoreactivity Induced by Vagal Nerve Stimulation with That Caused by Pharmacologically Diverse Antidepressants. *Journal of Pharmacology and Experimental Therapeutics* 2012;341(2):317-325

ALZET Comments: Desipramine; sertraline; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 250-350 g).

Q2136: H. Furmaga, *et al.* Vagal Nerve Stimulation Rapidly Activates Brain-Derived Neurotrophic Factor Receptor TrkB in Rat Brain. *PLoS One* 2012;7(5):U65-U74



ALZET Comments: Sertraline; desipramine; Ethanol; saline; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, adult, male, 250-350 g); nitrocellulose filters used; 10% ethanol used.

Q2005: C. ba-Delgado, *et al.* Analgesic antidepressants promote the responsiveness of locus coeruleus neurons to noxious stimulation: Implications for neuropathic pain. *Pain* 2012;153(7):1438-1449

ALZET Comments: Desipramine; duloxetine; Saline; cyclodextrin, methyl-beta; SC; Rat; 2ML1; 1 week; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 250-300 g).

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;.

Q1314: H. Sato, *et al.* Acute desipramine treatment reduces regional serotonin synthesis rates, while chronic treatment elevates rates, in a rat model of depression: An autoradiographic study. *NEUROCHEMISTRY INTERNATIONAL* 2011;58(7):759-766

ALZET Comments: Desipramine; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (FSL, FRL).

Q1054: S. L. Erickson, *et al.* Chronic desipramine treatment alters tyrosine hydroxylase but not norepinephrine transporter immunoreactivity in norepinephrine axons in the rat prefrontal cortex. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(9):1219-1232

ALZET Comments: Desipramine; Ethanol; IP; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; animal info (adult, male, Sprague Dawley); post op. care (penicillin); 10% ethanol used.

Q1018: C. Cottingham, *et al.* The Antidepressant Desipramine Is an Arrestin-biased Ligand at the alpha (2A)-Adrenergic Receptor Driving Receptor Down-regulation in Vitro and in Vivo. *Journal of Biological Chemistry* 2011;286(41):36063-36075

ALZET Comments: Desipramine; Ethanol; SC; Mice; 1002; 14 days; Controls received mp w/ saline; animal info (Arr3 -/-, wt); 15% ethanol used.

Q1615: M. D. S. Lapiz-Bluhm, *et al.* A cognitive deficit induced in rats by chronic intermittent cold stress is reversed by chronic antidepressant treatment. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2010;13(8):997-1009

ALZET Comments: Citalopram hydrobromide; desipramine hydrochloride; Ethanol; saline; IP; Rat; 2ML4; Controls received mp w/ vehicle; 10% ethanol used; animal info (Sprague Dawley, male, 220-240 g, adult);.

P9610: C. H. K. West, *et al.* Antidepressant drugs with differing pharmacological actions decrease activity of locus coeruleus neurons. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2009;12(5):627-641

ALZET Comments: Desipramine; mirtazapine; chlorpheniramine; Paroxetine; scopolamine; amphetamine; escitalopram; chlordiazepoxide; SC; IP; Rat; 2ML2; 14, 21 days; Controls received mp w/vehicle; dose-response (Fig 2-5); pumps replaced on day 14; good methods pg 629; animal info (male, Sprague Dawley, 5-7 mo old, 550-700g); "Importantly, use of minipumps also eliminates the need for repeated handling and injection of animals to administer the drug chronically." pg. 628; IP catheter used.

P9294: Z. R. Zhao, *et al.* Norepinephrine Transporter Regulation Mediates the Long-Term Behavioral Effects of the Antidepressant Desipramine. *Neuropsychopharmacology* 2008;33(13):3190-3200



ALZET Comments: Desipramine; Saline; ethanol; DMSO; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; dose-response (fig. 1); animal info (male, Sprague Dawley, 300-350 g.); 40% DMSO used; 10% EtOH used; behavioral testing (forced swim test).

P8892: N. E. Paterson, *et al.* The effects of chronic versus acute desipramine on nicotine withdrawal and nicotine self-administration in the rat. *Psychopharmacology* 2008;198(3):351-362

ALZET Comments: Desipramine; nicotine; Saline; water; SC; Rat; 2ML1; 2ML2; 2ML4; 7, 14, 28 days; pumps replaced; dependence; animal info (male, Wistar, 300-350g.); post op. care ("antibacterial preparation"); comparison of IP injections vs. SC mp; "The results of the present study indicated that chronic, but not acute, DMI treatment attenuated the anhedonic and somatic components of nicotine withdrawal and that chronic DMI treatment significantly decreased nicotine and food-maintained responding." pg. 358.

P9126: C. O. Bondi, *et al.* Chronic unpredictable stress induces a cognitive deficit and anxiety-like behavior in rats that is prevented by chronic antidepressant drug treatment. *Neuropsychopharmacology* 2008;33(2):320-331

ALZET Comments: Desipramine; escitalopram; Ethanol; saline; IP; Rat; 2ML4; Post op. care (penicillin); animal info (Sprague Dawley, 200-250 g.); 10% ethanol used; behavioral testing (chronic unpredictable stress).

9. Duloxetine

Q4103: M. J. Skelly, *et al.* Chronic treatment with prazosin or duloxetine lessens concurrent anxiety-like behavior and alcohol intake: evidence of disrupted noradrenergic signaling in anxiety-related alcohol use. *BRAIN AND BEHAVIOR* 2014;4(468-483

ALZET Comments: Prazosin; propranolol; duloxetine; DMSO; saline, sterile; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (male, Long Evans, adult, 300g); functionality of mp verified by residual volume; 10% DMSO used; stress/adverse reaction: (see pg. 472); post op. care (ketoprofen 3 mg/kg SC); behavioral testing (ethanol intake, open field test, locomotor activity, elevated plus maze); dependence; "Drug doses were calculated based on the estimated mean weight of animals in each group halfway through the drug delivery period (taking the mean weight at baseline and adding projected weight gain across 2 weeks)" pg 470; pumps removed after 4 weeks;.

Q2005: C. ba-Delgado, *et al.* Analgesic antidepressants promote the responsiveness of locus coeruleus neurons to noxious stimulation: Implications for neuropathic pain. *Pain* 2012;153(7):1438-1449

ALZET Comments: Desipramine; duloxetine; Saline; cyclodextrin, methyl-beta; SC; Rat; 2ML1; 1 week; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 250-300 g).

P8117: G. G. Gould, *et al.* Effect of chronic administration of duloxetine on serotonin and norepinephrine transporter binding sites in rat brain. *Biological Psychiatry* 2007;61(2):210-215

ALZET Comments: Duloxetine; desipramine; paroxetine; Ethanol; water; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum agent concentrations; dose-response (p.211); animal info (male, Sprague-Dawley, 125-150g).

P7266: L. Grandoso, *et al.* Alpha₂-Adrenoceptor involvement in the in vitro inhibitory effect of citalopram on a subpopulation of rat locus coeruleus neurons. *European Journal of Pharmacology* 2005;517(1-2):51-58

ALZET Comments: Citalopram; duloxetine; Saline; SC; Rat; 14 days; Controls received mp w/ vehicle; 5-HT reuptake inhibitor, noradrenaline reuptake inhibitor.

P4238: L. E. Rueter, *et al.* Electrophysiological characterization of the effect of long-term duloxetine administration on the rat serotonergic and noradrenergic systems. *J. Pharmacol. Exp. Ther* 1998;285(2):404-412

ALZET Comments: Duloxetine; Ethanol; Water; SC; Rat; 2,21 days; controls received mp w/vehicle; antidepressant; 50% ethanol used, which is not recommended by the manufacturer;.



10. Escitalopram

Q6998: K. L. Smith, *et al.* Opioid system modulators buprenorphine and samidorphan alter behavior and extracellular neurotransmitter concentrations in the Wistar Kyoto rat. *Neuropharmacology* 2019;146(316-326

ALZET Comments: Escitalopram; SC; Rat; 2ML4; 14 days; Dose (10 mg/kg/day); animal info (Wistar Kyoto rat); behavioral testing (Forced swim test, Marble burying test); dependence;

Q6975: M. Ebrahimzadeh, *et al.* Synergistic effect of aripiprazole and escitalopram in increasing serotonin but not norepinephrine neurotransmission in the rat hippocampus. *Neuropharmacology* 2019;146(12-18

ALZET Comments: Escitalopram; SC; Rat; 1003D, 2ML2; 2days, 14 days; Dose (5 mg/kg/day); animal info (Male Sprague-Dawley rats, 280-320 gr);.

Q6771: S. Schreiber, *et al.* Interaction between methylphenidate, methadone and different antidepressant drugs on antinociception in mice, and possible clinical implications. *World J Biol Psychiatry* 2017;18(4):300-307

ALZET Comments: methadone; escitalopram; venlafaxine; desipramine; clomipramine; SC; Mice; 2002; 14 days; Dose: methadone (0.5 mg/kg) venlafaxine (2.5 mg/kg); escitalopram (20mg/kg); desipramine (1mg/kg); clomipramine (0.5 mg/kg); animal info (Male ICR mice, 25-35g); dependence.

Q5741: M. S. Riga, *et al.* Subchronic vortioxetine treatment -but not escitalopram- enhances pyramidal neuron activity in the rat prefrontal cortex. *Neuropharmacology* 2017;113(Pt A):148-155

ALZET Comments: Escitalopram; SC; Rat; 2ML2; 2 weeks; Controls received mp w/ vehicle; animal info (175-200 g); post op. care (an analgesic (Buprenorphine: 0.5 mg/kg p.o every 12 h) and a prophylactic antibiotic (Enofloxacin 7.5 mg/kg s.c.) given during 2-3 consecutive days after surgery); Therapeutic indication (medial prefrontal cortex, electrophysiology); Dose (10 mg/kg/day);.

Q5182: G. Qesseveur, *et al.* Genetic dysfunction of serotonin 2A receptor hampers response to antidepressant drugs: A translational approach. *Neuropharmacology* 2016;105(142-53

ALZET Comments: Fluoxetine hydrochloride; escitalopram hydrochloride; Saline; SC; Mice; 1007D; 1002; 2, 21, 28 days; animal info (male, WT or 5-HT2A mutant, 10-14 weeks old, 25-35g); behavioral testing (tail suspension test; novelty surpassed feeding); behavioral testing (tail suspension test; novelty surpassed feeding); fluoxetine dose (18 mg/kg, free base).

Q4925: M. El Mansari, *et al.* Effects of acute and sustained administration of vortioxetine on the serotonin system in the hippocampus: electrophysiological studies in the rat brain. *Psychopharmacology (Berl)* 2015;232(13):2343-52

ALZET Comments: Vortioxetine; escitalopram; SC; Rat; 2 days; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dalwey, adult, 250-300g); Dose (Vortioxetine 5 mg/kg/day; escitalopram 5 mg/kg/day);.

Q4511: D. E. Ehrlich, *et al.* Prenatal stress, regardless of concurrent escitalopram treatment, alters behavior and amygdala gene expression of adolescent female rats. *NEUROPHARMACOLOGY* 2015;97(251-258

ALZET Comments: Escitalopram oxalate; Saline; SC; Rat; 2ML4; Controls received mp w/ vehicle; animal info (female, nulliparous Sprague Dalwey, 200-225g); behavioral testing (open field, social interaction, novel object recognition, elevated plus maze; teratology);.

Q3346: D. Kostyalik, *et al.* Chronic escitalopram treatment caused dissociative adaptation in serotonin (5-HT) 2C receptor antagonist-induced effects in REM sleep, wake and theta wave activity. *Experimental Brain Research* 2014;232(3):935-946

ALZET Comments: Escitalopram; Water, distilled; hydrochloric acid; Rat; 2ML4; 20 days; Controls received mp w/ vehicle; animal info (male, Wistar, 250-280g); behavioral testing (sleeping pattern); used electrodes from Plastics One to measure sleep;

Q3128: L. Westrich, *et al.* The effects of combining serotonin reuptake inhibition and 5-HT(7) receptor blockade on circadian rhythm regulation in rodents. *PHYSIOLOGY & BEHAVIOR* 2013;110(:):42-50



ALZET Comments: Escitalopram; Water; SC; Rat; 14 days; Controls received mp w/ saline; animal info (2 month old, Sprague Dawley); comparison of single dose vs mp pg.45 "Subchronic dosing with escitalopram in DD (10 mg/kg/day s.c.) via osmotic minipumps for 14 days yielded no significant change in wheel running onsets. A single dose of SB269970 (30 mg/kg s.c.), timed at ZT11 at the beginning of subchronic escitalopram dosing, produced a significant delay in activity onset"; behavioral testing (wheel running);.

Q2479: S. Vas, *et al.* Differential adaptation of REM sleep latency, intermediate stage and theta power effects of escitalopram after chronic treatment. *Journal of Neural Transmission* 2013;120(1):169-176

ALZET Comments: Escitalopram; Cyclodextrin, hydroxypropyl beta; Rat; 2ML4; 21 days; Control animals received mp w/ vehicle; animal info (Wistar, male, 250-280 g); 10% cyclodextrin used.

Q2591: A. L. Pehrson, *et al.* Lu AA21004, a novel multimodal antidepressant, produces regionally selective increases of multiple neurotransmitters-A rat microdialysis and electrophysiology study. *European Neuropsychopharmacology* 2013;23(2):133-145

ALZET Comments: Lu AA21004; escitalopram; Cyclodextrin, 2-hydroxypropyl-b-; SC; Rat; 2ML2; 3 days; Animal info (male, 250-350 g, Wistar, Sprague Dawley); post op. care (massage); "During the 3 days of treatment via minipumps, the skin surrounding the minipump was massaged daily, preventing skin irritation and stimulating reliable drug exposure." pg 135; 10-40% cyclodextrin used.

Q4775: Elizabeth I. Flandreau, *et al.* Escitalopram alters gene expression and HPA axis reactivity in rats following chronic overexpression of corticotropin-releasing factor from the central amygdala. *Psychoneuroendocrinology* 2013;38(1349-1361

ALZET Comments: escitalopram; PEG 300; SC; Rat; not specified; 4 weeks; 10 mg/kg/day dose; male, Wistar, PND70 rats; functionality of mp verified by plasma escitalopram concentrations (LC-MS/MS assay); behavioral testing (elevated plus maze (EPM), defensive withdrawal (DW), social interaction (SI));.

Q5516: C. H. Bourke, *et al.* Prenatal exposure to escitalopram and/or stress in rats produces limited effects on endocrine, behavioral, or gene expression measures in adult male rats. *Neurotoxicol Teratol* 2013;39(100-9

ALZET Comments: escitalopram; Saline; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; behavioral testing (defensive withdrawal, open field, sucrose consumption, elevated plus maze, acoustic startle response, forced swim test); Therapeutic indication (Depression); Dose (12.2 mg/kg);.

Q2900: C. H. Bourke, *et al.* Prenatal exposure to escitalopram and/or stress in rats. *Psychopharmacology* 2013;228(2):231-241

ALZET Comments: Escitalopram; Saline; SC; Rat; 2004; 28 days; Controls received mp w/ saline; animal info (Sprague-Dawley male, Nulliparous females, 200-225g), pregnant; half-life (p. 238); behavioral testing (maternal care behavior).

11. Fluoxetine

Q7074: C. Li, *et al.* Chronic fluoxetine treatment accelerates kindling epileptogenesis in mice independently of 5-HT2A receptors. *Epilepsia* 2018;59(7):e114-e119

ALZET Comments: Fluoxetine hydrochloride; DMSO; Saline; SC; Mice; 50% DMSO used; Controls received mp w/ vehicle; animal info (Male mice aged 11-14 weeks);.

Q5182: G. Qesseveur, *et al.* Genetic dysfunction of serotonin 2A receptor hampers response to antidepressant drugs: A translational approach. *Neuropharmacology* 2016;105(142-53

ALZET Comments: Fluoxetine hydrochloride; escitalopram hydrochloride; Saline; SC; Mice; 1007D; 1002; 2, 21, 28 days; animal info (male, WT or 5-HT2A mutant, 10-14 weeks old, 25-35g); behavioral testing (tail suspension test; novelty surpassed feeding); behavioral testing (tail suspension test; novelty surpassed feeding); fluoxetine dose (18 mg/kg, free base).



Q5631: K. Bravo, *et al.* Perinatal Fluoxetine Exposure Impairs the CO₂ Chemoreflex. Implications for Sudden Infant Death Syndrome. *Am J Respir Cell Mol Biol* 2016;55(3):368-76

ALZET Comments: Fluoxetine; DMSO; SC; Mice (pregnant); 2004; Controls received mp w/ vehicle (dimethyl sulfoxide 40%); animal info (CF-1 mice: 5-7 days of gestation); functionality of mp verified by Plasma fluoxetine concentration determined by HPLC with a diode array detector; 40% DMSO used; teratology; "Delivering fluoxetine by osmotic minipumps was less stressful for dams than were oral gavages or injections; this avoided maternal stress, which has consequences on fetal brain development. The plasma concentration of fluoxetine in dams was similar to the reported plasma level in patients under fluoxetine treatment" pg 372; Therapeutic indication (Hypercapnia; respiration); Dose (7 mg/kg/day);.

Q4580: S. M. Schumacher, *et al.* Paroxetine-Mediated GRK2 Inhibition Reverses Cardiac Dysfunction and Remodeling After Myocardial Infarction. *JOURNAL OF CARDIAC FAILURE* 2015;21(S109-S109

ALZET Comments: Paroxetine; fluoxetine; DMSO; water; SC; Mice; 1002; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6, myocardial infarction); functionality of mp verified by serum levels; ischemia (cardiac); Dose: paroxetine or fluoxetine (5 mg/kg/d).

Q4282: I. Rayen, *et al.* Developmental exposure to SSRIs, in addition to maternal stress, has long-term sex-dependent effects on hippocampal plasticity. *PSYCHOPHARMACOLOGY* 2015;232(1231-1244

ALZET Comments: Fluoxetine; Propylenediol; saline; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, adult, 250-300g); 50% propylenediol used; teratology; "These implants also reduced the effect of stress associated with repeated injections or oral gavage." pg 1233;.

Q4327: C. Betry, *et al.* Effect of the multimodal acting antidepressant vortioxetine on rat hippocampal plasticity and recognition memory. *PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY* 2015;58(38-46

ALZET Comments: Vortioxetine; fluoxetine; SR57227; Cyclodextrin, 2-hydroxypropyl-b-; SC; Rat; 1 day; 3 days; 14 days; Controls received mp w/ fluoxetine as positive control; animal info (male, Sprague Dawley, 260-320g); behavioral testing (object recognition testing);.

Q4070: A. Rodriguez-Gaztelumendi, *et al.* An altered spinal serotonergic system contributes to increased thermal nociception in an animal model of depression. *Experimental Brain Research* 2014;232(1793-1803

ALZET Comments: Fluoxetine; Propylene glycol; ethanol; water, distilled; SC; Rat; 2001; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-270g); 10% ethanol used; 50% propylene glycol used; behavioral testing (open field; tail flick test);.

Q5423: A. Rodriguez-Gaztelumendi, *et al.* An altered spinal serotonergic system contributes to increased thermal nociception in an animal model of depression. *Exp Brain Res* 2014;232(6):1793-803

ALZET Comments: Fluoxetine; Propylene Glycol; Ethanol; Water; Sc; Rat; 2001; 1 week; Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats, 250-270 g); 50% propylene glycol, 10% ethanol, 40% water; behavioral testing (open-field test, tail flick test); Bilateral olfactory bulbectomy model; Therapeutic indication (OB-associated thermal hyperalgesia); Dose (10 mg/kg);.

Q3358: I. Rayen, *et al.* Developmental fluoxetine exposure facilitates sexual behavior in female offspring. *Psychopharmacology* 2014;231(1):123-133

ALZET Comments: Fluoxetine; Propylenediol; saline; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250-300g, postpartum); 50% propylenediol used; behavioral testing (locomotor activity; sexual behavior testing); teratology; "...this mode of administration was chosen instead of repeated injections or oral gavage to pups, in order to minimize stress. In addition, minipumps have successfully been used during the postpartum period" pg125; effects of prenatal stress;.

Q3317: J. L. Pawluski, *et al.* Fluoxetine Dose and Administration Method Differentially Affect Hippocampal Plasticity in Adult Female Rats. *NEURAL PLASTICITY* 2014;;(;):U1-U9



ALZET Comments: Fluoxetine; Saline; propylenediol; SC; Rat; 2ML2; 2 weeks; Animal info (female, sprague dawley, 250-300g); functionality of mp verified by serum levels; 25% propylenediol used; comparison of oral dosing/food vs mp; dose-response (pg.5, figure 2); no stress (see pg.5); post op. care (carprofen 2.5-5 mg/kg);.

Q3430: L. Cardamone, *et al.* Chronic antidepressant treatment accelerates kindling epileptogenesis in rats. *NEUROBIOLOGY OF DISEASE* 2014;63(1):194-200

ALZET Comments: Fluoxetine hydrochloride; citalopram hydrobromide; DMSO; water, saline; SC; Rat; 2ML4; 8 weeks; Controls received mp w/ vehicle; animal info (male, Wistar, 9-11 weeks old); functionality of mp verified by blood plasma levels; pumps replaced every 4 weeks; 50% DMSO used; long-term study; "In addition, despite using a very high concentration of DMSO in the pumps, albeit at a very low release rate (60 ul/day), we noted no ill-effects of this with respect to the general health and well-being of the animals." pg 197; citalopram and fluoxetine are SSRI antidepressants;.

Q6757: I. Rayen, *et al.* Developmental fluoxetine exposure and prenatal stress alter sexual differentiation of the brain and reproductive behavior in male rat offspring. *Psychoneuroendocrinology* 2013;38(9):1618-29

ALZET Comments: Fluoxetine; Propylenediol; saline; SC; Rat; 2ML4; 4 weeks; Dose (5 mg/kg/day); 50% propylenediol used; Controls received mp w/ vehicle; animal info (adult female Sprague-Dawley rats (250—300 g); "Therefore, we chose this mode of delivery instead of repeated injections or oral gavage, to minimize the effect of repeated stress." pg. 1620;.

Q2897: C. Bety, *et al.* The rapid recovery of 5-HT cell firing induced by the antidepressant vortioxetine involves 5-HT(3) receptor antagonism. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2013;16(5):1115-1127

ALZET Comments: Fluoxetine; vortioxetine; SC; Rat; Animal info (male Sprague-Dawley, 250-300g); dose-response (pg.4); vortioxetine is a 5-HT3 receptor antagonist.

Q2423: J. L. Pawluski, *et al.* DEVELOPMENTAL FLUOXETINE EXPOSURE DIFFERENTIALLY ALTERS CENTRAL AND PERIPHERAL MEASURES OF THE HPA SYSTEM IN ADOLESCENT MALE AND FEMALE OFFSPRING. *Neuroscience* 2012;220(1):131-141

ALZET Comments: Fluoxetine; Propylenediol; saline; SC; Rat; 2ML4; 21 days; Control animals received mp w/ vehicle; animal info (Sprague Dawley, female, adult, post partum 1, 250-300 g).

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;.

Q1511: I. Rayen, *et al.* Fluoxetine during Development Reverses the Effects of Prenatal Stress on Depressive-Like Behavior and Hippocampal Neurogenesis in Adolescence. *PLoS One* 2011;6(9):U172-U180

ALZET Comments: Fluoxetine; Propylenediol; saline; SC; Rat; 2ML4; Controls received mp w/ vehicle; animal info (adult, female, Sprague-Dawley, 250-300 g, P1).

Q0355: S. B. Pinnock, *et al.* The Roles of BDNF, pCREB and Wnt3a in the Latent Period Preceding Activation of Progenitor Cell Mitosis in The Adult Dentate Gyrus by Fluoxetine. *PLoS One* 2010;5(10):U236-U243

ALZET Comments: K252a; fluoxetine; Saline; CSF/CNS; SC; Rat; 1002; 2ML2; 7, 14 days; Controls received mp w/ saline; animal info (male, Sprague-Dawley, 8 wks old, 200-250 g); multiple pumps per animal (2); cannula placement verified by examining its track on sections stained with cresyl violet.



Q1230: S. Mato, *et al.* Long-Term Fluoxetine Treatment Modulates Cannabinoid Type 1 Receptor-Mediated Inhibition of Adenylyl Cyclase in the Rat Prefrontal Cortex through 5-Hydroxytryptamine(1A) Receptor-Dependent Mechanisms. *MOLECULAR PHARMACOLOGY* 2010;77(3):424-434

ALZET Comments: Fluoxetine HCl; WAY100635; Propylene glycol; ethanol; water, distilled; SC; Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (male, Wistar, 200-250 g); 10% ethanol used.

P9479: A. Rodriguez-Gaztelumendi, *et al.* Altered CB₁ receptor-signaling in prefrontal cortex from an animal model of depression is reversed by chronic fluoxetine. *Journal of Neurochemistry* 2009;108(6):1423-1433

ALZET Comments: Fluoxetine HCl; Propylene glycol; ethanol; water, distilled; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-270 g.); 10% ethanol used; behavioral testing (open field).

P9789: S. B. Pinnock, *et al.* SYNERGISTIC EFFECTS OF DEHYDROEPIANDROSTERONE AND FLUOXETINE ON PROLIFERATION OF PROGENITOR CELLS IN THE DENTATE GYRUS OF THE ADULT MALE RAT. *Neuroscience* 2009;158(4):1644-1651

ALZET Comments: Fluoxetine; SC; Rat; 14 days; Animal info (male, Sprague Dawley, 8 wks old, 250-300 g.).

Q0819: J. E. Oh, *et al.* Paradoxical Anxiogenic Response of Juvenile Mice to Fluoxetine. *Neuropsychopharmacology* 2009;34(10):2197-2207

ALZET Comments: Fluoxetine; Saline; SC; Mice (neonate); 1007D; 7 days; Controls received mp w/ vehicle; animal info (Swiss Webster, C57Bl/6, male, pups 2 weeks old and adult 8 week old); male pups implanted with SC pumps at 2 weeks of age; incisions closed by wound glue; pumps removed at 3 weeks of age; no stress (see pg.2197); pump implantation/removal did not alter overall behavior in the novelty-induced hypophagia (NIH) test; behavioral testing (elevated plus maze, open-field, NIH tests, forced swim test; Dose: 2, 3, and 4 mg/kg/day).

12. Imipramine

Q5976: R. Biswas, *et al.* Imipramine blocks acute silicosis in a mouse model. *Part Fibre Toxicol* 2017;14(1):36

ALZET Comments: Imipramine; PBS; SC; Mice; 6 weeks, 10 weeks; Controls received mp w/ vehicle; animal info (C57Bl/6, 6-8 weeks); The incision was closed with vetbond. Post-op treatment: buprenorphine (0.05-0.10 mg/kg SC; Therapeutic indication (Pulmonary disease, silicosis);.

Q2124: N. Carrier, *et al.* Testosterone and imipramine have antidepressant effects in socially isolated male but not female rats. *Hormones and Behavior* 2012;61(5):678-685

ALZET Comments: Imipramine hydrochloride; Saline, sterile; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (adult, male, 250-270 g, female, 200-225 g, 2-3 mo old); replacement therapy (gonadectomy).

Q1848: N. Carrier, *et al.* Extracellular Signal-Regulated Kinase 2 Signaling in the Hippocampal Dentate Gyrus Mediates the Antidepressant Effects of Testosterone. *Biological Psychiatry* 2012;71(7):642-651

ALZET Comments: Imipramine hydrochloride; Saline; SC; Rat; 2ML4; 30 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, adult, 250-270 g).

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;.



Q0978: A. Blugeot, *et al.* Vulnerability to Depression: From Brain Neuroplasticity to Identification of Biomarkers. *Journal of Neuroscience* 2011;31(36):12889-12899

ALZET Comments: Flavone, 7,8-dihydroxy; imipramine; Saline, sterile; CSF/CNS; SC; Rat; 2004; 2002; 14, 22 days; Controls received mp w/ saline; animal info (male, Sprague Dawley, 324-349 g); 7,8-DHF is a TrkB receptor antagonist.

P9449: E. A. Stone, *et al.* Evaluation of the repeated open-space swim model of depression in the mouse. *Pharmacology Biochemistry and Behavior* 2008;91(1):190-195

ALZET Comments: Imipramine HCl, desmethyl; diazepam; fluoxetine; haloperidol; Saline; DMSO; water; SC; Mice; 1002; 14 days; Controls received mp w/either saline, 25, 50% or 100% DMSO; half-life (p. 191); animal info (male, Swiss Webster, 8-10 wks old); behavioral testing (swimming behavior, tail-suspension test, sucrose suspension test); "since drugs have relatively short half-lives in mice, to more closely mimic the human condition in which blood levels are maintained for prolonged periods, all agents were administered by osmotic minipump." (p. 191); all mice were housed singly for the duration of the experiment (3 weeks). Dose: desmethylimipramine in saline (10–11.5 mg/kg/d) in a 35–40 g mouse, fluoxetine dissolved at the same concentration in 50% DMSO; halodoperidol dissolved in 25%DMSO at 0.3–0.34 mg/kg/day (2 mg/ml) and diazepam in 100% DMSO at 1–1.1 mg/kg/day (6.66 mg/ml).

P9288: C. Becker, *et al.* Repeated social defeat-induced depression-like behavioral and biological alterations in rats: involvement of cholecystokinin. *Molecular Psychiatry* 2008;13(12):1079-1092

ALZET Comments: Imipramine; CI-988; Water, distilled; saline; SC; Rat; 2ML4; 25 days; Controls received mp w/ vehicle; no stress (see pg. 1089); animal info (male, Sprague Dawley, 8 wks old, 300-325 g., Long-Evans, 700-800); behavioral testing (social defeat paradigm); "We chose to give Imipramine... through an implanted mini-pump because (1) a relatively constant level of Imipramine can be delivered to the animals throughout the day and (2) the procedure is not stressful." (p. 1089).

P8097: M. Fujita, *et al.* In vivo and in vitro measurement of brain phosphodiesterase 4 in rats after antidepressant administration. *Synapse* 2007;61(2):78-86

ALZET Comments: Imipramine; Saline; SC; Rat; 20, 27 days; Controls received mp w/ vehicle; functionality of mp verified by residual volume; animal info (male, Sprague-Dawley, 268-345g.); Positron emission tomography (PET); "To avoid injection-induced stress and fluctuations of imipramine and the metabolite levels, we administered imipramine using osmotic minipump" (p.84).

P8069: H. A. Mitchell, *et al.* The effects of norepinephrine transporter inactivation on locomotor activity in mice. *Biological Psychiatry* 2006;60(10):1046-1052

ALZET Comments: Reboxetine; bupropion; imipramine; desipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 18-20 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; no stress (see p.1049); post op. care (Buprenorphine); animal info (male, female, C57BL6/J, 3-7 months old); 50% ETOH vehicle for desipramine; mp primed 1 day in 37 celsius saline.

P7901: T. H. Ahern, *et al.* The effects of chronic norepinephrine transporter inactivation on seizure susceptibility in mice. *Neuropsychopharmacology* 2006;31(4):730-738

ALZET Comments: Reboxetine; sertraline; desipramine; bupropion; imipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug levels; dose-response (fig. 4); comparison of IP injections vs. mp; stress/adverse reaction: (see pg. 731) Dbh -/- mice did not tolerate mp surgery well and showed signs of general malaise. All other mice strains showed no stress.; post op. care (buprenorphine); animal info (female, male, 3-7 month old; C57BL/6J NET -/- or wt; 257BL/6J 129SvEv Dbh -/-, +/-) 50% ethanol; mp primed 2 days in 37 celsius saline; "we achieved serum levels that fell within or very close to human therapeutic range for each drug with the exception of sertraline." (pg. 732).

P7514: C. H. K. West, *et al.* A selective test for antidepressant treatments using rats bred for stress-induced reduction of motor activity in the swim test. *Psychopharmacology* 2005;182(1):9-23



ALZET Comments: Amitriptyline HCl; venlafaxine HCl; clordiazepoxide HCl; imipramine HCl; phenelzine sulfate; scopolamine HBr; desipramine HCl; bupropion HCl; chlorpheniramine maleate; fluoxetine HCl; sertraline; amphetamine sulfate, D-; Water, sterile distilled; PEG; SC; Rat; 2ML2; 6,14 days; Controls received mp w/ vehicle; functionality of mp verified by agent blood levels; dose-response (fig. 5); animal info (male, female, susceptible, selectively bred); some animals had saline-filled catheter attached to mp to delay drug infusion by 5 days; "The most notable advantage of minipump delivery is that it eliminates stress resulting from daily injection of drug....minipumps also provide constant infusion of drug" (pg. 22).

P5337: L. A. B. Slot, *et al.* Experimental conditions for the continuous subcutaneous infusion of four central analgesics in rats. *Pharmacology Biochemistry and Behavior* 2002;72(4):943-951

ALZET Comments: Morphine HCl; Ketamine HCl; Imipramine HCl; gabapentin; Water, distilled; SC; Rat; 2ML2; 2 weeks; Controls received mp w/ saline; no stress (see pg. 947); 14 day stability verified by HPLC on all agents; the site of pump placement was massaged daily to avoid tissue adherence; opioid and non-opioid analgesics; body weight gain information provided.

P5883: E. Gur, *et al.* Effects of triiodothyronine and imipramine on basal 5-HT levels and 5-HT₁ autoreceptor activity in rat cortex. *European Journal of Pharmacology* 2002;457(1):37-43

ALZET Comments: Imipramine; SC; Rat; 2ML2; 2ML4; 2, 4 weeks; Controls received mp w/ saline.

P6585: F. C. Colpaert, *et al.* Large-amplitude 5-HT_{1A} receptor activation: a new mechanism of profound, central analgesia. *Neuropharmacology* 2002;43(6):945-958

ALZET Comments: F13640; morphine HCl; imipramine HCl; ketamine HCl; gabapentin; Water, double distilled; SC; Rat; 2ML2; 14 days; Controls received mp w/ saline; dose-response (fig. 3); comparison of IP & SC injections vs. mp; tolerance; dependence; "Continuous F 13640 infusion uniquely produced profound analgesia in this model of severe, chronic pain." (p. 955).

P4797: M. M. Grant, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on locus coeruleus electrophysiologic activity. *Biological Psychiatry* 2001;49(11):117-129

ALZET Comments: Desipramine, HCl; Imipramine; Phenelzine sulfate; Fluoxetine, HCl; Sertraline, HCl; Saline; PEG; SC; Rat; 2ML2; 2ML4; 14 or 30 days; Controls received mp w/ vehicle; antidepressant; functionality of mp verified by antidepressant blood levels vs. IP injection; dose-response (table, text p. 123-124); no stress (see p. 119 "consequences of daily handling and injection were therefore avoided in the present study"); desipramine, imipramine, and phenelzine were delivered in saline vehicle; fluoxetine and sertraline were delivered in 75% PEG and 25% saline; the agents are all clinical antidepressants;

P4171: C.-T. Lai, *et al.* Effects of phenelzine and imipramine on the steady state levels of mRNAs that encode glutamic acid decarboxylase (GAD67 and GAD65), the GABA transporter GAT-1 and GABA transaminase in rat cortex. *Naunyn-Schmiedeberg's Arch. Pharmacol* 1998;357(3):32-38

ALZET Comments: Phenelzine sulfate; Imipramine HCl; Water; SC; Rat; 3,21 days; functionality of mp verified by characteristic responses to phenelzine (GABA levels and MAO activity); antidepressant.

P3498: V. A.-M. I. Tanay, *et al.* Chronic administration of antipanic drugs alters rat brainstem GABA-A receptor subunit mRNA levels. *Neuropharmacology* 1996;35(9/10):1475-1482

ALZET Comments: Phenelzine; alprazolam; imipramine; buspirone; Water, sterile; DMSO; propylene glycol; SC; Rat; 21 days; Antidepressant; controls received mp w/ vehicle; pumps were turned in subcutaneous pocket to avoid fibrous tissue outgrowth.

13. Lithium

Q7135: G. Frindt, *et al.* Na restriction activates epithelial Na channels in rat kidney through two mechanisms and decreases distal Na(+) delivery. *J Physiol* 2018;596(16):3585-3602



ALZET Comments: Lithium Chloride; Water; SC; Rat; 2001D; 1 day; Dose (750 mM/day); Controls received mp w/ vehicle; animal info (Sprague–Dawley, 150-250 g); cardiovascular;.

Q3369: Q. Wu, *et al.* NR2B subunit of the NMDA glutamate receptor regulates appetite in the parabrachial nucleus. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2013;110(36):14765-14770
ALZET Comments: Lithium chloride; RO25-6981; bretazenil; Saline; CSF/CNS (fourth ventricle; parabrachial nucleus); Mice; 1002; 14 days; Controls received mp w/ vehicle or sham surgery; animal info (male, Agrp DTR/+ or WT); bilateral cannula used; dose-response (pg.14766, fig.3; pg.14769, fig.6); behavioral testing (food intake); tissue perfusion (fourth ventricle; parabrachial nucleus); Cannula placement verified; RO25-6981 is a NR2B antagonist; bilateral infusion;.

P9250: J. Dill, *et al.* Inactivation of glycogen synthase kinase 3 promotes axonal growth and recovery in the CNS. Journal of Neuroscience 2008;28(36):8914-8928
ALZET Comments: Lithium Chloride; Saline, physiological; SC; Mice; 2004; 28 days; Controls received mp w/ vehicle; enzyme inhibitor (Glycogen synthase kinase-3); animal info (female, C57BL/6, 8-10 wks old, spinal cord injury/laminectomy); behavioral testing (BBB locomotor scale, grid walking, foot print analysis).

P9776: D. J. Pulford, *et al.* Chronic lithium administration down regulates transthyretin mRNA expression in rat choroid plexus. Neuropsychiatric Disease and Treatment 2006;2(4):549-555
ALZET Comments: Lithium chloride; Water, sterile; SC; Rat; 28 days; Controls received mp w/ vehicle; animal info (male, Lister hooded, 257 g.).

P5723: S. C. Benoit, *et al.* Assessment of the aversive consequences of acute and chronic administration of the melanocortin agonist, MTII. International Journal of Obesity 2003;27(5):550-556
ALZET Comments: MTII; Lithium chloride; IP; Rat; 7 days; Controls received mp w/ saline; comparison of IP, IV, SC injections vs. IP mp; MTII is a melanocortin agonist.

P6711: S. C. Benoit, *et al.* Two novel paradigms for the simultaneous assessment of conditioned taste aversion and food intake effects of anorexic agents. PHYSIOLOGY & BEHAVIOR 2003;79(4-5):761-766
ALZET Comments: Lithium Chloride; IP; Rat; 2ML1; 7 days; Controls received mp w/ equimolar saline; comparison of IP injections vs. mp; no stress (see pg.764).

P2895: A. C. O'Connell, *et al.* Composition and flow rate of saliva and caries development in young rats following administration of lithium. Caries Res 1994;28(342-347)
ALZET Comments: Lithium carbonate; HCl; SC; Rat; no duration posted; antidepressant; controls received no operation.

P2249: L. A. Eckel, *et al.* Novel diet consumption and body weight gain are reduced in rats chronically infused with lithium chloride: mediation by the chemosensitive area postrema. Brain Res. Bull 1993;31(613-619)
ALZET Comments: Lithium chloride; Water; IP; Rat; 2001; 8 days; antidepressant; controls received empty pumps.

P2008: S. A. Qureshi, *et al.* Lithium-induced nephrotoxicity in rats following subcutaneous multiple injection and infusion using mini-osmotic pumps. Fundam. Appl. Toxicol 1992;18(616-620)
ALZET Comments: Lithium chloride; Saline; SC; Rat; 2ML2; 8 days; antidepressant; 'constant blood levels, produced by the sc infusion method, resulted in less nephrotoxicity compared to the fluctuating plasma levels produced by inj.'; functionality of mp verified by LiCl plasma levels; comparison of sc injections vs mp.

P1098: H. Klemfuss, *et al.* Potassium reduces lithium toxicity: Circadian rhythm actions are maintained. Life Sci 1987;40(2531-2538)
ALZET Comments: Lithium chloride; Water; SC; Rat; 2ML4; 30 days; controls received mp w/water.

P0857: J. C. Barnes, *et al.* Lithium and bupropion antagonise the phasic changes in locomotor activity caused by dopamine infused into the rat nucleus accumbens. Psychopharmacology 1986;89(311-316)



ALZET Comments: Dopamine HCl; Lithium; Sodium metabisulfite; CSF/CNS (nucleus accumbens); IP; Rat; 2002; 13 days; controls rec'd mps w/vehicle; mp connected to cannula in NC; mps & injection units primed overnight; lithium admin. ip; agents admin. simult. in 1 group; comparison of ip inject. vs mp infusion.

14. Maprotiline

Q0004: L. Bjartmar, *et al.* Long-term treatment with antidepressants, but not environmental stimulation, induces expression of NP2 mRNA in hippocampus and medial habenula. *Brain Research* 2010;1328(:):25-33

ALZET Comments: Amitriptyline; moclobemide; citalopram hydrobromide; maprotiline; SC; Rat; 3, 21 days; Controls received mp w/isotonic saline; enzyme inhibitor (monoamine oxidase-A); animal info (male, Sprague-Dawley, 200-250 g); "This method of delivery was chosen to avoid daily injections and thus manipulation of the animals." (p. 30); antidepressants.

P3352: K. G. Todd, *et al.* Chronic administration of the antidepressants phenelzine, desipramine, clomipramine, or maprotiline decreases binding to 5-hydroxytryptamine_{2A} receptors without affecting benzodiazepine binding sites in rat brain. *Cell. Molec. Neuro* 1995;15(3):361-370

ALZET Comments: Clomipramine; Fluoxetine; Desipramine; Phenelzine; Maprotiline; SC; Rat; 2ML4; 21 days; antidepressant; no comment posted.

P0694: K. G. Lloyd, *et al.* Upregulation of gamma-aminobutyric acid (GABA) B binding sites in rat frontal cortex: a common action of repeated administration of different classes of antidepressants and electroshock. *J. Pharmacol. Exp. Ther* 1985;235(1):191-199

ALZET Comments: Maprotiline; Nomifensine; Amitriptyline; Citalopram; Desipramine; Pargyline; Trazodone; Viloxazine; Zimeldine; SC; Rat; 2002; 6-18 days; comparison of agents effects; comparison of single dose ip injec vs. mp infusion and repeated ip injec of other psychotropic drugs vs. electroshock treatment; antihypertensive.

15. Mianserin

P2365: P. J. Mitchell, *et al.* Chronic treatment with clomipramine and mianserin increases the hierarchical position of subdominant rats housed in triads. *Behav. Pharmacology* 1992;3(239-247)

ALZET Comments: Clomipramine; Mianserin; Water; SC; Rat; 2002; 7/14 days; antidepressant; controls received mp w/ water or sham op; no stress (see pg. 241).

P1695: H. Kubota, *et al.* Mechanisms of the B-adrenoceptor down-regulation by the treatment with antidepressants in the rat cerebral cortex: effects of continuous administration of antidepressants by an osmotic pump. *Jpn. J. Psychiatry Neurol* 1990;44(1):135-136

ALZET Comments: Tunicamycin; Cycloheximide; Desipramine; Fluoxetine; Mianserin; Trazodone; CSF/CNS; SC; Rat; 2001; 2ML1; 4-7 days; comparison of sc injections vs. mp; cyclo. and tunica. delivered icv for 5 days.

P1756: K. Kurata, *et al.* Heterogeneous distribution of mianserin in rat brain during chronic continuous infusion. *Pharmacology* 1989;39(285-290)

ALZET Comments: Mianserin; DMSO; SC; Rat; 2ML2; 2, 14 days; functionality of mp verified by measuring residual volume, serum drug levels; tetracyclic antidepressant, 5HT antagonists.

P0338: M. Williams, *et al.* Chronic in vivo treatment with desmethylimipramine and mianserin does not alter adenosine A-1 radioligand binding in rat cortex. *Neurosci. Lett* 1983;35(47-51)

ALZET Comments: Desipramine; Mianserin; SC; Rat; 2ML2; 2-3 weeks; comparison of agents effects; DMI 2 wks, Mianserin 3 wks.



16. Milnacipran

Q6550: Y. Yoshino, *et al.* Endothelial nitric oxide synthase in rat brain is downregulated by sub-chronic antidepressant treatment. *Psychopharmacology (Berl)* 2017;234(11):1663-1669

ALZET Comments: Paroxetine hydrochloride; Milnacipran hydrochloride; Mirtazapine; Saline; SC; Rat; 2ML4; 14 days; Dose (Paroxetine: 10 mg/kg; milnacipran: 30 mg/kg; mirtazapine 10 mg/kg); Controls received mp w/ vehicle; animal info (Male adult Wistar rats weighing 180–200 g);.

P9846: R. Takeda, *et al.* Analgesic effect of milnacipran is associated with c-Fos expression in the anterior cingulate cortex in the rat neuropathic pain model. *NEUROSCIENCE RESEARCH* 2009;64(4):380-384

ALZET Comments: Milnacipran; Saline; SC; Rat; 2ML2; Controls received sham operation; animal info (Sprague Dawley, 320-350 g.); behavioral testing (withdrawal response); "The pump makes it possible to precisely and continuously administer systemic drug-delivery without any repeated harmful treatment" pg. 381.

P2179: M. B. Assie, *et al.* Effects of prolonged administration of milnacipran, a new antidepressant, on receptors and monoamine uptake in the brain of the rat. *Neuropharmacology* 1992;31(2):149-155

ALZET Comments: Milnacipran; Desipramine; PEG 300; Water; Rat; 2ML4; 27 days; antidepressant; controls received mp w/vehicle; functionality of mp verified by blood levels (p. 151); comparison of oral administration vs. mp; stress/adverse reaction: skin necrosis w/desipramine pumps; route not stated.

17. Mirtazapine

Q6550: Y. Yoshino, *et al.* Endothelial nitric oxide synthase in rat brain is downregulated by sub-chronic antidepressant treatment. *Psychopharmacology (Berl)* 2017;234(11):1663-1669

ALZET Comments: Paroxetine hydrochloride; Milnacipran hydrochloride; Mirtazapine; Saline; SC; Rat; 2ML4; 14 days; Dose (Paroxetine: 10 mg/kg; milnacipran: 30 mg/kg; mirtazapine 10 mg/kg); Controls received mp w/ vehicle; animal info (Male adult Wistar rats weighing 180–200 g);.

Q5373: N. A. Holtz, *et al.* Pharmacologically distinct pramipexole-mediated akinesia vs. risk-taking in a rat model of Parkinson's disease. *Prog Neuropsychopharmacol Biol Psychiatry* 2016;70(77-84

ALZET Comments: Pramipexole HCL; Mirtazapine; Pramipexole HCL; Mirtazapine; SC; Rat; 2002, 2ML4; 12 - 14 days; Controls received mp w/ vehicle; animal info (250-300 g, male Sprague-Dawley rats); For mirtazapine, saline brought to 5.5-6.0 pH with 1 N NaOH; good methods (pg. 79); neurodegenerative (Parkinson's disease); behavioral testing (forelimb step task); PPX is a dopamine D2 receptor agonist; Mirtazapine is an atypical antidepressant; akinesia and risk-taking rat model; Dose (PPX 0.3 and 1.2 mg/kg/day; Mirtazapine 5 mg/kg/day);.

Q5063: N. Ito, *et al.* Contribution of protein binding, lipid partitioning, and asymmetrical transport to drug transfer into milk in mouse versus human. *Pharm Res* 2013;30(9):2410-22

ALZET Comments: acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopyramide phosphate salt, labetalol hydrochloride, nitrofurantoin +-propranolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cephapirin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, praziquantel, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide.; DMSO; water; IP; mice; 1003D; animal info: lactating mice, postnatal age of 14 days; functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer.

Q0899: S. Yamamura, *et al.* Different actions for acute and chronic administration of mirtazapine on serotonergic transmission associated with raphe nuclei and their innervation cortical regions. *Neuropharmacology* 2011;60(4):550-560

ALZET Comments: Mirtazapine; HCl; Ringer's solution; SC; Rat; 2ML4; 21 days; Animal info (Sprague-Dawley, male, 5 wks old).



P9610: C. H. K. West, *et al.* Antidepressant drugs with differing pharmacological actions decrease activity of locus coeruleus neurons. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2009;12(5):627-641

ALZET Comments: Desipramine; mirtazapine; chlorpheniramine; Paroxetine; scopolamine; amphetamine; escitalopram; chlordiazepoxide; SC; IP; Rat; 2ML2; 14, 21 days; Controls received mp w/vehicle; dose-response (Fig 2-5); pumps replaced on day 14; good methods pg 629; animal info (male, Sprague Dawley, 5-7 mo old, 550-700g); "Importantly, use of minipumps also eliminates the need for repeated handling and injection of animals to administer the drug chronically." pg. 628; IP catheter used.

P4703: A. Besson, *et al.* Effects of the co-administration of mirtazapine and paroxetine on serotonergic neurotransmission in the rat brain. *European Neuropsychopharmacology* 2000;10(177-188)

ALZET Comments: Mirtazapine; Paroxetine;; Water; Ethanol;; SC;; Rat;; 2 or 21 days;; No stress (see pg; 178); Antidepressant treatment; 80:20 water/ethanol vehicle used in 2 day study; 50:50 water/ethanol vehicle used in 21 day study; multiple pumps per animal (2) used for mirtazapine-paroxetine combination group;.

P4647: N. Haddjeri, *et al.* Acute and long-term actions of the antidepressant drug mirtazapine on central 5-HT neurotransmission. *Journal of Affective Disorders* 1998;51(255-266)

ALZET Comments: Mirtazapine; Pindolol;; NaCl; Ascorbic acid;; SC;; Rat;; 2, 21 days;; controls received mp w/ vehicle; comparison of IV injections vs mp; antidepressant; pindolol infused for 2 days; mirtazapine administered for 21 days.

P3445: N. Haddjeri, *et al.* Effects of long-term treatment with the $\alpha(2)$ -adrenoceptor antagonist mirtazapine on 5-HT neurotransmission. *Naunyn-Schmiedeberg's Arch. Pharmacol* 1997;355(20-29)

ALZET Comments: Mirtazapine; ETHANOL; Water; SC; Rat; 21 days; controls received mp w/ vehicle; mirtazapine is also known as ORG 3770 or Remeron, and is a non-selective $\alpha(2)$ -adrenoceptor antagonist and antidepressant.

18. Nomifensine

P0694: K. G. Lloyd, *et al.* Upregulation of gamma-aminobutyric acid (GABA) B binding sites in rat frontal cortex: a common action of repeated administration of different classes of antidepressants and electroshock. *J. Pharmacol. Exp. Ther* 1985;235(1):191-199

ALZET Comments: Maprotiline; Nomifensine; Amitriptyline; Citalopram; Desipramine; Pargyline; Trazodone; Viloxazine; Zimeldine; SC; Rat; 2002; 6-18 days; comparison of agents effects; comparison of single dose ip injec vs. mp infusion and repeated ip injec of other psychotropic drugs vs. electroshock treatment; antihypertensive.

19. Nortriptyline

P2654: K. Brodin, *et al.* Clomipramine and clonazepam increase cholecystokinin levels in rat ventral tegmental area and limbic regions. *Eur. J. Pharmacol* 1994;263(175-180)

ALZET Comments: Nortriptyline; Amitriptyline; Clomipramine; Alaproclate; Clonazepam; Alcohol; Saline; SC; Rat; 2ML2; 14 days; antidepressant; controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose-response (Table 1; pg. 177); enzyme inhibitor; clonazepam is a benzodiazepene; the others are monoamine uptake inhibitors.

20. Paroxetine

Q6550: Y. Yoshino, *et al.* Endothelial nitric oxide synthase in rat brain is downregulated by sub-chronic antidepressant treatment. *Psychopharmacology (Berl)* 2017;234(11):1663-1669

ALZET Comments: Paroxetine hydrochloride; Milnacipran hydrochloride; Mirtazapine; Saline; SC; Rat; 2ML4; 14 days; Dose (Paroxetine: 10 mg/kg; milnacipran: 30 mg/kg; mirtazapine 10 mg/kg); Controls received mp w/ vehicle; animal info (Male adult Wistar rats weighing 180–200 g);.



Q4595: J. P. Steiner, *et al.* Interaction of Paroxetine with Mitochondrial Proteins Mediates Neuroprotection. *Neurotherapeutics* 2015;12(200-216)

ALZET Comments: Paroxetine; SC; Mice (transgenic); 2004; Controls received mp w/ saline; animal info (male, bp120 tg, adult, 8-9 weeks old); functionality of mp verified by residual volume; pumps primed overnight at 37C;.

Q4580: S. M. Schumacher, *et al.* Paroxetine-Mediated GRK2 Inhibition Reverses Cardiac Dysfunction and Remodeling After Myocardial Infarction. *JOURNAL OF CARDIAC FAILURE* 2015;21(S109-S109)

ALZET Comments: Paroxetine; fluoxetine; DMSO; water; SC; Mice; 1002; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6, myocardial infarction); functionality of mp verified by serum levels; ischemia (cardiac); Dose: paroxetine or fluoxetine (5 mg/kg/d).

Q3871: M. El Mansari, *et al.* Restoration of Serotonin Neuronal Firing Following Long-Term Administration of Bupropion but Not Paroxetine in Olfactory Bulbectomized Rats. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2015;18(U87-U94)

ALZET Comments: Bupropion; paroxetine; Water; ethanol; SC; Rat; 2 days; 14 days; 28 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 300-500g, olfactory bulbectomized); 50% ethanol used; behavioral testing (open field);.

Q2570: D. Geroe, *et al.* Cell-Based Screening Identifies Paroxetine as an Inhibitor of diabetic Endothelial Dysfunction. *Diabetes* 2013;62(3):953-964

ALZET Comments: Paroxetine; Rat; 28 days; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 225-250 g); pumps replaced after 2 weeks.

Q1811: M. L. Rovin, *et al.* Influence of chronic administration of antidepressant drugs on mRNA for galanin, galanin receptors, and tyrosine hydroxylase in catecholaminergic and serotonergic cell-body regions in rat brain. *Neuropeptides* 2012;46(2):81-91

ALZET Comments: Phenelzine; desipramine; paroxetine; DMSO; PEG; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, adult, 5-7 mo old); Osmotic minipumps were chosen for AD delivery because they slowly release drug over 14 days, thus eliminating the stress animals would experience by daily injections of the AD" pg 83; IP catheter used; wound clips used; enzyme inhibitor (monoamine oxidase); 50% DMSO used; 25% PEG used.

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;.

Q1200: M. H. Lee, *et al.* Rescue of adult hippocampal neurogenesis in a mouse model of HIV neurologic disease. *NEUROBIOLOGY OF DISEASE* 2011;41(3):678-687

ALZET Comments: Paroxetine; SC; Mice (transgenic); 2004; 28 days; Animal info (8-9 wks old, gp120-tg, wt); functionality of mp verified by residual volume.

Q1397: C. H. K. West, *et al.* Paroxetine-Induced Increase in Activity of Locus Coeruleus Neurons in Adolescent Rats: Implication of a Countertherapeutic Effect of an Antidepressant. *Neuropsychopharmacology* 2010;35(8):1653-1663



ALZET Comments: Paroxetine; DMSO; PEG 400; water, distilled; IP; Rat; 2ML2; 2, 4, 8, 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 45 days old); pumps replaced after 7 days; 50% DMSO used; 25% PEG 400 used; wound clips used; IP catheter used; The distal end of the tubing was then introduced through a small hole into the peritoneal cavity and secured to the abdominal wall while closing the hole with suture." pg 1654; "For duration of administration of 14 days in the juvenile animals, the minipump was replaced after 7 days, with the drug concentration adjusted at that time for the increased weight of the animal." pg 1654.

Q1594: R. Mongeau, *et al.* 5-HT_{2C} receptor activation prevents stress-induced enhancement of brain 5-HT turnover and extracellular levels in the mouse brain: modulation by chronic paroxetine treatment. *Journal of Neurochemistry* 2010;115(2):438-449

ALZET Comments: Paroxetine; DMSO; saline; SC; Mice; 2004; 3 weeks; Controls received mp w/ vehicle; animal info (2-3 mo old, male, SV129, C57BL/6J).

P9610: C. H. K. West, *et al.* Antidepressant drugs with differing pharmacological actions decrease activity of locus coeruleus neurons. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2009;12(5):627-641

ALZET Comments: Desipramine; mirtazapine; chlorpheniramine; Paroxetine; scopolamine; amphetamine; escitalopram; chlordiazepoxide; SC; IP; Rat; 2ML2; 14, 21 days; Controls received mp w/vehicle; dose-response (Fig 2-5); pumps replaced on day 14; good methods pg 629; animal info (male, Sprague Dawley, 5-7 mo old, 550-700g); "Importantly, use of minipumps also eliminates the need for repeated handling and injection of animals to administer the drug chronically." pg. 628; IP catheter used.

P9644: I. Skelin, *et al.* Flesinoxan challenge suggests that chronic treatment with paroxetine in rats does not desensitize receptors controlling 5-HT synthesis. *NEUROCHEMISTRY INTERNATIONAL* 2008;53(6-8):236-243

ALZET Comments: Paroxetine; Ethanol; water; SC; Rat; 2ML2; 14 days; Animal info (SD, male, 130-150g); 50% ethanol.

P8117: G. G. Gould, *et al.* Effect of chronic administration of duloxetine on serotonin and norepinephrine transporter binding sites in rat brain. *Biological Psychiatry* 2007;61(2):210-215

ALZET Comments: Duloxetine; desipramine; paroxetine; Ethanol; water; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum agent concentrations; dose-response (p.211); animal info (male, Sprague-Dawley, 125-150g).

P7726: G. G. Gould, *et al.* A comparison of the chronic treatment effects of venlafaxine and other antidepressants on serotonin and norepinephrine transporters. *Biological Psychiatry* 2006;59(5):408-414

ALZET Comments: Venlafaxine; sertraline; amitriptyline; paroxetine; desipramine; citalopram; Saline; water, deionized; ethanol; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug concentrations; dose-response (fig1); animal info (male, Sprague-Dawley, 150-200g); 50% EtoH in H₂O.

P7376: K. Hirano, *et al.* Effects of continuous administration of paroxetine on ligand binding site and expression of serotonin transporter protein in mouse brain. *Brain Research* 2005;1053(1-2):154-161

ALZET Comments: Paroxetine hydrochloride; Ethanol; water, distilled; SC; Mice; 2004; 5, 10, 15, 21 days; Controls received mp w/ vehicle; functionality of mp verified by plasma drug concentration; dose-response (fig. 1); half-life (p. 157) 3.4 hours after oral admin.; 50% ETOH; "The subcutaneous implantation of the drug-containing osmotic minipump enabled the continuous administration of paroxetine... and succeeded in maintaining the mouse plasma paroxetine concentrations within therapeutic levels." (p.158).

P6501: S. Benmansour, *et al.* Regulation of the norepinephrine transporter by chronic administration of antidepressants. *Biological Psychiatry* 2004;55(3):313-316

ALZET Comments: Desipramine; paroxetine; Ethanol; water; SC; Rat; 3,6 weeks; Controls received mp w/ vehicle; 50% ethanol.

P7088: B. Aibel, *et al.* Antihyperalgesic effects of cizolirtine in diabetic rats: Behavioral and biochemical studies. *Pain* 2004;110(1-2):22-32



ALZET Comments: Cizolirtine; paroxetine hydrochloride; Saline; DMSO; SC; Rat; 2ML2; 2 weeks; Controls received mp w/ vehicle; replacement therapy (STZ-induced diabetes); dose-response (fig. 4); 20% DMSO.

21. Phenzelzine

Q1811: M. L. Rovin, *et al.* Influence of chronic administration of antidepressant drugs on mRNA for galanin, galanin receptors, and tyrosine hydroxylase in catecholaminergic and serotonergic cell-body regions in rat brain. *Neuropeptides* 2012;46(2):81-91

ALZET Comments: Phenzelzine; desipramine; paroxetine; DMSO; PEG; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, adult, 5-7 mo old); Osmotic minipumps were chosen for AD delivery because they slowly release drug over 14 days, thus eliminating the stress animals would experience by daily injections of the AD" pg 83; IP catheter used; wound clips used; enzyme inhibitor (monoamine oxidase); 50% DMSO used; 25% PEG used.

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenzelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;.

P9373: F. Chenu, *et al.* Long-term administration of monoamine oxidase inhibitors alters the firing rate and pattern of dopamine neurons in the ventral tegmental area. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2009;12(4):475-485

ALZET Comments: Clorgyline; phenzelzine; deprenyl; SC; Rat; 2, 21 days; Controls received mp w/ saline; enzyme inhibitor (MAO, monoamine oxidase); animal info (male, Sprague Dawley, 250-300 g.).

P7514: C. H. K. West, *et al.* A selective test for antidepressant treatments using rats bred for stress-induced reduction of motor activity in the swim test. *Psychopharmacology* 2005;182(1):9-23

ALZET Comments: Amitriptyline HCl; venlafaxine HCl; clordiazepoxide HCl; imipramine HCl; phenzelzine sulfate; scopolamine HBr; desipramine HCl; bupropion HCl; chlorpheniramine maleate; fluoxetine HCl; sertraline; amphetamine sulfate, D-; Water, sterile distilled; PEG; SC; Rat; 2ML2; 6,14 days; Controls received mp w/ vehicle; functionality of mp verified by agent blood levels; dose-response (fig. 5); animal info (male, female, susceptible, selectively bred); some animals had saline-filled catheter attached to mp to delay drug infusion by 5 days; "The most notable advantage of minipump delivery is that it eliminates stress resulting from daily injection of drug....minipumps also provide constant infusion of drug" (pg. 22).

R0154: A. Frazer, *et al.* Delayed pharmacological effects of antidepressants. *Molecular Psychiatry* 2002;7(S23-S28)

ALZET Comments: Desipramine; Paroxetine; Sertraline; Phenzelzine; Rat; 4, 10, 15, 21 days; Antidepressant; controls received mp w/ vehicle; brain tissue distribution; review article mentions several pK studies on chronic infusion of antidepressants.

P4797: M. M. Grant, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on locus coeruleus electrophysiological activity. *Biological Psychiatry* 2001;49(117-129)

ALZET Comments: Desipramine, HCl; Imipramine; Phenzelzine sulfate; Fluoxetine, HCl; Sertraline, HCl;; Saline; PEG;; SC;; Rat;; 2ML2; 2ML4;; 14 or 30 days;; Controls received mp w/ vehicle; antidepressant; functionality of mp verified by antidepressant blood levels vs. IP injection; dose-response (table, text p. 123-124); no stress (see p. 119 "consequences of daily handling and injection were therefore avoided in the present study"); desipramine, imipramine, and phenzelzine were



delivered in saline vehicle; fluoxetine and sertraline were delivered in 75% PEG and 25% saline; the agents are all clinical antidepressants;.

P4171: C.-T. Lai, *et al.* Effects of phenelzine and imipramine on the steady state levels of mRNAs that encode glutamic acid decarboxylase (GAD67 and GAD65), the GABA transporter GAT-1 and GABA transaminase in rat cortex. *Naunyn-Schmiedeberg's Arch. Pharmacol* 1998;357(32-38)

ALZET Comments: Phenelzine sulfate; Imipramine HCl; Water; SC; Rat; 3,21 days; functionality of mp verified by characteristic responses to phenelzine (GABA levels and MAO activity); antidepressant.

P3498: V. A.-M. I. Tanay, *et al.* Chronic administration of antipanic drugs alters rat brainstem GABA-A receptor subunit mRNA levels. *Neuropharmacology* 1996;35(9/10):1475-1482

ALZET Comments: Phenelzine; alprazolam; imipramine; buspirone; Water, sterile; DMSO; propylene glycol; SC; Rat; 21 days; Antidepressant; controls received mp w/ vehicle; pumps were turned in subcutaneous pocket to avoid fibrous tissue outgrowth.

P3352: K. G. Todd, *et al.* Chronic administration of the antidepressants phenelzine, desipramine, clomipramine, or maprotiline decreases binding to 5-hydroxytryptamine_{2A} receptors without affecting benzodiazepine binding sites in rat brain. *Cell. Molec. Neuro* 1995;15(3):361-370

ALZET Comments: Clomipramine; Fluoxetine; Desipramine; Phenelzine; Maprotiline; SC; Rat; 2ML4; 21 days; antidepressant; no comment posted.

P2800: K. Allison, *et al.* Behavioural response to SKF 38393 and quinpirole following chronic antidepressant treatment. *Eur. J. Pharmacol* 1995;277(139-144)

ALZET Comments: Desipramine HCl; Clomipramine HCl; Phenelzine sulfate; Clorgyline HCl; Water, distilled; SC; Rat; 2ML4; 28 days; controls received mp w/ vehicle; all agents are antidepressants.

P2971: R. L. Sherry-McKenna, *et al.* Monoamine oxidase inhibitors: effects on tryptophan concentrations in the rat brain. *J. Neural Transm* 1994;41(155-163)

ALZET Comments: Phenelzine; Tranylcypromine, 4-methoxy-; Acetylphenelzine, N₂-; Tranylcypromine, 4-fluoro-; Tranylcypromine; Deprenyl; SC; IP; Rat; 28 days; antidepressant; controls received mp with vehicle; comparison of TCP and PLZ ip injections vs. mp.

P2832: K. F. McKenna, *et al.* Chronic administration of the antidepressant phenelzine and its N-acetyl analogue: effects on GABAergic function. *J. Neural Transm* 1994;41(115-122)

ALZET Comments: Phenelzine sulfate; Acetylphenelzine, N₂-; SC; Rat; 2ML2; 28 days; antidepressant; controls received mp with water.

22. Reboxetine

Q2003: Y. C. Ku, *et al.* Different involvement of ventral and dorsal norepinephrine pathways on norepinephrine reuptake inhibitor-induced locomotion and antidepressant-like effects in rats. *Neuroscience Letters* 2012;514(2):179-184

ALZET Comments: Reboxetine; Saline; SC; Rat; 2004; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, adult).

Q2721: A. A. Fossa, *et al.* Improved preclinical cardiovascular therapeutic indices with long-term inhibition of norepinephrine reuptake using reboxetine. *TOXICOLOGY AND APPLIED PHARMACOLOGY* 2012;264(3):343-350

ALZET Comments: Reboxetine; Water, sterile; SC; Rat; 2ML4; 28 days; Control animals received mp w/ vehicle; functionality of mp verified via residual volume.

P9879: Z. Zhao, *et al.* Association of Changes in Norepinephrine and Serotonin Transporter Expression with the Long-Term Behavioral Effects of Antidepressant Drugs. *Neuropsychopharmacology* 2009;34(6):1467-1481



ALZET Comments: Protriptyline; reboxetine; sertraline; venlafaxine; DMSO; saline; ethanol; SC; Rat; 2ML2; 2ML4; 14, 42 days; Controls received mp w/ vehicle; long-term study; pumps replaced after 21 days; animal info (male, Sprague Dawley, 300-350 g.); 50% DMSO used; 10% ethanol used.

P9743: T. Arunrut, *et al.* Differential behavioral and neurochemical effects of exercise, reboxetine and citalopram with the forced swim test. *LIFE SCIENCES* 2009;84(17-18):584-589

ALZET Comments: Reboxetine; citalopram; Saline; SC; Rat; 7 days; Controls received mp w/vehicle; animal info (male, Sprague Dawley).

P8663: V. S. Barbiero, *et al.* Chronic antidepressants induce redistribution and differential activation of alpha CaM kinase II between presynaptic compartments. *Neuropsychopharmacology* 2007;32(12):2511-2519

ALZET Comments: Reboxetine; fluoxetine; desipramine; Ethanol; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 170-200g); reboxetine is a selective norepinephrine reuptake inhibitor (NRI); fluoxetine is a selective serotonin reuptake inhibitor (SSRI); desipramine is a tricyclic antidepressant inhibiting norepinephrine release.

P8069: H. A. Mitchell, *et al.* The effects of norepinephrine transporter inactivation on locomotor activity in mice. *Biological Psychiatry* 2006;60(10):1046-1052

ALZET Comments: Reboxetine; bupropion; imipramine; desipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 18-20 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; no stress (see p.1049); post op. care (Buprenorphine); animal info (male, female, C57BL6/J, 3-7 months old); 50% ETOH vehicle for desipramine; mp primed 1 day in 37 celsius saline.

P7901: T. H. Ahern, *et al.* The effects of chronic norepinephrine transporter inactivation on seizure susceptibility in mice. *Neuropsychopharmacology* 2006;31(4):730-738

ALZET Comments: Reboxetine; sertraline; desipramine; bupropion; imipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug levels; dose-response (fig. 4); comparison of IP injections vs. mp; stress/adverse reaction: (see pg. 731) Dbh -/- mice did not tolerate mp surgery well and showed signs of general malaise. All other mice strains showed no stress.; post op. care (buprenorphine); animal info (female, male, 3-7 month old; C57BL/6J NET -/- or wt; 257BL/6J 129SvEv Dbh -/-, +/-) 50% ethanol; mp primed 2 days in 37 celsius saline; "we achieved serum levels that fell within or very close to human therapeutic range for each drug with the exception of sertraline." (pg. 732).

P7543: J. F. Cryan, *et al.* Differential behavioral effects of the antidepressants reboxetine, fluoxetine, and moclobemide in a modified forced swim test following chronic treatment. *Psychopharmacology* 2005;182(3):335-344

ALZET Comments: Reboxetine hydrobromide; fluoxetine hydrobromide; moclobemide; Ethanol; saline; SC; Rat; 2ML1; 2ML2; 3, 14 days; Controls received mp w/ vehicle or saline; functionality of mp verified by residual volume; dose-response (fig. 1); post op. care (providone-iodine antiseptic ointment); animal info (male, Sprague-Dawley, 350-500 g); 50% ethanol.

P6901: G. Bonanno, *et al.* Chronic antidepressants reduce depolarization-evoked glutamate release and protein interactions favoring formation of SNARE complex in hippocampus. *Journal of Neuroscience* 2005;25(13):3270-3279

ALZET Comments: Fluoxetine; reboxetine; desipramine; Ethanol; SC; Rat; 2ML2; 14 days; Comparison of IP injections vs. SC mp; 5% ethanol used.

P6998: E. Tiraboschi, *et al.* Selective phosphorylation of nuclear CREB by fluoxetine is linked to activation of CaM kinase IV and MAP kinase cascades. *Neuropsychopharmacology* 2004;29(10):1831-1840

ALZET Comments: Fluoxetine; desipramine; reboxetine; Ethanol; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; comparison of acute IP injections vs. mp; 5% ethanol.

P6933: E. Tiraboschi, *et al.* Antidepressants activate CaMKII in neuron cell body by Thr286 phosphorylation. *NeuroReport* 2004;15(15):2393-2396



ALZET Comments: Desipramine; reboxetine; Ethanol; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; comparison of IP injections vs. SC mp; 5% ethanol used; antidepressants.

P6795: A. A. Russo-Neustadt, *et al.* Hippocampal brain-derived neurotrophic factor expression following treatment with reboxetine, citalopram, and physical exercise. *Neuropsychopharmacology* 2004;29(12):2189-2199

ALZET Comments: Citalopram; reboxetine; SC; Rat; 2,7,14 days; Controls received mp w/ saline; "Reboxetine was infused via osmotic minipump in this experiment because sores developed on injection sites when reboxetine was administered IP (injection) for more than 7 consecutive days." (p. 2190).

23. Ritanserin

P3916: M. M. El, *et al.* In vivo electrophysiological characterization of 5-HT receptors in the guinea pig head of caudate nucleus and orbitofrontal cortex. *Neuropharmacology* 1997;36(4/5):577-588

ALZET Comments: Metergoline; Ritanserin; SC; Guinea pig; 4 day; antidepressant; controls received mp w/ NaCl; comparison of IV injections vs. mp.

24. Sertraline

Q4868: O. Otlivanchik, *et al.* Orexin signaling is necessary for hypoglycemia-induced prevention of conditioned place preference. *Am J Physiol Regul Integr Comp Physiol* 2016;310(R66-R73)

ALZET Comments: Sertraline; Ethanol; SC; Rat; 2001; 1 week; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 7-8 weeks old, 250-400g); 50% ethanol used; behavioral testing (open field); diabetes; Dose (7.5 mg/kg/day);

Q1779: H. Furmaga, *et al.* Comparison of Delta FosB Immunoreactivity Induced by Vagal Nerve Stimulation with That Caused by Pharmacologically Diverse Antidepressants. *Journal of Pharmacology and Experimental Therapeutics* 2012;341(2):317-325

ALZET Comments: Desipramine; sertraline; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 250-350 g).

Q2136: H. Furmaga, *et al.* Vagal Nerve Stimulation Rapidly Activates Brain-Derived Neurotrophic Factor Receptor TrkB in Rat Brain. *PLoS One* 2012;7(5):U65-U74

ALZET Comments: Sertraline; desipramine; Ethanol; saline; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, adult, male, 250-350 g); nitrocellulose filters used; 10% ethanol used.

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;

P9879: Z. Zhao, *et al.* Association of Changes in Norepinephrine and Serotonin Transporter Expression with the Long-Term Behavioral Effects of Antidepressant Drugs. *Neuropsychopharmacology* 2009;34(6):1467-1481



ALZET Comments: Protriptyline; reboxetine; sertraline; venlafaxine; DMSO; saline; ethanol; SC; Rat; 2ML2; 2ML4; 14, 42 days; Controls received mp w/ vehicle; long-term study; pumps replaced after 21 days; animal info (male, Sprague Dawley, 300-350 g.); 50% DMSO used; 10% ethanol used.

P8759: N. M. Sanders, *et al.* The selective serotonin reuptake inhibitor sertraline enhances counterregulatory responses to hypoglycemia. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2008;294(5):E853-E860

ALZET Comments: Sertraline; Ethanol; water, distilled; SC; Rat; 2001; 2ML4; 6, 20 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 370-460g); 50% EtOH used; endocrinology.

P8973: D. V. Rossi, *et al.* Chronic administration of venlafaxine fails to attenuate 5-HT_{1A} receptor function at the level of receptor-G protein interaction. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2006;9(4):393-406

ALZET Comments: Amitriptyline HCl; sertraline HCl; venlafaxine HCl; Water, sterile; ethanol; SC; Rat; 2ML4; 21 days; Controls received mp w/ saline; functionality of mp verified by serum drug concentrations; dose- response (fig. 1); animal info (male, Sprague Dawley, 200-275 g.); 40% ethanol used; behavioral testing (hypothermic response).

P7726: G. G. Gould, *et al.* A comparison of the chronic treatment effects of venlafaxine and other antidepressants on serotonin and norepinephrine transporters. *Biological Psychiatry* 2006;59(5):408-414

ALZET Comments: Venlafaxine; sertraline; amitriptyline; paroxetine; desipramine; citalopram; Saline; water, deionized; ethanol; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug concentrations; dose-response (fig1); animal info (male, Sprague-Dawley, 150-200g); 50% EtOH in H₂O.

P7901: T. H. Ahern, *et al.* The effects of chronic norepinephrine transporter inactivation on seizure susceptibility in mice. *Neuropsychopharmacology* 2006;31(4):730-738

ALZET Comments: Reboxetine; sertraline; desipramine; bupropion; imipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug levels; dose-response (fig. 4); comparison of IP injections vs. mp; stress/adverse reaction: (see pg. 731) Dbh -/- mice did not tolerate mp surgery well and showed signs of general malaise. All other mice strains showed no stress.; post op. care (buprenorphine); animal info (female, male, 3-7 month old; C57BL/6J NET -/- or wt; 257BL/6J 129SvEv Dbh -/-, +/-) 50% ethanol; mp primed 2 days in 37 celsius saline; "we achieved serum levels that fell within or very close to human therapeutic range for each drug with the exception of sertraline." (pg. 732).

P7514: C. H. K. West, *et al.* A selective test for antidepressant treatments using rats bred for stress-induced reduction of motor activity in the swim test. *Psychopharmacology* 2005;182(1):9-23

ALZET Comments: Amitriptyline HCl; venlafaxine HCl; clordiazepoxide HCl; imipramine HCl; phenelzine sulfate; scopolamine HBr; desipramine HCl; bupropion HCl; chlorpheniramine maleate; fluoxetine HCl; sertraline; amphetamine sulfate, D-; Water, sterile distilled; PEG; SC; Rat; 2ML2; 6,14 days; Controls received mp w/ vehicle; functionality of mp verified by agent blood levels; dose-response (fig. 5); animal info (male, female, susceptible, selectively bred); some animals had saline-filled catheter attached to mp to delay drug infusion by 5 days; "The most notable advantage of minipump delivery is that it eliminates stress resulting from daily injection of drug....minipumps also provide constant infusion of drug" (pg. 22).

25. Sulpiride

P2115: L.-W. Zhou, *et al.* Triazolam blocks the initial rotational effects of quinpirole but permits the later developing reduction of dopamine D₂-mediated rotational behavior and dopamine D₂ receptors. *Eur. J. Pharmacol* 1992;218(219-227)

ALZET Comments: Quinpirole HCl; Sulpiride; Triazolam; Ascorbic acid; DMSO; SC; mice; 2001; 6 days; Quinpirole is a dopamine agonist; antidepressant; stability verified in vitro for 7 days.

P1444: H. Ueda. Time course study of changes in the activity of rats during intraventricular infusion of 6-hydroxydopamine, haloperidol and sulpiride: a study of the relationship between an origin of the negative symptoms in schizophrenia and catecholamines. *J. Iwate Med. Assoc* 1988;40(3):385-398

ALZET Comments: Dopamine, 6-hydroxy-; Haloperidol; Sulpiride; CSF/CNS; Rat; 8 days; Japanese, English abstract.



P0630: B. Costall, *et al.* The continuity of dopamine receptor antagonism can dictate the long-term behavioural consequences of a mesolimbic infusion of dopamine. *Neuropharmacology* 1985;2(3):193-197

ALZET Comments: Dopamine HCl; Sulpiride; Nitrogen; Sodium metabisulfite; CSF/CNS (nucleus accumbens); IP; Rat; 13 days; mp model not stated; comparison of Sulp ip injec vs. mp infusion; 2 mp/rat - bilateral infusion; mp primed overnight; vehicles listed used w/DOP; concomitant Sulp admin. ip.

26. Tansospirone

P2873: S. Wieland, *et al.* Effect of chronic treatments with tansospirone and imipramine on serotonin-mediated behavioral responses and monoamine receptors. *Neuropharmacology* 1993;32(6):561-573

ALZET Comments: Tansospirone; Imipramine; 1-PP; Water, deionized; SC; Rat; 2ML2; 14 days, 24 hours; antidepressant; controls received mp with saline; comparison of sc injections vs. mp; 1-PP is a tansospirone metabolite; tansospirone is an azapirone; multiple pumps per animal (2).

P2279: R. Godbout, *et al.* Tansospirone and its metabolite, 1-(2-pyrimidinyl)-piperazine-I. effects of acute and long-term administration of tansospirone on serotonin neurotransmission. *Neuropharmacology* 1991;30(7):679-690

ALZET Comments: Tansospirone; Saline; SC; Rat; 2ML2; 14 days; controls received mp w/saline; tansospirone is SM-3997, a 5-HT_{1A} receptor ligand.

27. Tianeptine

P2785: G. Pineyro, *et al.* Effect of prolonged administration of tianeptine on 5-HT neurotransmission: an electrophysiological study in the rat hippocampus and dorsal raphe. *Naunyn-Schmiedeberg's Arch. Pharmacol* 1995;351(119-125)

ALZET Comments: Tianeptine; SC; Rat; 14 days; controls received mp w/ saline; tianeptine is a tricyclic antidepressant.

P3325: G. Pineyro, *et al.* Effect of acute and prolonged tianeptine administration on the 5-HT transporter: electrophysiological, biochemical and radioligand binding studies in the rat brain. *Naunyn-Schmiedeberg's Arch. Pharmacol* 1995;351(111-118)

ALZET Comments: Tianeptine; SC; Rat; 14 days; antidepressant; controls received mp w/saline; comparison of IV injections vs. mp; half-life of tianeptine is 2.5 hrs, (p.117).

28. Tranylcypromine

Q0143: S. Argueelles, *et al.* Degeneration of dopaminergic neurons induced by thrombin injection in the substantia nigra of the rat is enhanced by dexamethasone: Role of monoamine oxidase enzyme. *Neurotoxicology* 2010;31(1):55-66

ALZET Comments: Tranylcypromine; Saline; SC; Rat; 2002; 12 days; Animal info (female, albino, Wistar, 200-250 g.).

P5193: S. C. Stout, *et al.* Regulation of corticotropin-releasing factor neuronal systems and hypothalamic-pituitary-adrenal axis activity by stress and chronic antidepressant treatment. *Journal of Pharmacology and Experimental Therapeutics* 2002;300(3):1085-1092

ALZET Comments: Reboxetine methanesulfonate; fluoxetine HCl; Venlafaxine HCl; Tranylcypromine HCl; Saline; DMSO; SC; Rat; 2ML2; 2ML4; 26 or 27 days; antidepressant; Controls received mp w/ vehicle; functionality of mp verified by drug serum levels; 2ML2 pumps replaced after 2 weeks; 2ML4 pumps used for all antidepressants except fluoxetine, which required serial 2ML2 implantation due to solubility problems; venlafaxine given for 27 days; all other drugs infused for 26 days; fluoxetine vehicle was 12% DMSO.



P2971: R. L. Sherry-McKenna, *et al.* Monoamine oxidase inhibitors: effects on tryptophan concentrations in the rat brain. *J. Neural Transm* 1994;41(155-163

ALZET Comments: Phenelzine; Tranylcypromine, 4-methoxy-; Acetylphenelzine, N2-; Tranylcypromine, 4-fluoro-; Tranylcypromine; Deprenyl; SC; IP; Rat; 28 days; antidepressant; controls received mp with vehicle; comparison of TCP and PLZ ip injections vs. mp.

P2735: D. B. Goodnough, *et al.* Effects of low- and high-dose tranylcypromine on [3H]tryptamine binding sites in the rat hippocampus and striatum. *Neurochem. Res* 1994;19(1):5-8

ALZET Comments: Tranylcypromine; Water, distilled; SC; Rat; 2ML2; 4,10 or 28 days; antidepressant; controls received mp w/ water; enzyme inhibitor.

P2734: D. B. Goodnough, *et al.* Comparisons of the actions of high and low doses of the MAO inhibitor tranylcypromine on 5-HT2 binding sites in rat cortex. *J. Neural Transm* 1994;41(Suppl):127-134

ALZET Comments: Tranylcypromine; Water, distilled; SC; Rat; 2ML2; 4,10 or 28 days; antidepressant; controls received mp w/ water; enzyme inhibitor.

P2733: D. B. Goodnough, *et al.* Tranylcypromine does not enhance the effects of amitriptyline on 5-HT2 receptors in rat cerebral cortex. *J. Pharm. Sci* 1994;83(1):100-103

ALZET Comments: Amitriptyline; Tranylcypromine; Water, distilled; SC; Rat; 2ML2; 4, 10 or 28 days; antidepressant; controls received mp w/ vehicle; enzyme inhibitor; tranylcypromine is an MAO inhibitor; amitriptyline infused alone and in combination with tranylcypromine.

P2906: P. R. Paetsch, *et al.* Effects of chronic antidepressant treatment on B-adrenoceptor subtype binding in the rat cerebral cortex and cerebellum. *Mol. and Chem. Neuropathy* 1993;20(21-31

ALZET Comments: Desipramine HCl; Tranylcypromine HCl; Phenelzine sulfate; Water, distilled; SC; Rat; 2ML4; 28 days; antidepressant; controls received mp with vehicle.

P3067: D. D. Mousseau, *et al.* Effects of age and chronic antidepressant treatment on [3H]tryptamine and [3H]dihydroalprenolol binding to rat cortical membranes. *Cell. Molec. Neuro* 1993;13(1):3-13

ALZET Comments: Imipramine HCl; Desipramine HCl; Clomipramine HCl; Tranylcypromine HCl; Phenelzine sulfate; Clorgyline HCl; Deprenyl HCl; SC; Rat; 2002; 2ML4; 14,28 days; antidepressant; controls received mp with vehicle; drug concentrations determined from Greenshaw program.

P2972: R. L. Sherry-McKenna, *et al.* 4-Methoxytranylcypromine, a monoamine oxidase inhibitor: effects on biogenic amines in rat brain following chronic administration. *Biol. Psychiatry* 1992;31(881-888

ALZET Comments: Tranylcypromine; Tranylcypromine, 4-methoxy-; Water, distilled; SC; Rat; 28 days; antidepressant; controls received mp with vehicle.

P2406: P. R. Paetsch, *et al.* Effects of chronic antidepressant treatment on dopamine-related [3-H] SCH 23390 and [3H] spiperone binding in the rat striatum. *Cell. Molec. Neuro* 1992;12(6):597-606

ALZET Comments: Phenelzine sulfate; Tranylcypromine HCl; Desipramine HCl; Water; SC; Rat; 2ML4; 28 days; antidepressant; no comment posted.

29. Trazodone

Q2088: R. Ghanbari, *et al.* Electrophysiological impact of trazodone on the dopamine and norepinephrine systems in the rat brain. *European Neuropsychopharmacology* 2012;22(7):518-526

ALZET Comments: Trazodone; Cyclodextrin, hydroxypropyl beta; SC; Rat; 2, 14 days; Controls received mp w/ vehicle; animal info (Wistar, male, 280-320 g); 20% cyclodextrin used; electrophysiology.



Q1569: R. Ghanbari, *et al.* Sustained Administration of Trazodone Enhances Serotonergic Neurotransmission: In Vivo Electrophysiological Study in the Rat Brain. *Journal of Pharmacology and Experimental Therapeutics* 2010;335(1):197-206
ALZET Comments: Trazodone; Cyclodextrin, hydroxypropyl, beta-; SC; Rat; 2, 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 250-350 g); 20% cyclodextrin used; dose-response.

P1695: H. Kubota, *et al.* Mechanisms of the B-adrenoceptor down-regulation by the treatment with antidepressants in the rat cerebral cortex: effects of continuous administration of antidepressants by an osmotic pump. *Jpn. J. Psychiatry Neurol* 1990;44(1):135-136

ALZET Comments: Tunicamycin; Cycloheximide; Desipramine; Fluoxetine; Mianserin; Trazodone; CSF/CNS; SC; Rat; 2001; 2ML1; 4-7 days; comparison of sc injections vs. mp; cyclo. and tunica. delivered icv for 5 days.

P0694: K. G. Lloyd, *et al.* Upregulation of gamma-aminobutyric acid (GABA) B binding sites in rat frontal cortex: a common action of repeated administration of different classes of antidepressants and electroshock. *J. Pharmacol. Exp. Ther* 1985;235(1):191-199

ALZET Comments: Maprotiline; Nomifensine; Amitriptyline; Citalopram; Desipramine; Pargyline; Trazodone; Viloxazine; Zimeldine; SC; Rat; 2002; 6-18 days; comparison of agents effects; comparison of single dose ip injec vs. mp infusion and repeated ip injec of other psychotropic drugs vs. electroshock treatment; antihypertensive.

30. Tryptophan, Hydroxy

P1882: A. Baron, *et al.* Reduction in the elevated blood pressure of Dahl salt-sensitive rats treated chronically with L-5-hydroxytryptophan. *Pharmacology* 1991;42(15-22)

ALZET Comments: Tryptophan, L-5-hydroxy; SC; Rat; 2001; no duration posted; pumps replaced four times during study; incorrectly states model 2001 pumps at 2ul/hr, early study showed compound stability for 1 week.

P2495: M. J. Fregly, *et al.* Chronic treatment with L-5-hydroxytryptophan prevents the development of DOCA-salt-induced hypertension in rats. *J. Hypertens* 1987;5(621-628)

ALZET Comments: Tryptophan, L-5-hydroxy; SC; Rat; 2001; no duration posted; stability verified by HPLC after 6.5 days in pumps.

31. Tryptophan

Q3951: T. Laeger, *et al.* Leucine acts in the brain to suppress food intake but does not function as a physiological signal of low dietary protein. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 2014;307(R310-R320)

ALZET Comments: Arginine; cystine, histidine; isoleucine; leucine; lysine; methionine; phenylalanine; threonine; tryptophan; tyrosine; valine; CSF/CNS; Rat; 2002; 6 days; Animal info (male, Sprague Dawley, 5-7 weeks old);

Q3425: D. Burger, *et al.* Effects of a domain-selective ACE inhibitor in a mouse model of chronic angiotensin II-dependent hypertension. *Clinical Science* 2014;127(57-63)

ALZET Comments: Lisinopril; lisinopril-tryptophan; Saline; Mice (transgenic); 2 weeks; Controls received mp w/ vehicle; animal info (TtRhRen, 2-3 months old); cardiovascular; antihypertensive; lisinopril-tryptophan aka lisW-S; bp measured using tail cuff and radiotelemetry;

P2512: E. H. Y. Lee. Effects of tryptophan administration on tetrahydrobiopterin level in rat caudate nucleus. *Neurochem. Int* 1991;19(3):363-366

ALZET Comments: Tryptophan, L-; SC; Rat; 2001; 7 days; 24 hours; antidepressant; controls received sc injections of saline; comparison of sc injections vs. mp; stress/adverse reaction: pg. 364; connective tissue grew over mp opening.



P1254: R. I. Peters, *et al.* Tryptophan and serotonin metabolism after sustained tryptophan infusion. *Neurochem. Int* 1984;6(5):685-691

ALZET Comments: Tryptophan, l-; Ammonium hydroxide; SC; mice; 2001; 24, 96 hours; controls received mp w/ vehicle; dose-response (graph); NH4OH was used as vehicle for TRP due to the limited solubility of TRP in water and saline; no stress.

32. Venlafaxine

Q6771: S. Schreiber, *et al.* Interaction between methylphenidate, methadone and different antidepressant drugs on antinociception in mice, and possible clinical implications. *World J Biol Psychiatry* 2017;18(4):300-307

ALZET Comments: methadone; escitalopram; venlafaxine; desipramine; clomipramine; SC; Mice; 2002; 14 days; Dose: methadone (0.5 mg/kg) venlafaxine (2.5 mg/kg); escitalopram (20mg/kg); desipramine (1mg/kg); clomipramine (0.5 mg/kg); animal info (Male ICR mice, 25-35g); dependence.

Q4126: V. Tamasi, *et al.* Transcriptional Evidence for the Role of Chronic Venlafaxine Treatment in Neurotrophic Signaling and Neuroplasticity Including also Glutamatergic- and Insulin-Mediated Neuronal Processes. *PLoS One* 2014;9(U773-U796

ALZET Comments: Venlafaxine; NaCl; SC; Rat; 2001; 3 weeks; Controls received sham surgery; animal info (male, Dark Agouti, 8 weeks old; 150g); diabetes;.

Q1431: C. H. K. West, *et al.* Effects of chronic antidepressant drug administration and electroconvulsive shock on activity of dopaminergic neurons in the ventral tegmentum. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2011;14(2):201-210

ALZET Comments: Desipramine hydrochloride; imipramine hydrochloride; fluoxetine hydrochloride; paroxetine hydrochloride; sertraline hydrochloride; venlafaxine hydrochloride; bupropion hydrochloride; phenelzine sulfate; Polyethylene glycol; DMSO; water; water, distilled; SC; IP; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, albino, Sprague-Dawley, 550-700 g); functionality of mp verified by drug levels in circulation; good methods, pg 4; 25% DMSO used; IP catheter used; silastic tubing used; "The distal end of the silastic tubing, including the bulb, was then introduced surgically into the peritoneal cavity and the peritoneal wall sutured closed so that the bulb prevented the tubing from being withdrawn back into the subcutaneous space, thereby enabling... delivery of drug from the pump into the peritoneal cavity." pg 4;.

P9879: Z. Zhao, *et al.* Association of Changes in Norepinephrine and Serotonin Transporter Expression with the Long-Term Behavioral Effects of Antidepressant Drugs. *Neuropsychopharmacology* 2009;34(6):1467-1481

ALZET Comments: Protriptyline; reboxetine; sertraline; venlafaxine; DMSO; saline; ethanol; SC; Rat; 2ML2; 2ML4; 14, 42 days; Controls received mp w/ vehicle; long-term study; pumps replaced after 21 days; animal info (male, Sprague Dawley, 300-350 g.); 50% DMSO used; 10% ethanol used.

P9571: P. Vollmar, *et al.* The antidepressant venlafaxine ameliorates murine experimental autoimmune encephalomyelitis by suppression of pro-inflammatory cytokines. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2009;12(4):525-536

ALZET Comments: Venlafaxine; PBS; SC; Mice; 2002; 14 days; Controls received mp w/vehicle; animal info (female, SJL/J, 6-12 wks).

P9307: R. Mostany, *et al.* A role for nuclear beta-catenin in SNRI antidepressant-induced hippocampal cell proliferation. *Neuropharmacology* 2008;55(1):18-26

ALZET Comments: Venlafaxine HCl; Saline; SC; Rat; 2002; 14 days; Controls received mp w/ vehicle; dose-response (fig. 1); animal info (male, Albino Wistar, 175-200 g.).

P8973: D. V. Rossi, *et al.* Chronic administration of venlafaxine fails to attenuate 5-HT_{1A} receptor function at the level of receptor-G protein interaction. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2006;9(4):393-406



ALZET Comments: Amitriptyline HCl; sertraline HCl; venlafaxine HCl; Water, sterile; ethanol; SC; Rat; 2ML4; 21 days; Controls received mp w/ saline; functionality of mp verified by serum drug concentrations; dose- response (fig. 1); animal info (male, Sprague Dawley, 200-275 g.); 40% ethanol used; behavioral testing (hypothermic response).

P8069: H. A. Mitchell, *et al.* The effects of norepinephrine transporter inactivation on locomotor activity in mice. *Biological Psychiatry* 2006;60(10):1046-1052

ALZET Comments: Reboxetine; bupropion; imipramine; desipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 18-20 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; no stress (see p.1049); post op. care (Buprenorphine); animal info (male, female, C57BL6/J, 3-7 months old); 50% ETOH vehicle for desipramine; mp primed 1 day in 37 celsius saline.

P7726: G. G. Gould, *et al.* A comparison of the chronic treatment effects of venlafaxine and other antidepressants on serotonin and norepinephrine transporters. *Biological Psychiatry* 2006;59(5):408-414

ALZET Comments: Venlafaxine; sertraline; amitriptyline; paroxetine; desipramine; citalopram; Saline; water, deionized; ethanol; SC; Rat; 2ML4; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug concentrations; dose-response (fig1); animal info (male, Sprague-Dawley, 150-200g); 50% EtoH in H2O.

P7901: T. H. Ahern, *et al.* The effects of chronic norepinephrine transporter inactivation on seizure susceptibility in mice. *Neuropsychopharmacology* 2006;31(4):730-738

ALZET Comments: Reboxetine; sertraline; desipramine; bupropion; imipramine; venlafaxine; Saline; ethanol; IP; Mice; 2004; 21 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug levels; dose-response (fig. 4); comparison of IP injections vs. mp; stress/adverse reaction: (see pg. 731) Dbh -/- mice did not tolerate mp surgery well and showed signs of general malaise. All other mice strains showed no stress.; post op. care (buprenorphine); animal info (female, male, 3-7 month old; C57BL/6J NET -/- or wt; 257BL/6J 129SvEv Dbh -/-, +/-) 50% ethanol; mp primed 2 days in 37 celsius saline; "we achieved serum levels that fell within or very close to human therapeutic range for each drug with the exception of sertraline." (pg. 732).

P7514: C. H. K. West, *et al.* A selective test for antidepressant treatments using rats bred for stress-induced reduction of motor activity in the swim test. *Psychopharmacology* 2005;182(1):9-23

ALZET Comments: Amitriptyline HCl; venlafaxine HCl; clordiazepoxide HCl; imipramine HCl; phenelzine sulfate; scopolamine HBr; desipramine HCl; bupropion HCl; chlorpheniramine maleate; fluoxetine HCl; sertraline; amphetamine sulfate, D-; Water, sterile distilled; PEG; SC; Rat; 2ML2; 6,14 days; Controls received mp w/ vehicle; functionality of mp verified by agent blood levels; dose-response (fig. 5); animal info (male, female, susceptible, selectively bred); some animals had saline-filled catheter attached to mp to delay drug infusion by 5 days; "The most notable advantage of minipump delivery is that it eliminates stress resulting from daily injection of drug....minipumps also provide constant infusion of drug" (pg. 22).

33. Viloxazine

P0694: K. G. Lloyd, *et al.* Upregulation of gamma-aminobutyric acid (GABA) B binding sites in rat frontal cortex: a common action of repeated administration of different classes of antidepressants and electroshock. *J. Pharmacol. Exp. Ther* 1985;235(1):191-199

ALZET Comments: Maprotiline; Nomifensine; Amitriptyline; Citalopram; Desipramine; Pargyline; Trazodone; Viloxazine; Zimeldine; SC; Rat; 2002; 6-18 days; comparison of agents effects; comparison of single dose ip injec vs. mp infusion and repeated ip injec of other psychotropic drugs vs. electroshock treatment; antihypertensive.

P0552: A. Pilc, *et al.* Chronic antidepressants and GABA 'B' receptors: a GABA hypothesis of antidepressant drug action. *Life Sci* 1984;35(21):2149-2154

ALZET Comments: Amitriptyline; Citalopram; Desipramine; Pargyline; Viloxazine; Saline; SC; Rat; 2002; 18 days; comparison of acute ip injec vs. mp infusion; comparison of agents effects; antihypertensive.



34. Zimeldine

P0694: K. G. Lloyd, *et al.* Upregulation of gamma-aminobutyric acid (GABA) B binding sites in rat frontal cortex: a common action of repeated administration of different classes of antidepressants and electroshock. *J. Pharmacol. Exp. Ther* 1985;235(1):191-199

ALZET Comments: Maprotiline; Nomifensine; Amitriptyline; Citalopram; Desipramine; Pargyline; Trazodone; Viloxazine; Zimeldine; SC; Rat; 2002; 6-18 days; comparison of agents effects; comparison of single dose ip injec vs. mp infusion and repeated ip injec of other psychotropic drugs vs. electroshock treatment; antihypertensive.