

## Recent References on the Administration of Antiviral Agents Using ALZET® Osmotic Pumps

#### **Acyclovir**

**Q3927:** N. Ito, et al. Organic Cation Transporter/Solute Carrier Family 22a is Involved in Drug Transfer into Milk in Mice. Journal of Pharmaceutical Sciences 2014;103(3342-3348

**Agents:** Acyclovir; cimetidine; clindamycin; metformin; terbutaline; verapamil; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** 72 hours;

**ALZET Comments:** Animal info (female, lactating, Bcrp KO or WT FVB); functionality of mp verified by plasma and milk concentrations; no stress "All mice survived the surgical procedure and appeared to be lactating normally, and all pups thrived throughout the course of the experiment." (see pg. 3343);

**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

**Agents:** 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. **Vehicle:** DMSO; water; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** Not Stated;

**ALZET Comments:** 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.

**Q7594:** K. Valerie, *et al.* Substantially improved in vivo radiosensitization of rat glioma with mutant HSV-TK and acyclovir. Cancer Gene Therapy 2001;8(1):3-8

Agents: Acyclovir Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML1; Duration: 7 days;

**ALZET Comments:** Dose (100mg/kg); Controls received Ad-beta-gal treatment and mp w/ agent; animal info (female, Fischer 344, 150-160g); cancer (glioma);

**P0379:** D. Myerson, *et al.* Prophylactic and therapeutic treatment with acyclovir of genital herpes in the guinea pig (41717). Proc. Soc. Exp. Biol. Med 1983;174(147-152

**Agents:** Acyclovir, sodium **Vehicle:** Saline; **Route:** SC; **Species:** Guinea pig; **Pump:** 2ML2; **Duration:** 1 week; **ALZET Comments:** comparison of ip inject vs. mp infusion; article states incorrectly that 2ML2 is spent after 7 days

#### **Amantadine**

**Q6943:** E. F. Brigham, *et al.* Pharmacokinetic/Pharmacodynamic Correlation Analysis of Amantadine for Levodopa-Induced Dyskinesia. J Pharmacol Exp Ther 2018;367(2):373-381

Agents: Amantadine Vehicle: Sodium acetate; Route: SC; Species: Rat; Pump: 2ML2; Duration: Not Stated;

ALZET Comments: Dose (22.5, 45, or 83 mg/kg per day); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats);

**Q3272:** E. Y. K. Huang, *et al.* Amantadine Ameliorates Dopamine-Releasing Deficits and Behavioral Deficits in Rats after Fluid Percussion Injury. PLoS One 2014;9(1):U118-U131

Agents: Amantadine Vehicle: Saline; Route: SC; Species: Rat; Pump: 2006; Duration: 8 weeks;

ALZET Comments: Control animals received mp w/ vehicle; animal info (male, SD, 200-250 g, 6 wks old); long-term study

**P4224:** M. B. Hesselink, *et al.* Brain penetration and in vivo recovery of NMDA receptor antagonists amantadine and memantine: a quantitative microdialysis study. Pharmaceut. Res 1999;16(5):637-642

Agents: Memantine; Amantadine Vehicle: Water; Route: SC; Species: Rat; Pump: 2ML2; Duration: Not Stated;

**ALZET Comments:** Dose-response; serum levels





**P4321:** M. B. Hesselink, *et al.* Adaptations of NMDA and dopamine D<sub>2</sub>, but not of muscarinic receptors following 14 days administration of uncompetitive NMDA receptor antagonists. Journal of Neural Transmission 1999;106(409-421 **Agents:** MK-801; Memantine; Amantadine **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 3,14 days; **ALZET Comments:** Controls received sham surgeries; comparison of S.C. injections vs. mp; half-life (p. 411); "In the clinical situation, depending on dosing schedule, only minor fluctuations in the steady-state plasma levels of the aminoadamantanes is observed. The only way to mimic this in animals is by continuous infusion of the drug using ALZET osmotic minipumps." (p.

**P3920:** L. Stitz, et al. Lack of antiviral effect of amantadine in borna disease virus infection. Med Microbiol Immunol 1998;186(195-200

**Agents:** Adamantane, 1-amino- **Vehicle:** Water, sterile distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days; **ALZET Comments:** functionality of mp verified by serum levels; comparison of oral doses vs. mp; immunology; agent is NMDA antagonist also called amantadine or 1-adamantanamide

**R0187:** W. Danysz, *et al.* Aminoadamantanes as NMDA Receptor Antagonists and Antiparkinsonian Agents - Preclinical Studies. Neurosci Biobehav Rev 1997;21(4):455-468

**Agents:** Amantadine; memantine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7, 14 days; **ALZET Comments:** Neurodegenerative (Parkinson's disease)

#### **Azidothymidine**

411)

**P2211:** A. F. Tarantal, *et al.* Pre and postnatal treatment of the rhesus macaque (Macaca mulatta) with azidothymidine: I. fetal studies. Pediatr. Aids HIV Infection: Fetus to Adolescent 1994;5(1):10-19

**Agents:** Azidothymidine **Vehicle:** Sodium hydroxide; **Route:** SC; **Species:** Monkey (pregnant); **Pump:** 2ML4; **Duration:** 28 days; **ALZET Comments:** Controls received mp w/vehicle; functionality of mp verified by plasma levels of AZT; teratology; AZT is azidothymidine, also known as zidovudine; multiple pumps per animal (3-4); "Circulating levels of AZT remained constant during the course of treatment and were achieved by the first (24 hr.) sample (p. 11); antiretroviral drug

**P2093:** M. Sinet, *et al.* Efficacy of continuous zidovudine infusion at early stages of retroviral infection in mice. J. Acquir. Immune Defic. Syndr 1992;5(577-582

**Agents:** Azidothymidine **Vehicle:** Propylene glycol; Water; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 5 days; **ALZET Comments:** Functionality of mp verified by plasma AZT levels; comparison of b.i.d. s.c. injections vs. mp; good methods; pK; half-life (p.577); continuous infusion significantly more effective than bolus injection; antiretroviral drug

**P1928:** J. A. Bilello, *et al.* Use of a neonatal murine retrovirus model to evaluate the long-term efficacy and toxicity of antiviral agents. Annals of the New York Academy of Sciences 1990;616(238-251

**Agents:** Azidothymidine **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (pregnant); **Pump:** 2001; **Duration:** 21 days; **ALZET Comments:** Pumps replaced after each week to achieve 3 weeks duration; immunology; teratology; oral delivery of AZT resulted in highly variable plasma levels; antiretroviral drug

**P1644:** J. M. Gallo, et al. Pump delivery of azidothymidine: potential for constant concentrations and improved brain delivery. J. Controlled Release 1989;9(249-253

**Agents:** Azidothymidine **Vehicle:** Not Stated; **Route:** IA (carotid); **Species:** Rat; **Pump:** 2001; **Duration:** 3, 7 days; **ALZET Comments:** Dose-response; blood levels; comparison of IV injections vs. mp; good methods; antiviral; alkaline pH of 11 increased solubility and stability of AZT; antiretroviral drug

#### **Ganciclovir (2015-Present)**

**Q10870:** X. Zhang, *et al.* Ablating Adult Neural Stem Cells Improves Synaptic and Cognitive Functions in Alzheimer Models. Stem Cell Reports 2021;16(1):89-105

Agents: Ganciclovir Vehicle: Saline; Route: SC; Species: Mice; Pump: 2004; Duration: 7 days;

**ALZET Comments:** Dose: (20 mg/kg/day); 0.9% sterile saline vehicle used; animal info: APP/PS1 (Jax, 34,832) and hAPP-J20 mice (Jax MMRRC, 034836); behavioral testing (MWM and Y-maze tests); Ganciclovir aka (GCV)







**Q9293:** I. Jakovcevski, et al. Impact of Depletion of Microglia/Macrophages on Regeneration after Spinal Cord Injury. Neuroscience 2021;459(129-141

Agents: Ganciclovir Vehicle: PBS; Route: SC; Species: Mice; Pump: 1004; Duration: 28 days;

ALZET Comments: Dose (50 mg/ml); animal info (three-month-old female TK mice); spinal cord injury;

**Q8599:** L. Katsouri, et al. Ablation of reactive astrocytes exacerbates disease pathology in a model of Alzheimer's disease. Glia 2020;68(5):1017-1030

Agents: Ganciclovir Vehicle: Saline; Route: CSF/CNS (right lateral ventricle); Species: Mice; Duration: 2 weeks;

**ALZET Comments:** Dose (11 μg/ul/hr); Controls received mp w/ vehicle; animal info (APP23/GFAP-TK double transgenic mice, 9 months old); behavioral testing (Object location task; Y maze); Ganciclovir aka GCV; neurodegenerative (Alzheimer's disease);

**Q8450:** N. Drost, *et al.* The Amyloid-beta rich CNS environment alters myeloid cell functionality independent of their origin. Scientific Reports 2020;10(1):7152

Agents: Ganciclovir Vehicle: CSF, Artificial; Route: CSF/CNS (right lateral ventricle); Species: Mice; Pump: 2001; 2004;

**Duration:** 6 weeks;

**ALZET Comments:** Dose (2.5 mg); animal info (APPPS1 mice; CX3CR1-GFP mice; CD11b-HSVTK+/– mice); Ganciclovir aka Cymeven; neurodegenerative (Alzheimer's disease);

**Q9094:** P. Varma, et al. Targeting Seizure-Induced Neurogenesis in a Clinically Relevant Time Period Leads to Transient But Not Persistent Seizure Reduction. Journal of Neuroscience 2019;39(35):7019-7028

Agents: Ganciclovir Vehicle: Saline; Route: SC; Species: Mice; Pump: 2004; Duration: 8 weeks;

**ALZET Comments:** Dose (150 mg/kg/day); Controls received mp w/ vehicle; animal info (6 weeks old); pumps replaced every 4 weeks; neurodegenerative (Seizure);

**Q7949:** E. Butti, et al. Neural Stem Cells of the Subventricular Zone Contribute to Neuroprotection of the Corpus Callosum after Cuprizone-Induced Demyelination. J Neurosci 2019;39(28):5481-5492

Agents: ganciclovir Vehicle: water, double distilled; Route: SC; Species: Mice; Pump: 2002; Duration: 4 weeks;

**ALZET Comments:** Dose (100 mg/kg/d); Controls were WT and received mp w/ agent; animal info (6-8 weeks, female, C57BL/6 and NestinTK); pumps replaced every 2 weeks; neurodegenerative (multiple sclerosis);

**Q6925:** S. Kalin, *et al.* CNS myeloid cells critically regulate heat hyperalgesia. J Clin Invest 2018;128(7):2774-2786 **Agents:** Ganciclovir **Route:** CSF/CNS (lateral ventricle); **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 4 weeks; **ALZET Comments:** animal info (150- to 200-dayold adult male hemizygous CD11b-HSVTK (TK) mice (4) or their transgene-negative littermates); ALZET brain infusion kit used;

**Q7908:** Z. C. Hesp, *et al.* Proliferating NG2-Cell-Dependent Angiogenesis and Scar Formation Alter Axon Growth and Functional Recovery After Spinal Cord Injury in Mice. J Neurosci 2018;38(6):1366-1382

Agents: Ganciclovir Vehicle: Saline, physiological; Route: CSF/CNS (lateral ventricle); Species: Mice; Pump: 1002; 1007D;

**Duration:** 7, 11, 14 days;

**ALZET Comments:** 

**Q7124:** M. Cusimano, *et al.* Selective killing of spinal cord neural stem cells impairs locomotor recovery in a mouse model of spinal cord injury. J Neuroinflammation 2018;15(1):58

Agents: Ganciclovir Vehicle: Water; Route: SC; Species: Mice; Pump: 2002; Duration: 28 days;

**ALZET Comments:** Dose (100 mg/kg/day); animal info (NestinTK); pumps replaced every 2 weeks; neurodegenerative (Spinal Chord);

**Q5714:** W. Xu, et al. Myelin Basic Protein Regulates Primitive and Definitive Neural Stem Cell Proliferation from the Adult Spinal Cord. Stem Cells 2017;35(2):485-496

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 5 days; **ALZET Comments:** animal info (GFAP-TK); spinal cord injury; Brain Coordinates (0.2 mm AP from bregma, 0.7 mm ML, and 2.5 mm DV below the dura);



**Q5885:** R. L. Reeve, et al. Quiescent Oct4(+) Neural Stem Cells (NSCs) Repopulate Ablated Glial Fibrillary Acidic Protein(+) NSCs in the Adult Mouse Brain. Stem Cells 2017;35(9):2071-2082

**Agents:** Ara-C; ganciclovir **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1007D; **Duration:** 3 days; 7 days; 14 days; **ALZET Comments:** animal info (Oct4 CKO;tk); Brain coordinates (10.2 mm anterior, 10.7 mm lateral, depth of 2.5 mm below the skull, relative to bregma)

**Q6356:** J. Mircetic, *et al.* Development of a genetic sensor that eliminates p53 deficient cells. Nat Commun 2017;8(1):1463 **Agents:** Ganciclovir **Vehicle:** Water; **Route:** SC; **Species:** Mice (nude); **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Dose (20 mg/kg/day); Controls received mp w/ vehicle; animal info (12 week old NMRI (nu/nu) mice);

**Q5709:** H. Williams, et al. Suppression of neointima formation by targeting beta-catenin/TCF pathway. Bioscience Reports 2016;36(6):

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2002; 2004; Duration: 21 days;

ALZET Comments: Controls received mp w/ PBS; animal info (C57BL6J); Dose (25 mg/kg/day);

**Q4845:** A. G. Kotini, *et al.* Escape Mutations, Ganciclovir Resistance, and Teratoma Formation in Human iPSCs Expressing an HSVtk Suicide Gene. MOLECULAR THERAPY 2016;5(**Agents:** Ganciclovir **Vehicle:** PBS; **Route:** SC; **Species:** Mice (NSG); **Pump:** 1007D; **Duration:** 2 weeks;

**ALZET Comments:** animal info (female, NSG, 8 weeks old); pumps replaced every week; cancer (teratoma); Dose (5 mg/kg/day);

**Q5285:** N. H. Varvel, et al. Replacement of brain-resident myeloid cells does not alter cerebral amyloid-beta deposition in mouse models of Alzheimer's disease. J Exp Med 2015;212(11):1803-9

Agents: Valganciclovir Vehicle: PBS; Route: CSF/CNS (ventricle); Species: mice; Pump: 2004; Duration: 2 weeks; ALZET Comments: Controls received mp w/ vehicle; animal info (Female hemizygous TK mice crossed w/ male hemizygous APPPS1 or hemizygous APP23); ALZET brain infusion kit 3 used; good methods (pg. 11807); post op. care (paracetamol, i.p. 5 mg/kg daily; acetaminophen i.p. 5 mg/kg daily); brain tissue distribution; Dental cement used; Cannula placement verified via staining; anesthetized using ketamine and xylazine; Brain coordinates; from bregma: +0.1 mm anteroposterior, 1.0 mm lateral, and 2.5 mm dorsoventral; Dose (50 mg/ml);

**Q4258:** D. O. Seo, *et al.* Adult Hippocampal Neurogenesis Modulates Fear Learning through Associative and Nonassociative Mechanisms. JOURNAL OF NEUROSCIENCE 2015;35(11330-11345

Agents: Ganciclovir Vehicle: PBS; Route: CSF/CNS; Species: Mice; Pump: 1002; Duration: 2 weeks;

**ALZET Comments:** Control animals received mp w/ vehicle; animal info (8 wks old, DCX-TK transgenic, wt); ALZET brain infusion kit 3 used

**Q4578:** U. Schneider, et al. Microglia inflict delayed brain injury after subarachnoid hemorrhage. Acta Neuropathologica 2015:130(215-231

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 9 days; **ALZET Comments:** Animal info (CD11b-HSVTK, 14-14 weeks old, 22-25g); ALZET brain infusion kit used; immunology; noted 230 ul reservoir;

**Q4290:** K. Rolon-Reyes, et al. Microglia Activate Migration of Glioma Cells through a Pyk2 Intracellular Pathway. PLoS One 2015;10(U2306-U2323

**Agents:** Ganciclovir **Route:** CSF/CNS (intratumoral); **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ saline, normal; animal info (male, CD11b-HSVTK transgenic); ALZET brain infusion kit used; cancer (glioma GL261);

**Q5254:** S. Prokop, *et al.* Impact of peripheral myeloid cells on amyloid-beta pathology in Alzheimer's disease-like mice. J Exp Med 2015;212(11):1811-8

**Agents:** Ganciclovir **Vehicle:** CSF, artificial; **Route:** CSF/CNS (lateral ventricles); **Species:** Mice; **Pump:** 2001; **Duration:** 10 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (APPPS1 transgenic mice); brain infusion cannula used; neurodegenerative (Alzheimer's); Dose (2.5 mg/ml); Therapeutic indication (Alzheimer's Disease);



**Q4509:** K. J. Dixon, et al. Endogenous Neural Stem/Progenitor Cells Stabilize the Cortical Microenvironment after Traumatic Brain Injury. JOURNAL OF NEUROTRAUMA 2015;32(753-764

Agents: Ganciclovir sodium Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: 4 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (CD1 nestin TK, adult); pumps replaced every 2 weeks; behavioral testing (motor function/rotarod test); traumatic brain injury;

**Q4373:** K. O. Cho, et al. Aberrant hippocampal neurogenesis contributes to epilepsy and associated cognitive decline. Nature Communications 2015;6(U1-U13

Agents: Ganciclovir Vehicle: Water, distilled; Route: SC; Species: Mice; Pump: 2004; Duration: 4 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL6 or Nestin-TH, 6 weeks old); behavioral testing (epilepsy behavior, open field, memory); pumps removed after 4 weeks; epilepsy;

**Q4340:** M. L. Bustos, *et al.* Depletion of Bone Marrow CCSP-Expressing Cells Delays Airway Regeneration. MOLECULAR THERAPY 2015;23(561-569

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 15 days; **ALZET Comments:** Animal info (CCtk or WT);

**Q3378:** A. A. Swan, *et al.* Characterization of the Role of Adult Neurogenesis in Touch-Screen Discrimination Learning. Hippocampus 2014;24(1581-1591

Agents: Ganciclovir Vehicle: Saline, sterile; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;

**ALZET Comments:** Animal info (GFAP TK tg, wt); "prevent necrosis at the drug infusion site, the pumps were gently rotated within the subcutaneous space every other day." pg 1582

**Q3618:** N. Sachewsky, et al. Primitive Neural Stem Cells in the Adult Mammalian Brain Give Rise to GFAP-Expressing Neural Stem Cells. STEM CELL REPORTS 2014;2(810-824

**Agents:** Ganciclovir; Ara-C **Vehicle:** PBS; saline; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 21 days; 7 days:

ALZET Comments: Animal info (GFAP-TK); ischemia (cerebral); 2% AraC; 200uM GCV;

**Q3811:** R. E. Bennett, et al. Acute Reduction of Microglia Does Not Alter Axonal Injury in a Mouse Model of Repetitive Concussive Traumatic Brain Injury. Journal of Neurotrauma 2014;31(1647-1663

**Agents:** Valganciclovir **Vehicle:** Saline, sterile; **Route:** Not Stated; **Species:** Mice; **Pump:** 1002; 2004; **Duration:** Not Stated; **ALZET Comments:** Controls received mp w/ vehicle; animal info (CD11b-TK +/-,6-8 weeks); post op. care (antibacterial ointment; heating pad); cyanoacrylate adhesive; Cannula placement verified via histological analysis; used Plastics One Cannula; pumps primed at 37C for 36-48 hours; pumps removed after 7 days and reimplanted after two closed-skull injuries; traumatic brain injury;

**Q3143:** C. R. Sun, *et al.* Conditional Ablation of Neuroprogenitor Cells in Adult Mice Impedes Recovery of Poststroke Cognitive Function and Reduces Synaptic Connectivity in the Perforant Pathway. Journal of Neuroscience 2013;33(44):17314-17325 **Agents:** Ganciclovir **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 4 weeks; 8 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (male, 6 weeks old); pumps replaced every 2 weeks; ischemia (stroke); behavioral testing (Barnes maze test, ladder test, cat walk test);

**Q3079:** J. O. Groves, *et al.* Ablating Adult Neurogenesis in the Rat Has No Effect on Spatial Processing: Evidence from a Novel Pharmacogenetic Model. PLoS Genetics 2013;9(9):U87-U102

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (transgenic); **Pump:** 2ML4; **Duration:** 8 weeks; **ALZET Comments:** Controls received mp w/ vehicle; animal info (male, GFAP-TK, 8 weeks); pumps replaced every 4 weeks; dose-response (p11); behavioral testing (Morris water maze, spatial working memory, food neophobia, anxiety tests, radial maze, open field); long-term study;





**Q3490:** S. A. Grathwohl, *et al.* Replacement of osmotic minipumps to extend the intracerebral infusion time of compounds into the mouse brain. Biosensors and Bioelectronics 2013;55(2):75-78

Agents: Valganciclovir Vehicle: PBS; Route: CSF/CNS; Species: Mice; Pump: 2004; Duration: 2 weeks; 4 weeks;;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, hemizygous CD11b-HSVTK); ALZET brain infusion kit 3 used; post op. care (Paracetamol IP 5 mg/kg/day up to 3 days); Pumps primed in 37C PBS;

**Q3057:** M. L. Bustos, et al. Bone Marrow Cells Expressing Clara Cell Secretory Protein Increase Epithelial Repair After Ablation of Pulmonary Clara Cells. MOLECULAR THERAPY 2013;21(6):1251-1258

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 5 days; 10 days;

ALZET Comments: Animal info (CCtk, four month old, 24g); pumps used to induce symptoms

**Q2151:** X. M. Wang, *et al.* Conditional Depletion of Neurogenesis Inhibits Long-Term Recovery after Experimental Stroke in Mice. PLoS One 2012;7(6):U384-U391

**Agents:** Ganciclovir **Vehicle:** PBS; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** 1003D; **Duration:** 14 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (HSV-TK Tg, CD1); incorrectly listed Model 1003D as 0.25 ul/hr; MCAO; ischemia (cerebral)

**Q2437:** F. Sun, et al. Ablation of Neurogenesis Attenuates Recovery of Motor Function after Focal Cerebral Ischemia in Middle-Aged Mice. PLoS One 2012;7(10):U92-U99

Agents: Ganciclovir Vehicle: PBS; Route: Not Stated; Species: Mice; Pump: Not Stated; Duration: 14 days;

**ALZET Comments:** Control animals received mp w/ vehicle; animal info (DCX-TK+, DCX-TL-, 12 mo old, male); infusion rate of 0.25 ul/hr)

**Q5668:** M. V. Sofroniew. Transgenic techniques for cell ablation or molecular deletion to investigate functions of astrocytes and other GFAP-expressing cell types. Methods Mol Biol 2012;814(531-44

**Agents:** Ganciclovir **Vehicle:** Saline; **Route:** SC; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 7, 21, 42 days; **ALZET Comments:** animal info (mGFAP-TK mice, 30 grams); comparison of daily injections vs mp; Dose (10 mg/kg/day);

**Q2625:** Y. Niibori, *et al.* Suppression of adult neurogenesis impairs population coding of similar contexts in hippocampal CA3 region. Nature Communications 2012;3(;):U271-U277

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2002; Duration: Not Stated;

ALZET Comments: Animal info (TK+, wt, 8 wks old)

**Q5387:** S. M. Lehmann, et al. An unconventional role for miRNA: let-7 activates Toll-like receptor 7 and causes neurodegeneration. Nat Neurosci 2012;15(6):827-35

**Agents:** Ganciclovir **Vehicle:** CSF, artificial; **Route:** CSF/CNS (ventricles); **Species:** Mice; **Pump:** 2001; **Duration:** 10 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (C57Bl/6J-CD11b-HSVTK mice); functionality of mp verified by brain samples; brain infusion kit used; neurodegenerative (Alzheimer's Disease); Ablation of microglia done through administration of Ganciclovir; Dose (2 mg/mL);

**Q2403:** J. Chen, et al. A restricted cell population propagates glioblastoma growth after chemotherapy. Nature 2012;488(7412):522-U121

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 2002; 2004; **Duration:** 10 weeks; **ALZET Comments:** Control animals received mp w/ PBS; animal info (Mut7, 8-10 wks old); pumps replaced every 4 weeks; long-term study; cancer (glioblastoma)

**Q2315:** E. Butti, et al. Subventricular zone neural progenitors protect striatal neurons from glutamatergic excitotoxicity. Brain 2012;135(;):3320-3335

**Agents:** Ganciclovir; ara-C; HU210 **Vehicle:** Water, distilled; PBS; DMSO; Tween; URB597; **Route:** SC; CSF/CNS; CSF/CNS (striatum); **Species:** Mice; **Pump:** 2002; 1007D; **Duration:** 7, 28 days;

**ALZET Comments:** Animal info (NestinfloxGFPfloxTK); pumps replaced after 14 days; brain infusion kit 3 used; incorrectly listed Model 1007; enzyme inhibitor (fatty acid amid hydrolase); HU210 is a cannabinoid receptor agonist





**Q2952:** N. S. Burghardt, et al. Adult-born hippocampal neurons promote cognitive flexibility in mice. Hippocampus 2012;22(9):1795-1808

Agents: Ganciclovir Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 56 days;

**ALZET Comments:** Controls received mp w/ ganciclovir; animal info (male, 129Sv/Ev, 23-27wks old; GFAP-TK transgenic); multiple pumps used (2); behavioral testing (p.1796)

**Q1910:** M. E. Bernard, et al. Repopulation of the Irradiation Damaged Lung with Bone Marrow-derived Cells. In Vivo 2012;26(1):9-18

**Agents:** Ganciclovir **Vehicle:** Saline, normal; **Route:** SC; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 24 hours; **ALZET Comments:** Controls received mp w/ vehicle; animal info (FVB/NHsd, HSV-TK-CCSP transgenic littermates, 6-10 wks old)

Q0783: H. Y. Zhai, et al. Microglia/Macrophages Promote Glioma Progression. Glia 2011;59(3):472-485

Agents: Ganciclovir; macrophage/microglia inhibitory factor; tuftsin Vehicle: Not Stated; Route: CSF/CNS (intratumoral);

Species: Mice; Pump: Not Stated; Duration: 14, 28 days;

**ALZET Comments:** Negative controls received mp w/ saline; animal info (12-16 wks old, male, CD11b-HSVTK +/-, 25-30 g, C57BL/6); cancer (glioma); Plastics One guide cannula used; macrophage/microglia inhibitory factor also known as MIF/TKP is a tripeptide; tuftsin also known as threonine-lysine-proline-arginin or TKPR

**Q1416:** J. Yong, et al. Multimodality Imaging of beta-Cells in Mouse Models of Type 1 and 2 Diabetes. Diabetes 2011;60(5):1383-1392

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 14 days;

**ALZET Comments:** Animal info (C57BL/6 MIP-TF, 8 wks old)

**Q0942:** J. Wright, *et al.* Age-Related Changes in the Oligodendrocyte Progenitor Pool Influence Brain Remodeling after Injury. Developmental Neuroscience 2011;32(5-6):499-509

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: 2 weeks;

ALZET Comments: Controls received mp w/ distilled water; animal info (P14, 2 wks old)

**Q1400:** J. P. Wisor, *et al.* Cerebral microglia mediate sleep/wake and neuroinflammatory effects of methamphetamine. Brain, Behavior, and Immunity 2011;25(4):767-776

Agents: Ganciclovir Vehicle: HCl; saline; Route: CSF/CNS; Species: Mice; Pump: 2004; Duration: 30 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (CD11b-TKmt-30, tg); incorrectly listed Model 2004 rate as 2.5 ul/hr

**Q1952:** L. Wei, *et al.* Affiliative Behavior Requires Juvenile, But Not Adult Neurogenesis. Journal of Neuroscience 2011;31(40):14335-14345

**Agents:** Ganciclovir **Vehicle:** PBS, sterile; **Route:** SC; CSF/CNS; **Species:** Mice (transgenic); **Pump:** 2004; 1004; **Duration:** Not Stated:

ALZET Comments: Animal info (TK-GFP); brain infusion kit 3 used; "the skull was dried with acetone" pg 14336

**Q1697:** L. Van Landeghem, *et al.* Enteric glia promote intestinal mucosal healing via activation of focal adhesion kinase and release of proEGF. American Journal of Physiology Gastrointestinal and Liver Physiology 2011;300(6):G976-G987

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 7 days;

**ALZET Comments:** Animal info (GFAP-HSVtk Tg, 22 wks old)

**Q1112:** H. Han, et al. Synergistic effects of galectin-1 and reactive astrocytes on functional recovery after contusive spinal cord injury. Archives of Orthopaedic and Trauma Surgery 2011;131(6):829-839

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 1007D; Duration: Not Stated;

**ALZET Comments:** Animal info (16-18 wks old)





**Q0695:** C. A. Blaiss, *et al.* Temporally Specified Genetic Ablation of Neurogenesis Impairs Cognitive Recovery after Traumatic Brain Injury. Journal of Neuroscience 2011;31(13):4906-4916

Agents: Ganciclovir Vehicle: Water, deionized; Route: SC; Species: Mice; Pump: 2002; Duration: 2 weeks; 30 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (6 wks old, male, wild-type, nestin-HSV-tk); wound clips used; behavioral testing (Morris water maze, fear conditioning)

**Q2223:** K. Arnold, *et al.* Sox2(+) Adult Stem and Progenitor Cells Are Important for Tissue Regeneration and Survival of Mice. Cell Stem Cell 2011;9(4):317-329

Agents: Ganciclovir Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 1, 2 weeks;

ALZET Comments: Animal info (Sox2-TK, wt, 3, 10-wks old); 7 or 14 day pumps used

**Q0507:** M. M. Mirrione, et al. Microglial ablation and lipopolysaccharide preconditioning affects pilocarpine-induced seizures in mice. NEUROBIOLOGY OF DISEASE 2010;39(1):85-97

**Agents:** Ganciclovir **Vehicle:** Saline; PBS; **Route:** CSF/CNS (hippocampus); **Species:** Mice; **Pump:** 1002; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ vehicle; post op. care (buprenorphine HCl); animal info (CD1 1b-, HSVTk +/-, wt, male, female, adult, 20-25 g); Plastics One guide cannula used

**P9957:** K. L. Jin, et al. Transgenic ablation of doublecortin-expressing cells suppresses adult neurogenesis and worsens stroke outcome in mice. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2010;107(17):7993-7998

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 14 days; **ALZET Comments:** Controls received mp w/ saline; animal info (DCX-Tk); incorrectly stated 1003D pumps used

**Q0771:** G. J. Huang, *et al.* A Genetic and Functional Relationship between T Cells and Cellular Proliferation in the Adult Hippocampus. PLOS BIOLOGY 2010;8(12):U107-U116

Agents: Ganciclovir Vehicle: Not Stated; Route: CSF/CNS; Species: Mice; Pump: 2004; Duration: 4 weeks;

ALZET Comments: Animal info (GFAP-tk, nestin-tk); ALZET brain infusion kit 3 used

**P9471:** A. C. Zemke, *et al.* Molecular Staging of Epithelial Maturation Using Secretory Cell-Specific Genes as Markers. American Journal of Respiratory Cell and Molecular Biology 2009;40(3):340-348

**Agents:** Ganciclovir **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 6, 9 days; **ALZET Comments:** Controls received no treatment; animal info (male, CCSP-HSVtK, 8-10 wks old); airway injury model

**P9511:** R. Uchibori, *et al.* Retroviral vector-producing mesenchymal stem cells for targeted suicide cancer gene therapy. JOURNAL OF GENE MEDICINE 2009;11(5):373-381

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice (nude); **Pump:** Not Stated; **Duration:** 28 days; **ALZET Comments:** Controls received mp w/ PBS; animal info (6 wks old, male, Balb/c, nu/nu); gene therapy

**P9836:** R. M. Teisanu, *et al.* Prospective Isolation of Bronchiolar Stem Cells Based Upon Immunophenotypic and Autofluorescence Characteristics. Stem Cells 2009;27(3):612-622

**Agents:** Ganciclovir **Vehicle:** PBS; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** 2001D; **Duration:** 24 hours; **ALZET Comments:** Animal info (2-6 months old, CCSP-HSV+k)

**P9446:** J. C. Snyder, *et al.* Reparative Capacity of Airway Epithelium Impacts Deposition and Remodeling of Extracellular Matrix. American Journal of Respiratory Cell and Molecular Biology 2009;40(6):633-642

**Agents:** Ganciclovir **Vehicle:** Saline, pyrogen free; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 3, 6, 9, 10 days;

ALZET Comments: Controls received no treatment; animal info (adult, FVB/N CCtK); airway injury model







**P9804:** B. H. Singer, et al. Conditional Ablation and Recovery of Forebrain Neurogenesis in the Mouse. Journal of Comparative Neurology 2009;514(6):567-582

Agents: Ganciclovir Vehicle: Saline; Route: CSF/CNS; Species: Mice; Pump: 2004; Duration: 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; no stress (572); ALZET brain infusion kit 3 used; animal info (8-12 wks old, Nestin tk<sup>+</sup>. wt); "we did not observe any differences in the overt behavior of wild-type or nestin-tk<sup>+</sup> mice, and there was no mortality following GCV administration." pg 572

**Q0815:** R. D. Madison, et al. SCHWANN CELL INFLUENCE ON MOTOR NEURON REGENERATION ACCURACY. Neuroscience 2009;163(1):213-221

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;

ALZET Comments: Controls received mp w/ saline; animal info (TK, male, female, 20-22 q); incorrectly listed Model 1007 used

**P9704:** S. Kaneko, *et al.* IL-7 and IL-15 allow the generation of suicide gene-modified alloreactive self-renewing central memory human T lymphocytes. Blood 2009;113(5):1006-1015

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (NOD/SCID); **Pump:** Not Stated; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/PBS; animal info (6-8 wks old, female, NOD/Scid); "ALZET pumps...were implanted subcutaneously to ensure drug release at a constant rate" pg 1008

**P9232:** T. S. Yu, et al. Traumatic Brain Injury-Induced Hippocampal Neurogenesis Requires Activation of Early Nestin-Expressing Progenitors. Journal of Neuroscience 2008;28(48):12901-12912

**Agents:** Ganciclovir **Vehicle:** Water, deionized; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 4, 5 weeks; **ALZET Comments:** Controls received mp w/ vehicle; pumps replaced every 2 weeks; animal info (C57BL/6, 6 wks old, dHSV-TK, wt, brain injury (CC1))

**P9379:** G. Gowing, *et al.* Ablation of Proliferating Microglia Does Not Affect Motor Neuron Degeneration in Amyotrophic Lateral Sclerosis Caused by Mutant Superoxide Dismutase. Journal of Neuroscience 2008;28(41):10234-10244 **Agents:** Ganciclovir **Route:** CSF/CNS (intrathecal); **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 30 days;

**ALZET Comments:** Controls received mp w/ saline; animal info (CD11b-Tkmt-30-SOD1G93A Tg, 85 days old); neurodegenerative (ALS); IP injection of ganciclovir given 24 hours before and during mp implantation surgery; behavioral testing (hindlimb reflex); "chronic and systemic injection of the nucleoside analog ganciclovir is lethal for CD11b-Tkmut30 transgenic mice, and ganciclovir is not highly diffusable within CNS tissue... To overcome this constraint, we proceeded with direct delivery of ganciclovir to the spinal cord via an osmotic pump connected to a cannula located in the intrathecal space."

**P8782:** S. Giraud, *et al.* Transient depletion of dividing T lymphocytes in mice induces the emergence of regulatory T cells and dominant tolerance to islet allografts. American Journal of Transplantation 2008;8(5):942-953

**Agents:** Ganciclovir **Vehicle:** Water, pyrogen-free; **Route:** SC; **Species:** Mice; Mice (transgenic); **Pump:** 2001; 2002; **Duration:** 7, 14 days;

ALZET Comments: STZ-induced diabetes, animal info (FVB EpCD4TK, FVB/N, B6 islet allograft, skin allograft)

**P8323:** M. A. Shibata, *et al.* Electrogene therapy using endostatin, with or without suicide gene therapy, suppresses murine mammary tumor growth and metastasis. Cancer Gene Therapy 2007;14(3):268-278

Agents: Ganciclovir Vehicle: Saline; Route: SC; Species: Mice; Pump: 2002; Duration: 8 weeks;

**ALZET Comments:** Controls received mp w/ agent and empty control vector; pumps replaced every 14 days; no stress (see pg. 271); cancer (mammary adenocarcinoma); animal info (BALB/C, female, 20-24 grams)

**P8243:** M. D. Saxe, *et al.* Paradoxical Influence of hippocampal neurogenesis on working memory. Proceedings of the National Academy of Sciences 2007;104(11):4642-4646

**Agents:** Ganciclovir **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 8 weeks; **ALZET Comments:** Controls received mp w/ agent but did not contain GFAP-Tk Tg; pumps replaced after 4 weeks, with 2 weeks in between implantations; no stress (see pg. 4643); animal info (male, C57BL/6-BALB/C, 12-20 weeks old); "Because this system has previously been shown to cause gastrointestinal toxicity at high doses (16), we delivered a constant low dose of GCV for several weeks via SC osmotic minipumps...This modification achieved a nearly complete reduction in hippocampal neurogenesis...but resulted in no effects on activity, body weight, food consumption, or (GI) pathology." (p. 4643)





**P8865:** M. Kobayashi, *et al.* Tissue-targeted in vivo gene transfer coupled with histone deacetylase inhibitor depsipeptide (FK228) enhances adenoviral infection in rat renal cancer allograft model systems. Urology 2007;70(6):1230-1236

Agents: Ganciclovir Vehicle: Not Stated; Route: IP; Species: Rat; Pump: Not Stated; Duration: 7 days;

ALZET Comments: Gene therapy; animal info (male, ACI, 6-8 wks old)

**P8110:** Y. Iwasaki, et al. Gene therapy of liver tumors with human liver-specific nanoparticles. Cancer Gene Therapy 2007;14(1):74-81

**Agents:** Ganciclovir **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat (nude); **Pump:** Not Stated; **Duration:** 12 days; **ALZET Comments:** Controls received mp w/ agent and plasmid w/out gene therapy gene; no stress (see p.78); cancer (liver); gene therapy; animal info (male, F344/N, nu/nu, 5 wks old, 180g., NuE hepatic tumors); GCV acts as pro-drug for HSV-tk expression plasmid gene therapy

**P7923:** A. R. Simard, et al. Bone marrow-derived microglia play a critical role in restricting senile plaque formation in Alzheimer's disease. Neuron 2006;49(4):489-502

**Agents:** Ganciclovir **Vehicle:** Saline; HCL; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 28 days; **ALZET Comments:** Controls received mp w/ vehicle; ALZET brain infusion kit 3 used; neurodegenerative (Alzheimer's disease); animal info (15-24 weeks old)

**P8337:** M. D. Saxe, *et al.* Ablation of hippocampal neurogenesis impairs contextual fear conditioning and synaptic plasticity in the dentate gyrus. Proceedings of the National Academy of Sciences 2006;103(46):17501-17506

Agents: Ganciclovir Vehicle: Saline, sterile; Route: SC; Species: Mice (transgenic); Pump: Not Stated; Duration: 6 weeks; ALZET Comments: Animal info (male, C57BL/6, BALB/C, 12-20 weeks old)

**P8074:** D. J. Myer, *et al.* Essential protective roles of reactive astrocytes in traumatic brain injury. Brain 2006;129(2761-2772 **Agents:** Ganciclovir **Vehicle:** Saline, sterile physiological; **Route:** SC; **Species:** Mice (transgenic); Mice; **Pump:** Not Stated; **Duration:** 7 days;

**ALZET Comments:** Animal info (C57BL/, wt or GFAP-TK Tg, contusion injury by controlled cortical impact); traumatic brain injury

**P7936:** A. Bondanza, et al. Suicide gene therapy of graft-versus-host disease induced by central memory human T lymphocytes. Blood 2006;107(5):1828-1836

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (NOD/SCID); **Pump:** 2001; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ saline; animal info (female, NOD/SCID, 6-8 weeks old, GvHD); gene therapy

**P7655:** M. Ito, *et al.* Stem cells in the hair follicle bulge contribute to wound repair but not to homeostasis of the epidermis. Nature Medicine 2005;11(12):1351-1354

**Agents:** Ganciclovir **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice (SCID); **Pump:** 2002; **Duration:** 2 weeks; **ALZET Comments:** Controls received mp w/ vehicle; comparison of SC injections vs. mp; animal info (Krt 1-15-HSV-TK transgenic skin grafted onto CB17I cr-scid/scid)

**P6992:** D. Wolfe, et al. Safety and biodistribution studies of an HSV multigene vector following intracranial delivery to non-human primates. Gene Therapy 2004;11(23):1675-1684

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** SC; **Species:** Monkey (Rhesus); **Pump:** 2ML1; 2ML2; **Duration:** 4,5,34,35 days; **ALZET Comments:** Pumps replaced after 2 weeks; no stress (see pg. 1677); cancer (glioblastoma); toxicology; MRI; multiple pumps per animal (2); gene therapy

**P6886:** S. D. Reynolds, *et al.* Airway injury in lung disease pathophysiology: selective depletion of airway stem and progenitor cell pools potentiates lung inflammation and alveolar dysfunction. American Journal of Physiology Lung Cellular and Molecular Physiology 2004;287(6):L1256-L1265

**Agents:** Ganciclovir **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 6,14 days; **ALZET Comments:** Controls received mp w/ vehicle; comparison of acute GCV vs. mp; no stress (see pg. L1262); "No evidence of infection at the pump insertion site, pneumonia or sepsis was noted in mice in either exposure protocol, at any time point."







**P6734:** K. U. Hong, *et al.* Basal cells are a multipotent progenitor capable of renewing the bronchial epithelium. American Journal of Pathology 2004;164(2):577-588

**Agents:** Ganciclovir; uridine, bromodeoxy- **Vehicle:** Saline; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 8 days, 24 hours;

ALZET Comments: Controls received mp w/ BrdU; 2002 pump used for 8 days of BrdU infusion; GCV infused for 24 hours

**P6504:** J. R. Faulkner, *et al.* Reactive astrocytes protect tissue and preserve function after spinal cord injury. Journal of Neuroscience 2004;24(9):2143-2155

**Agents:** Ganciclovir **Vehicle:** Saline, sterile physiological; **Route:** SC; **Species:** Mice (transgenic); **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ vehicle

**P6238:** C. M. Morshead, *et al.* The ablation of glial fibrillary acidic protein-positive cells from the adult central nervous system results in the loss of forebrain neural stem cells but not retinal stem cells. European Journal of Neuroscience 2003;18(1):76-84 **Agents:** Ganciclovir **Vehicle:** Saline, physiological; **Route:** CSF/CNS; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 3 days:

ALZET Comments: Controls received mp w/ vehicle

**P5657:** M. Herraiz, et al. Liver failure caused by herpes simplex virus thymidine kinase plus ganciclovir therapy is associated with mitochondrial dysfunction and mito chondrial DNA depletion. Human Gene Therapy 2003;14(5):463-472

Agents: Ganciclovir Vehicle: Saline; Route: IP; Species: Rat; Pump: 2ML2; Duration: 3,7,10 days;

**ALZET Comments:** Controls received mp w/ saline; gene therapy

**P5596:** F. Doetsch, et al. EGF converts transit-amplifying neurogenic precursors in the adult brain into multipotent stem cells. Neuron 2002;36(6):1021-1034

**Agents:** Epidermal growth factor; Ganciclovir **Vehicle:** Saline; BSA; PBS; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; 1002; **Duration:** 7 hours; 6 days;

**ALZET Comments:** Controls received mp w/ vehicle; Gene therapy; peptides; EGF was diluted in BSA-containing saline and infused for 7 hours, or 6 days in 1007D pumps; Ganciclovir was diluted in PBS and infused for 6 days via 1002 pumps

**Q7394:** Y. Zhou, *et al.* Ablation of pituitary pro-opiomelanocortin (POMC) cells produces alterations in hypothalamic POMC mRNA levels and midbrain mu opioid receptor binding in a conditional transgenic mouse model. Journal of Neuroendocrinology 2001;13(9):808-17

Agents: sodium ganciclovir Vehicle: Saline; Route: SC; Species: Mice; Pump: 2001; Duration: 1 week;

**ALZET Comments:** Dose (190 mg/kg/day); Controls received mp w/ vehicle; animal info (adult, male, TK+/+); sodium ganciclovir aka Cytovene is an antiherpes agent; subsequent booster injections of 100 mg/kg ganciclovir, three times per week, for 1-2 weeks after 1 week of osmotic pump delivery;

**Q7710:** K. L. von Eckardstein, *et al.* Short-term neuropathological aspects of in vivo suicide gene transfer to the F98 rat glioblastoma using liposomal and viral vectors. Histol Histopathol 2001;16(3):735-44

Agents: Ganciclovir Vehicle: Saline; Route: CSF/CNS; Species: Rat; Pump: Not Stated; Duration: 14 days;

**ALZET Comments:** Dose (100 mg/kg/d); Controls received mp w/ vehicle; animal info (Adult, Male, Fischer); Ganciclovir aka GCV; ALZET brain infusion kit 3-5 used; Brain coordinates (2.6 mm lateral and 1.0 mm frontal to the bregma, 5.0 mm deep);

**Q6848:** J. Liu, et al. Selective T-cell subset ablation demonstrates a role for T1 and T2 cells in ongoing acute graft-versus-host disease: a model system for the reversal of disease. Blood 2001;98(12):3367-3375

Agents: Ganciclovir Vehicle: PBS; Route: SC; Species: Mice (transgenic); Pump: 2004; Duration: 28 days;

ALZET Comments: Dose (3.75 mg/d); Controls received mp w/ vehicle; animal info (6-8 week AKR and B10.BR male mice);



**Q7553:** K. U. Hong, *et al.* Clara cell secretory protein-expressing cells of the airway neuroepithelial body microenvironment include a label-retaining subset and are critical for epithelial renewal after progenitor cell depletion. American Journal of Respiratory Cell and Molecular Biology 2001;24(6):671-81

**Agents:** ganciclovir; uridine, bromodeoxy-; Thymidine, 3H- **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001D; **Duration:** 24 hours; 8 days; 9 days;

**ALZET Comments:** Dose ((ganciclovir 10 mg/day), (BrdU 20 mg/ml at 0.5µl/h), ([3H]-TdR 1 mCi/ml)); Controls received mp w/ vehicle; animal info (2-4-months, male, CCtk transgenic); "GCV pumps were removed at Day 2 of recovery and replaced with 14-d miniosmotic pumps delivering 0.5µl/h of sterile 20 mg/ml BrdU in normal saline solution. Animals were killed on Day 10 of recovery (continuous labeling for 8 d)." p.672;

**P4512:** V. Thomas-Vaslin, et al. Prolonged allograft survival through conditional and specific ablation of alloreactive T cells expressing a suicide gene. Transplantation 2000;69(10):2154-2161

**Agents:** Ganciclovir **Vehicle:** Water; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2001; 2002; **Duration:** 7, 14 days; **ALZET Comments:** Functionality of mp verified by ganciclovir plasma levels by liquid chromatography; immunology; transplantation

**P5767:** S. D. Reynolds, *et al.* Conditional clara cell ablation reveals a self-renewing progenitor function of pulmonary neuroendocrine cells. American Journal of Physiology Lung Cellular and Molecular Physiology 2000;278(6):L1256-L1263 **Agents:** Ganciclovir **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 6,12 days; **ALZET Comments:** Controls received mp w/ vehicle; gene therapy

**P4580:** T. G. Bush, et al. Leukocyte infiltration, neuronal degeneration, and neurite outgrowth after ablation of scar-forming, reactive astrocytes in adult transgenic mice. Neuron 1999;23(297-308

**Agents:** Ganciclovir; memantine **Vehicle:** Saline, sterile physiological; **Route:** SC; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 7, 14 days;

ALZET Comments: gene therapy; ganciclovir infused for 7 days; memantin infused for 14 days

**Q5560:** B. Lambrecht. Dendritic cells are required for the development of chronic eosinophilic airway inflammation in response to inhaled antigen in sensitized mice. Journal of Immunology 1998;160(8):4090-4097

Agents: Ganciclovir Vehicle: PBS; Route: SC; Species: Mice (transgenic); Pump: 2001; Duration: 7 days;

**ALZET Comments:** Controls received mp w/ vehicle (PBS); Immunology (Eosinophilic Airway Inflammation); Therapeutic indication (Asthma); Dose (50 mg/kg/day)

**P4579:** T. G. Bush, *et al.* Fulminant jejuno-ileitis following ablation of enteric glia in adult transgenic mice. Cell 1998;93(189-201 **Agents:** Ganciclovir **Vehicle:** Saline, sterile physiological; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2004; 2001; 2002; 1007D; **Duration:** 7, 14, 28 days;

**ALZET Comments:** Controls received no treatment; gene therapy

**P4467:** J. L. Cohen, *et al.* Prevention of graft-versus-host disease in mice using a suicide gene expressed in T lymphocytes. Blood 1997;89(12):4636-4645

Agents: Ganciclovir Vehicle: PBS; Route: SC; Species: Mice; Pump: 2001; Duration: 7 days;

**ALZET Comments:** Controls received mp w/vehicle; functionality of mp verified by plasma levels; comparison of IP injections vs. mp; immunology; Gene therapy

**P3921:** S. Benedetti, *et al.* Limited efficacy of the hsv-tk/gcv system for gene therapy of malignant gliomas and perspectives for the combined transduction of the interleukin-4 gene. Human Gene Therapy 1997;8(1345-1353

**Agents:** Ganciclovir **Vehicle:** Water; **Route:** Not Stated; **Species:** Rat; Mice (nude); **Pump:** 2002; 2ML2; **Duration:** 2 weeks; **ALZET Comments:** Comparison of IP injections vs. mp; cancer; gene therapy

**P3574:** M. Franken, et al. Epstein-barr virus-driven gene therapy for EBV-related lymphomas. Nature Medicine 1996;2(12):1379-1382

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice (SCID); **Pump:** Not Stated; **Duration:** 7 days; **ALZET Comments:** Controls received p w/ saline; comparison of ip injections vs. mp; cancer; gene therapy







**P3047:** H. Wallace, *et al.* Consequences of thyroid hormone deficiency induced by the specific ablation of thyroid follicle cells in adult transgenic mice. J. Endocrinol 1994;143(107-120

Agents: Ganciclovir Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: 2002; Duration: 14 days;

ALZET Comments: Controls received mp with PBS; comparison of ip injections vs. mp

**P2284:** P. T. Golumbek, et al. Herpes simplex-1 virus thymidine kinase gene is unable to completely eliminate live, nonimmunogenic tumor cell vaccines. J. Immunother 1992;12(224-230

**Agents:** Ganciclovir **Vehicle:** Not Stated; **Route:** SC; **Species:** mice; **Pump:** 2002; **Duration:** 2, 4 weeks; **ALZET Comments:** Controls received mp w/vehicle; pumps replaced; immunology; Gene therapy

P2129: H. Wallace, et al. Specific ablation of thyroid follicle cells in adult transgenic mice. Endocrinology 1991;129(6):3217-3226

Agents: Ganciclovir Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2002; Duration: 14 days;

ALZET Comments: Controls received mp with saline; also called DHPG

#### **PMEA**

**P1963:** J. S. Lee, *et al.* Transplacental antiretroviral therapy with 9-(2-phosphonylmethoxyethyl)adenine is embryotoxic in transgenic mice. J. Acquir. Immune Defic. Syndr 1991;4(833-838

ALZET Comments: PMEA; Mice; no duration posted; comparison of ip injections vs. mp; teratology; antiviral agent.

#### R-95288

**P3720:** T. Agatsuma, et al. Protection of hu-PBL-SCID/beige mice from HIV-1 infection by a 6-mer modified oligonucleotide, R-95288. Antiviral Res 1997;34(121-130

**ALZET Comments:** R-95288; Saline; IP; SC; mice (SCID); 2002; no duration posted; controls received mp w/saline; antisense; mice were transplanted w/human peripheral blood leukocytes; R-95288 protects human chimeric mice against HIV-1 infection; AIDS.

#### Ribavirin

**P9134:** M. C. Georges-Courbot, et al.  $Poly(I)-poly(C_{12}U)$  but not ribavirin prevents death in a hamster model of Nipah Virus infection. Antimicrobial Agents and Chemotherapy 2006;50(5):1768-1772

**ALZET Comments:** Ribavirin; 6-aza-uridine; SC; Hamster; 2ML2; 14 days; Controls received mp w/ PBS; toxicology; animal info (2 months old, golden); Ribavirin is an antiviral agent; 6-aza-uridine is a triazmenucleoside.

**P5453:** N. Charlier, et al. Infection of SCID mice with Montana Myotis leukoencephalitis virus as a model for flavivirus encephalitis. Journal of General Virology 2002;83(1887-1896

ALZET Comments: Ribavirin; SC; Mice (SCID); 2002; 14 days; Ribavirin is an antiviral; antiretroviral.

#### SID791

**P3587:** R. Datema, et al. Antiviral efficacy in vivo of the anti-human immunodeficiency virus bicyclam SDZ SID 791 (JM 3100), an inhibitor of infectious cell entry. Antimicrob. Agents Chemother 1996;40(3):750-754

**ALZET Comments:** SID 791; Saline, sterile; SC; Mice (SCID); mice; 2002; no duration posted; functionality of mp verified by plasma levels; dose-response; comparison of sc injections vs. mp; immunology; SID 791 is a bicyclam which inhibits HIV replication in vivo; human fetal liver & thymus transplanted into SCID mice.