



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

1. Angiostatin

P8109: A. E. M. Dirkx, *et al.* Anti-angiogenesis therapy can overcome endothelial cell anergy and promote leukocyte-endothelium interactions and infiltration in tumors. *FASEB Journal* 2006;20(6):621-630

ALZET Comments: Anginex; endostatin; BSA; angiostatin; Saline; SC; Mice; 2 weeks; 7, 11 days; Controls received mp w/ BSA or no treatment; dose-response (fig.5); cancer (melanoma, colon carcinoma); animal info (C57BL/6).

P6632: J. M. Vogten, *et al.* Angiostatin inhibits experimental liver fibrosis in mice. *International Journal of Colorectal Disease* 2004;19(4):387-394

ALZET Comments: Angiostatin; PBS; SC; Mice; 2002; 2 weeks; Controls received mp w/ vehicle; no stress (see pg. 389).

P6134: J. C. Reijneveld, *et al.* Angiostatin prolongs the survival of mice with leptomeningeal metastases. *European Journal of Clinical Investigation* 2003;33(1):76-81

ALZET Comments: Angiostatin; Water, distilled; SC; Mice; 2001; 7 days; Controls received mp w/ vehicle; cancer (melanoma); angiogenesis inhibitor; "angiostatin was administered through a continuous infusion...the continuous administration of angiogenesis inhibitors has greater therapeutic efficacy than the more commonly used twice-daily injections." p. 80.

P5342: E. A. T. Velde, *et al.* Enhanced antitumour efficacy by combining conventional chemotherapy with angiostatin or endostatin in a liver metastasis model. *British Journal of Surgery* 2002;89(10):1302-1309

ALZET Comments: Angiostatin; SC; Mice; 2001; Cancer; angiogenesis inhibitor.

P5052: E. A. te Velde, *et al.* Adverse effects of the antiangiogenic agent angiostatin on the healing of experimental colonic anastomoses. *ANNALS OF SURGICAL ONCOLOGY* 2002;9(3):303-309

ALZET Comments: Angiostatin; PBS; SC; mice; 2001; 4-7 days; controls received mp w/ vehicle; stability by mouse cornea neovascularization assay (p. 304); cancer; wound healing; angiogenesis inhibitor.

P4657: T. A. Drixler, *et al.* Continuous administration of angiostatin inhibits accelerated growth of colorectal liver metastases after partial hepatectomy. *Cancer Research* 2000;60(1761-1765)

ALZET Comments: Angiostatin; PBS; SC; mice; 2001; 2002; 7, 14 days; Controls received mp w/ vehicle; dose-response (p. 1763); comparison of SC injections vs. mp; half-life (p. 1761); cancer; angiogenesis inhibitor; this study shows that continuous administration of angiostatin significantly improves inhibition of angiogenesis and tumor growth suppression compared to injections.

2. Ara-C

Q7174: M. Batailler, *et al.* Pineal-dependent increase of hypothalamic neurogenesis contributes to the timing of seasonal reproduction in sheep. *Sci Rep* 2018;8(1):6188

ALZET Comments: Ara-C; CNS/CSF (third ventricle); Sheep; 2ML4; 4 Weeks; Dose (500ug/day); animal info (Ewes, 58.8 ± 4.5 kg , 59.4 ± 4 kg)); Ara-C aka cytosine-b-D-arabinofuranoside; Ara-C aka cytosine-b-D-arabinofuranoside;.

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

ALZET Comments: Ara-C; ganciclovir; CSF/CNS; Mice; 1007D; 3 days; 7 days; 14 days; animal info (Oct4 CKO;tk);.

Q5941: A. Cebrian-Silla, *et al.* Unique Organization of the Nuclear Envelope in the Post-natal Quiescent Neural Stem Cells. *Stem Cell Reports* 2017;9(1):203-216



ALZET Comments: Ara-C; CSF/CNS; Mice; 6 days; animal info (Wild-type CD1 mice); Ara-C is an antimetabolic agent a.k.a. cytosine-b-D-arabinofuranoside;.

Q5975: F. Bicker, *et al.* Neurovascular EGFL7 regulates adult neurogenesis in the subventricular zone and thereby affects olfactory perception. *Nat Commun* 2017;8(15922)

ALZET Comments: Ara-C; CSF/CNS (lateral ventricle); Mice (knockout); 2001; 7 days; Animal info (2 months); ALZET Brain infusion kit used; Dose (2%);.

Q5508: F. Zhang, *et al.* In Vivo Targeted MR Imaging of Endogenous Neural Stem Cells in Ischemic Stroke. *Molecules* 2016;21(9):

ALZET Comments: Ara-C; CSF/CNS; mice; 1007D; 7 days; animal info (C57BL6J, 8-10 weeks old, 20-25g); ischemia (cerebral);.

Q5072: B. Tighilet, *et al.* Reactive Neurogenesis and Down-Regulation of the Potassium-Chloride Cotransporter KCC2 in the Cochlear Nuclei after Cochlear Deafferentation. *Frontiers in Pharmacology* 2016;7(**ALZET Comments:** Ara-C; muscimol; NaCl; CSF, artificial; CSF/CNS (fourth ventricle); Cat; 2ML4; 3 days; 30 days; Controls received mp w/ vehicle; animal info (male, adult, 4-5kg); post op. care (antibiotics for 7 days; analgesic for 3 days);.

Q4838: H. JIA, *et al.* PREVENTION OF TRAUMA-INDUCED COCHLEAR FIBROSIS USING INTRACochlear APPLICATION OF ANTI-INFLAMMATORY AND ANTIPROLIFERATIVE DRUGS. *neuroscience* 2016;316(261-278)

ALZET Comments: Dexamethasone; Ara-C; Perilymph, artificial; Ear (cochlea); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (Wistar, adult); animal info (Wistar, adult); stability verified by (incubation in 37C saline for 7 days see pg 268); one cochlea received vehicle only, while other received drug;.

Q5323: A. V. Apkarian, *et al.* Role of adult hippocampal neurogenesis in persistent pain. *Pain* 2016;157(2):418-28

ALZET Comments: Ara-C; Saline; CSF/CNS (lateral ventricle); mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (C57Bl/6 male mice, 8-9 wks old); dose-response (pg 421); behavioral testing (touch and cold sensitivity of injured paw, Von Frey, Tail suspension test, Open field, Black-box emergence test); "Mice show full behavioral and functional recovery soon after surgery" pg 419; Brain coordinates; 0.4mm posterior to the bregma, 1mm lateral to the midline, and 2 mm ventral to the skull.

Q3789: D. Sun, *et al.* Inhibition of Injury-Induced Cell Proliferation in the Dentate Gyrus of the Hippocampus Impairs Spontaneous Cognitive Recovery after Traumatic Brain Injury. *Journal of Neurotrauma* 2015;32(495-505)

ALZET Comments: Ara-C; CSF, artificial; CSF/CNS; Rat; 1007D; 7 days; Control animals received mp w/ vehicle; ALZET Brain infusion kit 2 used; animal info (male, 3-4 mo old, Sprague Dawley).

Q4538: S. Morita, *et al.* Vascular endothelial growth factor-dependent angiogenesis and dynamic vascular plasticity in the sensory circumventricular organs of adult mouse brain. *CELL AND TISSUE RESEARCH* 2015;359(865-884)

ALZET Comments: Ara-C; Saline; CSF/CNS; Mice; 2002; 10 days; Controls received mp w/ vehicle; animal info (male, C57BL6J, adult, P70-P84); comparison of IP injection vs mp; cardiovascular; "This infusion method is effective for suppressing cell proliferation in the subventricular zone and minimizes surgery damage to brain tissues" pg 867;.

Q5159: L. K. Hamilton, *et al.* Aberrant Lipid Metabolism in the Forebrain Niche Suppresses Adult Neural Stem Cell Proliferation in an Animal Model of Alzheimer's Disease. *Cell Stem Cell* 2015;17(4):397-411

ALZET Comments: Ara-C; Oleic Acid; AB142089; CSF/CNS (cerebroventricular); mice; 1007D; 1004; 6 days; 25 days; Controls received mp w/ vehicle; animal info: 2-month-old WT or 3xTg-AD mice; functionality of mp verified by Analysis of brain sections by IMS; cancer; dose-response (pg 407); neurodegenerative (NSC impairment); enzyme inhibitor (SCD-1 inhibitor – AB142089); Dose: 500 mM Oleic Acid; 10mM C12 Oleic Acid conjugated to vehicle; 10mM C13 Oleic Acid conjugated to vehicle; 2% AraC; 40 mM SCD-1 inhibitor.

Q5154: A. Ghanbari, *et al.* Depletion of neural stem cells from the subventricular zone of adult mouse brain using cytosine b-Arabinofuranoside. *Brain Behav* 2015;5(11):e00404



ALZET Comments: Ara-C; Saline; CSF/CNS (right lateral ventricle); Mice; 1007D; 1 week; 2 weeks; Controls received sham operation and mp w/ vehicle; animal info: Five-week-old male C57-BL6 mice; pumps replaced once after 7 days; ALZET brain infusion kit 3 used; good methods (pg 2); post op. care (0.5 mg/kg buprenorphine every 12 h for 48 hours); cyanoacrylate adhesive (Loctite 454); delayed delivery (6-12 hours); Dose: 2% Ara-C in Saline; Brain coordinates; Paxinos mouse brain Atlas: Anterior-Posterior (AP): -0.2, Medial-Lateral (ML): +0.9 from the bregma point and Dorsal-Ventral: +2.7 from the top of skull.

Q4420: S. Furutachi, *et al.* Slowly dividing neural progenitors are an embryonic origin of adult neural stem cells. NATURE NEUROSCIENCE 2015;18(657-+)

ALZET Comments: Ara-C; PBS; CSF/CNS; Mice; 1007D; 6 days; Animal info (Rosa26-rtTA or RE-mCMV-H2B-GFP); ALZET brain infusion kit 3 used;

3. Azacytidine

Q1107: J. J. U. Guo, *et al.* Neuronal activity modifies the DNA methylation landscape in the adult brain. Nature Neuroscience 2011;14(10):1345-U172

ALZET Comments: RG108; azacytidine, 5-; CSF/CNS; Mice; 1003D; 3 days; Controls received mp w/ saline; animal info (wt, Gadd45b KO, 8-10 wks old, male); enzyme inhibitor (DNA methyltransferases).

P0604: D. S. Zaharko, *et al.* Plasma kinetics and effects of 5,6-dihydro-5-azacytidine in mice and L1210 tumor. Invest. New Drugs 1985;3(35-41)

ALZET Comments: Azacytidine, 5,6-dihydro-5-; PBS; SC; mice; 2001; 4 days; cancer chemotherapy; pumps primed in PBS for 24 hr. prior to implant; solubility limit of DHAC is 820mg/ml at room temp; comparison with previous injec. & acute infusion data.

4. Bevacizumab

R0378: B. Halle, *et al.* Convection-enhanced Drug Delivery for Glioblastoma: A Systematic Review Focused on Methodological Differences in the Use of the Convection-enhanced Delivery Method. Asian J Neurosurg 2019;14(1):5-14

ALZET Comments: Etoposide, Bevacizumab, IMCA12, Interleukin-13-PE38, Tetrakis Chlorin; CSF/CNS (intratumoral); Mice, Rat; 2001D, 1003D, 1007D, 1004, 2004; 24 hours, 3, 7, 21, 28 days; ALZET brain infusion kit 1,2, and 3 used; cancer (Glioblastoma);

Q7219: Y. X. Liu, *et al.* Delivery of bevacizumab by intracranial injection: assessment in glioma model. Onco Targets Ther 2018;11(2673-2683)

ALZET Comments: Bevacizumab; PBS; CSF/CNS (intratumoral); Mice; Pump model not stated; 28 days; Dose (25 ug/ul); Controls received mp w/ vehicle; comparison of weekly IV injections vs intratumoral delivery via minipump; cancer (Glioma); "Localized BEV delivery by Alzet micro-osmotic pumps is more effective in reducing tumor size and tumor cell infiltration when compared with systemic administration."

Q4636: W. J. Wang, *et al.* Effects of convection-enhanced delivery of bevacizumab on survival of glioma-bearing animals. Neurosurgical Focus 2015;38(U112-U119)

ALZET Comments: Bevacizumab; Saline; CSF/CNS (intratumoral); Mice (nude); 1004; 28 days; Controls received mp w/ vehicle; animal info (athymic, nu/nu); ALZET brain infusion kit used; cancer (glioma); immunology; "Bevacizumab was delivered into the tumor using chronic pump-mediated delivery, defined as "convection-enhanced delivery" or CED. This CED method was used because it has the advantage of achieving the desirable drug concentration in the microenvironment of the glioma while avoiding the use of high initial doses." pg 2;

Q4537: K. Morishita, *et al.* Postinfarction Cardiac Remodeling Proceeds Normally in Granulocyte Colony-Stimulating Factor Knockout Mice. AMERICAN JOURNAL OF PATHOLOGY 2015;185(1899-1911)



ALZET Comments: Bevacizumab; Saline; SC; Mice; 1002; 4 weeks; Controls received mp w/ vehicle; animal info (G-CSF-KO, 10-12 weeks); cardiovascular;.

Q2990: J. W. Shim, *et al.* VEGF, which is elevated in the CSF of patients with hydrocephalus, causes ventriculomegaly and ependymal changes in rats. *Experimental Neurology* 2013;247(1):703-709

ALZET Comments: Vascular endothelial growth factor-A165; Bevacizumab; Saline; BSA; CSF/CNS; Rat; 2001D; 1 day; Controls received mp w/vehicle, or (saline, BSA); Peptides; animal info (male Sprague-Dawley rats, 250g); Brain infusion kit (2) used;.

P9819: R. Savai, *et al.* Evaluation of Angiogenesis Using Micro-Computed Tomography in a Xenograft Mouse Model of Lung Cancer. *NEOPLASIA* 2009;11(1):48-56

ALZET Comments: Bevacizumab; IV (jugular); Mice (nude); 2002; 14 days; Controls received mp w/ distilled water; animal info (female, C57BL/6, 5-7 wks old, BALB/c, nu/nu, 7-8 wks old); pump implanted IP; bevacizumab is a anti-VEGF antibody; "This delivery (using ALZET pumps) mimics local delivery of antivascular agents and can be used effectively alone or in combination with cytotoxic chemotherapy for site-specific drug delivery for lung cancer treatment. As expected, continuous infusion of bevacizumab decreased lung tumor volume and tumor perfusion, with an added survival advantage compared to the untreated group." pg 55; cancer (lung); antibody.

5. Bleomycin

Q7149: K. Kamio, *et al.* Resolution of bleomycin-induced murine pulmonary fibrosis via a splenic lymphocyte subpopulation. *Respir Res* 2018;19(1):71

ALZET Comments: Bleomycin; Saline; SC; Mice; 2001; 7 days; Dose (100 mg/kg/day); Controls received mp w/ vehicle; animal info (C57BL/6); gene therapy; .

Q5913: T. Watanabe, *et al.* Optimization of a murine and human tissue model to recapitulate dermal and pulmonary features of systemic sclerosis. *PLoS One* 2017;12(6):e0179917

ALZET Comments: Bleomycin; Saline; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; dose-response pg 5); Pumps removed on day 10; Dose (1, 10, 60, 110 u/kg);.

Q6078: X. Liang, *et al.* Inhibition of FKBP10 Attenuates Hypertrophic Scarring through Suppressing Fibroblast Activity and Extracellular Matrix Deposition. *J Invest Dermatol* 2017;137(11):2326-2335

ALZET Comments: Bleomycin sulfate; SC; Mice; 1004; 56 days; Dose (2.8 mg/ml); animal info (12 week old C57/BL6 mice);.

Q5874: A. P. Grzegorzewska, *et al.* Dimethyl Fumarate ameliorates pulmonary arterial hypertension and lung fibrosis by targeting multiple pathways. *Sci Rep* 2017;7(41605)

ALZET Comments: Bleomycin; PBS; SC; Mice; 1007D; 7 days; animal info (6–8 week old male C57BL/6 mice); pulmonary fibrosis model wherein fibrosis was induced by osmotic pump-delivery of bleomycin; Dose (1.8 Unit/mouse);.

Q6151: K. Fujiwara, *et al.* Inhibition of Cell Apoptosis and Amelioration of Pulmonary Fibrosis by Thrombomodulin. *Am J Pathol* 2017;187(10):2312-2322

ALZET Comments: Bleomycin; Saline; SC; Mice; 10 days; Dose (100 mg/kg); Controls received mp w/ vehicle; animal info (Nine-week-old female WT mice weighing 19 to 21 g);.

Q5470: M. Urawa, *et al.* Protein S is protective in pulmonary fibrosis. *J Thromb Haemost* 2016;14(8):1588-99

ALZET Comments: Bleomycin; Saline; SC; Mice; 7 days; Controls received mp w/ vehicle; animal info (male, hPS-TG or C57BL/6, 18-22g, 8-12 weeks old); cardiovascular; Dose (100 mg/kg);.

Q4851: R. Lemaire, *et al.* Resolution of Skin Fibrosis by Neutralization of the Antifibrinolytic Function of Plasminogen Activator Inhibitor. *ARTHRITIS & RHEUMATOLOGY* 2016;68(2):473-483



ALZET Comments: Bleomycin; SC; Mice; 1 week; animal info (C57Bl6, 6-10 weeks old); Dose (100 mg/kg);.

Q4183: W. T. Wu, *et al.* Synergistic Effect of Bolus Exposure to Zinc Oxide Nanoparticles on Bleomycin-Induced Secretion of Pro-Fibrotic Cytokines without Lasting Fibrotic Changes in Murine Lungs. *International Journal of Molecular Sciences* 2015;16(660-676

ALZET Comments: Bleomycin sulfate; Saline; SC; Mice; 2001; 7 days; Controls received mp w/ vehicle; animal info (female, C57BL6J, 9 weeks old, 19-22g); cardiovascular;.

Q3974: M. R. Liang, *et al.* A modified murine model of systemic sclerosis: bleomycin given by pump infusion induced skin and pulmonary inflammation and fibrosis. *LABORATORY INVESTIGATION* 2015;95(342-350

ALZET Comments: Bleomycin; Saline; SC; Mice; 2004; 1 week; 2 weeks; 3 weeks; 4 weeks; Controls received mp w/ vehicle; animal info (C57BL6, 6-8 weeks old); no stress (see pg. 344); immunology;.

6. Carboplatin

Q3399: W. L. Yang, *et al.* Radiation therapy combined with intracerebral administration of carboplatin for the treatment of brain tumors. *Radiation Oncology* 2014;9(1):U20-U28

ALZET Comments: Carboplatin; CSF/CNS; Rat; 2001; 7 days; animal info (male, Fischer, 200-220 g, F98 glioma bearing); cancer (glioma); comparison of mp with convection enhanced delivery (CED).

Q2878: N. Zhidkov, *et al.* Continuous Intraperitoneal Carboplatin Delivery for the Treatment of Late-Stage Ovarian Cancer. *MOLECULAR PHARMACEUTICS* 2013;10(9):3315-3322

ALZET Comments: Carboplatin; PBS; IP; Mice (SCID); 1002; 14 days; Controls received mp w/ saline; toxicology; animal info (6-8 week old female SCID); comparison of bolus injection vs mp; cancer (ovarian).

Q2949: T. Y. Huo, *et al.* Preparation, Biodistribution and Neurotoxicity of Liposomal Cisplatin following Convection Enhanced Delivery in Normal and F98 Glioma Bearing Rats. *PLoS One* 2012;7(11):U98-U107

ALZET Comments: Carboplatin; Rat; Animal info (F98 Glioma bearing rats); cancer (brain); infusion of carboplatin via alzet minipump along with radiotherapy produced a 2.5 to 3.6 fold increase in the mean survival time of F98 glioma bearing rats with a subset of cured animals;.

Q2351: L. Bobyk, *et al.* Intracerebral delivery of Carboplatin in combination with either 6 MV Photons or monoenergetic synchrotron X-rays are equally efficacious for treatment of the F98 rat glioma. *JOURNAL OF EXPERIMENTAL & CLINICAL CANCER RESEARCH* 2012;31(1):U1-U7

ALZET Comments: Carboplatin; Dextrose; CSF/CNS; Rat; 2001; 7 days; Animal info (F98 glioma bearing); cancer; brain tissue distribution.

Q1415: W. L. Yang, *et al.* Convection enhanced delivery of carboplatin in combination with radiotherapy for the treatment of brain tumors. *Journal of Neuro-oncology* 2011;101(3):379-390

ALZET Comments: Carboplatin; Saline, normal; CSF/CNS (striatum); Rat; 2001; 7 days; ~Controls received mp w/ vehicle; animal info (Fischer, 220-240 g); cancer (glioma); "Prolonged infusion of carboplatin by means of Alzet osmotic pumps yielded the longest MST (mean survival time), and 2 of 5 rats were cured of their tumors." pg 388; 45]. "It is noteworthy that in this study the brainstem was not damaged by direct infusion of 200 ul of carboplatin (0.5 mg/ml), and that there was no neurotoxicity until a lethal dose (dose (greater than/equal to) 1.0 mg/ml) was administered." pg 388.

Q0589: T. Iwasa, *et al.* Marked anti-tumour activity of the combination of YM155, a novel survivin suppressant, and platinum-based drugs. *British Journal of Cancer* 2010;103(1):36-42

ALZET Comments: YM-155; cisplatin; carboplatin; DMSO; IV; Mice (nude); 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, nude, BALB/cAnNCrj-nu/nu, 5 weeks old); 0.1% DMSO used; cancer.



7. CDDP

P6470: S. Ohtsukasa, *et al.* Increased expression of CEA and MHC class I in colorectal cancer cell lines exposed to chemotherapy drugs. *Journal of Cancer Research and Clinical Oncology* 2003;129(12):719-726

ALZET Comments: CDDP; fluorouracil, 5-; IP; Mice; 1007D; 14 days; Controls received mp w/ saline; pumps replaced after 7 days; cancer (colorectal); CDDP (Cisdiamminedichloroplatinum II); is a chemotherapeutic agent.

8. Cetuximab

Q2710: K. M. Talasila, *et al.* EGFR wild-type amplification and activation promote invasion and development of glioblastoma independent of angiogenesis. *Acta Neuropathologica* 2013;125(5):683-698

ALZET Comments: Cetuximab; CSF/CNS (intratumoral); Rat (nude); 2ML4; 4 weeks; Control animals received mp w/ PBS; animal info (rnu/rnu Rowett); ALZET brain infusion kit 2 used; convection enhanced delivery (CED); tissue perfusion (intratumoral).

P9680: T. Martens, *et al.* Inhibition of glioblastoma growth in a highly invasive nude mouse model can be achieved by targeting epidermal growth factor receptor but not vascular endothelial growth factor receptor-2. *Clinical Cancer Research* 2008;14(17):5447-5458

ALZET Comments: Cetuximab; CSF/CNS (intratumoral); Mice (nude); 2004; Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioblastoma); ALZET brain infusion kit 2 used; animal info (NMRI- nu/nu, 6-8 wks old); cetuximab is a monoclonal antibody against EGFR.

9. Cisplatin

R0291: N. Foray. Comment to the paper "Efficacy of intracerebral delivery of cisplatin in combination with photon irradiation for treatment of brain tumors" from Rousseau *et al.*, in press. *Journal of Neuro-oncology* 2011;101(1):161-163

ALZET Comments: Cisplatin; CSF/CNS; Rat; Animal info (Fisher); glioma; CED, convection enhanced delivery.

Q0589: T. Iwasa, *et al.* Marked anti-tumour activity of the combination of YM155, a novel survivin suppressant, and platinum-based drugs. *British Journal of Cancer* 2010;103(1):36-42

ALZET Comments: YM-155; cisplatin; carboplatin; DMSO; IV; Mice (nude); 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, nude, BALB/cAnNCrj-nu/nu, 5 weeks old); 0.1% DMSO used; cancer.

R0266: E. E. L. Swan, *et al.* Inner ear drug delivery for auditory applications. *Advanced Drug Delivery Reviews* 2008;60(15):1583-1599

ALZET Comments: Cisplatin; Sodium thiosulfate; Brain-derived neurotrophic factor; Fibroblast growth factor; D-JNKI-1; BN82270; Tetrodotoxin; Perilymph, artificial; Dexamethasone; Methylprednisone; Caroverine; Methionine, D-; Thiourea; Liposome, cationic; Neomycin; SC; Ear (round window membrane); Ear (cochlea); Ear (scala tympani); Ear; Guinea pig; 3, 7, 14, 28 days; Gene therapy; peptides; no stress; enzyme inhibitor (peroxidase); stress/adverse reaction (see pg 1593) "Ref #161 found local trauma and inflammatory responses"; tissue perfusion (scala tympani, cochlea, round window membrane); comparison of middle ear injections vs. mp; Review, see pgs. 1587 - 1589, 1591, 1593 - 1595, refs #49, 50, 60, 63, 72, 75, 102, 104, 180, 181, 194-201.

P8870: Y. I. Chirino, *et al.* Selective iNOS inhibition reduces renal damage induced by cisplatin. *TOXICOLOGY LETTERS* 2008;176(1):48-57

ALZET Comments: 1400W; cisplatin; Saline; SC; Rat; 2001; 3 days; Controls received mp w/ vehicle; enzyme inhibitor (iNOS); animal info (male, Wistar, 230-275g.).

P8712: G. P. Vasvari, *et al.* Combination of thalidomide and cisplatin in an head and neck squamous cell carcinomas model results in an enhanced antiangiogenic activity in vitro and in vivo. *International Journal of Cancer* 2007;121(8):1697-1704



ALZET Comments: Cisplatin; IP; Mice (NOD/SCID); 1002; 4 weeks; Controls received no treatment; pumps replaced after 2 weeks; no stress (see pg. 1699); cancer (head/neck squamous cell carcinoma); animal info (female, NOD/SCID, 6-8 wks old, 15-25g).

P5673: F. L. C. Wolters, *et al.* Systemic co-treatment with alpha-melanocyte stimulating hormone delays hearing loss caused by local cisplatin administration in guinea pigs. *Hearing Research* 2003;179(1-2):53-61

ALZET Comments: Cisplatin; Saline; Ear (cochlea); Guinea pig; 2002; 1 week; Tissue perfusion (cochlea).

P5734: M. Berrada, *et al.* Tumor treatment by sustained intratumoral release of 5-fluorouracil: Effects of drug alone and in combined treatments. *INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS* 2002;54(5):1550-1557

ALZET Comments: Fluorouracil, 5-; cisplatin; PBS; IP; Mice; 1007D; 7 days; Controls received mp w/ PBS; comparison of IP injections vs. mp; cancer; cisplatin also called cis-platinum or cis-DDP.

P4972: S. J. O'Leary, *et al.* Perilymphatic application of cisplatin over several days in albino guinea pigs: dose-dependency of electrophysiological and morphological effects. *Hearing Research* 2001;154(135-145)

ALZET Comments: Cisplatin; Saline; Ear (cochlea); Guinea pig; 2002; 7 days; tissue perfusion (scala tympani); dose-response (Fig. 1-8); ototoxicity; in-house cochlear cannula used (modified); hearing loss; "the pump model has several advantages: 1) there appears to be less inter-animal variability than via systemic administration; 2) cisplatin dosage can be studied parametrically; 3) the effects of systemic toxicity are avoided" (p. 144).

10. Cyclophosphamide

P9990: J. Mercapide, *et al.* Primary gene-engineered neural stem/progenitor cells demonstrate tumor-selective migration and antitumor effects in glioma. *International Journal of Cancer* 2010;126(5):1206-1215

ALZET Comments: Cyclophosphamide; CSF/CNS; Mice (nude); Controls received mp w/ sterile saline; animal info (6 wks old, female).

P7768: J. E. Damber, *et al.* The anti-tumour effect of low-dose continuous chemotherapy may partly be mediated by thrombospondin. *Cancer Chemotherapy and Pharmacology* 2006;58(3):354-360

ALZET Comments: Cyclophosphamide; paclitaxel; Saline; SC; Rat; 2ML1; 10 days; Controls received mp w/ vehicle; cancer (AT-1 adenocarcinoma); animal info (adult, male, copenhagen); "Continuous/metronomic therapy may achieve a more pronounced anti-tumoural effect and significantly diminish the side effects compared with conventional bolus MTD-type chemotherapy." (p. 359).

P1969: G. Tagliabue, *et al.* Antitumor activity of 1,4-bis (2'-chloroethyl)-1,4-diazabicyclo-[2.2.1] heptane dimaleate (dabis maleate) in M5076 and its subline resistant to cyclophosphamide M5/CTX. *Ann. Oncol* 1992;3(233-236)

ALZET Comments: Dabis maleate; Cyclophosphamide; Water; SC; mice; 3 days; cancer.

P4591: W. Reiners, *et al.* Teratogenesis and pharmacokinetics of cyclophosphamide after drug infusion as compared to injection in the mouse during day 10 of gestation. *Pharmacokinetics in Teratogenesis* 1987;II(Chap. 4):41-48

ALZET Comments: Cyclophosphamide; NaCl; PEG 300;; SC;; mice;; 2001;; 24 hours;; functionality of mp verified by plasma levels; comparison of bolus injections vs. mp; half-life (p. 42);.

P1723: D. S. Zaharko. Immunological concepts and the combination of cyclophosphamide with 5-aza-2'-deoxycytidine on L1210 in vivo. *J. Immunopharmacol* 1985;7(2):195-202

ALZET Comments: Cyclophosphamide; Cytidine, 5-aza-2'-deoxy-; SC; mice; 2001; 12 hours; comparison of ip injections vs. mp; immunology.

R0079: H. Nau, *et al.* Controlled-rate drug administration in testing for toxicity, in particular teratogenicity toward interspecies bioequivalence. In 'Topics in Pharmaceutical Sciences,' D. D. Breimer and P. Speiser (eds.), Elsevier Science Publishers B. V. , 1985 1985;143-157



ALZET Comments: Cyclophosphamide; Valproic acid; SC; mice; no duration posted; pump model not stated; review; dose-response (graph); half-life; comparison of injections vs. mp infusion; teratology.

11. Doxorubicin

Q7146: X. Jing, *et al.* MicroRNA-29b Regulates the Mitochondria-Dependent Apoptotic Pathway by Targeting Bax in Doxorubicin Cardiotoxicity. *Cell Physiol Biochem* 2018;48(2):692-704

ALZET Comments: Doxorubicin; Saline; SC; Rats; 2002; 14 days; Controls received mp w/ vehicle; Dose (30 mg/kg body weight); animal info (Male Wistar rats); .

Q6233: I. Piotrowska, *et al.* Early transcriptional alteration of histone deacetylases in a murine model of doxorubicin-induced cardiomyopathy. *PLoS One* 2017;12(6):e0180571

ALZET Comments: Doxorubicin; PBS; SC; Mice; 2002; 14 days; Dose (15 µg/g); Controls received mp w/ vehicle; animal info (CBA x C57BL/6 F1 female mice); cardiovascular; "Local toxicity or vesicant effects of doxorubicin (tissue damage from escaping out of the vein) do not occur with Alzet pumps and so were also absent" pg. 4;

Q6018: J. Cornillie, *et al.* In Vivo Antitumoral Efficacy of PhAc-ALGP-Doxorubicin, an Enzyme-Activated Doxorubicin Prodrug, in Patient-Derived Soft Tissue Sarcoma Xenograft Models. *Mol Cancer Ther* 2017;16(8):1566-1575

ALZET Comments: Doxorubicin hydrochloride; PBS; IP; Mice; 1007D; 7 days; Controls received mp w/ vehicle; cancer (Sarcoma); Therapeutic indication (Cancer; soft tissue sarcoma; xenograft model);.

Q2267: R. Knoell, *et al.* Telethonin Deficiency Is Associated With Maladaptation to Biomechanical Stress in the Mammalian Heart. *Circulation Research* 2011;109(7):758-U153

ALZET Comments: Doxorubicin; Mice; 21 days; Animal info (telethonin KO, 26-38 wks old); infusion rate of 0.5 ul/hr.

P9568: T. Loch, *et al.* Different extent of cardiac malfunction and resistance to oxidative stress in heterozygous and homozygous manganese-dependent superoxide dismutase-mutant mice. *Cardiovascular Research* 2009;82(3):448-457

ALZET Comments: Doxorubicin; PBS; SC; Mice; 2002; 2 weeks; Controls received mp w/vehicle; animal info (4.5 mo. old).

P8944: P. Wenzel, *et al.* ALDH-2 deficiency increases cardiovascular oxidative stress - Evidence for indirect antioxidative properties. *Biochemical and Biophysical Research Communications* 2008;367(1):137-143

ALZET Comments: Nitroglycerin; acetaldehyde; doxorubicin; Ethanol; SC; IP; Mice; 3, 4 days; Controls received mp w/ vehicle; cardiovascular; animal info (10 wks old, male, ALDH-2 null); nitroglycerin also known as glycerol trinitrate, GTN; "chronic (in contrast to short term/acute) treatment with doxorubicin lead to a more pronounced increase in mitochondrial ROS formation and to a greater extent of endothelial as well as smooth muscle dysfunction" pg. 141.

P7120: A. Khan, *et al.* Infusion rates and drug distribution in brain tumor models in rats. *Journal of Neurosurgery (Pediatrics 1)* 2005;102(53-58

ALZET Comments: Carboplatin; doxorubicin; transferrin-doxorubicin; CSF/CNS; Rat; 2ML1; 2001; 7 days; Cancer (glioma, gliosarcoma); brain tissue distribution; CNS infusion rate study; "...the use of intratumoral infusions significantly increase survival in comparison with bolus injections and conventional systemic treatments." P. 53; flexible tipped cannula components were from Plastics One; in some cases the tubing/cannula were left empty after implantation to allow the tissue to seal before fluid flow.

P7394: M. Guarnieri, *et al.* Flexible versus rigid catheters for chronic administration of exogenous agents into central nervous system tissues. *Journal of Neuroscience Methods* 2005;144(2):147-152

ALZET Comments: Doxorubicin; carboplatin; Dextrose solution; saline; CSF/CNS (parenchyma); Rat; 2001; Animal info (F, Fischer, 220 g); Functionality of mp verified by pump examination, post infusion; stability verified by previous studies, 14 days; good methods (p. 148); cancer (glioma); brain tissue distribution; Plastics One cannula used (stainless steel); "replacement of rigid infusion tubes [cannulae] with flexible tubing increases the reliability of local CNS drug infusions.



Rigid catheters [cannulae] may allow backflow of the infused drug along the path of the catheters into the subdural space." (P. 147).

12. Endostatin

Q3697: C. H. S. Lin, *et al.* Endostatin and kidney fibrosis in aging: a case for antagonistic pleiotropy? *American Journal of Physiology-Heart and Circulatory Physiology* 2014;306(H1692-H1699)

ALZET Comments: Peptide, endostatin mP1; DMSO; PBS; SC; Mice; 2004; 28 days; Controls received mp w/ vehicle; animal info (C57, 2 months old); 50% DMSO used; peptides; femoral artery ligation; cardiovascular;

P8275: K. Tanabe, *et al.* Endostatin peptide, an inhibitor of angiogenesis, prevents the progression of peritoneal sclerosis in a mouse experimental model. *Kidney International* 2007;71(3):227-238

ALZET Comments: Endostatin (1-27), human; PBS; SC; Mice; 2004; 24 days; Controls received mp w/ vehicle; dose-response (fig. 1); no stress (see pg. 234); animal info (male, ICR, female, 6 weeks old, 27 grams, peritoneal sclerosis); "Continuous administration of endostatin peptide via subcutaneous osmotic minipumps did not produce any harmful side effects...In addition, treatment with endostatin peptide did not give rise to any pathological alterations in the heart, liver, or kidney, and failed to affect wound repair" (p. 234); nephrology.

P8357: W. J. M. Mulder, *et al.* Early in vivo assessment of angiostatic therapy efficacy by molecular MRI. *FASEB Journal* 2007;21(2):378-383

ALZET Comments: Endostatin; anginex; SC; Mice; 2 weeks; 3 days; Controls received mp w/ saline; cancer (melanoma); peptides; MRI; animal info (C57BL/6, 6 weeks old); antiangiogenesis.

P8793: D. Kurosaka, *et al.* The effect of endostatin evaluated in an experimental animal model of collagen-induced arthritis. *SCANDINAVIAN JOURNAL OF RHEUMATOLOGY* 2007;36(6):434-441

ALZET Comments: Endostatin; PBS; IP; Mice; 2 weeks; Controls received mp w/ vehicle; animal info (1J, 6 week); "compared with the once daily dosing regimen, the administration of endostatin by an osmotic pump achieved a similar arthritis-inhibiting effect at one-tenth of the dose...the administration method using osmotic pump is useful." pg. 434.

Q5875: S. DK. The HUVEC/Matrigel Assay. An In Vivo Assay of Human Angiogenesis Suitable for Drug Validation. *Methods in Molecular Biology* 2007;360(253-68)

ALZET Comments: Endostatin, recomb. human; SC; Mice; 1002, 2004; 14, 28 days; functionality of mp verified by endostatin plasma levels; Endostatin released from the osmotic pumps can be detected throughout the experimental period as demonstrated by analysis of endostatin in serum by using an ELISA kit from CytImmune Sciences"; Therapeutic indication (cancer, antiangiogenesis); Dose (2 ug/h);

R0235: J. Folkman. Angiogenesis. *Annual Review of Medicine* 2006;57(1-18)

ALZET Comments: Endostatin, recomb.; IP; Mice; Cardiovascular; ALZET see pg. 8.

P8109: A. E. M. Dirkx, *et al.* Anti-angiogenesis therapy can overcome endothelial cell anergy and promote leukocyte-endothelium interactions and infiltration in tumors. *FASEB Journal* 2006;20(6):621-630

ALZET Comments: Anginex; endostatin; BSA; angiostatin; Saline; SC; Mice; 2 weeks; 7, 11 days; Controls received mp w/ BSA or no treatment; dose-response (fig.5); cancer (melanoma, colon carcinoma); animal info (C57BL/6).

P7564: K. Ichinose, *et al.* Antiangiogenic endostatin peptide ameliorates renal alterations in the early stage of a type 1 diabetic nephropathy model. *Diabetes* 2005;54(10):2891-2903

ALZET Comments: Endostatin, human (1-27); PBS; SC; Mice; 2004; 2 weeks; Controls received mp w/ vehicle; replacement therapy (STZ diabetes); dose-response (fig. 2); no stress (see pg.2892); peptides; animal info (female, C57BL/6, 21-26 g).



13. Etoposide

R0378: B. Halle, *et al.* Convection-enhanced Drug Delivery for Glioblastoma: A Systematic Review Focused on Methodological Differences in the Use of the Convection-enhanced Delivery Method. *Asian J Neurosurg* 2019;14(1):5-14

ALZET Comments: Etoposide, Bevacizumab, IMCA12, Interleukin-13-PE38, Tetrakis Chlorin; CSF/CNS (intratumoral); Mice, Rat; 2001D, 1003D, 1007D, 1004, 2004; 24 hours, 3, 7, 21, 28 days; ALZET brain infusion kit 1,2, and 3 used; cancer (Glioblastoma);

Q5425: A. M. Sonabend, *et al.* Convection-enhanced delivery of etoposide is effective against murine proneural glioblastoma. *Neuro Oncol* 2014;16(9):1210-9

ALZET Comments: Etoposide; PBS; CSF/CNS (intratumoral); Mice; 1007D; 7 days; Controls received mp w/ vehicle; ALZET brain infusion kit 3 used; cancer (proneural glioblastoma); dose-response/dose escalation study (pg. 1212); Toxicology (pg. 1212); Adhesive glue purchased from Scienceware; Cannula penetration depth 2mm; CED stands for convection enhanced delivery; Therapeutic indication (proneural glioblastoma); Dose (200, 400, 600, 800 uM etoposide);

P9777: S. Giraud, *et al.* In vitro apoptotic induction of human glioblastoma cells by Fas ligand plus etoposide and in vivo antitumour activity of combined drugs in xenografted nude rats. *INTERNATIONAL JOURNAL OF ONCOLOGY* 2007;30(273-281

ALZET Comments: Fas ligand; etoposide; dexamethasone; CSF, artificial; CSF/CNS (intratumoral); Rat (nude); 1002; 15 days; Tissue perfusion (tumor); functionality of mp verified by residual volume; cancer (glioblastoma); animal info (female 2 months old, 159 g.).

P5213: D. Peng, *et al.* Transduction of hepatocellular carcinoma (HCC) using recombinant adeno- associated virus (rAAV): in vitro and in vivo effects of genotoxic agents. *J Hepatol* 2000;32(6):975-985

ALZET Comments: Etoposide; IP; Rat; 1 week; Functionality of mp verified by measuring etoposide concentration in tumor tissue; cancer; etoposide (VP-16) is a chemotherapeutic agent.

P2546: G. de Haan, *et al.* Hemotoxicity by prolonged etoposide administration to mice can be prevented by simultaneous growth factor therapy. *Cancer Res* 1995;55(324-329

ALZET Comments: Erythropoietin; Granulocyte-colony stimulating factor; Etoposide; SC; mice; 7 days; dose-response curves (pg. 326-328); cancer; peptides; etoposide is VP-16-213; EPO and VP-16-213 given in same pump initially, but this inactivated the G-CSF; multiple pumps per animal (1-2) for G-CSF/VP-16 mice.

P2305: A. M. E. Claessen, *et al.* Locoregional administration of etoposide, but not of interleukin 2, facilitates active specific immunization in guinea pigs with advanced carcinoma. *Cancer Res* 1992;52(2440-2446

ALZET Comments: Interleukin-2; Etoposide; SC; Guinea pig; 2001; 2002; 1 and 2 weeks; comparison of local injections vs. mp (table, p. 2442); cancer.

P1471: A. M. Claessen, *et al.* Cell-mediated immunity is enhanced by cytostatic drugs continuously released at the site of antigenic stimulation. *Cancer Immunol. Immunother* 1989;28(131-135

ALZET Comments: Etoposide; Fluorouracil, 5-; SC; Guinea pig; 2001; 7 days; comparison of sc injections vs. mp infusion; cancer/immunology; VP-16-213 is etoposide.

14. Fluorouracil

R0357: L. Kucerova, *et al.* Targeted antitumor therapy mediated by prodrug-activating mesenchymal stromal cells. *Cancer Lett* 2017;408(1-9

ALZET Comments: Fluorouracil, 5-; CSF/CNS (ventricle); Rat; cancer (glioblastoma); "The use of Alzet osmotic pumps delivered the prodrug directly to the brain at a constant and defined pace, and therefore reduced the dose of the prodrug required for the same therapeutic effect." pg.5;



Q1661: J. M. Atkinson, *et al.* An Integrated In Vitro and In Vivo High-Throughput Screen Identifies Treatment Leads for Ependymoma. *CANCER CELL* 2011;20(3):384-399

ALZET Comments: Fluorouracil, 5-; SC; Mice (nude); 2001D; Animal info (CD-1, 8 wks old, 23-28 g); cancer.

Q0812: S. Tsukioka, *et al.* Oral fluoropyrimidine S-1 combined with leucovorin is a promising therapy for colorectal cancer: Evidence from a xenograft model of folate-depleted mice. *Molecular Medicine Reports* 2009;2(3):393-398

ALZET Comments: Fluorouracil, 5-; Saline, sterile; SC; Mice (nude); 2002; 14 days; Animal info (BALB/cA-nu/nu, 4-5 wks old); cancer (colorectal); "oral S-1/LV therapy inhibited the growth of COL-1 tumors more effectively than the infusion of 5-FU/LV when administered at doses of similar toxicity" pg 397.

P9489: P. Albertsson, *et al.* Low-dose continuous 5-fluorouracil infusion stimulates VEGF-A-mediated angiogenesis. *Acta Oncologica* 2009;48(3):418-425

ALZET Comments: Fluorouracil, 5-; NaCl; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; no stress (see pg. 420); pumps primed; "No animal died during the surgical procedure or post surgical period"; angiogenesis; "The animals behaved normally and there were no signs of diarrhea or stomatitis." pg 240.

P8790: H. Terazono, *et al.* Modulatory effects of 5-fluorouracil on the rhythmic expression of circadian clock genes: A possible mechanism of chemotherapy-induced circadian rhythm disturbances. *Biochemical Pharmacology* 2008;75(8):1616-1622

ALZET Comments: Fluorouracil, 5-; SC; Mice; 2001; 7 days; Controls received mp w/ saline; animal info (male, ICR, 7 wks old).

P7931: S. Yurimoto, *et al.* Enhancement of the anti-tumor activity of S-1 by low-dose cisplatin in mice bearing the sarcoma-180 model. *Anti-cancer Drugs* 2005;16(10):1109-1114

ALZET Comments: Fluorouracil, 5-; IP; Mice; 1007D; 8 days; Cancer (sarcoma-180); animal info (six week old, male, 30 grams); tumor cells in abdomen; chemotherapeutic.

P7764: L. Pukac, *et al.* HGS-ETR1, a fully human TRAIL-receptor 1 monoclonal antibody, induces cell death in multiple tumour types in vitro and in vivo. *British Journal of Cancer* 2005;92(8):1430-1441

ALZET Comments: Fluorouracil, 5-; SC; Mice (nude); 2002; 14 days; Controls received no treatment; cancer (colon); animal info (female, Swiss, athymic, 7-8 wk old, 20g.).

P7261: K. Nakano, *et al.* Enhanced efficacy of conditionally replicating herpes simplex virus (G207) combined with 5-fluorouracil and surgical resection in peritoneal cancer dissemination models. *JOURNAL OF GENE MEDICINE* 2005;7(5):638-648

ALZET Comments: Fluorouracil, 5-; IP; Mice (SCID); hamster; 2 weeks; Cancer (gastric, gall bladder carcinoma); pyrimidine synthesis inhibitor.

15. Gefitinib

Q0420: S. C. Peng, *et al.* A novel role of CPEB3 in regulating EGFR gene transcription via association with Stat5b in neurons. *NUCLEIC ACIDS RESEARCH* 2010;38(21):7446-7457

ALZET Comments: Endothelial growth factor, recomb.; gefitinib; DMSO; CSF, artificial; BSA; CSF/CNS; Mice; 1004; 14 days; Controls received mp w/ vehicle; animal info (8 wks old, male, C57BL/6J); behavioral testing (Morris water maze test); gefitinib is a chemotherapeutic.

Q0956: S. Agarwal, *et al.* Distribution of Gefitinib to the Brain Is Limited by P-glycoprotein (ABCB1) and Breast Cancer Resistance Protein (ABCG2)-Mediated Active Efflux. *Journal of Pharmacology and Experimental Therapeutics* 2010;334(1):147-155

ALZET Comments: Gefitinib; DMSO; IP; Mice; 1003D; 24, 48 hours; Animal info (wt, Mdr1a/b -/- Bcrp1 -/-); dose-response (Table 1); half-life (p.149) "1 hour in mice"; wound clips used; chemotherapeutic.



16. Imatinib

Q6168: R. C. Nayak, *et al.* The signaling axis atypical protein kinase C lambda/iota-Satb2 mediates leukemic transformation of B-cell progenitors. *Nat Commun* 2019;10(1):1-16

ALZET Comments: Ro-31-8220; imatinib; PBS; SC; Mice (transgenic); 2002; 14 days; Dose (Ro-31-8220 (1 mM); imatinib (0.5 mM)); Controls received mp w/ vehicle; animal info (6-12 week old transgenic mice); enzyme inhibitor (Protein Kinase C);

Q6491: Tucheng Sun, *et al.* Imatinib inhibits angiotensin II-induced aortic dissection through the c-Abl signaling pathway. *International Journal for Clinical Experimental Pathology* 2017;10(5):5316-5324

ALZET Comments: Angiotensin II; Imatinib mesylate; Saline; SC; Mice; 1002; 2 weeks; Dose (Angiotensin II: 3 mg/kg/day; Angiotensin II + Imatinib mesylate: 60 mg/kg per day); 0.9% saline used; Controls received mp w/ vehicle; animal info (12-30 week old C57BL/6 male mice weighing 25-35g); enzyme inhibitor (tyrosine kinase, c-Abl); cardiovascular; Pump incorrectly noted as model #1014D.

Q5735: R. Callahan, *et al.* Original Research: Featured Article: Imatinib mesylate (Gleevec) inhibits Notch and c-Myc signaling: Five-day treatment permanently rescues mammary development. *Exp Biol Med (Maywood)* 2017;242(1):53-67

ALZET Comments: Imatinib mesylate; Saline; SC; Mice (pregnant); 2001; 5 days; Controls received mp w/ vehicle; animal info (10 weeks old); cancer (Breast); Imatinib mesylate a.k.a Gleevec ; Therapeutic indication (Mammary gland development, Breast cancer); Dose (21 mg/mouse/week); enzyme inhibitor (tyrosine kinase);

Q4546: R. J. Napier, *et al.* Low Doses of Imatinib Induce Myelopoiesis and Enhance Host Anti-microbial Immunity. *PLoS Pathogens* 2015;11(U1651-U1677)

ALZET Comments: Imatinib mesylate; Water; SC; Mice; 1007D; 2002; 28 days; Controls received mp w/ vehicle; animal info (male, C57BL6, 6 weeks old); functionality of mp verified by serum levels; dose-response (pg.9); immunology; enzyme inhibitor (tyrosine kinase);

Q3443: J. Chu, *et al.* Pharmacological Modulation of GSAP Reduces Amyloid-beta Levels and Tau Phosphorylation in a Mouse Model of Alzheimer's Disease with Plaques and Tangles. *JOURNAL OF ALZHEIMERS DISEASE* 2014;41(729-737)

ALZET Comments: Imatinib; CSF, artificial; CSF/CNS (intrathecal); Mice (transgenic); 1007D; 1 week; Controls received mp w/ vehicle; animal info (triple transgenic ABBP, PS1, P301L); neurodegenerative (Alzheimer's); "Since it is known that the drug does not penetrate the blood-brain barrier efficiently, it is possible that the contradictory results reflect this property of the drug. For this reason in the current study, we delivered Imatinib by means of implanted osmotic minipumps directly in the brains of the triple transgenic mice" pg 730; Imatinib aka STI571 aka Gleevec; used dental cement; enzyme inhibitor (tyrosine kinase);

Q1933: J. M. Launay, *et al.* Serotonin 5-HT(2B) receptors are required for bone-marrow contribution to pulmonary arterial hypertension. *Blood* 2012;119(7):1772-1780

ALZET Comments: Imatinib mesylate; Mice; 5 weeks; Controls received mp w/ vehicle; animal info (5HT-2b -/-, adult, 7-9 wks old); imatinib mesylate also known as Gleevec or STI-571; hypoxia; enzyme inhibitor (tyrosine kinase);

17. Marimastat

Q4525: D. C. Marshall, *et al.* Selective Allosteric Inhibition of MMP9 Is Efficacious in Preclinical Models of Ulcerative Colitis and Colorectal Cancer. *PLoS One* 2015;10(U2689-U2714)

ALZET Comments: Marimastat; DMSO; water; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, Lewis); 50% DMSO used; behavioral testing (resting posture, gait);



Q2230: S. G. N. Mazurek, *et al.* Functional biomarkers of musculoskeletal syndrome (MSS) for early in vivo screening of selective MMP-13 inhibitors. *Journal of Pharmacological and Toxicological Methods* 2011;64(1):89-96

ALZET Comments: Marimastat; DMSO; water; SC; Rat; 2ML2; 15-17 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 180-370); wound clips used; enzyme inhibitor (matrix metalloproteinase, MMP-13).

Q1475: J. Frant, *et al.* Orally Active, Antimetastatic, Nontoxic Diphenyl Ether-Derived Carbamoylphosphonate Matrix Metalloproteinase Inhibitors. *ChemMedChem* 2011;6(8):1471-1477

ALZET Comments: Marimastat; Propylene glycol; DMSO; SC; Rat; 2ML2; 2 weeks; animal info (male, Lewis, 150-180 g); 50% DMSO used.

P9727: J. B. Skipper, *et al.* In vivo Efficacy of Marimastat and Chemoradiation in Head and Neck Cancer Xenografts. *ORL-JOURNAL FOR OTO-RHINO-LARYNGOLOGY AND ITS RELATED SPECIALTIES* 2009;71(1):1-5

ALZET Comments: Marimastat; DMSO; SC; Mice (nude); 2002; 14 days; Controls received mp w/vehicle; cancer; animal info (3 mo old, female).

P8016: J. S. Fridman, *et al.* Selective inhibition of ADAM metalloproteases as a novel approach for modulating ErbB pathways in cancer. *Clinical Cancer Research* 2007;13(6):1892-1902

ALZET Comments: Marimastat; INCB3619; SC; Mice; mice (nude); 7, 14 days; Controls received mp w/ vehicle; enzyme inhibitor (metalloprotease); cancer (squamous cell carcinoma, breast, lung carcinoma); toxicology; animal info (BALB/c, CD-1 nu/nu); ErbB ligand shedding inhibitor; half-life (pg 1894) "<2h in the mouse" 6.1h in larger animals.

P5943: N. Wada, *et al.* Reduced angiogenesis in peritoneal dissemination of gastric cancer through gelatinase inhibition. *CLINICAL & EXPERIMENTAL METASTASIS* 2003;20(5):431-435

ALZET Comments: Marimastat; DMSO; water; SC; Mice (SCID); 2002; 2 weeks; controls received mp w/ vehicle; enzyme inhibitor (matrix metalloprotease); marimastat, the broad-spectrum matrix metalloproteinase inhibitor was dissolved in 50% DMSO; angiogenesis inhibitor.

P5338: M. Kimata, *et al.* Matrix metalloproteinase inhibitor, marimastat, decreases peritoneal spread of gastric carcinoma in nude mice. *Japanese Journal of Cancer Research* 2002;93(7):834-841

ALZET Comments: Marimastat; DMSO; SC; Mice (nude); 28 days; Controls received mp w/ vehicle; pumps replaced after 14 days; gastric cancer; enzyme inhibitor; matrix metalloproteinase inhibitor; 50% DMSO vehicle.

P5454: P. Charoenrat, *et al.* A synthetic matrix metalloproteinase inhibitor prevents squamous carcinoma cell proliferation by interfering with epidermal growth factor receptor autocrine loops. *International Journal of Cancer* 2002;100(5):527-533

ALZET Comments: Marimastat; DMSO; Water, sterile; SC; Mice; 2002; 17 days; Controls received mp w/ vehicle; cancer; enzyme inhibitor (matrix metalloproteinase).

18. Metacept 1

P9572: C. Restall, *et al.* A novel histone deacetylase inhibitor augments tamoxifen-mediated attenuation of breast carcinoma growth. *International Journal of Cancer* 2009;125(2):483-487

ALZET Comments: Metacept 1; DMSO; cremophor; saline; SC; Mice; 26 days; Half-life (p.483) 20 min.; cancer (breast); animal info (female BALB/c); enzyme inhibitor (histone deacetylase); chemotherapeutic.

19. Methotexate

Q6622: I. M. Moore, *et al.* Effects of Intraventricular Methotrexate on Neuronal Injury and Gene Expression in a Rat Model: Findings From an Exploratory Study. *Biol Res Nurs* 2016;18(5):505-14

ALZET Comments: Methotrexate; CSF, artificial; CSF/CNS (left lateral ventricle); Rat; 1003D; 1 day; Dose (2 mg/kg or 4 mg/kg); Controls received mp w/ vehicle; ALZET brain infusion kit 2 used; Brain coordinates (2 mm left of sagittal suture and



1 mm posterior to coronal suture to a depth of 3.5 mm); Cannula placement verified via injection of Evan's blue dye; cyanoacrylate adhesive;.

Q4967: M. A. Fischer, *et al.* Flaviviruses are sensitive to inhibition of thymidine synthesis pathways. *J Virol* 2013;87(17):9411-9

ALZET Comments: Methotrexate, Floxuridine; DMSO; SC; Mice; 50% DMSO used; animal info (AG129 mice); comparison of IP injections vs mp; Agents are small-molecule inhibitors of dengue virus; immunology;.

P9442: J. Scholz, *et al.* Low-dose methotrexate reduces peripheral nerve injury-evoked spinal microglial activation and neuropathic pain behavior in rats. *Pain* 2008;138(1):130-142

ALZET Comments: Methotrexate; dexamethasone; CSF, artificial; PBS; CSF/CNS (intrathecal); Rat; 7, 14 days; Controls received mp w/ vehicle; dose-response (fig. 7); comparison of IP injections vs. mp; enzyme inhibitor (dihydrofolate reductase); animal info (male, Sprague Dawley, 160-200 g., SNI); behavioral testing (paw withdrawal, mechanical allodynia, cold allodynia); "sustained intrathecal treatment may therefore suppress microglial activation much more efficiently than intermittent high-dose bolus injections." (p. 140).

P7278: E. D. Lobo, *et al.* Application of anti-methotrexate Fab fragments for the optimization of intraperitoneal methotrexate therapy in a murine model of peritoneal cancer. *Journal of Pharmaceutical Sciences* 2005;94(9):1957-1964

ALZET Comments: Methotrexate; IP; Mice; 1003D; 72 hours; Controls received ip bolus saline injection; dose-response (fig. 3); cancer (peritoneal sarcoma); toxicology; mp primed overnight in 37 degrees saline.

P6106: E. D. Lobo, *et al.* Application of pharmacokinetic-pharmacodynamic modeling to predict the kinetic and dynamic effects of anti-methotrexate antibodies in mice. *Journal of Pharmaceutical Sciences* 2003;92(8):1665-1676

ALZET Comments: Methotrexate; Saline; IP; Mice; Controls received mp w/ vehicle; IP catheter used; pump model or duration not stated.

P6105: E. D. Lobo, *et al.* Pharmacokinetic-pharmacodynamic modeling of methotrexate-induced toxicity in mice. *Journal of Pharmaceutical Sciences* 2003;92(8):1654-1664

ALZET Comments: Methotrexate; Saline; IP; Mice; 1003D; 2001D; 2001; 1,3,7 days; Controls received mp w/ vehicle; mtx plasma levels taken; dose-response (p. 1659); comparison of bolus injections vs. IP mp; toxicology; IP catheter used.

20. Other

Q2575: L. Li, *et al.* Brain Efflux Index To Investigate the Influence of Active Efflux on Brain Distribution of Pemetrexed and Methotrexate. *Drug Metabolism and Disposition* 2013;41(3):659-667

ALZET Comments: Pemetrexed; IP; Mice; 1003D; 72 hours; animal info (C57BL/6, male, Bcrp 1 -/-); post op. care (ibuprofen in the drinking water); pemetrexed is an antifolate; chemotherapeutic;.

Q2916: A. Z. Dudek, *et al.* Brain Metastases from Renal Cell Carcinoma in the Era of Tyrosine Kinase Inhibitors. *Clinical Genitourinary Cancer* 2013;11(2):155-160

ALZET Comments: Sorafenib; sunitinib; DMSO; saline; IP; 1003D; Animal info (Friend virus B-type (FVB) wild type, and Abcb1a/b knockout mice); cancer (renal carcinoma and brain metastases); cancer; enzyme inhibitor (tyrosine kinase); chemotherapeutic.

Q2576: S. Agarwal, *et al.* Function of the Blood-Brain Barrier and Restriction of Drug Delivery to Invasive Glioma Cells: Findings in an Orthotopic Rat Xenograft Model of Glioma. *Drug Metabolism and Disposition* 2013;41(1):33-39

ALZET Comments: Erlotinib; DMSO; IP; Mice; 1003D; 48 hours; Animal info (Mdr1ab -/-, Bcrp1 -/-, 8-10 wks old); wound clips used; half-life ("approximately 1 hour") pg 34; cancer (glioma); "Erlotinib half-life in mice has been reported to be approximately 1 hour (Marchetti et al., 2008), so an infusion lasting 48 hours was considered to be sufficient to attain steady state in both the brain and plasma." pg 34; chemotherapeutic; enzyme inhibitor (tyrosine kinase);.



Q1928: T. L. Wang, *et al.* Brain Distribution of Cediranib Is Limited by Active Efflux at the Blood-Brain Barrier. *Journal of Pharmacology and Experimental Therapeutics* 2012;341(2):386-395

ALZET Comments: Cediranib; DMSO; IP; Mice; 1003D; 72 hours; Animal info (wt, Mdr1a/b -/-, Bcrp1 -/-, and Mdr1a/b -/-, Bcrp1 -/-); cancer (glioma); enzyme inhibitor (tyrosine kinase); chemotherapeutic.

Q2729: K. G. Roberts, *et al.* Genetic Alterations Activating Kinase and Cytokine Receptor Signaling in High-Risk Acute Lymphoblastic Leukemia. *CANCER CELL* 2012;22(2):153-166

ALZET Comments: Ruxolitinib; Dimethylacetamide; propylene glycol; SC; Mice; 4 weeks; Control animals received mp w/ vehicle; animal info (BCR-JAK2); enzyme inhibitor (JAK2, janus kinase 2); cancer; chemotherapeutic; 40% DMA used; 60% propylene glycol used;.

Q2184: R. K. Mittapalli, *et al.* Impact of P-Glycoprotein (ABCB1) and Breast Cancer Resistance Protein (ABCG2) on the Brain Distribution of a Novel BRAF Inhibitor: Vemurafenib (PLX4032). *Journal of Pharmacology and Experimental Therapeutics* 2012;342(1):33-40

ALZET Comments: Vemurafenib; DMSO; propylene glycol; saline; IP; Mice; 48 hours; Animal info (wt, Mdr1a/b -/-, Bcrp1 -/-); infusion rate of 1 ul/hr; wound clips used; brain tissue distribution; cancer (breast); vemurafenib also known as PLX4032; 40% DMSO used; chemotherapeutic.

Q2314: S. L. Maude, *et al.* Targeting JAK1/2 and mTOR in murine xenograft models of Ph-like acute lymphoblastic leukemia. *Blood* 2012;120(17):3510-3518

ALZET Comments: Ruxolitinib; Dimethylacetamide; propylene glycol; SC; Mice (NSG); 3-4 weeks; Control animals received mp w/ vehicle; animal info (NOD SCID, nonobese); ruxolitinib also known as INCB018424; stress/adverse effects "One ruxolitinib-treated mouse... experienced a wound dehiscence at the subcutaneous pump surgical site" pg 3512; cancer (leukemia); chemotherapeutic; 40% DMA used; 60% propylene glycol used;.

Q1785: P. Albertsson, *et al.* Low-dosage metronomic chemotherapy and angiogenesis: topoisomerase inhibitors irinotecan and mitoxantrone stimulate VEGF-A-mediated angiogenesis. *APMIS* 2012;120(2):147-156

ALZET Comments: Irinotecan; mitoxantrone; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, adult); chemotherapeutic;.

Q1219: L. Martiniova, *et al.* Pharmacologic Modulation of Serine/Threonine Phosphorylation Highly Sensitizes PHEO in a MPC Cell and Mouse Model to Conventional Chemotherapy. *PLoS One* 2011;6(2):U67-U74

ALZET Comments: LB1; PBS; IP; Mice (nude); 1002; 2 weeks; Controls received mp w/ vehicle; animal info (female, athymic, NCr-nu, 6-10 wks old); cancer; enzyme inhibitor (serine/threonine protein phosphatase 2A, PP2A); chemotherapeutic.

Q0921: R. T. Hinkle, *et al.* Treatment with a corticotrophin releasing factor 2 receptor agonist modulates skeletal muscle mass and force production in aged and chronically ill animals. *BMC MUSCULOSKELETAL DISORDERS* 2011;12(;):U1-U12

ALZET Comments: PG-873637; Saline, physiological; SC; Rat; 1, 3, 5 months; Controls received mp w/ vehicle; animal info (F344, female, 24 mo old, myocardial infarction); long-term study; pumps replaced every 28 days; PG873637 is a CRF2R selective agonist; 28-day pumps used; new agent; chemotherapeutic.

Q0773: P. Cuevas, *et al.* Antiglioma effects of a new, low molecular mass, inhibitor of fibroblast growth factor. *Neuroscience Letters* 2011;491(1):1-7

ALZET Comments: Dobesilate; PBS; CSF/CNS (intratumoral); Rat; 2004; 27 days; Controls received mp w/ vehicle; cancer (glioma); Compound, also known as (2,5-dihydroxyphenyl-sulfonate or 2,5DHPS) is an FGF inhibitor; chemotherapeutic.

Q1745: M. E. Balasis, *et al.* Combination of Farnesyltransferase and Akt Inhibitors Is Synergistic in Breast Cancer Cells and Causes Significant Breast Tumor Regression in ErbB2 Transgenic Mice. *Clinical Cancer Research* 2011;17(9):2852-2862

ALZET Comments: Tipifarnib; Cyclodextrin, 2-hydroxypropyl-b-; DMSO; Mice; 2002; 14 days; Animal info (MMTV/neu); 20% cyclodextrin used; enzyme inhibitor (farnesyltransferase); cancer (breast); chemotherapeutic.



Q1442: S. Agarwal, *et al.* The Role of the Breast Cancer Resistance Protein (ABCG2) in the Distribution of Sorafenib to the Brain. *Journal of Pharmacology and Experimental Therapeutics* 2011;336(1):223-233

ALZET Comments: Sorafenib; DMSO; IP; Mice; 1003D; 48 hours; Animal info (FVB wild-type, *Mdr1a/b* *-/-*, *Bcrp1* *-/-*, *Mdr1a/b* *-/-*, *Bcrp1* *-/-*); half-life pg 226 "Sorafenib half-life in plasma and brain after an intravenous dose was determined to be 1.6 and 0.9 h, respectively. Therefore an infusion lasting 48 h was considered to be sufficiently long to attain steady state in both plasma and brain."; good methods, pg 226 "In the intraperitoneal infusion studies, the apparent plasma clearance (CL_{app}) was calculated by using the equation, $CL_{app} = k(0)/C_{ss}$, where, $k(0)$ is the rate of infusion into the peritoneal cavity normalized to body weight (ng/h/kg), and C_{ss} is the plasma concentration at steady state (ng/ml)."; enzyme inhibitor (biaryl-urea RAF kinase, tyrosine kinase); cancer (glioma); chemotherapeutic.

Q0715: M. A. Shibata, *et al.* Raloxifene inhibits tumor growth and lymph node metastasis in a xenograft model of metastatic mammary cancer. *BMC CANCER* 2010;10(:):U1-U14

ALZET Comments: Raloxifene; DMSO; ethanol; SC; Mice; 2002; 6 weeks; Animal info (female, 6 wks old, BALB/c); pumps replaced every other week; cancer (metastatic breast cancer); stress/adverse reaction: "one animal died from an overdose of anesthesia when the osmotic mini-pumps were changed" (see pg. 7 of 14); raloxifene is a novel selective estrogen receptor modulator; chemotherapeutic.

Q0420: S. C. Peng, *et al.* A novel role of CPEB3 in regulating EGFR gene transcription via association with Stat5b in neurons. *NUCLEIC ACIDS RESEARCH* 2010;38(21):7446-7457

ALZET Comments: Endothelial growth factor, recomb.; gefitinib; DMSO; CSF, artificial; BSA; CSF/CNS; Mice; 1004; 14 days; Controls received mp w/ vehicle; animal info (8 wks old, male, C57BL/6J); behavioral testing (Morris water maze test); gefitinib is a chemotherapeutic.

Q0306: K. Norrby, *et al.* Dalteparin, a low-molecular-weight heparin, promotes angiogenesis mediated by heparin-binding VEGF-A in vivo. *APMIS* 2010;118(12):949-957

ALZET Comments: Dalteparin; epirubicin; Saline; SC; Rat; 2002; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (adult, male, Sprague-Dawley, 6-7 wks old, 218-223 g.); cancer; multiple pumps per animal (2); dalteparin is a low-molecular-weight heparin; epirubicin is a chemotherapeutic.

P9917: B. W. Murray, *et al.* Small-molecule p21-activated kinase inhibitor PF-3758309 is a potent inhibitor of oncogenic signaling and tumor growth. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2010;107(20):9446-9451

ALZET Comments: PF-3758309; Mice (nude); 9 days; Dose response; enzyme inhibitor (P21-activated kinase); animal info (athymic, CRL breed, 6-8 weeks); cancer; chemotherapeutic.

Q0584: K. D. Lynn, *et al.* GU81, a VEGFR2 antagonist peptoid, enhances the anti-tumor activity of doxorubicin in the murine MMTV-PyMT transgenic model of breast cancer. *BMC CANCER* 2010;10(:):U1-U13

ALZET Comments: GU81; IP; Mice (transgenic); 19 days; Animal info (MMTV-PyMT/Fvb tg, 6 wks old); possibly Model 2004 used (100 ul in 19 days = 0.22 ul/hr); cancer (breast); GU81 is a VEGFR2 antagonist peptoid; chemotherapeutic.

Q0664: J. M. Argiles, *et al.* PATTERNS OF GENE EXPRESSION IN MUSCLE AND FAT IN TUMOR-BEARING RATS: EFFECTS OF CRF2R AGONIST ON CACHEXIA. *Muscle & Nerve* 2010;42(6):936-949

ALZET Comments: PG-873637; SC; Rat; Controls received mp w/ NaCl; animal info (male, Wistar, 5 wks old); cancer; PG-873637 is a CRF2R agonist; chemotherapeutic.

Q0956: S. Agarwal, *et al.* Distribution of Gefitinib to the Brain Is Limited by P-glycoprotein (ABCB1) and Breast Cancer Resistance Protein (ABCG2)-Mediated Active Efflux. *Journal of Pharmacology and Experimental Therapeutics* 2010;334(1):147-155

ALZET Comments: Gefitinib; DMSO; IP; Mice; 1003D; 24, 48 hours; Animal info (wt, *Mdr1a/b* *-/-* *Bcrp1* *-/-*,); dose-response (Table 1); half-life (p.149) "1 hour in mice"; wound clips used; chemotherapeutic.



Q0673: C. L. Roland, *et al.* Cytokine Levels Correlate with Immune Cell Infiltration after Anti-VEGF Therapy in Preclinical Mouse Models of Breast Cancer. *PLoS One* 2009;4(11):U41-U53

ALZET Comments: GU81; IP; Mice (NOD/SCID); 1, 3, 4 weeks; Controls received IP IgG injection; animal info (6-8 wks old, female, NOD/SCID, BALB/c); cancer (breast); chemotherapeutic.

P9572: C. Restall, *et al.* A novel histone deacetylase inhibitor augments tamoxifen-mediated attenuation of breast carcinoma growth. *International Journal of Cancer* 2009;125(2):483-487

ALZET Comments: Metacept 1; DMSO; cremophor; saline; SC; Mice; 26 days; Half-life (p.483) 20 min.; cancer (breast); animal info (female BALB/c); enzyme inhibitor (histone deacetylase); chemotherapeutic.

P9538: A. Kazi, *et al.* Blockade of Protein Geranylgeranylation Inhibits Cdk2-Dependent p27^{Kip1} Phosphorylation on Thr187 and Accumulates p27^{Kip1} in the Nucleus: Implications for Breast Cancer Therapy. *MOLECULAR AND CELLULAR BIOLOGY* 2009;29(8):2254-2263

ALZET Comments: GGTI-2418; Polyethylene glycol; DMSO; SC; Mice (nude); 14 days; Controls received mp w/vehicle; cancer (breast); 20% DMSO used; enzyme inhibitor (geranylgeranyltransferase I); chemotherapeutic.

Q0104: B. Hokschi, *et al.* Taurolidine in the prevention and therapy of lung metastases. *European Journal of Cardio-thoracic Surgery* 2009;36(6):1058-1063

ALZET Comments: Taurolidine; IV; Rat; 7 days; Controls received tumoral implantation w/o mp; animal info (275-380 g, bdx); 2ML sized pump used; chemotherapeutic.

P9597: D. M. Beauvais, *et al.* Syndecan-1 regulates $\alpha_v\beta_3$ and $\alpha_v\beta_5$ integrin activation during angiogenesis and is blocked by synstatin, a novel peptide inhibitor. *Journal of Experimental Medicine* 2009;206(3):691-705

ALZET Comments: Synstatin (82-130); synstatin (94-119); synstatin (92-119); cyclic RGDfv; cyclic RADfv; PBS; DMSO; H₂O, double distilled; Mice (nude); 2004; 4 weeks; Controls received mp w/vehicle, or PBS; cancer; peptides; animal info (6-8 wks old, female, athymic, BALB/c); 50% DMSO used; chemotherapeutic.

Q0602: P. Beauparlant, *et al.* Preclinical development of the nicotinamide phosphoribosyl transferase inhibitor prodrug GMX1777. *Anti-cancer Drugs* 2009;20(5):346-354

ALZET Comments: GMX1777; NaCl; IV (jugular); Mice (nude; SCID); 2001D; 24 hours; Controls received mp w/ vehicle; animal info (BalbC nude, CB17, SCID/SCID, female); comparison of 72 h infusion pump vs 24 h mp; cancer (refractory solid tumors and lymphomas); "The 24 h infusion was the most effective administration schedule identified in mouse xenograft models" pg 352-353; cancer; chemotherapeutic.

P9278: R. Nasr, *et al.* Eradication of acute promyelocytic leukemia-initiating cells through PML-RARA degradation. *Nature Medicine* 2008;14(12):1333-1342

ALZET Comments: Bortezomib; cyclic AMP; H89; SC; Mice (nude); mice (transgenic); 1, 3, 6, 7 days; Controls received no treatment; enzyme inhibitor (PKA); cancer (acute promyelocytic leukemia); animal info (nude, PLZF-RARA-RARA-PLZF; PML-RARA5873A Tg); Bortezomib is a proteasom inhibitor; chemotherapeutic;.

Q0501: C. K. Donawho, *et al.* ABT-888, an orallyactive poly(ADP-ribose) polymerase inhibitor that potentiates DNA-damaging agents in preclinical tumor models. *Clinical Cancer Research* 2007;13(9):2728-2737

ALZET Comments: ABT-888; Saline; SC; Mice (nude; SCID); 2002; 14 days; Controls received mp w/ vehicle; dose-response (pg 2732, fig. 2); cancer; animal info (C57BL/6, SCID); chemotherapeutic; "ABT-888 administered... via (minipump) not only potentiated cyclophosphamide... but also caused tumor regression, whereas the cyclophosphamide monotherapy only slightly delayed tumor growth." pg 2733.

P8159: S. Bihorel, *et al.* Influence of hydroxyurea on imatinib mesylate (gleevec) transport at the mouse blood-brain barrier. *Drug Metabolism and Disposition* 2006;34(12):1945-1949

ALZET Comments: Imatinib mesylate; hydroxyurea; Saline; SC; Rat; 2ML2; 7, 14 days; Half-life (p. 1948) hydroxyurea <1 hour in rats; enzyme inhibitor (ribonucleotide reductase, tyrosine kinase); cancer (glioblastoma); animal info (Hanover Wistar, 270-310 grams); ATP competitive inhibitor; A.K.A, Gleevec or STI571; chemotherapeutic.



P7931: S. Yurimoto, *et al.* Enhancement of the anti-tumor activity of S-1 by low-dose cisplatin in mice bearing the sarcoma-180 model. *Anti-cancer Drugs* 2005;16(10):1109-1114

ALZET Comments: Fluorouracil, 5-; IP; Mice; 1007D; 8 days; Cancer (sarcoma-180); animal info (six week old, male, 30 grams); tumor cells in abdomen; chemotherapeutic.

P8287: T. Manabe, *et al.* New infusion device for trans-tissue, sustained local delivery of anticancer agent to surgically resected tissue: Potential use for suppression of local recurrence of pancreatic cancer. *JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART B-APPLIED BIOMATERIALS* 2005;73B(1):203-207

ALZET Comments: Gemcitabine; SC; Mice (nude); 1007D; 7 days; Tissue perfusion (intratumoral); comparison of IP injections; cancer (pancreatic); animal info (five week old); pump used as part of a novel infusion device; pictures of device p. 205; PE tubing used to connect pump to perfusion device; continuous infusion resulted in macroscopically undetectable tumors after day 6; chemotherapeutic;.

P6394: M. Sudoh, *et al.* A new animal model of continuous catheterization for investigating mechanisms of arteritis associated with chemotherapy. *LIFE SCIENCES* 2004;74(24):3025-3032

ALZET Comments: Fluorouracil, 5-FU; peplomycin; Saline, heparinized; IA (abdominal aorta); Rat; 2ML1; 7 days; Controls received mp w/ vehicle; cancer; chemotherapeutic agents; PE-10 and 60 used; tubing attached using a moment binding agent (alon-alfa); catheter schematic p. 3027; pump placed IP.

P6260: R. B. Gibbs, *et al.* Effects of raloxifene and estradiol on hippocampal acetylcholine release and spatial learning in the rat. *Psychoneuroendocrinology* 2004;29(6):741-748

ALZET Comments: Raloxifene; Estradiol, 17B-; DMSO; Cyclodextrin, 2-hydroxypropyl-b- (molecusol); SC; Rat; 2004; Controls received mp w/ vehicle; replacement therapy (ovariectomy); pumps replaced every 28 days; 20% cyclodextrin & 1% DMSO used; incorrectly states pumping rate as 2.5 ul/hr; behavioral study; research diets; chemotherapeutic.

P7697: O. Stoeltzing, *et al.* Inhibition of integrin alpha beta 1 function with a small peptide (ATN-161) plus continuous 5-FU infusion reduces colorectal liver metastases and improves survival in mice. *Int. J. Cancer* 2003;104(4):496-503

ALZET Comments: Fluorouracil, 5-; Saline; IP; Mice; 2002; 2 weeks; Controls received mp w/ vehicle; cancer; angiogenesis; "In preliminary studies..., we observed severe side effects with 5-FU...biweekly injections...thus, we chose to deliver 5-FU by continuous infusion...to minimize toxicity. Additionally, studies have demonstrated an increased efficacy of chemotherapeutic agents when administered continuously." (p. 497).

P6470: S. Ohtsukasa, *et al.* Increased expression of CEA and MHC class I in colorectal cancer cell lines exposed to chemotherapy drugs. *Journal of Cancer Research and Clinical Oncology* 2003;129(12):719-726

ALZET Comments: CDDP; fluorouracil, 5-; IP; Mice; 1007D; 14 days; Controls received mp w/ saline; pumps replaced after 7 days; cancer (colorectal); CDDP (Cisdiamminedichloroplatinum II); is a chemotherapeutic agent.

P5136: C. Morales, *et al.* Antitumoral effect of irinotecan (CPT-11) on an experimental model of malignant neuroectodermal tumor. *Journal of Neuro-oncology* 2002;56(219-226

ALZET Comments: Irinotecan (CPT-11); Saline; IP; Rat; 2004; 28 days; functionality of mp verified by residual content; comparison of IP and intratumoral injections vs. mp; no stress (see p. 222): animals tolerated the pumps: no infections or peritoneal fibrosis were observed; cancer; enzyme inhibitor (topoisomerase I); animals with pumps showed less toxicity: "schedules of continuous administration of CPT-11 were more efficacious and less toxic..." (p. 223); chemotherapeutic;.

P5213: D. Peng, *et al.* Transduction of hepatocellular carcinoma (HCC) using recombinant adeno- associated virus (rAAV): in vitro and in vivo effects of genotoxic agents. *J Hepatol* 2000;32(6):975-985

ALZET Comments: Etoposide; IP; Rat; 1 week; Functionality of mp verified by measuring etoposide concentration in tumor tissue; cancer; etoposide (VP-16) is a chemotherapeutic agent.

P3566: G. Veerman, *et al.* Antitumor activity of prolonged as compared with bolus administration of 2',2'-difluorodeoxycytidine in vivo against murine colon tumors. *Cancer Chemother. Pharmacol* 1996;335-342



ALZET Comments: Gemcitabine; SC; Mice; 1003D; 1007D; 3, 7 days; Functionality of mp verified by in vitro testing; comparison of ip and bench-mounted infusion pump injections vs. mp; half-life (p. 1996); cancer; toxicology; "...prolonged infusion of gemcitabine can give a better antitumor activity than bolus injections and shows promise of being active in clinical trials." (p. 335); 2',2'-difluorodeoxycytidine is gemcitabine; chemotherapeutic;.

21. Paclitaxel

Q5313: M. Cadamuro, *et al.* Low-Dose Paclitaxel Reduces S100A4 Nuclear Import to Inhibit Invasion and Hematogenous Metastasis of Cholangiocarcinoma. *Cancer Res* 2016;76(16):4775-84

ALZET Comments: Paclitaxel; Cremophor EL, Ethanol; IP; Mice (SCID); 1004; 2 weeks; Controls received mp w/ vehicle; animal info (SCID mice 6–8 weeks old); functionality of mp verified by bioluminescence imaging to check metastatic spread; 50% Cremophor, 50% ethanol used; cancer (Cholangiocarcinoma); Xenograft model; Dose (2.6 mg/kg/d);.

Q5562: P. G. Popovich, *et al.* Independent evaluation of the anatomical and behavioral effects of Taxol in rat models of spinal cord injury. *Exp Neurol* 2014;261(97-108)

ALZET Comments: Paclitaxel; Cremophor; ethanol; CSF/CNS (intrathecal); Rat; 2004; 28 days; Controls received mp w/ vehicle; animal info (Female Sprague-dawley rats, 10 weeks old, 215 g); functionality of mp verified by (pg. 100); good methods (pg. 99); spinal cord injury; post op. care (wound clips used; cages maintained at 37 degrees during recovery; daily injections of Gentocin (5 mg/kg) and saline for 7 days); Taxol aka Paclitaxel; Taxol is an anti-neoplastic microtubule stabilizing agent; reduces fibroglotic scarring caused by dorsal spinal hemisection; injury recovery; ALZET rat intrathecal catheter used for custom designed catheter; Therapeutic indication (spinal cord injury); Dose (256 ng/day);.

Q2550: Z. L. Zhou, *et al.* A combination of taxol infusion and human umbilical cord mesenchymal stem cells transplantation for the treatment of rat spinal cord injury. *Brain Research* 2012;1481(;):79-89

ALZET Comments: Paclitaxel; Ethanol; cremophor EL; CSF/CNS (intrathecal); Rat; 2004; 28 days; Control animals received mp w/ PBS; animal info (Sprague Dawley, female, 200-250 g); Paclitaxel also known as Taxol; 50% ethanol used; 50% cremophor EL used; spinal cord injury.

Q2383: K. Serizawa, *et al.* Paclitaxel-Induced Endothelial Dysfunction in Living Rats Is Prevented by Nicorandil via Reduction of Oxidative Stress. *JOURNAL OF PHARMACOLOGICAL SCIENCES* 2012;119(4):349-358

ALZET Comments: Paclitaxel; DMSO; cremophor EL; water, distilled; SC; Rat; mice; 2ML1; 1007D; 1 week; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 250-300; ICR, male, 10-11 wks old); post op. care (bupivacaine); 50% DMSO used; 25% Cremophor EL used.

Q5522: V. Vassileva, *et al.* Effects of sustained and intermittent paclitaxel therapy on tumor repopulation in ovarian cancer. *Mol Cancer Ther* 2008;7(3):630-7

ALZET Comments: Paclitaxel; Saline; IP; Mice; 14 days; animal info (CD1 Immunocompromised); Ovarian cancer; "The Alzet pumps provided continuous release of paclitaxel directly at the tumor site, allowing for enhanced drug penetration into the inner layers of the tumor and greater tumor cell kill." Pg. 637; paclitaxel aka Taxol; Therapeutic indication (Ovarian cancer); Dose (20 mg/kg/wk);.

P7768: J. E. Damber, *et al.* The anti-tumour effect of low-dose continuous chemotherapy may partly be mediated by thrombospondin. *Cancer Chemotherapy and Pharmacology* 2006;58(3):354-360

ALZET Comments: Cyclophosphamide; paclitaxel; Saline; SC; Rat; 2ML1; 10 days; Controls received mp w/ vehicle; cancer (AT-1 adenocarcinoma); animal info (adult, male, copenhagen); "Continuous/metronomic therapy may achieve a more pronounced anti-tumoural effect and significantly diminish the side effects compared with conventional bolus MTD-type chemotherapy." (p. 359).

22. TIMP



P5373: M. Takahashi, *et al.* *In vivo* glioma growth requires host-derived matrix metalloproteinase 2 for maintenance of angioarchitecture. *Pharmacological Research* 2002;46(2):155-163

ALZET Comments: TIMP-1; TIMP-2; PBS; CSF/CNS (intratumoral); Rat; 2002; 3, 7, or 14 days; Controls received mp w/ vehicle; tissue perfusion (tumor); functionality of mp verified by immunohistochemistry of agents; cancer; enzyme inhibitor; ALZET brain infusion kit used; MMP inhibitors (tissue inhibitors of metalloprotease = TIMP); rat glioma model.

23. Topotecan

Q6792: G. M. Shackelford, *et al.* Continuous and bolus intraventricular topotecan prolong survival in a mouse model of leptomeningeal medulloblastoma. *PLoS One* 2019;14(1):e0206394

ALZET Comments: Topotecan; Saline; CSF/CNS (ventricle); Mice; 2004; 28 days; Dose (5.28 µg/day); Controls received mp w/ vehicle; animal info (J:NU mice (homozygous for the Foxn1nu mutation); comparison of bolus dosing vs mp; cancer (Leptomeningeal medulloblastoma);

Q6341: G. Pascual-Pasto, *et al.* Increased delivery of chemotherapy to the vitreous by inhibition of the blood-retinal barrier. *J Control Release* 2017;264(34-44

ALZET Comments: Topotecan; SC; Mice (nude); 2001D; cancer;

Q3002: F. Lin, *et al.* Abcc4 Together with Abcb1 and Abcg2 Form a Robust Cooperative Drug Efflux System That Restricts the Brain Entry of Camptothecin Analogues. *Clinical Cancer Research* 2013;19(8):2084-2095

ALZET Comments: Topotecan; Glucose; SC; Mice; 1003D; Animal info (WT, Abcg2^{-/-}, Abcb1a/b^{-/-}, Abcc4^{-/-}, 8-14 wks old); Camptothecins brain distribution (Fig. 5).

Q1881: H. S. Huang, *et al.* Topoisomerase inhibitors unsilence the dormant allele of Ube3a in neurons. *Nature* 2012;481(7380):185-U90

ALZET Comments: Topotecan; Tartaric acid; saline; CSF/CNS; Mice; 2001; 2002; 5, 14 days; Animal info (Ube3a m⁺/pYfP); cyanoacrylate adhesive used; schematic of cannula insertion (Fig 3a).

Q1723: K. A. Lopez, *et al.* Convection-Enhanced Delivery of Topotecan into a PDGF-Driven Model of Glioblastoma Prolongs Survival and Ablates Both Tumor-Initiating Cells and Recruited Glial Progenitors. *Cancer Research* 2011;71(11):3963-3971

ALZET Comments: Topotecan hydrochloride; CSF/CNS (frontal subcortical white matter); Rat; 2ML1; 1, 4, 7 days; Controls received mp w/ PBS; ALZET brain infusion kit II used; cyanoacrylate adhesive used; cancer (glioma); convection enhanced delivery.

Q2212: I. A. Aljuffali, *et al.* Enhanced antitumor activity of low-dose continuous administration schedules of topotecan in prostate cancer. *CANCER BIOLOGY & THERAPY* 2011;12(5):407-420

ALZET Comments: Topotecan; Saline; SC; Mice (nude); 28 days; Controls received mp w/ vehicle; animal info (NCr, male); cancer (prostate).

24. Vinblastine

P8780: P. Albertsson, *et al.* Dose effects of continuous vinblastine chemotherapy on mammalian angiogenesis mediated by VEGF-A. *Acta Oncologica* 2008;47(2):293-300

ALZET Comments: Vinblastine sulfate; Saline, physiological; SC; Rat; 2001; 2ML1; 6-10 days; Controls received mp w/ vehicle; dose-response (fig. 2); no stress (see pg. 296); cancer; animal info (male, Sprague Dawley, 217-219g.).

P8474: G. Klement, *et al.* Continuous low-dose therapy with vinblastine and VEGF receptor-2 antibody induces sustained tumor regression without overt toxicity. *Journal of Clinical Investigation* 2000;105(8):15-24



ALZET Comments: Vinblastine sulfate; Saline; SC; Mice (SCID); 3 weeks; Controls received IP injections; comparison of IP injections vs. mp; no stress (see pg. R19); cancer (neuroblastoma); toxicology; animal info (SCID, 4-6 weeks old, 15-20 grams); IP bolus given at start of mp treatment.

P4402: D.-D. Vu, *et al.* In vivo model for the experimental manipulation of calcified tissues: A surgical approach for accessing the odontogenic organ and associated tissues of the rat incisor;. *Journal of Histochemistry and Cytochemistry* 1999;47(3):323-336

ALZET Comments: Vinblastine sulfate; fetuin-gold; BSA, dinitrophenol-tagged-; Saline, physiological; Bone; Rat; 1003D; 2001D; 1, 3 days; controls received mp with vehicle; tissue perfusion (alveolar bone); "Minipumps...are advantageous compared to microinjection because they can deliver, in a controlled and continuous manner, relatively large amounts of experimental agents through a bony window" p. 325;.

P4575: J. van Asperen, *et al.* Comparative pharmacokinetics of vinblastine after a 96-hour continuous infusion in wild-type mice and mice lacking mdr1a P-Glycoprotein. *The Journal of Pharmacology and Experimental Therapeutics* 1999;289(1):329-333

ALZET Comments: Vinblastine; Dextrose; SC; Mice; 2001; 96 hours; Functionality of mp verified by plasma levels; half-life (p. 330); antineoplastic.

P1935: G. B. Sivolapenko, *et al.* Xenogenic monoclonal antibodies in the management of cancer: control of their in vivo immunogenicity and induction of specific unresponsiveness using an antibody-drug immunoconjugate. *Br. J. Cancer* 1991;64(281-287

ALZET Comments: Vinblastine; SC; rabbit; 2ML1; no duration posted; cancer.

P1379: M. Kanje, *et al.* A new method for studies of the effects of locally applied drugs on peripheral nerve regeneration in vivo. *Brain Research* 1988;439(116-121

ALZET Comments: Actinomycin D; Cycloheximide; Mitomycin C; Vinblastine; Ringer's solution; CSF/CNS (sciatic nerve); Rat; 2001; 2002; 3, 4, 6 days; mp connected to silicone cuff; functionality of mp verified in vivo with dye; tissue perfusion.

25. Vincristine

Q3282: Y. Yang, *et al.* Spinal Changes of a Newly Isolated Neuropeptide Endomorphin-2 Concomitant with Vincristine-Induced Allodynia. *PLoS One* 2014;9(2):U627-U638

ALZET Comments: Vincristine; IV (jugular); Rat; 2002; 2 weeks; Control animals received mp w/ saline; animal info (adult, male, Sprague Dawley, 200 g).

Q3517: M. F. Jarvis, *et al.* A peripherally acting, selective T-type calcium channel blocker, ABT-639, effectively reduces nociceptive and neuropathic pain in rats. *Biochemical Pharmacology* 2014;89(536-544

ALZET Comments: Vincristine sulfate; IV (jugular); Rat; 2002; 14 days; Animal info (male, Sprague Dawley, 200-420g); behavioral testing (paw withdrawal); pumps primes overnight; used PE-60 catheter tubing; chemotherapy-induced neuropathic pain model;.

Q3089: X. T. Ji, *et al.* Spinal Astrocytic Activation Contributes to Mechanical Allodynia in a Rat Chemotherapy-Induced Neuropathic Pain Model. *PLoS One* 2013;8(4):U440-U451

ALZET Comments: Vincristine; Saline; IV (jugular); Rat; 2002; 14 days; Controls received mp w/ vehicle; animal info (male, adult, sprague dawley, 200g); behavioral testing (Rotarod test, Von Frey monofilaments, Hargreaves' method); "Implantation of the mini-osmotic pump is a simple procedure with the advantages of performing only once, providing reliable intravenous drug delivery, taking little time to perform, and good tolerance" pg 9; Used to induce chemotherapy-induced neuropathic pain in rat model.

Q1941: G. F. Xi, *et al.* Efficacy of interstitial continuous vincristine infusion in a bioluminescent rodent intracranial tumor model. *Journal of Neuro-oncology* 2012;106(2):261-270



ALZET Comments: Vincristine; Saline; CSF/CNS (striatum); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Fischer 344, 180-220 g); ALZET brain infusion kit used.

P8148: P. Honore, *et al.* A-740003 [N-(1-[[cyanoimino](5-quinolinylamino)methyl]amino)-2,2-dimethylpropyl)-2-(3,4-dimethoxyphenyl)acetamide], a novel and selective P2X₇ receptor antagonist, dose-dependently reduces neuropathic pain in the rat. *Journal of Pharmacology and Experimental Therapeutics* 2006;319(3):1376-1385

ALZET Comments: Vincristine sulfate; IV (jugular); Rat; 2002; 14 days; Animal info (male, Sprague-Dawley, 200-300g.); mp primed overnight; chemotherapy-induced neuropathic pain model.