



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

Q11245: I. Bhutada, *et al.* CDK7 and CDK9 inhibition interferes with transcription, translation, and stemness, and induces cytotoxicity in GBM irrespective of temozolomide sensitivity. *Neuro-Oncology* 2024;26(1):70-84

Agents: SNS032 **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Strain:** SCID; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: animal info: 8 weeks-old; ALZET BIK 3 used; good methods see Supp. data; cancer (Glioblastoma);

Q11231: A. H. Shah, *et al.* Human endogenous retrovirus K contributes to a stem cell niche in glioblastoma. *The Journal of Clinical Investigation* 2023;133(13):

Agents: Abacavir **Vehicle:** Saline; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Strain:** Athymic nude; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose (12.3 mg/kg/d); controls received mp w/ saline; abacavir is a commercially available nucleoside reverse transcriptase inhibitor

Q11015: D. E. Vatner, *et al.* Exercise enhancement by RGS14 disruption is mediated by brown adipose tissue. *Aging Cell* 2023;22(4):e13791

Agents: U0126 **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Strain:** RGS14 KO; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Dose (10 mg/kg day); animal info: RGS14 KO mice and WT littermates; U0126 is a selective MAPK inhibitor; aging, cardiovascular (exercise capacity)

Q10957: Y. Li, *et al.* Simultaneous late-gadolinium enhancement and T1 mapping of fibrosis and a novel cell-based combination therapy in hypertensive mice. *Biomedicine & Pharmacotherapy* 2023;158(114069)

Agents: Serelaxin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (0.5/mg/kg/day); animal info (12 week-old male K/DOCA/salt injured mice, weighing approximately 25–30 g); Blood pressure measured via Tail cuff; (p.9) see Fig. 3; cardiovascular; Therapeutic indication (hypertension);

Q11012: P. S. Upadhyayula, *et al.* Dietary restriction of cysteine and methionine sensitizes gliomas to ferroptosis and induces alterations in energetic metabolism. *Nature Communications* 2023;14(1):1187

Agents: RLS3 **Vehicle:** DMSO; PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Dose: 500 nm; 0.5% DMSO used; Controls received mp w/ vehicle; animal info: 8 weeks; RAS-selective lethal 3 (RSL3), a well-known inhibitor of glutathione peroxidase 4 (GPX4); convection-enhanced delivery; cancer (glioblastoma)

Q10977: S. Parker, *et al.* Immunotoxin- α CD40 therapy activates innate and adaptive immunity and generates a durable antitumor response in glioblastoma models. *Science Translational Medicine* 2023;15(eabn5649)

Agents: D2C7; α CD40 **Vehicle:** Mouse serum albumin; PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Strain:** C57BL/6; **Pump:** 1007D; **Duration:** 72 hours;

ALZET Comments: Dose: 0.2 μ g D2C7, 10 to 300 μ g α CD40; Controls received mp w/ vehicle; animal info: Female 7-8 weeks old 16 to 20 g; D2C7 is a recomb antibody immunotoxin; CD40 is immunoregulatory, belongs to tumor necrosis factor family; tumor brain coordinates (0.5 mm anterior and 2.0 mm lateral to bregma); cancer (Glioblastoma); convection enhanced delivery

Q10918: R. Ge, *et al.* A Novel Tumor-Promoting Role for Nuclear Factor IX in Glioblastoma Is Mediated through Transcriptional Activation of GINS1. *Molecular Cancer Research* 2023;21(3):189-198

Agents: Doxorubicin **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1003D; **Duration:** Not Stated;

ALZET Comments: animal info (Male; Mice; BALB/cJ genetic background); enzyme inhibitor (Topo isomerase 2); cyanoacrylate adhesive; cancer (Glioblastoma); Therapeutic indication (Glioblastoma);

Q10579: J. Kopecky, *et al.* Intratumoral Administration of the Antisecretory Peptide AF16 Cures Murine Gliomas and Modulates Macrophage Functions. *Scientific Reports* 2022;12(1):4609

Agents: Temozolomide; AF16 **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Dose (180 mg/72 μ l; 300 μ g/72 μ l); animal info (C57BL/6 Female; 8-10 weeks old); peptides; immunology;



Q11216: A. Kopecky. Novel methods of malignant brain tumor utilizing the tumor microenvironment. Lund University, Faculty of Medicine 2022;

Agents: Trimetazidine **Vehicle:** Saline; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Strain:** Not Stated; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Dose (180µg); Controls received mp w/ vehicle; comparison of single injection w/ mp; cancer (Glioblastoma multiforme); immunology; "This route circumvents the blood-brain barrier that normally excludes a wide spectrum of chemotherapeutics from being used in malignant brain tumor patients due to their impassable electrochemical characteristics."

Q8458: J. Enriquez Perez, *et al.* Convection-enhanced delivery of temozolomide and whole cell tumor immunizations in GL261 and KR158 experimental mouse gliomas. BMC Cancer 2020;20(1):7

Agents: Temozolomide **Vehicle:** PBS; Saline; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Dose (2.4mg/Kg/day); 0.9% NaCl used; Controls received mp w/ vehicle; animal info (C57BL/6 female mice 8–10weeks old); ALZET brain infusion kit 3 used; Brain coordinates (1.5 mm to the right and 1.0 mm anterior of the bregma);

Q7039: X. Yu, *et al.* Synergistic antitumor effects of 9.2.27-PE38KDEL and ABT-737 in primary and metastatic brain tumors. PLoS One 2019;14(1):e0210608

Agents: 9.2.27-PE38KDEL immunotoxin, ABT-737 **Vehicle:** PBS, captisol, mouse serum albumin; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 1007D; **Duration:** 3 days;

ALZET Comments: 5% Captisol and 2% mouse serum albumin used; animal info (Nude mice (22–30 g, 6–8 weeks); ALZET brain infusion kit 3 used; cancer (glioblastoma); "Convection-enhanced delivery (CED), utilizing osmotic pumps, has been successfully used to bypass the blood-brain barrier and to deliver ITs directly into brain tumors" pg.12 ;

Q7065: G. Mastrella, *et al.* Targeting APLN/APLNR improves anti-angiogenic efficiency and blunts pro-invasive side effects of VEGFA/VEGFR2-blockade in glioblastoma. Cancer Research 2019;79(9):2298-2313

Agents: apelin-F13A, DC101, Antibody,anti-VEGFR2 **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1002; 2004; **Duration:** 14 and 28 days;

ALZET Comments: Dose (30 or 60 µg of apelin-F13A, 0.8 mg of DC101); ALZET brain infusion kit 3 used; cancer (glioblastoma);

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-Australasian Journal of Animal Sciences 2019;14(1):5-14

Agents: Etoposide, Bevacizumab, IMCA12, Interleukin-13-PE38, Tetrakis Chlorin **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice, Rat; **Pump:** 2001D, 1003D, 1007D, 1004, 2004; **Duration:** 24 hours, 3, 7, 21, 28 days;

ALZET Comments: ALZET brain infusion kit 1,2, and 3 used; cancer (Glioblastoma);

R0380: A. Clavreul, *et al.* Nanocarriers and nonviral methods for delivering antiangiogenic factors for glioblastoma therapy: the story so far. Int J Nanomedicine 2019;14(2497-2513

Agents: Bevacizumab; RNA, small interfering (anti-HIF-1α/PEG); Immunotoxin, DTAT/DTATEGF; Endostatin; 17-ODYA; Miconazole; **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral), IV; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: This review describes methods (including convection-enhanced delivery devices, implantable polymer devices, nanocarriers, and cellular vehicles) to deliver antiangiogenic factors to intracranial tumors.

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

Agents: Bevacizumab **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: 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."



Q10099: G. D. Arnone, *et al.* Localized targeted antiangiogenic drug delivery for glioblastoma. *Journal of Neuro-Oncology* 2018;137(2):223-231

Agents: Bevacizumab; Irinotecan **Vehicle:** Not Stated; **Route:** CSF/CNS (Intratumoral); **Species:** Mice;

ALZET Comments: Dose: Bevacizumab (10 mg/kg); dose-response (Studies have shown a dose dependent effect of bevacizumab on glioma cells such that low doses affect the vascularity of the tumor cells but higher doses may have additional specific antitumoral effects, independent of vascular regression.[48]); Controls received mp w/ vehicle; animal info (female rats); cancer: (Glioblastoma multiforme (GBM)); "Genetic therapy has also been considered among investigators as an approach for continuous local delivery of antiangiogenic inhibitors"

Q5934: D. Yu, *et al.* Multiplexed RNAi therapy against brain tumor-initiating cells via lipopolymeric nanoparticle infusion delays glioblastoma progression. *Proc Natl Acad Sci U S A* 2017;114(30):E6147-E6156

Agents: RNA, small interfering; **Route:** CSF/CNS (intratumoral); **Species:** mice (nude); **Pump:** 1002, 2002; **Duration:** 14 days;

ALZET Comments: animal info (athymic nude, 6-8 weeks old); ALZET brain infusion kit 3 used; cancer (glioblastoma); "Because repeated surgery introduces stress and pain that may impact the survival of the experimental animals, we opted for the convection-enhanced delivery (CED) strategy using an Alzet osmotic pump to deliver a continuous supply of the nano RNAi combination..." pg E6151;

Q5091: X. Wang, *et al.* Affinity-controlled protein encapsulation into sub-30 nm telodendrimer nanocarriers by multivalent and synergistic interactions. *Biomaterials* 2016;101(258-71

Agents: Telodendrimer nanoparticles, peptide-incorporated **Route:** CSF/CNS **Species:** Mice (nude); **Duration:** 7 days;

ALZET Comments: Controls received mp w/ free peptide; animal info (female, athymic nude NCRU-Sp/Sp, 8 weeks old); cancer (glioblastoma U87); tissue perfusion (intratumoral); pumps primed overnight at 37C; Dose (0.5 ug/h); Brain coordinates (0.5 mm anterior to bregma and 2.5 mm lateral of midline);

Q6614: D. Markowitz, *et al.* Pharmacological Inhibition of the Protein Kinase MRK/ZAK Radiosensitizes Medulloblastoma. *Mol Cancer Ther* 2016;15(8):1799-808

Agents: M443 **Vehicle:** PBS; DMSO; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Duration:** 2 weeks;

ALZET Comments: 0.01% DMSO used; animal info (4 week old female athymic mice); enzyme inhibitor (MRK); Brain coordinates (2 mm to the right and 1 mm posterior to the lambda); cancer (Medulloblastoma); Industry authored (Fatimo Innovation LLC);

Q5861: I. V. Guzhova, *et al.* HSP70-based anti-cancer immunotherapy. *Hum Vaccin Immunother* 2016;12(10):2529-2535

Agents: HSP70, human recomb. **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Rat;

ALZET Comments: comparison of intracranial injections vs mp; cancer (Glioma); peptides; "Such injections, particularly those done using an osmotic pump, caused a significant delay in tumor growth and increase the survival of tumor-bearing animals." pg 2532; Therapeutic indication (Cancer, Glioma);

Q4673: M. Zamykal, *et al.* Inhibition of intracerebral glioblastoma growth by targeting the insulin-like growth factor 1 receptor involves different context-dependent mechanisms. *NEURO-ONCOLOGY* 2015;17(1076-1085

Agents: IMC-A12 **Vehicle:** Saline; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 2004; **Duration:** 3 weeks; 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (Foxn1nu, 6-8 weeks old); cancer (glioblastoma);

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

Agents: Bevacizumab **Vehicle:** Saline; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 1004; **Duration:** 28 days;

ALZET Comments: 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;



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);

Q3780: R. Hiramatsu, *et al.* Tetrakis(p-Carboranylthio-Tetrafluorophenyl)Chlorin (TPFC): Application for Photodynamic Therapy and Boron Neutron Capture Therapy. *Journal of Pharmaceutical Sciences* 2015;104(962-970)

Agents: Tetrakis(p-carboranylthiotetrafluorophenyl) Chlorin **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001D;
ALZET Comments: Animal info (male, 200-250 g, F344 Fischer); ALZET brain infusion kit 2 used; TPFC, also known as Tetrakis(p-Carboranylthio-Tetrafluorophenyl)Chlorin, is a carboranyl-containing chlorin of high boron content; cancer (glioma); tissue perfusion; convection-enhanced delivery

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

Agents: Etoposide **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: 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);

Q3212: S. Eberstaal, *et al.* Intratumoral COX-2 inhibition enhances GM-CSF immunotherapy against established mouse GL261 brain tumors. *International Journal of Cancer* 2014;134(11):2748-2753

Agents: Parecoxib; valdecoxib **Vehicle:** Not Stated; **Route:** IP; CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1004; **Duration:** 7 days; 34 days;
ALZET Comments: Animal info (C57BL/6, female, 8-10 wks old); cancer; tissue perfusion (intratumoral)

Q4703: M. Benadiba, *et al.* Growth inhibitory effects of the Diruthenium-Ibuprofen compound, [Ru(2)Cl(lbp)(4)], in human glioma cells in vitro and in the rat C6 orthotopic glioma in vivo 1993. *JOURNAL OF BIOLOGICAL INORGANIC CHEMISTRY* 2014;19(1025-1035)

Agents: Diruthenium-ibuprofen **Vehicle:** Ethanol; CSF, artificial; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Animal info (female, Wistar, 250-350g); ALZET brain infusion kit used; 15% ethanol used; comparison of injection vs mp; cancer (glioma); tissue perfusion (intratumoral, glioma); "Using the orthotopic C6 model the effects of either chronic 14-day treatment by intra-peritoneal injection of chronic 14-day intra-tumour infusion by an Alzet osmotic pump attached to a brain infusion cannula were tested. Tumour growth was reduced by both routes of administration with the osmotic pump appearing to be the less harmful route in terms of haematological responses." pg 1033; Diruthenium-Ibuprofen aka Rulbp;

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

Agents: Cetuximab **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Rat (nude); **Pump:** 2ML4; **Duration:** 4 weeks;
ALZET Comments: Control animals received mp w/ PBS; animal info (rnu/rnu Rowett); ALZET brain infusion kit 2 used; convection enhanced delivery (CED); tissue perfusion (intratumoral)

Q2557: S. Gopinath, *et al.* Cathepsin B and uPAR regulate self-renewal of glioma-initiating cells through GLI-regulated Sox2 and Bmi1 expression. *Carcinogenesis: Integrative Cancer Research* 2013;34(3):550-559

Agents: Plasmid, pCU; plasmid, SV **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Control animals received mp w/ PBS; animal info (5 wks old, female, nude); infusion rate of 0.25 ul/hr; pCU plasmid is a bicistronic shRNA construct directed against both uPAR and cathepsin B; cancer (glioblastoma)



Q2864: S. Fritzell, *et al.* Intratumoral temozolomide synergizes with immunotherapy in a T cell-dependent fashion. *Cancer Immunology, Immunotherapy* 2013;62(9):1463-1474

Agents: Temozolomide **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Animal info (C57BL/6, female, syngenic, 8-10 wks old); ALZET brain infusion kit 3 used; cyanoacrylate; tissue perfusion (intratumoral); temozolomide (TMZ) is an alkylating agent

Q2463: V. Chandramohan, *et al.* Recombinant anti-podoplanin (NZ-1) immunotoxin for the treatment of malignant brain tumors. *International Journal of Cancer* 2013;132(10):2339-2348

Agents: Immunotoxin, NZ-1; immunotoxin, P588 **Vehicle:** PBS-HSA; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;

ALZET Comments: Control animals received mp w/ vehicle; tissue perfusion (intratumoral); cancer (brain)

Q3328: L. Biddlestone-Thorpe, *et al.* ATM Kinase Inhibition Preferentially Sensitizes p53-Mutant Glioma to Ionizing Radiation. *Clinical Cancer Research* 2013;19(12):3189-3200

Agents: KU-60019 **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 1007D; 1002; 2002; **Duration:** 7 days; 19 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, nude, athymic, 15-20g, 5-6 weeks old); ALZET brain infusion kit 3 used; cancer (glioma); tissue perfusion (glioma); "To reach meaningful drug concentrations of KU-60019 within the tumor, the BBB/BBB need to be bypassed or drugs administered locally. Both osmotic pumps, as well as clinically used CED, partially bypass the BBB/BBB and deliver drugs directly to the tumor to improve efficacy and reduce potential systemic toxicity" pg3194; KU-60019 is a kinase inhibitor

Q3684: J. V. Berg, *et al.* Intratumoral IL-12 combined with CTLA-4 blockade elicits T cell-mediated glioma rejection. *Journal of Experimental Medicine* 2013;210(13):2803-2811

Agents: Interleukin-12, murine **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 1004; 2004; **Duration:** 28 d
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6); cancer (glioma); tissue perfusion (tumor; glioma); immunology; pumps primed at 37C; pumps explanted after 28 days;

Q1975: R. R. Kotipatruni, *et al.* Apoptosis Induced by Knockdown of uPAR and MMP-9 is Mediated by Inactivation of EGFR/STAT3 Signaling in Medulloblastoma. *PLoS One* 2012;7(9):U893-U905

Agents: RNA, small hairpin **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2001;
ALZET Comments: Animal info (nude); tissue perfusion (tumor); cancer

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

Q0781: A. Schulte, *et al.* A Distinct Subset of Glioma Cell Lines with Stem Cell-like Properties Reflects the Transcriptional Phenotype of Glioblastomas and Overexpresses CXCR4 as Therapeutic Target. *Glia* 2011;59(4):590-602

Agents: AMD 3100 **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2004;
ALZET Comments: Controls received mp w/ PBS; animal info (6-8 wks old, NMRI-nu/nu); ALZET brain infusion kit 2 used;

Q1161: D. Kesanakurti, *et al.* Suppression of MMP-2 Attenuates TNF-alpha Induced NF-kappa B Activation and Leads to JNK Mediated Cell Death in Glioma. *PLoS One* 2011;6(5):U239-U252

Agents: RNA, small interfering, MMP-2 **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumorally); **Species:** Mice (nude); **Pump:** 2004; **Duration:** Not Stated;

ALZET Comments: Animal info (athymic, female, nu/nu, 4-6 wks old); cancer (glioma); tissue perfusion (intratumorally); MMP2 siRNA



Q1158: S. Kawabata, *et al.* Convection enhanced delivery of carboranylporphyrins for neutron capture therapy of brain tumors. *Journal of Neuro-oncology* 2011;103(2):175-185

Agents: Porphyrin, H2TCP; porphyrin, H2TBP; porphyrin, H2DCP **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Rat (pregnant); **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: Controls received no treatment; animal info (Fischer, CD, pregnant, 220-240 g); comparison of convection enhanced delivery (CED) vs mp; cancer (glioma); tissue perfusion (intratumoral); Compounds also known as 5,10,15,20-tetra-(4-nido-carboranylphenyl) tetrabenzoporphyrin, 5,10,15,20-tetra-(4-nido-carboranylphenyl)porphyrin and 5,15-di-[3,5-(nido-carboranylmethyl)phenyl]porphyrin; "The animals that received of H2TBP by Alzet pump had longer MSTs than those that received it by CED (43.8 vs. 33.8 days), demonstrating that Alzet pump delivery was more effective than CED"

Q1468: W. Giraldo, *et al.* Toxicity and delivery methods for the linamarase/linamarin/glucose oxidase system, when used against human glioma tumors implanted in the brain of nude rats. *Cancer Letters* 2011;313(1):99-107

Agents: Linamarase; linamarin; glucose oxidase **Vehicle:** PBS; saline; **Route:** CSF/CNS (intratumoral); SC; **Species:** Rat (nude); **Pump:** 2001; 2ML1; **Duration:** 5, 7 days;

ALZET Comments: animal info (Wistar, 200 g, rnu/rnu); tissue perfusion (intratumoral); ALZET brain infusion kit used; stress/adverse effects "we have found abnormal speed variations in the rate of delivery of the lin/ GO cocktail when an osmotic pump connected to a brain infusion flow moderator device by a catheter was used, maybe causing some of the premature deaths." pg 106; "Three rats died by toxicity 40, 48 and 72 h from the beginning of the treatment, and the systemic treatment was ended in all of them after the first death" pg 104; cancer (glioma)

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

Agents: Dobesilate **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2004; **Duration:** 27 days; **ALZET Comments:** Controls received mp w/ vehicle; cancer (glioma);

Q0095: N. O. Schmidt, *et al.* Inhibition of thromboxane synthase activity improves glioblastoma response to alkylation chemotherapy. *Translational Oncology* 2010;3(1):43-49

Agents: Furegrelate **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2004; **Duration:** 4 weeks; **ALZET Comments:** Controls received mp w/ vehicle; tissue perfusion (tumor); functionality of mp verified by residual volume; stress/adverse reaction: (see pg. 46) "hemosiderin deposits"; cancer (glioma); ALZET BIK used; animal info (Swiss, 4-6 wks old)

Q0707: Y. Tange, *et al.* Novel Antitumor Effect of Carboplatin Delivered by Intracerebral Microinfusion in a Rat Malignant Glioma Model. *NEUROLOGIA MEDICO-CHIRURGICA* 2009;49(12):572-579

Agents: Carboplatin **Vehicle:** Glucose, D-; Evans blue; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001; **Duration:** 3, 7 days;

ALZET Comments: Animal info (male, F344/N Slc, Fischer 220-260 g); brain tissue distribution; ALZET brain infusion kit used; stability verified (4 weeks) pg 573; cancer (glioma); MRI; brain tissue distribution; "... continuous intracerebral microinfusion using the osmotic mini-pump can provide broader distribution of agents than growth of the brain tumor."; "intracerebral microinfusion can attain clinically favorable drug distribution from a single infusion point." pg 576

P9478: A. K. Schauff, *et al.* Inhibition of invasion-associated thromboxane synthase sensitizes experimental gliomas to gamma-radiation. *Journal of Neuro-oncology* 2009;91(3):241-249

Agents: Furegrelate **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 1002; **Duration:** 14 days; **ALZET Comments:** Controls were untreated; enzyme inhibitor (thromboxane synthase TXSA); cancer (glioma); tissue perfusion (tumor); ALZET brain infusion kit 3 used; animal info (NMRI)

P9618: J. Rousseau, *et al.* EFFICACY OF INTRACEREBRAL DELIVERY OF CARBOPLATIN IN COMBINATION WITH PHOTON IRRADIATION FOR TREATMENT OF F98 GLIOMA-BEARING RATS. *INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS* 2009;73(2):530-536

Agents: Carboplatin **Vehicle:** Dextrose; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001; **Duration:** 6 days; **ALZET Comments:** Controls received mp w/vehicle; no stress (see pg. 532); cancer (glioma); ALZET brain infusion kit 2 used; animal info (male, Fisher, 230-260g); "Surgery for pump implantation was well tolerated." pg. 532; "It is noteworthy that the brainstem was not damaged by direct infusion of 200 ul of carboplatin (0.5 mg/mL) at a flow rate of 1uL/h." pg. 535;



P9661: J. A. Miyake, *et al.* Gamma-linolenic acid inhibits both tumour cell cycle progression and angiogenesis in the orthotopic C6 glioma model through changes in VEGF, Flt1, ERK1/2, MMP2, cyclin D1, pRb, p53 and p27 protein expression. *Lipids in Health and Disease* 2009;8(1):U1-U10

Agents: Gamma linolenic acid **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2002; **Duration:** 14d
ALZET Comments: Controls received mp w/vehicle; cancer (glioma); ALZET brain infusion kit used; animal info (adult, female, Wistar, 250-350)

P9944: A. Agrawal, *et al.* Functional Delivery of siRNA in Mice Using Dendriworms. *ACS Nano* 2009;3(9):2495-2504

Agents: RNA, small interfering; epidermal growth factor receptor; dendriworm, dye-labeled; RNA, small interfering, GFP, dendriworm, dye-labeled **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Duration:** 3, 7 days;
ALZET Comments: Tissue perfusion (tumor); cancer (glioblastoma); incorrectly stated pump model 2007; Plastics One cannula used; animal info (Swiss Webster)

P9206: D. Zagorac, *et al.* Antiangiogenic effect of inhibitors of cytochrome P450 on rats with glioblastoma multiforme. *Journal of Cerebral Blood Flow and Metabolism* 2008;28(8):1431-1439

Agents: Miconazole; Octadecynoic acid, 17- **Vehicle:** Ethanol; CSF, artificial; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (CYP epoxygenase); tissue perfusion (tumor); ALZET brain infusion kit used; animal info (male, Fisher, 8-10 wks old); 10% ethanol used; antiangiogenesis

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

Agents: Cetuximab **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2004;
ALZET Comments: 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

P9768: G. S. Kang, *et al.* Effects, in an in-vivo model system, of 1,2,3,4-tetrahydroisoquinoline on glioma. *Anti-Cancer Drugs* 2008;19(9):859-870

Agents: EDL-155 **Vehicle:** HBSS; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Tissue perfusion (tumor); comparison of IP injections vs. mp; cancer (glioma); animal info (male, Sprague Dawley, 250-350 g); EDL-155 also known as 1-(biphenyl-4-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-6,7-diol

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)

Agents: Fas ligand; etoposide; dexamethasone **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intratumoral); **Species:** Rat (nude); **Pump:** 1002; **Duration:** 15 days;

ALZET Comments: functionality of mp verified by residual volume; animal info (female 2 months old, 159 g.)

P8366: M. I. Dorrell, *et al.* Combination angiostatic therapy completely inhibits ocular and tumor angiogenesis. *Proceedings of the National Academy of Sciences* 2007;104(3):967-972

Agents: Vascular endothelial growth factor, aptamer; EMD472523; T2-TrpRS **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001D; 2ML2; 2ML4; **Duration:** 3,6 days; 24 hours;
ALZET Comments: Controls received mp w/ vehicle; cancer (gliosarcoma); animal info (male, Fischer, 344); EMD472523 is an integrin antagonist, VEGF aptamer is chemically identical to Macugen; T2 is a proteolytic fragment of tryptophan tRNA synthetase; all agents have angiostatic activity; tissue perfusion (tumor)



P8208: T. Martens, *et al.* A novel one-armed anti-c-met antibody inhibits glioblastoma growth in vivo. *Clinical Cancer Research* 2006;12(20):6144-6152

Agents: Antibody, anti-c-Met, OA5D5 **Vehicle:** Histidine; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2004; **Duration:** 12, 21, 28 days;

ALZET Comments: Controls received mp w/ vehicle; cancer (glioblastoma); ALZET brain infusion kit 2 used; animal info (male, NMRI-nu/nu, 6-8 wks old); "Because the OA-5D5 antibody is a relatively large but stable molecule, convection-enhanced drug delivery (by mp) was ideally suited to deliver it in our orthotopic model." (p.6151); tissue perfusion (tumor)

P7904: T. C. Harding, *et al.* AAV serotype 8-mediated gene delivery of a soluble VEGF receptor to the CNS for the treatment of glioblastoma. *MOLECULAR THERAPY* 2006;13(5):956-966

Agents: Adeno-associated virus serotype 8 vector, recomb. **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: Controls received mp w/ AAV control; cancer (glioblastoma multiforme, u-251 MG); gene therapy; animal info (male, athymic, 6 wk. old); "Implantation of the mini pump allows the slow infusion of a rAAV vector...to transduce more effectively the intracranial tumor mass." (pg. 962); antiangiogenesis

P8145: C. Grommes, *et al.* Inhibition of in vivo glioma growth and invasion by peroxisome proliferator-activated receptor gamma agonist treatment. *Molecular Pharmacology* 2006;70(5):1524-1533

Agents: Pioglitazone **Vehicle:** DMSO; PBS; **Route:** CSF/CN; **Species:** Rat; **Pump:** 2ML4; **Duration:** 3, 6, 9, 14, 21 days;

ALZET Comments: Controls received mp w/ vehicle; comparison of oral admin. vs. mp; no stress (see p.1532); stability verified by in vitro incubation at 37 celsius for 21 days; cancer (glioma); ALZET brain infusion kit used; animal info (Sprague-Dawley, 200-250g.); 0.1% DMSO; Antineoplastic; tissue perfusion (tumor)

R0238: S. Boeckle, *et al.* Optimizing targeted gene delivery: Chemical modification of viral vectors and synthesis of artificial virus vector systems. *AAPS Journal* 2006;8(4):E731-E742

Agents: Virus, synthetic RNA **Vehicle:** Not Stated; **Route:** Intratumoral; **Species:** Mice (nude);

ALZET Comments: Cancer (glioblastoma); "Control animals within 30 days after tumor implantation, all treated animals survived for >1 year and were completely cured." (p. E738); gene therapy

P7975: P. Pyrko, *et al.* The role of contortrostatin, a snake venom disintegrin, in the inhibition of tumor progression and prolongation of survival in a rodent glioma model. *Journal of Neurosurgery* 2005;103(3):526

Agents: Contortrostatin **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ PBS; plasma levels taken; cancer (glioma); brain tissue distribution; snake venom disintegrin; "agent was well tolerated by animals and lacks obvious neurotoxic side effects. All the contortrostatin treated mice survived the entire treatment period and continued to do well for seven more days after the termination." tygon tubing used;

P7283: T. Ozawa, *et al.* Toxicity, biodistribution, and convection-enhanced delivery of the boronated porphyrin BOPP in the 9L intracerebral rat glioma model. *International Journal of Radiation Oncology Biology Physics* 2005;63(1):247-252

Agents: Porphyrin, boronated **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: Controls received no treatment; dose-response; comparison of IV injections vs. mp;

P7197: J. A. MacKay, *et al.* Distribution in brain of liposomes after convection enhanced delivery; modulation by particle charge, particle diameter, and presence of steric coating. *Brain Research* 2005;1035(2):139-153

Agents: Liposomes; FITC-dextran-lysine **Vehicle:** Saline; Tris buffer; **Route:** CSF/CNS (caudate putamen); CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: Tissue perfusion (intratumoral); comparison of acute CSF/CNS injection vs. mp; half-life (p. 151) 9.9 hours; cancer (glioblastoma); ALZET brain infusion kit 2 used; brain tissue distribution; post op. care (buprenorphine)



- P7434:** K. Kawakami, *et al.* Evidence that IL-13R alpha-2 chain in human glioma cells is responsible for the antitumor activity mediated by receptor-directed cytotoxin therapy. *Journal of Immunotherapy* 2005;28(3):193-202
Agents: Interleukin-13-PE38; interleukin-13Ra2, pME18S- **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral);
Species: Mice (nude); **Pump:** 1003D; 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle or antisense IL-13Ra2 plasmid vector; pumps replaced after 3 days; cancer (glioblastoma); cyanoacrylate adhesive; convection enhanced delivery; IL-13Ra2 cDNA encoding plasmid vector; "the upregulated IL-13 Ra2 chain was successfully targeted with a continuous infusion of IL-13 cytotoxin." (p. 199)
- R0208:** Y. Shoji, *et al.* Current status of delivery systems to improve target efficacy of oligonucleotides. *Current Pharmaceutical Design* 2004;10(7):785-796
Agents: Oligonucleotide, antisense **Vehicle:** Not Stated; **Route:** SC; Intratumoral; **Species:** Not Stated;
ALZET Comments: Cancer (adenocarcinoma); surgical sutures used to immobilize the pumps
- P5950:** N. O. Schmidt, *et al.* Antiangiogenic therapy by local intracerebral microinfusion improves treatment efficiency and survival in an orthotopic human glioblastoma model. *Clinical Cancer Research* 2004;10(4):1255-1262
Agents: Endostatin, recomb. murine **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2004;
Duration: 21 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by residual volume; comparison of SC injections vs. chronic ICV mp; no stress (see pg. 1261); cancer (glioma); ALZET brain infusion kit 1 used (per Dr. Carroll); MRI; "The direct infusion of therapeutic compounds into brain tumors can overcome some of the obstacles of drug delivery." p. 1255; BIK's removed prior to MRI; "no signs of intracranial bleeding due to the presence of the pumps or antiangiogenic treatment were observed..." (p. 1261); angiogenesis inhibitor; surgical glue used to affix cannula to the skull
- P9779:** T. Ozawa, *et al.* Antitumor effects of specific telomerase inhibitor GRN163 in human glioblastoma xenografts1. *NEURO-ONCOLOGY* 2004;218-226
Agents: GRN163, FITC- **Route:** CSF/CNS (intratumoral); **Species:** Rat (nude); **Pump:** 1007D; **Duration:** 7, 14 days
ALZET Comments: Tissue perfusion (tumor); enzyme inhibitor (telomerase); animal info (6-8 wks old, male, athymic)
- P7081:** A. Matsuno, *et al.* In vivo growth suppression of rat C6 glioma transplanted in rat brain using antisense oligonucleotide for microtubule-associated protein 1A messenger ribonucleic acid. *British Journal of Haematology* 2004;18(4):343-346
Agents: Oligodeoxynucleotide, phosphorothisate antisense; oligodeoxynucleotide, phosphorothisate sense; oligodeoxynucleotide, phosphorothisate scramble **Vehicle:** Saline, sterile; **Route:** CSF/CNS (intratumoral); **Species:** Rat;
Pump: 1007D; **Duration:** 1 week;
ALZET Comments: Controls received mp w/ sense or scrambled oligos; antisense (microtubule-associated protein 1A); cancer
- P7077:** F. Lefranc, *et al.* Characterization of gastrin-induced proangiogenic effects in vivo in orthotopic U373 experimental human glioblastomas and in vitro in human umbilical vein endothelial cells. *Clinical Cancer Research* 2004;10(24):8250-8265
Agents: Gastrin-17 **Vehicle:** Saline; **Route:** CSF/CNS (intratumoral); **Species:** Rat (nude); **Pump:** 1002; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; stability verified; cancer (glioma)
- P6554:** G. O. Hjortland, *et al.* Immunotoxin treatment targeted to the high-molecular-weight melanoma-associated antigen prolonging the survival of immunodeficient rats with invasive intracranial human glioblastoma multiforme. *Journal of Neurosurgery* 2004;100(2):320-327
Agents: Antibody, monoclonal 9.2.27 - pseudomonas exotoxin A; dye, evans blue **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral);
Species: Rat (nude); **Pump:** 2001D; **Duration:** 24 hours;
ALZET Comments: Controls received mp w/ PBS; cancer (glioma biopsy tumors); ALZET brain infusion kit used; brain tissue distribution; mp primed in sterile saline at 37 degrees Celsius for 4 hours; mp removed after 3 days



P6720: C. S. Gondi, *et al.* RNAi-mediated inhibition of cathepsin B and uPAR leads to decreased cell invasion, angiogenesis and tumor growth in gliomas. *Oncogene* 2004;23(8):8486-8496

Agents: RNA, small interfering; Virus, EV/SV vector **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioma); gene therapy; antiangiogenesis; siRNA (cathepsin B); pump model not stated (0.25 ul/hr); "...local intracranial delivery of pcu using mini-osmotic pumps effectively inhibited human malignant glioma growth."

P6775: U. Gawlick, *et al.* A conjugate of a tumor-targeting ligand and a T cell costimulatory antibody to treat brain tumors. *Bioconjugate Chemistry* 2004;15(5):1137-1145

Agents: Antibody, anti-CD28 Fab/Folate; gadolinium **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by MRI w/ gadolinium infusion; comparison of IV, SC, ICV injections vs. mp; cancer (brain, choroid plexus); brain tissue distribution; MRI; cyanoacrylate adhesive; "The strongest effect on tumor growth assessed of anti-CD28 fab/Folate." (p. 1143). Plastics One cannula used

P6764: S. Frewert, *et al.* Intratumoral infusion of interleukin-1 beta and interferon-gamma; induces tumor invasion with macrophages and lymphocytes in a rat glioma model. *Neuroscience Letters* 2004;364(3):145-148

Agents: Interleukin-1, beta recomb. rat; Interferon-gamma, recomb. rat **Vehicle:** Saline, physiological; albumin, human serum; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 1003D; **Duration:** 48 hours;

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioma)

P6535: W. Fischer, *et al.* Human alpha-lactalbumin made lethal to tumor cells (HAMLET) kills human glioblastoma cells in brain xenografts by an apoptosis-like mechanism and prolongs survival. *Cancer Research* 2004;64(6):2105-2112

Agents: Lactalbumin, alpha; HAMLET; radio-isotopes **Vehicle:** ¹²⁵I tracer; saline; **Route:** CSF/CNS (intratumoral); **Species:** Rat (nude); **Pump:** 2001D; **Duration:** 1 day;

ALZET Comments: Tissue perfusion (tumor); functionality of mp verified by autoradiography on brain sections; no stress (see pg. 2108); cancer (glioblastoma); brain tissue distribution; agent is called HAMLET or (human alpha lact albumin made lethal to tumor cells); "...there were no signs of edema or tissue damage in the surrounding brain, including the cortex, which had been penetrated by the [26 gauge] infusion cannula." p. 2108

P6557: K. H. Chi, *et al.* Antisense thymidylate synthase electrogene transfer to increase uptake of radiolabeled iododeoxyuridine in a murine model. *Journal of Nuclear Medicine* 2004;45(3):478-484

Agents: Uridine; iodoeoxy; radio-isotopes **Vehicle:** Saline, normal; ¹³¹I tracer; **Route:** Intratumoral; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ PBS; cancer; "The present study was designed to increase the extent of cellular uptake of ¹³¹I-IdUrd in experimental tumors by using a miniosmotic pump." (p. 483)

P5835: I. Svechnikova, *et al.* Apoptosis and tumor remission in liver tumor xenografts by 4-phenylbutyrate. *INTERNATIONAL JOURNAL OF ONCOLOGY* 2003;22(3):579-588

Agents: Phenylbutyrate, 4- **Vehicle:** PBS; **Route:** Intratumoral; **Species:** Rat (nude); **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Tissue perfusion (intratumoral); cancer; 4-phenylbutyrate is a derivative of the short-chain fatty acid, butyrate, also a low toxicity cytostatic compound

P6540: P. M. Grossi, *et al.* Efficacy of intracerebral microinfusion of trastuzumab in an Athymic rat model of intracerebral metastatic breast cancer. *Clinical Cancer Research* 2003;9(15):5514-5520

Agents: Herceptin; antibody, anti-Her2 monoclonal; radio-isotopes **Vehicle:** Saline; ¹²⁵I tracer; **Route:** IP; CSF/CNS (intratumoral); **Species:** Rat (athymic); **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Tissue perfusion (tumor); herceptin serum levels (p. 5516); comparison of systemic IP mp vs. intracerebral mp infusion; cancer (breast); brain tissue distribution; radiolabeled herceptin (trastuzumab) was also infused intratumorally, peritumorally, and i.p to study tissue distribution



P5819: C. Giussani, *et al.* Local intracerebral delivery of endogenous inhibitors by osmotic minipumps effectively suppresses glioma growth in vivo. *Cancer Research* 2003;63(12):2499-2505

Agents: Platelet factor-4; MMP-2 (hemopexin fragment) **Vehicle:** PBS; **Route:** SC; CSF/CNS (intratumoral); **Species:** Mice; **Pump:** 2004; **Duration:** 28,94 days;

ALZET Comments: Controls received mp w/ PBS; tissue perfusion (tumor); dose-response (p.2502); comparison of IP injections SC systemic mp infusion vs. local intracranial mp infusion; long-term study; pumps replaced after 28 days in some groups; stability verified by in vitro assay; cancer (glioma); Angiogenesis inhibitors; COOH terminal fragment of PF-4 used; In vitro activity of agents confirmed for up to 16 days; "In conclusion, our data demonstrates that local intracerebral delivery of endogenous inhibitors by osmotic minipumps is a very effective modality for the treatment of aggressive tumors..." (p.2505); tissue perfusion (tumor);

P5357: T. L. Walker, *et al.* Enhanced *In Vivo* tumour response from combination of carboplatin and low-dose c-myc antisense oligonucleotides. *Anticancer Research* 2002;22(4):2237-2245

Agents: Oligonucleotide, antisense **Vehicle:** Water, sterile; **Route:** SC; intratumoral; **Species:** Rat; **Pump:** 1003D; **Duration:** 86h

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (intratumoral); cancer; antisense; 50mm long catheter filled w/ 15 ul of vehicle to enable 15 hr delayed delivery of antisense; c-myc antisense used

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

Agents: TIMP-1; TIMP-2 **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2002; **Duration:** 3, 7, or 14 days;

ALZET Comments: 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

P5820: D. R. Sorensen, *et al.* Combination of endostatin and a protein kinase C alpha DNA enzyme improves the survival of rats with malignant glioma. *NEOPLASIA* 2002;4(6):474-479

Agents: Endostatin, recomb human **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2ML2; **Duration:** 28 days;

ALZET Comments: Tissue perfusion (tumor); cancer (glioma); ALZET brain infusion kit used; Angiogenesis inhibitor; 5 ul/hr pump used; "Rats treated with a continuous intracranial delivery of endostatin lived significantly longer than untreated controls". (p 477)

P6148: H. A. Leaver, *et al.* Highly unsaturated fatty acid induced tumor regression in glioma pharm acodynamics and bioavailability of gamma linolenic acid in an implantation glioma model: effects on tumour biomass, apoptosis and neuronal t issue histology. *Prostaglandins Leukotrienes and Essential Fatty Acids* 2002;67(5):283-292

Agents: Linolenic acid, gamma **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Not Stated; **Pump:** 2001;

Duration: 3,7 days;

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (tumor); cancer (glioma); ALZET brain infusion kit used

P5664: M. Hagedorn, *et al.* Domain swapping in a COOH-terminal fragment of platelet factor 4 generates potent angiogenesis inhibitors. *Cancer Research* 2002;62(23):6884-6890

Agents: Platelet factor 4 peptides **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** 2004;

Duration: 30 days;

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (intratumoral); dose-response (p. 6888; fig 6); cancer; peptides; glioma; antiangiogenesis.

Q7212: O. Engebraaten, *et al.* Intratumoral immunotoxin treatment of human malignant brain tumors in immunodeficient animals. *Int J Cancer* 2002;97(6):846-52

Agents: Antibody, anti-EGF receptor; Immunotoxin (Tfn-CRM107); Immunotoxin (425.3-PE) **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); Rat (nude); **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: ALZET brain infusion kit used;



P5271: M. M. Davies, *et al.* Effect of manipulation of primary tumour vascularity on metastasis in an adenocarcinoma model. *British Journal of Cancer* 2002;86(1):123-129

Agents: Fibroblast growth factor, basic **Vehicle:** Saline; **Route:** IV (jugular); Intratumoral; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (intratumoral); cancer; peptides; bFGF delivered either by systemic IV infusion or intratumorally

P5059: M. M. Davies, *et al.* Basic fibroblast growth factor infusion increases tumour vascularity, blood flow and chemotherapy uptake. *Acta Oncologica* 2002;41(1):84-90

Agents: Fibroblast Growth Factor, Basic **Vehicle:** Saline; **Route:** IV (jugular); Intratumoral;; **Species:** Rat; **Duration:** 10,14,28 d

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (tumor); cancer; one group received 10-day saline infusion by pump, followed by 14-day bFGF or saline infusion from a second pump

P5489: P. Cuevas, *et al.* Inhibition of rat glioma growth by neomycin. Preliminary report. *Neurological Research* 2002;24(6):522-524

Agents: Neomycin **Vehicle:** PBS; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2004; **Duration:** 26 days;

ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (tumor); cancer

P5531: Y. Chen, *et al.* Effects of irradiated tumor vaccine and continuous localized infusion of granulocyte-macrophage colony-stimulating factor on neuroblastomas in mice. *Journal of Pediatric Surgery* 2002;37(9):1298-1304

Agents: Colony-stimulating factor, GM **Vehicle:** PBS; BSA; **Route:** SC (tumor vaccine injection site); **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ PBS; immunology; GM-CSF is recombinant murine; tissue perfusion

P4825: H. H. Engelhard, *et al.* Therapeutic effects of sodium butyrate on glioma cells in vitro and in the rat C6 glioma model. *Neurosurgery* 2001;48(3):616-625

Agents: Butyrate, sodium **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;

ALZET Comments: Controls received w/ saline; tissue perfusion (tumor); functionality of mp verified by residual volume; dose-response (graph on p. 621); cancer (glioma); Butyrate, sodium is a naturally occurring four-carbon fatty acid;

P4815: S. Hautmann, *et al.* Treatment of metastatic hormone-refractory prostate adenocarcinoma (MatLyLu) in Copenhagen rats with micro-osmotic interleukin-2 pumps. *Anticancer Research* 2000;20(4495-4498)

Agents: Interleukin-2 **Vehicle:** Albumin, human; **Route:** SC; Peritumoral (orthotopic); **Species:** Rat; **Pump:** 2002;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by in vitro assay; no stress (see p. 4496); good methods pumps weighed p. 4496; cancer (prostate); immunology; peptides; rats had a prostatic adenocarcinoma tumor implanted; Albumin vehicle was 20% concentration; SC & peritumoral orthotopic implantation; Note: these pumps were left in for 28 days

P5754: I. Galve-Roperh, *et al.* Anti-tumoral action of cannabinoids: involvement of sustained ceramide accumulation and extracellular signal-regulated kinase activation. *Nat Med* 2000;6(3):313-319

Agents: WIN-55212-2; Cannabinol, delta-9-tetrahydro- **Vehicle:** PBS; BSA; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Tissue perfusion (tumor); cancer; WIN-55,212-2 is a potent synthetic cannabinol agonist

P4112: S. Hautmann, *et al.* Treatment of metastatic hormone refractory adenocarcinoma of the prostate (mat ly ly) with micro-osmotic interleukin-2 pump in male copenhagen rats. *Eur. Urol* 1998;34(265-266)

Agents: Interleukin-2 **Vehicle:** Albumin; **Route:** Intratumoral; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/albumin; tissue perfusion (intratumoral); cancer (prostate); immunology; peptides

P3783: E. Tsuchida, *et al.* The effect of UCN-01 (7-hydroxystaurosporine), a potent inhibitor of protein kinase C, on fractionated radiotherapy or daily chemotherapy of a murine fibrosarcoma. *Int. J. Radiat. Oncol. Biol. Phys* 1997;39(5):1153-1161

Agents: UCN-01 **Vehicle:** Citric acid; **Route:** Intratumoral; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Tissue perfusion (tumor); cancer; enzyme inhibitor



P3523: J. J. Viola, *et al.* In situ cyclopentenyl cytosine infusion for the treatment of experimental brain tumors. *Cancer Research* 1995;55(1306-1309

Agents: Cyclopentenyl cytosine **Vehicle:** Saline, normal; **Route:** IP; intratumoral; **Species:** Rat; **Pump:** 2ML2; 2ML4; **Duration:** 6, 28 days;

ALZET Comments: controls received mp w/ saline; tissue perfusion (tumor); cancer; ALZET brain infusion kit used; SC pump connected to IP catheter; IP catheter used

P2481: Y. Ikeda, *et al.* Therapeutic effects of local delivery of dexamethasone on experimental brain tumors and peritumoral brain edema. *J. Neurosurg* 1993;79(716-721

Agents: Dexamethasone **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Rabbit; **Duration:** 6, 10 days;

ALZET Comments: Controls received no treatment; tissue perfusion (tumor); comparison of injections vs. mp; local vs. systemic treatment, graph pg. 719