



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

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 Res* 2019;

ALZET Comments: apelin-F13A, DC101, Antibody, anti-VEGFR2; CSF, artificial; CSF/CNS (tumor); Mice; 1002; 2004; 14 and 28 days; Dose (30 or 60 µg of apelin-F13A, 0.8 mg of DC101); apelin-F13A is a mutant APLNR ligand, DC101 is a VEGFR2-blocking antibody; 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 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; 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.”.

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

ALZET Comments: RNA, small interfering; CSF/CNS (intratumoral); mice (nude); 1002, 2002; 14 days; 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

ALZET Comments: Telodendrimer nanoparticles, peptide-incorporated; CSF/CNS (Intratumoral); Mice (nude); 7 days; 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

ALZET Comments: M443; PBS; DMSO; CSF/CNS (intratumoral); Mice (nude); 2 weeks; 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

ALZET Comments: HSP70, human recomb.; CSF/CNS (intratumoral); Rat; 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



ALZET Comments: IMC-A12; Saline; CSF/CNS (intratumoral); Mice; 2004; 3 weeks; 4 weeks; Controls received mp w/ vehicle; animal info (Foxn1nu, 6-8 weeks old); cancer (glioblastoma); tissue perfusion (glioblastoma); IMC-A12 aka cixutumumab;

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;

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

ALZET Comments: Ganciclovir; CSF/CNS (intratumoral); Mice (transgenic); 2004; 7 days; 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)

ALZET Comments: Tetrakis(p-carboranylthiotetrafluorophenyl) Chlorin; CSF/CNS (intratumoral); Rat; 2001D; 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

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);

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

ALZET Comments: Parecoxib; valdecoxib; IP; CSF/CNS (intratumoral); Mice; 1004; 7 days; 34 days; 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)

ALZET Comments: Diruthenium-ibuprofen; Ethanol; CSF, artificial; CSF/CNS (intratumoral); Rat; 2002; 14 days; 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 RuIbp;

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).



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

ALZET Comments: Plasmid, pCU; plasmid, SV; CSF/CNS (intratumoral); Mice (nude); 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

ALZET Comments: Temozolomide; CSF/CNS (intratumoral); Mice; 1003D; 3 days; 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

ALZET Comments: Immunotoxin, NZ-1; immunotoxin, P588; PBS-HSA; CSF/CNS (intratumoral); Mice; 1003D; 3 days; Control animals received mp w/ vehicle; tissue perfusion (intratumoral); cancer (brain).

Q7211: V. Chandramohan, *et al.* Recombinant anti-podoplanin (NZ-1) immunotoxin for the treatment of malignant brain tumors. *Int J Cancer* 2013;132(10):2339-48

ALZET Comments: Immunotoxin, NZ-1-(scdsFv)-PE38KDEL; Immunotoxin, P588-(scdsFv)-PE38KDEL; PBS, human serum albumin; CSF/CNS (intratumoral); Mice (NSG); 1003D; 3 days; 0.2% PBS-HSA used; Controls received mp w/ vehicle; animal info (Male NOD scid gamma (NSG) mice (20–30 g; 12 weeks)); cancer (glioblastoma, medulloblastoma);

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

ALZET Comments: KU-60019; PBS; CSF/CNS (intratumoral); Mice (nude); 1007D; 1002; 2002; 7 days; 19 days; 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/BTB need to be bypassed or drugs administered locally. Both osmotic pumps, as well as clinically used CED, partially bypass the BBB/BTB 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

ALZET Comments: Interleukin-12, murine; PBS; CSF/CNS (intratumoral); Mice; 1004; 2004; 28 days; 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

ALZET Comments: RNA, small hairpin; CSF/CNS (intratumoral); Mice (nude); 2001; Animal info (nude); tissue perfusion (tumor); cancer.

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

ALZET Comments: Ganciclovir; macrophage/microglia inhibitory factor; tuftsin; CSF/CNS (intratumoral); Mice; 14, 28 days; 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



ALZET Comments: AMD 3100; CSF/CNS (intratumoral); Mice (nude); 2004; Controls received mp w/ PBS; animal info (6-8 wks old, NMRI-nu/nu); ALZET brain infusion kit 2 used; cancer (glioma).

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

ALZET Comments: RNA, small interfering, MMP-2; CSF/CNS (intratumorally); Mice (nude); 2004; 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

ALZET Comments: Porphyrin, H2TCP; porphyrin, H2TBP; porphyrin, H2DCP; CSF/CNS (intratumoral); Rat (pregnant); 2001D; 24 hours; 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" pg 181.

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

ALZET Comments: Linamarase; linamarin; glucose oxidase; PBS; saline; CSF/CNS (intratumoral); SC; Rat (nude); 2001; 2ML1; 5, 7 days; 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

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.

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

ALZET Comments: Furegrelate; PBS; CSF/CNS (intratumoral); Mice (nude); 2004; 4 weeks; 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 brain infusion kit 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

ALZET Comments: Carboplatin; Glucose, D-; Evans blue; CSF/CNS (intratumoral); Rat; 2001; 3, 7 days; 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

ALZET Comments: Furegrelate; CSF/CNS (intratumoral); Mice (nude); 1002; 14 days; 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

ALZET Comments: Carboplatin; Dextrose; CSF/CNS (intratumoral); Rat; 2001; 6 days; 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; tissue perfusion (tumor).

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

ALZET Comments: Gamma linolenic acid; CSF, artificial; CSF/CNS (intratumoral); Rat; 2002; 14 days; 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

ALZET Comments: RNA, small interfering; epidermal growth factor receptor; dendriworm, dye-labeled; RNA, small interfering, GFP, dendriworm, dye-labeled; CSF/CNS (intratumoral); Mice; 3, 7 days; 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

ALZET Comments: Miconazole; octadecynoic acid, 17-; Ethanol; CSF, artificial; CSF/CNS (intratumoral); Rat; 1002; 14 days; 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

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.

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

ALZET Comments: EDL-155; HBSS; CSF/CNS (intratumoral); Rat; 2001; 7 days; 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

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.).

P8366: M. I. Dorrell, *et al.* Combination angiostatic therapy completely inhibits ocular and tumor angiogenesis. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2007;104(3):967-972

ALZET Comments: Vascular endothelial growth factor, aptamer; EMD472523; T2-TrpRS; PBS; CSF/CNS (intratumoral); Rat; 2001D; 2ML2; 2ML4; 3,6 days; 24 hours; 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

ALZET Comments: Antibody, anti-c-Met, OA5D5; Histidine; CSF/CNS (intratumoral); Mice (nude); 2004; 12, 21, 28 days; 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

ALZET Comments: Adeno-associated virus serotype 8 vector, recomb.; CSF/CNS (intratumoral); Rat; 2001D; 24 hours; Controls received mp w/ AAV control; cancer (glioblastoma multiforme, u-251 MG); gene therapy; animal info (male, athymic, 6 wk. old); rAAV contains soluble VEGF inhibitor, sVEGFR1/R2; "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

ALZET Comments: Pioglitazone; DMSO; PBS; CSF/CNS (intratumoral); Rat; 2ML4; 3, 6, 9, 14, 21 days; 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

ALZET Comments: Virus, synthetic RNA; Intratumoral; Mice (nude); 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

ALZET Comments: Contortrostatin; CSF/CNS (intratumoral); Mice; 2 weeks; 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." p. 533; tygon tubing used; tissue perfusion (tumor).

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

ALZET Comments: Porphyrin, boronated; PBS; CSF/CNS (intratumoral); Rat; 2001D; 24 hours; Controls received no treatment; dose-response; comparison of IV injections vs. mp; cancer (brain glioma); toxicology.

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

ALZET Comments: Liposomes; FITC-dextran-lysine; Saline; tris buffer; CSF/CNS (caudate putamen); CSF/CNS (intratumoral); Rat; 2001D; 24 hours; 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

ALZET Comments: Interleukin-13-PE38; interleukin-13Ra2, pME18S-; CSF/CNS (intratumoral); Mice (nude); 1003D; 1007D; 7 days; 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

ALZET Comments: Oligonucleotide, antisense; SC; intratumoral; 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

ALZET Comments: Endostatin, recomb. murine; PBS; CSF/CNS (intratumoral); Mice (nude); 2004; 21 days; 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

ALZET Comments: GRN163, FITC-; CSF/CNS (intratumoral); Rat (nude); 1007D; 7, 14 days; Tissue perfusion (tumor); enzyme inhibitor (telomerase); cancer (glioma); 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 Neurosurgery 2004;18(4):343-346

ALZET Comments: Oligodeoxynucleotide, phosphorothisate antisense; oligodeoxynucleotide, phosphorothisate sense; oligodeoxynucleotide, phosphorothisate scramble; Saline, sterile; CSF/CNS (intratumoral); Rat; 1007D; 1 week; Controls received mp w/ sense or scrambled oligos; antisense (microtubule-associated protein 1A); cancer (glioma).

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

ALZET Comments: Gastrin-17; Saline; CSF/CNS (intratumoral); Rat (nude); 1002; 7 days; 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

ALZET Comments: Antibody, monoclonal 9.2.27 - pseudomonas exotoxin A; dye, evans blue; PBS; CSF/CNS (intratumoral); Rat (nude); 2001D; 24 hours; 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(8486-8496

ALZET Comments: RNA, small interfering; Virus, EV/SV vector; PBS; CSF/CNS (intratumoral); Mice (nude); 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

ALZET Comments: Antibody, anti-CD28 Fab/Folate; gadolinium; PBS; CSF/CNS (intratumoral); Mice (transgenic); 1002; 14 days; 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

ALZET Comments: Interleukin-1, beta recomb. rat; Interferon-gamma, recomb. rat; Saline, physiological; albumin, human serum; CSF/CNS (intratumoral); Rat; 1003D; 48 hours; 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

ALZET Comments: Lactalbumin, alpha; HAMLET; radio-isotopes; ¹²⁵I tracer; saline; CSF/CNS (intratumoral); Rat (nude); 2001D; 1 day; 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

ALZET Comments: Uridine; iodoeoxy; radio-isotopes; Saline, normal; ¹³¹I tracer; Intratumoral; Mice; 2001; 7 days; Controls received mp w/ PBS; cancer; "The present study was designed to increase the extent of cellular uptake of ¹³¹I-IldUrd 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

ALZET Comments: Phenylbutyrate, 4-; PBS; Intratumoral; Rat (nude); 2ML1; 7 days; 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

ALZET Comments: Herceptin; antibody, anti-Her2 monoclonal; radio-isotopes; Saline; ¹²⁵I tracer; IP; CSF/CNS (intratumoral); Rat (athymic); 2ML1; 7 days; 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

ALZET Comments: Platelet factor-4; MMP-2 (hemopexin fragment); PBS; SC; CSF/CNS (intratumoral); Mice; 2004; 28 or 94 days; 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

ALZET Comments: Oligonucleotide, antisense; Water, sterile; SC; intratumoral; Rat; 1003D; 86 hours; 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



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.

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

ALZET Comments: Endostatin, recomb human; CSF/CNS (intratumoral); Rat; 2ML2; 28 days; 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 pharmacodynamics and bioavailability of gamma linolenic acid in an implantation glioma model: effects on tumour biomass, apoptosis and neuronal tissue histology. *PROSTAGLANDINS LEUKOTRIENES AND ESSENTIAL FATTY ACIDS* 2002;67(5):283-292

ALZET Comments: Linolenic acid, gamma; PBS; CSF/CNS (intratumoral); 2001; 3-7 days; 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

ALZET Comments: Platelet factor 4 peptides; PBS; CSF/CNS (intratumoral); Mice (nude); 2004; 30 days; 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

ALZET Comments: Antibody, anti-EGF receptor; Immunotoxin (Tfn-CRM107); Immunotoxin (425.3-PE); CSF/CNS (intratumoral); Mice (nude); Rat (nude); 2001D; 24 hours; ALZET brain infusion kit used;

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

ALZET Comments: Fibroblast growth factor, basic; Saline; IV (jugular); Intratumoral; Rat; 2004; 28 days; 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

ALZET Comments: Fibroblast Growth Factor, Basic; Saline; IV (jugular); Intratumoral;; Rat; 10, 14, or 28 days; 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

ALZET Comments: Neomycin; PBS; CSF/CNS (intratumoral); Rat; 2004; 26 days; 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

ALZET Comments: Colony-stimulating factor, GM; PBS; BSA; SC (tumor vaccine injection site); Mice; 1002; 14 days; 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



ALZET Comments: Butyrate, sodium;; CSF/CNS (intratumoral);; Rat;; 2ML2;; 2 weeks;; 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)

ALZET Comments: Interleukin-2;; Albumin, human;; SC; Peritumoral (orthotopic); Rat;; 2002;; 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

ALZET Comments: WIN-55212-2; Cannabinol, delta-9-tetrahydro-; PBS; BSA; CSF/CNS (intratumoral); Rat; 2001; 7 days; 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)

ALZET Comments: Interleukin-2; Albumin; intratumoral; Rat; no duration posted; 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

ALZET Comments: UCN-01; Citric acid; intratumoral; mice; 2001; 7 days; 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 Res* 1995;55(1306-1309)

ALZET Comments: Cyclopentenyl cytosine; Saline, normal; IP; intratumoral; Rat; 2ML2; 2ML4; 6, 28 days; 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)

ALZET Comments: Dexamethasone; intratumoral; rabbit; 6, 10 days; controls received no treatment; tissue perfusion (tumor); comparison of injections vs. mp; local vs. systemic treatment, graph pg. 719.

P1707: B. F. Kimler, *et al.* Combination of radiation therapy and intracranial bleomycin in the 9L rat brain tumor model. *Int. J. Radiat. Oncol. Biol. Phys* 1990;18(1115-1121)

ALZET Comments: Bleomycin; CSF/CNS (intratumoral); cattle; Rat; 2001; 2002; 7, 14 days; Antibiotic; controls received pumps with saline only; tissue perfusion (tumor); dose-response (graph, p. 1117); comparison of ip injections vs. mp.

P1470: G. Bouvier, *et al.* Intratumoral chemotherapy with multiple sources. *Ann. N. Y. Acad. Sci* 1989;531(212-214)

ALZET Comments: Cisplatin; CSF/CNS (intratumoral); human; 2002; no duration posted; mp connected to multiple microcatheters and cannulae; tissue perfusion (tumor); cancer/immunology.

R0088: R. E. Harbaugh, *et al.* Use of implantable pumps for central nervous system drug infusions to treat neurological disease. *Neurosurgery* 1988;23(693-698)

ALZET Comments: Cisplatin; CSF/CNS (intratumoral); human; Rat; 2001; 2002; no duration posted; tissue perfusion (tumor); cancer/immunology.