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

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);

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 ;

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);

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);

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.

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.”

Agents: Bevacizumab Vehicle: Not Stated; Route: CSF/CNS (Intratumoral); Species: Mice; Pump: Not Stated; Duration: Not Stated;
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 specificantitumoral 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”
**Agents:** RNA, small interfering **Vehicle:** Not Stated; **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;

**Agents:** Telodendrimer nanoparticles, peptide-incorporated **Vehicle:** Not Stated; **Route:** CSF/CNS (Intratumoral); **Species:** Mice (nude); **Pump:** Not Stated; **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 37°C; Dose (0.5 ug/h); Brain coordinates (0.5 mm anterior to bregma and 2.5 mm lateral of midline);

**Agents:** M443 **Vehicle:** PBS; DMSO; **Route:** CSF/CNS (intratumoral); **Species:** Mice (nude); **Pump:** Not Stated; **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);

**Agents:** HSP70, human recomb. **Vehicle:** Not Stated; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
**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); tissue perfusion (glioblastoma); IMC-A12 aka cixutumumab;

**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;

**Agents:** Ganciclovir **Vehicle:** Not Stated; **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 trangenic); ALZET brain infusion kit used; cancer (glioma GL261);
Agents: Tetrakis (pcarboranylthiotetrafluorophenyl) Chlorin Vehicle: Not Stated; Route: CSF/CNS (intratumoral); Species: Rat; Pump: 2001D; Duration: Not Stated;
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

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)

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)

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;

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 (mu/mu Rowett); ALZET brain infusion kit 2 used; convection enhanced delivery (CED); tissue perfusion (intratumoral)

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)

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

**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)


**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/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


**Agents:** Interleukin-12, murine  
**Vehicle:** PBS;  
**Route:** CSF/CNS (intratumoral);  
**Species:** Mice;  
**Pump:** 1004; 2004;  
**Duration:** Not Stated;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL6); cancer (glioma); tissue perfusion (tumor; glioma); immunology; pumps primed at 37°C; pumps explanted after 28 days;


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


**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


**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;


**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

**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”  pg 181


**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)


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


**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 brain infusion kit used; animal info (Swiss, 4-6 wks old)


**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


**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)

**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; 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();U1-U10

**Agents:** Gamma linolenic acid  
**Vehicle:** CSF, artificial;  
**Route:** CSF/CNS (intratumoral);  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 14 days;

**ALZET Comments:** Controls received mp w/vehicle; cancer (glioma); ALZET brain infusion kit used; animal info (adult, female, Wistar, 250-350)


**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)


**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


**Agents:** Cetuximab  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (intratumoral);  
**Species:** Mice (nude);  
**Pump:** 2004;  
**Duration:** 15 days;

**ALZET Comments:** Tissue perfusion (tumor); functionality of mp verified by residual volume; cancer (glioblastoma); ALZET brain infusion kit 2 used; animal info (NMRI- nu/nu, 6-8 wks old); cetuximab is a monoclonal antibody against EGFR


**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


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

**ALZET Comments:** Tissue perfusion (tumor); functionality of mp verified by residual volume; cancer (glioblastoma); animal info (female 2 months old, 159 g.)
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)

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)

Agents: Adeno-associated virus serotype 8 vector, recombi. Vehicle: 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

Agents: Pioglitazone Vehicle: DMSO; PBS; Route: CSF/CNS (intratumoral); 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)

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

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;

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;
**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 (buprenophine)

**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)

**Agents:** Oligonucleotide, antisense  
**Vehicle:** Not Stated  
**Route:** SC; Intratumoral  
**Species:** Not Stated  
**ALZET Comments:** Cancer (adenocarcinoma); surgical sutures used to immobilize the pumps

**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

**Agents:** GRN163, FITC  
**Route:** CSF/CNS (intratumoral)  
**Species:** Rat (nude)  
**Pump:** 1007D  
**Duration:** 7, 14 days  
**ALZET Comments:** Tissue perfusion (tumor); enzyme inhibitor (telomerase); cancer (glioma); animal info (6-8 wks old, male, athymic)

**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

**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)

**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(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."


**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


**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)


**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


**Agents:** Uridine; iododeoxy; 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)


**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

**Agents:** Herceptin; antibody, anti-Her2 monoclonal; radio-isotopes **Vehicle:** Saline; **125**I 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 (transituzumab) was also infused intratumorally, peritumorally, and i.p to study tissue distribution


**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);


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

**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


**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 **Vehicle:** Not Stated; **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 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

**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

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.


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;


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 (tumor); cancer; peptides; bFGF delivered either by systemic IV infusion or intratumorally


Agents: Fibroblast Growth Factor, Basic Vehicle: Saline; Route: IV (jugular); Intratumoral; Species: Rat; Pump: Not Stated; Duration: 10,14,28 days;
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


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


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


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;


Agents: Interleukin-2 Vehicle: Albumin, human; Route: SC; Peritumoral (orthotopic); Species: Rat; Pump: 2002; Duration: Not Stated;
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
**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

**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

**Agents:** UCN-01  
**Vehicle:** Citric acid;  
**Route:** Intratumoral;  
**Species:** Mice;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** Tissue perfusion (tumor); cancer; enzyme inhibitor

**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

**Agents:** Dexamethasone  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (intratumoral);  
**Species:** Rabbit;  
**Pump:** Not Stated;  
**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

**Agents:** Bleomycin  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (intratumoral);  
**Species:** Cattle; Rat;  
**Pump:** 2001; 2002;  
**Duration:** 7, 14 days;  
**ALZET Comments:** Antibiotic; controls received pumps with saline only; tissue perfusion (tumor); dose-response (graph, p. 1117); comparison of ip injections vs. mp

**Agents:** Cisplatin  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (intratumoral);  
**Species:** Human;  
**Pump:** 2002;  
**Duration:** Not Stated;  
**ALZET Comments:** mp connected to multiple microcatheters and cannulae; tissue perfusion (tumor); cancer/immunology

**Agents:** Cisplatin  
**Vehicle:** Not Stated;  
**Route:** CSF/CNS (intratumoral);  
**Species:** Human;  
**Pump:** 2001; 2002;  
**Duration:** Not Stated;  
**ALZET Comments:** Tissue perfusion (tumor); cancer/immunology