



References on the Administration of Erythropoietin Using ALZET® Osmotic Pumps

Q9979: D. Szczesny, *et al.* Proof-of-concept study on improved efficacy of rHuEPO administered as a long-term infusion in rats. *Pharmacological Reports* 2020;72(5):1264-1270

Agents: Human recombinant erythropoietin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days; **ALZET Comments:** Dose (1333 IU/kg, 667 IU/kg, and 333 IU/kg.); 0.9% Saline used; Controls received mp w/ vehicle; Human recombinant erythropoietin aka rHuEPO; dependence;

Q8440: S. Dey, *et al.* Sex-specific brain erythropoietin regulation of mouse metabolism and hypothalamic inflammation. *JCI Insight* 2020;5(5):

Agents: Erythropoietin, recombinant human **Vehicle:** Saline; **Route:** CSF/CNS (lateral cerebral ventricle); **Species:** Mice; **Pump:** 2006; **Duration:** 14 days;

ALZET Comments: Dose (3000 U/kg); Controls received mp w/ vehicle; animal info (Tg21 mice); recombinant human Erythropoietin aka recombinant human EPO; ALZET brain infusion kit 3 used; Brain coordinates (midline, 1.00 mm; antero-posterior, 0.34 mm; dorsoventral, 2.30 mm); dental cement used; replacement therapy (Erythropoietin);

Q8045: E. K. Kim, *et al.* Local Subcutaneous Injection of Erythropoietin Might Improve Fat Graft Survival, Whereas Continuous Infusion Using an Osmotic Pump Device Was Harmful by Provoking an Overwhelming Foreign Body Reaction in a Nude Mouse Model. *Archives of Aesthetic Plastic Surgery* 2018;24(3):128-133

Agents: Erythropoietin **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week;

ALZET Comments: Dose (1,000 IU of EPO); animal info (36 weeks old, CD-1, Male, 20-25 g); EPO aka hemangiogenic and antiapoptotic factor ; dependence;

Q4880: E. H. Sanchez-Mendoza, *et al.* Implantation of Miniosmotic Pumps and Delivery of Tract Tracers to Study Brain Reorganization in Pathophysiological Conditions. *Journal of Visualized Experiments* 2016;107(1-9)

Agents: Erythropoietin, recombinant human **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 30 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6); good methods (Jove Video; picture of pump and implantation pg. 4); ischemia (cerebral); post op. care (Carprofen 4 mg/kg); behavioral testing (rotarod test; hand grip strength); cyanoacrylate adhesive; "In this work we have shown the method of implantation of minipumps with a cannula connected to the skull in order to deliver the plasticity promoting protein rhEpo directly into the ventricle, thus circumventing the BBB." pg 8; Cannula placement verified via histologic analysis "The are no evident severe tissue alterations based on Nissl staining as compared to the corresponding contralateral area";

Q6648: M. Rauner, *et al.* Increased EPO Levels Are Associated With Bone Loss in Mice Lacking PHD2 in EPO-Producing Cells. *J Bone Miner Res* 2016;31(10):1877-1887

Agents: Erythropoietin, recomb. human **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (knockout); Mice (transgenic); **Pump:** Not Stated; **Duration:** 30 days;

ALZET Comments: Dose (3 U EPO/day or 10 U EPO/day); Controls received mp w/ vehicle; animal info (8-12 week old WT and *Osx:cre-PHD2f/f* and *Vav:cre-PHD2f/f* mice);

Q4450: S. Hiram-Bab, *et al.* Erythropoietin directly stimulates osteoclast precursors and induces bone loss. *FASEB JOURNAL* 2015;29(1890-1900)

Agents: Erythropoietin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (transgenic); **Pump:** Not Stated; **Duration:** 10 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Tg6, 12 weeks old);

Q3130: G. B. Wang, *et al.* The AKT/mTOR pathway mediates neuronal protective effects of erythropoietin in sepsis. *MOLECULAR AND CELLULAR BIOCHEMISTRY* 2014;385(1-2):125-132

Agents: Erythropoietin, human recombinant **Vehicle:** PBS; BSA; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 week;

ALZET Comments: Controls received mp w/ vehicle or sham surgery; animal info (Sprague Dawley, 120 days old, 240-280g); behavioral testing (open field exploration, inhibitory avoidance, Morris water maze);



Q3518: M. S. Jeffers, *et al.* Epidermal Growth Factor and Erythropoietin Infusion Accelerate Functional Recovery in Combination With Rehabilitation. *Stroke* 2014;45(185-+

Agents: Epidermal Growth Factor; erythropoietin **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 14 days;

ALZET Comments: Animal info (male, Sprague Dawley); pumps replaced every 7 days; ischemia (cerebral); behavioral testing (staircase test); pumps removed 7 days after serial implantation;

Q3269: Y. F. Wang, *et al.* Bioengineered sequential growth factor delivery stimulates brain tissue regeneration after stroke. *Journal of Controlled Release* 2013;172(1):1-11

Agents: Epidermal growth factor; erythropoietin **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 14 days;

ALZET Comments: Animal info (male, C57BL6, 9-11 weeks old); EGF-PGF pumps replaced after 7 days with pump filled with ETO; ALZET brain infusion kit 3 used; comparison of epicortical composite vs mp; stress/adverse reaction: "Unlike the ICV catheter/minipump, which causes significant tissue damage, the epicortical composite provides a minimal invasiveness and no tissue damage." (see pg.9); immunology; Pumps implanted 4 days after stroke; BIK implanted same day as stroke;

Q2546: J. Unden, *et al.* Post-ischemic continuous infusion of erythropoietin enhances recovery of lost memory function after global cerebral ischemia in the rat. *BMC Neuroscience* 2013;14(;):U1-U8

Agents: Erythropoietin **Vehicle:** Saline; **Route:** IV (jugular); **Species:** Rat; **Pump:** 2001D; 1003D; **Duration:** 72 hours;

ALZET Comments: Control animals received mp w/ vehicle; animal info (Wistar, male, 300-350 g); silastic tubing used

Q2677: L. M. Yamaleyeva, *et al.* Cell Therapy with Human Renal Cell Cultures Containing Erythropoietin-Positive Cells Improves Chronic Kidney Injury. *STEM CELLS TRANSLATIONAL MEDICINE* 2012;1(5):373-383 **Erythropoietin**

Agents: Erythropoietin, recomb. human **Vehicle:** Saline; **Route:** IP; **Species:** Rat (nude); **Pump:** 2ML4; **Duration:** Not Stated;

ALZET Comments: Animal info (athymic, male, 10-15 wks old); pump functionality measured via residual volume

Q1294: R. Reitmeir, *et al.* Post-acute delivery of erythropoietin induces stroke recovery by promoting perilesional tissue remodelling and contralesional pyramidal tract plasticity. *Brain* 2011;134(;):84-99

Agents: Erythropoietin **Vehicle:** NaCl; **Route:** CSF/CNS; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6/j, male, 23-25 g, 8-10 wks); ALZET brain infusion kit 3 used; ischemia (focal cerebral)

Q1055: A. Erlandsson, *et al.* Immunosuppression promotes endogenous neural stem and progenitor cell migration and tissue regeneration after ischemic injury. *Experimental Neurology* 2011;230(1):48-57

Agents: Epidermal growth factor, recomb. human; erythropoietin; cyclosporine A **Vehicle:** Not Stated; **Route:** CSF/CNS; SC; **Species:** Mice (NOD/SCID); **Pump:** 1007D; **Duration:** Not Stated;

ALZET Comments: Animal info (male, C57/BL6, 8-10 wks old); pumps replaced after 7 days; ALZET brain infusion kit 3 used

Q1286: C. D. Price, *et al.* Effect of continuous infusion of asialoerythropoietin on short-term changes in infarct volume, penumbra apoptosis and behaviour following middle cerebral artery occlusion in rats. *Clinical and Experimental Pharmacology and Physiology* 2010;37(2):185-192

Agents: Erythropoietin, asialo- **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 4 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-275 g)

Q0577: A. Kondo, *et al.* Erythropoietin exerts anti-epileptic effects with the suppression of aberrant new cell formation in the dentate gyrus and upregulation of neuropeptide Y in seizure model of rats. *Brain Research* 2009;1296(;):127-136

Agents: Erythropoietin, human, recomb.; antibody, anti-EPO **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 days; 24 hours;

ALZET Comments: Controls received mp w/ rat serum albumin, or control mouse IgG; animal info (male, Fischer 344, 10-12 wks old, 200-250 g, SLC)



P9496: T. Kadota, *et al.* Continuous intraventricular infusion of erythropoietin exerts neuroprotective/rescue effects upon Parkinson's disease model of rats with enhanced neurogenesis. *Brain Research* 2009;1254(1):120-127

Agents: Erythropoietin **Vehicle:** Albumin, rat serum; saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week; **ALZET Comments:** Controls received mp w/ vehicle; animal info (Sprague Dawley, 220-250 g.)

Q0293: B. J. Jobst, *et al.* Endothelial Cell Seeding Fails to Prevent Intimal Hyperplasia Following Arterial Injury in the Rat Carotid Model. *Cardiovascular Drugs and Therapy* 2009;23(5):343-353

Agents: Granulocyte-colony stimulating factor, human, recomb.; erythropoietin, human, recomb. **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** 2ML1; **Duration:** 48 hours; **ALZET Comments:** Controls received mp w/ saline; animal info (male, CD, 250 g, splenectomy)

Q0263: M. Jing, *et al.* The combined therapy of intrahippocampal transplantation of adult neural stem cells and intraventricular erythropoietin-infusion ameliorates spontaneous recurrent seizures by suppression of abnormal mossy fiber sprouting. *Brain Research* 2009;1295(203-217)

Agents: Erythropoietin, human, recomb. **Vehicle:** Saline; Albumin, rat serum; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (male, 190-210 g)

P9369: L. Belayev, *et al.* A novel neurotrophic therapeutic strategy for experimental stroke. *Brain Research* 2009;1280(117-123)

Agents: Erythropoietin **Vehicle:** Saline; **Route:** IV (femoral); **Species:** Rat; **Pump:** 2ML1; **Duration:** 3 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Long-Evans, 280-330 g., MCAO)

P8932: S. Oya, *et al.* Region-specific proliferative response of neural progenitors to exogenous stimulation by growth factors following ischemia. *NeuroReport* 2008;19(8):805-810

Agents: Epidermal growth factor, recomb. human; Fibroblast growth factor-2, recomb. human; Insulin-like growth factor I, recomb. human; Erythropoietin, recomb. rat; Brain-derived neurotrophic factor, recomb. human; DDL4, recomb. mouse **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days; **ALZET Comments:** Ischemia; animal info (male, Wistar, 8wks old, 280-300 g.); bilateral infusion

P9049: M. Hack, *et al.* A systemic combination therapy with granulocyte-colony stimulating factor plus erythropoietin aggravates the healing process of balloon-injured rat carotid arteries. *Cardiovascular Drugs and Therapy* 2008;22(5):351-362

Agents: Granulocyte-colony stimulating factor-, recomb. human; Erythropoietin **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ saline; peptides; animal info (male, Sprague Dawley, 300-350 g., splenectomy); "We used implantable osmotic minipumps to guarantee continuous systemic delivery of the tested cytokines over the first even days upon intraperitoneal deposition." pg. 353

P8660: J. Soliz, *et al.* Soluble erythropoietin receptor is present in the mouse brain and is required for the ventilatory acclimatization to hypoxia. *Journal of Physiology-London* 2007;583(1):329-336

Agents: Erythropoietin receptor, soluble **Vehicle:** Phosphate buffer; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days; **ALZET Comments:** Controls received mp w/ vehicle; ALZET brain infusion kit used; animal info (male C57/BL6, 3 months old, hypoxia)

Q0248: B. Kolb, *et al.* Growth factor-stimulated generation of new cortical tissue and functional recovery after stroke damage to the motor cortex of rats. *Journal of Cerebral Blood Flow and Metabolism* 2007;27(9):983-997

Agents: Erythropoietin; Epidermal growth factor **Vehicle:** CSF, artificial; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7, 14 days; **ALZET Comments:** Controls received mp w/ vehicle; peptides; animal info (male, Long-Evans, 90-110 days old); ischemia (cerebral); behavioral testing (forelimb asymmetry, forelimb inhibition (swimming), reaching); some animals received 7 days EGF



P8429: B. L. Frederiksen, *et al.* Does erythropoietin augment noise induced hearing loss? *Hearing Research* 2007;223(1-2):129-137

Agents: Erythropoietin **Vehicle:** Not Stated; **Route:** Ear (round window); **Species:** Guinea pig; **Pump:** 1007D; **Duration:** 1 week;
ALZET Comments: Controls received mp w/ saline; replacement therapy (noise-induced hearing impairment); comparison of acute admin. vs. mp; peptides; animal info (male, Dunkin-Hartley); tissue perfusion (round window); mp primed 6 hours in 37 Celsius saline; correct catheter placement confirmed

P7614: S. Malhotra, *et al.* Ischemic preconditioning is mediated by erythropoietin through PI-3 kinase signaling in an animal model of transient ischemic attack. *Journal of Neuroscience Research* 2006;83(1):19-27

Agents: Erythropoietin receptor, soluble **Vehicle:** PBS; BSA; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ vehicle; peptides; ischemia (cerebral); animal info (male, Wistar, 200-225 g); MCAO

P5948: K. Prass, *et al.* Hypoxia-induced stroke tolerance in the mouse is mediated by erythropoietin. *Stroke* 2003;34(8):1981-1986

Agents: Erythropoietin, soluble receptor **Vehicle:** PBS; BSA; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1003D; **Duration:** 64 hours;

ALZET Comments: Controls received mp w/ vehicle; peptides; ischemia (cerebral); human EPO used; 0.1%BSA used in vehicle

P5801: T. Shingo, *et al.* Erythropoietin regulates the in vitro and in vivo production of neuronal progenitors by mammalian forebrain neural stem cells. *J Neurosci* 2001;21(24):9733-9743

Agents: Erythropoietin; antibody, rabbit anti-EPO neutralizing; rabbit IgG **Vehicle:** Saline; albumin, mouse serum; rat serum; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 6 days;

ALZET Comments: Controls received mp w/ vehicle; peptides; Erythropoietin (EPO) Recomb. Human, antibody & IgG were dissolved in 0.9% saline with 1 mg/ml mouse serum albumin; pump/cannula schematic (p. 9739 fig A)

P4619: B. R. Walker, *et al.* Nitric oxide-dependent pulmonary vasodilation in polycythemic rats. *American Journal of Physiology Heart and Circulatory Physiology* 2000;279(H2382-H2389)

Agents: Erythropoietin **Vehicle:** Saline; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 weeks;

ALZET Comments: controls received mp w/vehicle; peptides; cardiovascular

P4291: I. Roeder, *et al.* Interactions of erythropoietin, granulocyte colony-stimulating factor, stem cell factor, and interleukin-11 on murine hematopoiesis during simultaneous administration. *Blood* 1998;91(9):3222-3229

Agents: Interleukin-11; Stem cell factor; Granulocyte-colony stimulating factor, PEGylated; Erythropoietin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2002; 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ saline; functionality of mp verified by pilot studies; no stress (see pg. 3223); peptides; recomb. human interleukin-11, EPO, & G-CSF used; recomb. rat stem cell factor used (pegylated);agents were given in every combination;

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

Agents: Erythropoietin; Granulocyte-colony stimulating factor; Etoposide **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 7 days;

ALZET Comments: Dose-response curves (pg. 326-328); cancer; peptides; etoposide is VP-16-213; EPO and VP-16-213 given in same pump initially, but this inactivated the G-CSF; multiple pumps per animal (1-2) for G-CSF/VP-16 mice

P2737: A. Hoffman, *et al.* Continuous versus pulsatile administration of erythropoietin (EPO) via the uterus in anemic rats. *Int. J. Pharmaceutics* 1994;111(197-202)

Agents: Erythropoietin **Vehicle:** Not Stated; **Route:** Intrauterine; **Species:** Rat; **Pump:** 2002; **Duration:** 5 days;

ALZET Comments: controls received intrauterine bolus of saline; replacement therapy (gentamicin-induced anemia); comparison of iv bolus and intrauterine bolus vs. mp; peptides; mp implanted subdermally in abdomen; "administration of drug at a constant rate produces considerably greater biological effect than that observed in the pulsatile mode." (pg. 200); tissue perfusion (uterus); recomb. human EPO used



P2523: T. Berney, *et al.* Murine autoimmune hemolytic anemia resulting from Fc-gamma receptor-mediated erythrophagocytosis: protection by erythropoietin but not by interleukin-3, and aggravation by granulocyte-macrophage colony-stimulating factor. *Blood* 1992;79(11):2960-2964

Agents: Erythropoietin; Interleukin-3; Colony-stimulating factor, GM **Vehicle:** PBS; Glycerol; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Immunology; peptides

P2970: T. Shibata, *et al.* Interleukin 3 perfusion prevents death due to acute anemia induced by monoclonal antierythrocyte autoantibody. *J. Exp. Med* 1990;171(1809-1814

Agents: Interleukin-3; Colony-stimulating factor, GM; Erythropoietin **Vehicle:** PBS; Glycerol; LPS, e. coli; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** Not Stated;

ALZET Comments: Controls received mp with vehicles +/- LPS; immunology; peptides; recomb. mouse GM-CSF & IL-3 used; recomb. human EPO used