



References on the Administration of Clozapine-N-Oxide Using ALZET® Osmotic Pumps

- Q10701:** C. Toledo, *et al.* Medullary Astrocytes Mediate Irregular Breathing Patterns Generation in Chronic Heart Failure Through Purinergic P2X7 Receptor Signalling. *EBioMedicine* 2022;80(104044)
Agents: Clozapine-N-oxide dihydrochloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
ALZET Comments: Dose (100 mg/kg); Controls received mp w/ vehicle; animal info (Male Sprague Dawley; 16 weeks old; Wild-type); gene therapy;
- Q10467:** W. T. Doucette, *et al.* Chronic chemogenetic manipulation of ventral pallidum targeted neurons in male rats fed an obesogenic diet. *Brain Research* 2022;1784(147886)
Agents: Clozapine-N-oxide **Vehicle:** Acetic acid; saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 1 month;
ALZET Comments: Dose: 6 mg/kg/day; animal info (Male; Fed high-fat/high-sugar diet); post op. care (ketoprofen 3 mg/kg); Clozapine-N-oxide aka CNO; gene therapy; good methods ("Pumps were evaluated post-explant. We confirmed in each case that the CNO solution was evacuated from the pumps and that CNO had not precipitated out of solution within the pump.")
- Q10518:** G. Dobrzanski, *et al.* Impact of somatostatin interneurons on interactions between barrels in plasticity induced by whisker deprivation. *Scientific Reports* 2022;12(1):17992
Agents: Clozapine N-oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week;
ALZET Comments: Dose (1 mg/ml); 0.9% saline used; Controls received mp w/ vehicle; animal info (Male; SOM-IRES-Cre mice; 2-3 months old);
- Q10342:** H. Sotoyama, *et al.* Resting-state dopaminergic cell firing in the ventral tegmental area negatively regulates affiliative social interactions in a developmental animal model of schizophrenia. *Translational Psychiatry* 2021;11(1):236
Agents: Clozapine-N-oxide **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 10 days; 13 days;
ALZET Comments: Dose: (1.5 mg/kg/day); Controls received mp w/ vehicle; animal info: EGF model rats; (postnatal week 10–12); behavioral testing: locomotion test in an open field chamber; social interaction; Clozapine-N-oxide aka (CNO); neurodegenerative
- Q9507:** P. B. Tran, *et al.* Prolonged chemogenetic inhibition of nociceptors in a murine surgical model of osteoarthritis: effects on immune responses in dorsal root ganglia. *Osteoarthritis and Cartilage* 2020;28(**Agents:** Clozapine-N-oxide **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (10-week old male NaV1.8-Pdi C57BL/6 mice); Clozapine-N-oxide aka CNO; immunology;
- Q8840:** G. A. Rodriguez, *et al.* Chemogenetic attenuation of neuronal activity in the entorhinal cortex reduces Abeta and tau pathology in the hippocampus. *PLOS Biology* 2020;18(8):e3000851
Agents: Clozapine-N-Oxide **Vehicle:** DMSO; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Dose (1 mg/kg/day); 0.05% DMSO used; Clozapine-N-Oxide aka CNO ; neurodegenerative (Alzheimer's Disease);
- Q8862:** J. Jiang, *et al.* Activation of hypothalamic AgRP and POMC neurons evokes disparate sympathetic and cardiovascular responses. *American Journal of Physiology and Heart Circulatory Physiology* 2020;319(5):H1069-H1077
Agents: Clozapine-N-Oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** Not Stated;
ALZET Comments: Dose (2 mg/kg/day); Controls received mp w/ vehicle; animal info (Ten- to twelve-week- old-male mice); Clozapine-N-oxide aka CNO; cardiovascular;



Q8454: E. A. Dulka, *et al.* Chemogenetic Suppression of GnRH Neurons during Pubertal Development Can Alter Adult GnRH Neuron Firing Rate and Reproductive Parameters in Female Mice. *eNeuro* 2020;7(3):

Agents: Clozapine-N-oxide **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (0.3 mg/kg); 2.75% DMSO used; Controls received mp w/ vehicle; animal info (Transgenic mice (C57Bl6/J), 2 weeks old); Clozapine-N-oxide aka CNO; dependence;

Q9077: B. Stutz, *et al.* Dopamine neuronal protection in the mouse Substantia nigra by GHSR is independent of electric activity. *Molecular Metabolism* 2019;24(120-138

Agents: Clozapine-N-oxide; Salvinorin B **Vehicle:** DMSO; Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (CNO- 0.3 mg/kg or Salvinorin B- 5 mg/kg); Controls received mp w/ vehicle; animal info (); Clozapine-N-oxide aka CNO, excitatory DREADD agonist, Salvinorin B aka inhibitory DREADD agonist ; neurodegenerative (Parkinson's Disease);

Q7611: A. Obeidat, *et al.* Nociceptive neuroplasticity of the murine knee joint precedes severe structural joint damage in a surgical model of OA. *Osteoarthritis and Cartilage* 2019;27(**Agents:** Clozapine N-oxide **Vehicle:** Vehicle; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (10 weeks old, Male); behavioral testing (Pressure Application Measurement, Up-Down staircase Test); Clozapine N-Oxide aka CNO; enzyme inhibitor (Nociceptor inhibitor); dependence;

Q7925: N. D. Jayaraj, *et al.* Reducing CXCR4-mediated nociceptor hyperexcitability reverses painful diabetic neuropathy. *J Clin Invest* 2018;128(6):2205-2225

Agents: Clozapine-N-Oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; Clozapine-N-oxide aka CNO; diabetes;

Q5793: F. Donato, *et al.* Stellate cells drive maturation of the entorhinal-hippocampal circuit. *Science* 2017;355(6330):

Agents: Clozapine-N-oxide **Vehicle:** Saline; **Route:** SC; **Species:** Mice (neonate); **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (11-14 days); clozapine-N-oxide (CNO) Therapeutic indication (learning and memory); Dose (1 mg/kg);

Q5965: X. Mason. Neural Circuit Mechanisms Underlying the Exacerbation of Alzheimer's Disease by Chronic Stress. Doctoral dissertation, Harvard Medical School 2015;

Agents: Clozapine-N-oxide **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: animal info (Adult male Swiss Webster mice); neurodegenerative (Alzheimer's disease);