Pharmacology Discovery Services

A Eurofins Discovery Partner Lab

Chemotherapy-induced peripheral neuropathy

Test the efficacy of analgesic agents to alleviate chemotherapy-induced neuropathic pain

Preclinical Pain *In Vivo* Services

Pharmacology Discovery Services is a partner lab of Eurofins Discovery specialized in *in vivo* rodent model testing for preclinical drug discovery. We have conducted *in vivo* testing for pain disorders for both efficacy and side-effect profiling for over 50 years. All pain *in vivo* models are validated in a dose-dependent manner with approved benchmark positive controls to assure high-quality reproducible data is provided to our clients. To meet the needs of your specific Pain drug discovery project, we also have the flexibility and expertise to develop custom *in vivo* models.

Available Pain Models

Acute	Neuropathic
Tail Flick	SNL (Chung) Model
Post-Operative Pain (Brennan)	CCI (Bennett) Model
Inflammatory	Chemotherapy-induced (CIPN); Taxol
Formalin	CIPN; Oxaliplatin
Acetic Acid Writhing	STZ Induced-Diabetic Pain
Carrageenan-induced	MIA Induced-Osteoarthritis Pain
CFA-induced	Bone Cancer Pain

Chemotherapy-Induced Peripheral Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is a serious complication associated with anticancer drugs. Pain and autonomic peripheral neuropathy often occur during chemotherapy treatment and can be a potential factor for the interruption of cancer treatment with an increased risk of mortality. The presence of CIPN is noted as hyperalgesia (increased response to a noxious stimuli) or allodynia (nociceptive response to a normally innocuous stimuli). Changes to peripheral nerves produce nerve hyperexcitability and pain from sensitivity to mechanical or cold stimuli. CIPN is a common side effect in 20-80% of patients receiving Taxol or Oxaliplatin. However, no effective treatment for this complication has been developed. Similarly, in rats after multiple treatments with these chemotherapy drugs, a significant increase in sensitivity to mechanical or cold stimuli is observed[1,2].

Pharmacology Discovery Services offers two CIPN rat models to support the evaluation of the analgesic activity of your lead compounds; the platinum-based drug, Oxaliplatin, and the microtubule-stabilizing drug, paclitaxel (Taxol®). The models employ the mechanical allodynia test to assess the neuropathic pain. A sharp withdrawal of the hind paw to light mechanical stimuli indicates the presence of allodynia. The cold allodynia test can be employed as a second measurement in the rat Oxaliplatin model. Thus, the models can serve as an early assessment for evaluating the therapeutic efficacy of new analgesic agents.

Chemotherapy-induced peripheral neuropathy

Chemotherapy-Induced Neuropathic Pain, Oxaliplatin, Rat, Item# 504700

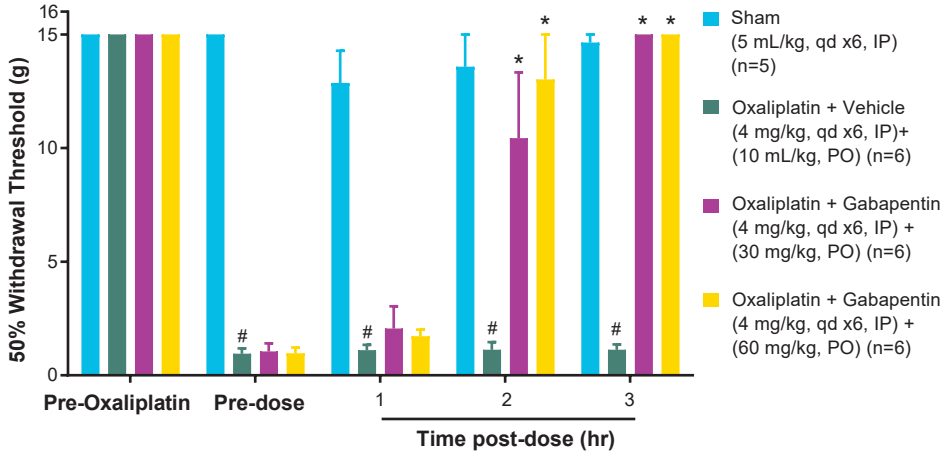

Figure 1. Withdrawal response (g) to von Frey monofilaments assessing mechanical allodynia in the hind paw. # p<0.05, treated vs. sham control; unpaired Student's t-test. * p<0.05, treated vs. vehicle control; one-way ANOVA followed by Dunnett's test.

Animals: Male Sprague Dawley (SD) rats

Induction: Six doses of Oxaliplatin (4 mg/kg) are intraperitoneal (IP) administered to rats over 17 days.

Verification of allodynia: The rats are verified if the development of allodynia on Day 21.

Efficacy test: Test articles are administered and efficacy is assessed at a specified time on Day 22. The model can be extended over a longer time course.

Behavioral end points: Mechanical allodynia (50% withdrawal threshold; g); Cold allodynia (Optional)

Positive control: Gabapentin (60 mg/kg, PO) at 2 and 3 hours post-dose

Turnaround time: 45 Days

Chemotherapy-Induced Neuropathic Pain, Paclitaxel, Rat, Item# 504400

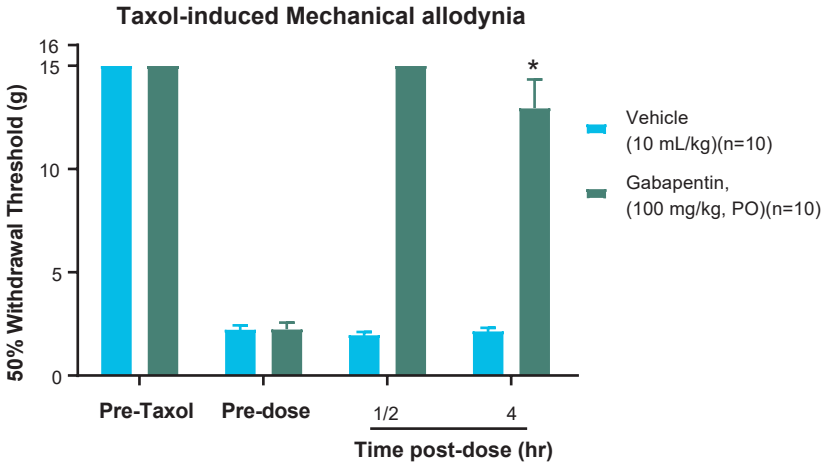

Figure 2. Withdrawal response (g) to von Frey monofilaments assessing mechanical allodynia in the hind paw. *p<0.05, treated vs. vehicle control; one-way ANOVA followed by Dunnett's test.

Species: Male Sprague Dawley (SD) rats

Induction: Four doses of Paclitaxel (4 mg/kg) are IP administered to rats over 7 days.

Verification of allodynia: The rats are verified for the development of allodynia on Day 13.

Efficacy test: Test articles are administered and efficacy is assessed at a specified time on Day 14. The model can be extended over a longer time course.

Behavioral end points: Mechanical allodynia (50% withdrawal thresholds; g); thermal hyperalgesia (seconds)

Positive control: Gabapentin (100 mg/kg, PO) typically at 2 hrs post dose

Turnaround time: 45 Days

Related Models		
Model	Species	Item #
Analgesia, Neuropathic Pain, Spinal Nerve Ligation	Mouse	504250
Analgesia, Neuropathic Pain, Chung Model	Rat	504200
Analgesia, Neuropathic Pain, Bennett Model, Nerve Ligation	Rat	504100

References

1. Zheng H, Xiao WH, Bennett GJ. Functional deficits in peripheral nerve mitochondria in rats with paclitaxel- and oxaliplatin-evoked painful peripheral neuropathy. *Exp Neurol.* 2011 Dec;232(2):154-61. doi: 10.1016/j.expneurol.2011.08.016
2. Areti A, Yerra VG, Naidu V, Kumar A. Oxidative stress and nerve damage: role in chemotherapy induced peripheral neuropathy. *Redox Biol.* 2014;2: 289-295.

For more information on *in vivo* pain services, please visit: pharmacologydiscoveryservices.com