Aim of Investigation:
Chemotherapy-induced peripheral neuropathy (CIPN) is a dose limiting side effect in the use of the platinum-based antineoplastic drug oxaliplatin as a treatment for colorectal cancer. Currently there is no treatment available to reverse the neurotoxicity which presents as pain, sensory loss and cold allodynia in up to 80% of patients. The aim of this study is to investigate if pregabalin can reverse the mechanical allodynia caused by oxaliplatin in CIPN.

Methods:
CIPN was induced in 10 male C57BL6 mice (6 weeks-old) with a single intraperitoneal injection of oxaliplatin (15 mg/kg i.p.) and in male SD rats (180-210 g) (5 or 10 mg/kg i.p.). Signs of thermal and mechanical allodynia were assessed from baseline to 14-19 days after injection by Cold/Hot plate (Bioseb, France) at 15°C (rats) and 20°C (mice) and hand-held von Frey (vF) hairs of gradually increasing weights (0.07, 0.16, 0.4, 0.6 and 1g). Pregabalin at 3 mg/kg and 10 mg/kg p.o. was administered to reverse the mechanical allodynia in mice and at 30mg/kg p.o. in rats.

Results: Mice

![Figure 1: Development of mechanical allodynia in C57Bl6 mice.](image1)

Development of mechanical allodynia following Oxaliplatin in C57Bl6 mice.

- Figure 1: Development of mechanical allodynia following Oxaliplatin in C57Bl6 mice.

![Figure 2: Development of thermal allodynia in C57Bl6 mice.](image2)

Development of thermal allodynia following Oxaliplatin in C57Bl6 mice.

- Figure 2: Development of thermal allodynia in C57Bl6 mice.

Results: Rats

![Figure 3: Development of mechanical allodynia following Oxaliplatin in Sprague Dawley rats.](image3)

Development of mechanical allodynia following Oxaliplatin in Sprague Dawley rats.

- Figure 3: Development of mechanical allodynia following Oxaliplatin in Sprague Dawley rats.

![Figure 4: Development of thermal allodynia following Oxaliplatin in Sprague Dawley rats.](image4)

Development of thermal allodynia following Oxaliplatin in Sprague Dawley rats.

- Figure 4: Development of thermal allodynia following Oxaliplatin in Sprague Dawley rats.

Conclusions:
The phenotype produced by systemic administration of oxaliplatin in rodents i.e. that of both thermal and mechanical hyperalgesia is similar to that observed in man; supporting the clinical translatability of this model. In the rat, oxaliplatin produced dose-dependent effects on mechanical and thermal allodynia. A single dose of pregabalin was able to reverse mechanical allodynia in the rat and mouse models of oxaliplatin-induced peripheral neurotoxicity.
Pregabalin was clearly more potent against mechanical allodynia than thermal allodynia in rats supporting the different pathological mechanisms underlying these two symptoms.

References: