THE NIH HEAL INITIATIVE PRECLINICAL SCREENING PLATFORM FOR PAIN EFFORTS TO VALIDATE TWO MODELS OF CHEMOTHERAPY-INDUCED PAINFUL NEUROPATHY IN THE RAT

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Background and aims: The National Institutes of Health Helping to End Addiction Long-term[SM] Initiative, or NIH HEAL Initiative[SM], Preclinical Screening Platform for Pain (PSPP) program PSPP is collaborating with PsychoGenics, Inc. to validate preclinical models and endpoints to enable screening and profiling of assets with the goal of accelerating the discovery and development of new non-opioid, non-addictive pain therapeutics. Here, we describe the validation and optimization of the paclitaxel and oxaliplatin models of chemotherapy-induced peripheral neuropathy in the rat.
Methods: Adult male and female Sprague Dawley rats (N=10, each sex, each experiment) were administered either paclitaxel (2 mg/kg, i.p., 4 mg/kg, i.p. or 2 mg/kg, i.v.), on 4 alternate days or oxaliplatin (3 mg/kg, i.v.) 2 days per week for 4 weeks. Hind paw tactile sensitivity using von Frey filaments and hind paw cold sensitivity using the acetone test were evaluated in both models. Effects of mechanical and cold priming of the hind paws on the development of hypersensitivity as well as the effects of chemotherapeutic agents on these endpoints were evaluated for a maximum period of 8 weeks.
Results: The careful evaluation of paclitaxel or oxaliplatin, taking pharmacokinetic parameters into consideration produced similar bilateral hind paw tactile and cold hypersensitivity which were significantly inhibited by morphine sulfate in a dose dependent manner.
Conclusions: The rigorous validation of the paclitaxel and oxaliplatin models of chemotherapy-induced peripheral neuropathy further highlights efforts within the NIH HEAL Initiative's PSPP program to validate endpoints and models for evaluating novel assets.