Efforts to accelerate development of non-opioid, non-addictive pain therapeutics within the NIH HEAL Initiative Preclinical Screening Platform for Pain and validation examples

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Background: The NIH HEAL Initiative Preclinical Screening Platform for Pain (PSPP) program has a goal of accelerating the discovery and development of new non-opioid, non-addictive pain therapeutics. In collaboration with PsychoGenics, Inc. preclinical models and endpoints are validated to enable screening and profiling of assets. 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 SD rats (N=10/sex/experiment) were administered either paclitaxel on 4 alternate days or oxaliplatin 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 and 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 PSPP program to validate endpoints and models for evaluating novel assets.