NIH HEAL Initiative: NINDS Preclinical Screening Platform for Pain (PSPP)

Sarah A. Woller[1], Amir P. Tamiz[1], Mark Urban[2], Mark Varney[2], Emer Leahy[2], Taleen Hanania[2], Smriti Iyengar[1]
[1]National Institute of Neurological Disorders and Stroke, National Institutes of Health, Rockville, MD 20852
[2]PsychoGenics Inc., Paramus, NJ 07652

Abstract

The National Institute of Neurological Disorders and Stroke (NINDS) aims to enhance pain management and accelerate the discovery and development of new non-addictive pain therapeutics as part of the recently launched NIH Helping to End Addiction Long-term (HEAL) Initiative, a trans-agency effort to provide scientific solutions to the opioid crisis. With NIH HEAL Initiative support, the NINDS Preclinical Screening Platform for Pain (PSPP) has been set up to accelerate identification of novel approaches to treat both acute and chronic pain conditions. Under NINDS direction, preclinical testing of submitted agents is performed by contract facilities on a blinded and confidential basis at no cost to the PSPP participants. Test candidates are evaluated in a suite of *in vivo* pain-related assays as well as drug abuse liability following *in vitro* receptor profiling, pharmacokinetic, and side-effect profile assessment. In vivo pain-related assays include models of acute to chronic pain and persistent pain mechanisms, as well as specific models of neuropathic, nociceptive and neuroplastic pain. A key feature of the PSPP is the flexibility to continuously acquire and validate innovative new models and endpoints that more closely represent human pain conditions. PSPP provides researchers from academia and industry, in the US and internationally, an efficient, rigorous, one-stop *in vivo* screening resource to identify and profile novel non-opioid, non-addictive therapeutic candidates, including small molecules, biologics, natural products and devices for the treatment of pain. This presentation will elaborate on the progress made within this novel non-opioid, non-addictive pain therapeutic discovery and development program and its efforts to engage the drug discovery and device development community.

Preclinical Screening Platform for Pain (PSPP)

The goal of the PSPP is to provide a platform to identify and profile non-addictive, non-opioid therapeutics for pain.

- One-stop resource for preclinical screening of potential therapeutic agents
- Assets accepted include small molecules, biologics, devices, or natural products
- Under NINDS direction, preclinical screening of assets is performed by contract facilities on a blinded and confidential basis
- Assets are accepted from worldwide academic institutions and industry
- PSPP is now accepting assets for evaluation on an ongoing basis
- No cost to PSPP participants

PSPP Testing Strategy: Screen, Profile, Validate

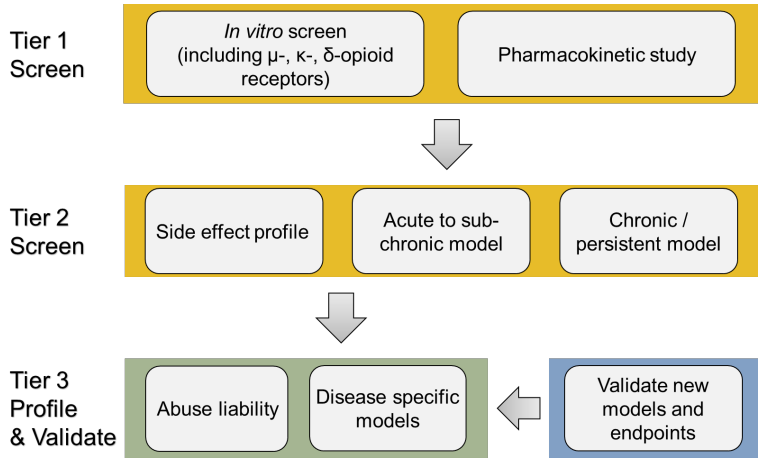
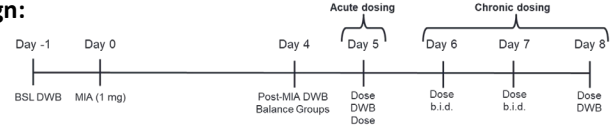


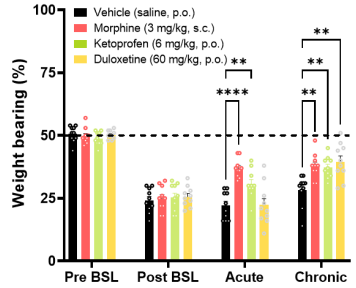
FIGURE 1: PSPP employs a multi-tier strategy for screening and profiling submitted assets.

Model Development and Endpoint Validation

Example: MIA model of osteoarthritis (OA) in the rat
Goal: Evaluate the effects of reference analgesics on dynamic weight bearing (DWB) in the rat MIA model of OA following acute and chronic dosing:
Method: 1 mg intraarticular MIA injection into left knee
Endpoint: dynamic weight bearing (DWB) assessed 1 hour after dosing
Reference compounds (n=10/group, male): morphine (3 mg/kg s.c.), ketoprofen (6 mg/kg p.o.), duloxetine (60 mg/kg p.o.), vehicle (saline p.o.)
Design:



Result: Following MIA injection, male rats put less weight on the left hindpaw. This imbalance is partially reversed after a single injection of morphine or ketoprofen and is further reversed following chronic dosing with morphine, ketoprofen, or duloxetine. * p <.05 relative to vehicle at each time by 2-way RM ANOVA with Dunnett's multiple comparison. Future studies will assess female rats and additional endpoints.



PSPP Participation and Eligibility

PSPP is currently accepting assets for evaluation continuously, on an ongoing basis.

For eligibility and participation inquiries, contact:

Dr. Smriti Iyengar, Program Director, smriti.iyengar@nih.gov, or
Dr. Sarah Woller, Scientific Project Manager, sarah.woller@nih.gov

For more information about PSPP, visit:
https://heal.nih.gov/research/preclinical-translational/screening-platform

Or scan here: