P313 Effect of Tail RFID Microchips on Growth Kinetics and Immune Response in Preclinical Oncology Mouse Models

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Mice are the most common laboratory animal for preclinical oncology studies, and because they are socially housed, a simple and efficient method for identifying individuals is required. Various types of radiofrequency identification (RFID) microchips are available for animal identification. There was a concern that implant of foreign objects, such as microchips, could affect an animal's immune response to immune-modulating compounds or immuno-oncology tumor models. Many microchips also require a large gauge needle for insertion in the subcutaneous space, which could interfere locally with a subcutaneous tumor model. For this project, 67 female BALB/c mice were implanted with RFID tail microchips, and 66 were not. Microchip implant occurred 2-4 d before subcutaneous implant of CT26.WT murine colon carcinoma tumors. Eight days post-implant, mice were sorted into groups for efficacy analysis (increase in time on study, incidence of regression, tumor doubling time) or sample collection based on tumor volume. Pro-inflammatory cytokine levels were measured through blood collections 1 d prior and 1, 7, and 14 d post microchip implant. Levels of several cytokines were minimally elevated in naïve mice with RFID microchips compared to those without the microchips 24 h post microchip implant; however, differences were no longer seen by 7 d post-implant. Immunohistochemistry of mouse tail sections (base of tail at site of RFID chip implant) also revealed no meaningful immune infiltration at the site of RFID microchip implantation. RFID microchips were shown to have minimal impact on baseline tumor growth kinetics and response to anti-mPD-1 in study mice. Flow cytometry analysis of tumors, spleen, and blood also revealed little to no difference in myeloid or lymphoid cell populations between microchipped and control mice. The use of the tail RFID microchips for identification does not appear to have a biological impact on the immune system of mice used for preclinical oncology research studies and is a technique refinement in RFID microchip systems.

P314 Extended-Release Buprenorphine, an FDA-indexed Analgesic, Attenuates Mechanical Hypersensitivity in Rats

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A new extended-release buprenorphine (XR), an FDA-indexed analgesic, was recently introduced to the laboratory animal community. The efficacy and dosing of XR for rats have not been extensively evaluated. This study aimed to investigate XR's efficacy in attenuating postoperative hypersensitivity in rat incisional pain models. We hypothesized that postoperative hypersensitivity attenuation achieved with XR (a low or high dose) would be similar to that of sustained-release buprenorphine in this model. Male adult Sprague-Dawley rats (n = 32) were randomly assigned to 1 of the 4 treatment groups: 1) Saline (Saline, 0.9% NaCl, 5 mL/kg, SC; once); 2) sustained-release buprenorphine (Bup-SR; 1.2 mg/kg, SC, once); 3) low dose extended-release buprenorphine (XR-Lo; 0.65 mg/kg, SC, once); 4) high dose extended-release buprenorphine (XR-Hi; 1.3 mg/kg, SC, once). A 1 cm longitudinal skin incision was made on the plantar hind paw 5 min after drug administration. Mechanical and thermal hypersensitivity was evaluated 1 d before surgery (D-1), 4 h after surgery (D0), and 3 d after surgery (D1, D2, and D3). The plasma buprenorphine concentration (n = 39) was measured from D0-D3. Clinical observations were recorded daily, and a gross necropsy was performed on D3. Mechanical (D0-D2) and thermal (D0-D3) hypersensitivity were observed in the Saline group. Bup-SR, XR-Lo, and XR-Hi effectively attenuated mechanical hypersensitivity for D0-D2. Plasma buprenorphine concentrations remained above the efficacious concentration of 1 ng/ml on D0 and D1 in all treatment groups. There were no abnormal clinical signs; however, injection site reactions were evident on D3 in the Bup-SR (71%), XR-Lo (75%), and XR-Hi (87%) groups. This study indicates that postoperative hypersensitivity attenuation with a low or high dose of XR is similar to Bup-SR. XR 0.65 mg/kg is recommended to attenuate postoperative mechanical hypersensitivity for up to 48 h in rats in an incisional pain model.

P315 Long-lasting, Highly Concentrated Buprenorphine Solution Provides Prolonged Therapeutic Blood Levels and Prolonged Mechanical Pain Responses In Rats

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A long-lasting, highly concentrated veterinary formulation of buprenorphine has been used to provide prolonged analgesia in cats, nonhuman primates, and mice. The use of a long-lasting formulation could prove beneficial in the management of pain in rats, which typically require dosing every 4-6 h to maintain adequate analgesia. LHC-Bup was evaluated in this study to determine if this formulation would provide similar prolonged analgesia in Sprague-Dawley rats. The pharmacokinetics were assessed after subcutaneous injection of 0.5 mg/kg LHC-Bup in male and female rats. Blood was collected via jugular venipuncture into a heparinized tube, and plasma levels were evaluated at 0.25, 0.5, 1, 2, 4, 8, 12, 24, 36, 48, and 72 h. Both male and female rats had a peak plasma level of Bup at 15 min after administration with a steady decrease by 24 h to 0.72 ± 0.3 ng/ml and 1.35 ± 0.51 ng/ml, in males and females, respectively. Administration of LHC-Bup maintained plasma levels of Bup above the purported therapeutic level of 1 ng/mL for over 12 h. The efficacy was assessed using a Randall-Selitto analgesiometer to measure mechanical pain tolerance after LHC-Bup administration. Male rats had an increased paw withdraw at 1 ($p < 0.01$), 3 ($p < 0.01$), 6 ($p=0.02$), and 12 ($p=0.09$) hours post-administration, tolerating a maximum pressure of 817.81 ± 215.48 g during the testing period, compared to the saline control that never tolerated more than 228.46 ± 114.96 g. Females had an increased paw withdraw at 1 ($p < 0.01$), 3 ($p < 0.01$), 6 ($p < 0.01$), 12 ($p=0.08$) and 24 ($p= 0.04$) hours post-administration, reaching a maximum threshold of 898.15 ± 204.50 g compared to 255.53 ± 116.40 g in the saline control. Based on these findings, LHC-Bup is a suitable formulation for the treatment of pain in rats at a dose of 0.5 mg/kg subcutaneously every 12 h in males and every 24 h in females.

P316 Ability of the Colony Stimulating Factor 1 Receptor (csf1r)-inhibitor, Plx5622 to Ablate Resident Retinal Microglia in Sprague Dawley Rats

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Retinal microglia participate in the pruning and maintenance of retinal neurons during development but are also active participants in phagocytosis of photoreceptors in retinal degenerative diseases. However, their exact contribution to photoreceptor degeneration remains unclear. We developed 2 novel rat models of inherited retinal disease, *Pde6b*$^{-/-}$ and *Mak*$^{-/-}$, via CRISPR-Cas9-meditated genome editing to characterize the role of retinal microglia and test whether depletion of these resident immune cells is feasible in the rat retina. Photoreceptor loss in *Pde6b*$^{-/-}$ and *Mak*$^{-/-}$ rat lines were characterized using standard immunohistochemistry against common retinal proteins and activated microglia. To deplete microglia, we treated