NP 1/16/2018

Column E Explanation

Registration Number: 91-R-0059, ID 1268

Number used in this study: 26 animals.

Species used in this study: Spiny mice

High dose LPS (lipopolysaccharide) injection to test endotoxic reaction - LPS are found in the outer membrane of Gram-negative bacteria, and elicit strong immune responses in animals. High dose LPS injections will be used to test endotoxic reaction as a measure of the inflammatory response in this new, non-traditional model rodent. The inflammatory response in Spiny Mice will be compared to standard well delineated inflammatory responses in Mus musculus. We will determine if inflammation has a role in ongoing neurogenesis and regenerative processes in Spiny Mice.

We have just begun to investigate endotoxic reaction in this unique species and will continue to characterize their baseline species reaction relative to well known reactions in Mus musculus. In an initial pilot experiment we observed mortality in 7/12 animals tested with a single dose of 12.5 mg/kg. Of the 7 animals found dead in this initial pilot, 5 were females. All deaths were reported to IACUC. As a corrective action plan, we restricted further experiments to males. We have now tested a total cohort of 29 Acomys (2/17 males with mortality) and observed clinical signs ranging from none (subclinical) to mild hunching, squinting, weight loss, slightly increased respiratory rate, and decreased activity. These mortality rates are considerably less than observed in concurrent Mus musculus cohorts tested under a different protocol. These data support our hypothesis that Acomys have increased homeostatic capacity which contributes to their regenerative wound healing abilities.

Since we are studying the effects of LPS on inflammation, we cannot use anti-inflammatory agents in conjunction with LPS. Furthermore, exogenous opioid administration also has immunomodulatory effects, including inhibition of antibody and cellular responses, natural killer cell activity, cytokine expression, chemokine-induced chemotaxis, and phagocytic activity. Although the exact mechanisms are unknown, the effects likely are due to opioid receptor binding on immune cells and indirect activation of the hypothalamic–pituitary–adrenal axis and sympathetic nervous system. Additionally, morphine-treated mice appear to be more susceptible to LPS, because of a combination of immunosuppression, decreased gastrointestinal transit time, and increased bacterial translocation (Comp Med. 2008 Apr; 58(2): 120–128) These points suggest that, even if analgesics were required, finding an agent that would not interfere with this established endotoxemia model is be difficult. Therefore, we monitor each animal very closely during the period of study and keep the numbers of animals to a minimum in each experiment.

High dose LPS treated animals are monitored two times daily by study personnel until euthanized or recovered: Animals are monitored for signs of pain (decreased activity, ungroomed appearance, hunched posture, daily body weight measurements), in addition to overall appearance and standard health monitoring as per animal care department's standard protocols.