Column E Explanation

Registration Number: 91-R-0059, ID 1268

Number used in this study: 19 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 are 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 is being compared to standard well delineated inflammatory responses in Mus musculus. We are determining if inflammation has a role in ongoing neurogenesis and regenerative processes in Spiny Mice.

In the past year, we have exclusively focused on our analyses on 12.5 mg/kg injections with sac at 1 hour. We have not observed any mortality within this short survival time post LPS administration. Our protocol is also approved for long-term (5 day) 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.

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.