Developmental Immunotoxicology Assessment in the Rat: Age, Gender and Strain Considerations

Rodney R. Dietert¹, Terry L. Bunn¹, Gregory S Ladics², and Michael P. Holsapple³. ¹College of Veterinary Medicine, Cornell University; ²Haskell Laboratories, E.I. du pont de Nemours, Inc.; and ³Environmental Research and Consulting Laboratories, The Dow Chemical Company.

The goals of this project were to determine the conditions for optimal immune assessment following in utero exposure to lead (Pb) and to evaluate the roles of age of assessment, gender, and genetic strain of rat on the observed immunotoxicologic outcomes following exposure. A combined delayed-type hypersensitivity response (DHR) to keyhole limpet hemocyanin (KLH) and anti-KLH IgG antibody were assessed as potential biomarkers for developmental immunotoxicity with age, gender, site of antigenic challenge, and strain as variables. Studies were conducted using both male and female Crl:CD®(SD)BR or Fisher 344 rats. The heavy metal, Pb, was used as a known developmental immunotoxin. IgG antibody against KLH antigen was measured using an enzyme linked immunosorbant assay (ELISA). Following sensitization with KLH, animals received a challenge injection in either the earlobe or footpad with KLH and the DTH measured 24 hours later using a spring-loaded caliper. Sprague-Dawley (CD) weanlings produced lower levels of antibody and a decreased DHR compared with adults; only adult males had a significantly increased DHR while both male and female adults produced higher levels of antibody than both genders of weanlings. The DHR was greater in young animals when challenged in the footpad vs. the earlobe. Females had optimum antibody levels with a DHR challenge in the earlobe whereas males had optimum levels when challenged in the footpad. In a strain comparison between weanlings exposed in utero to control or 250 ppm Pb acetate in drinking water and rats examined at five weeks of age, the CD vs. F344 rats had higher antibody responses; in contrast, F344 rats exhibited an elevated DHR. Pb exposure in utero via the pregnant dams produced differential gender effects in the juveniles of both strains. Females had a significantly decreased Pb-induced DHR (p<0.5) whereas males did not. These results suggest that the DHR and anti-KLH IgG are suitable as biomarkers of developmental immunotoxicity and, based on the Pb results, assessment can be performed in juvenile rats. Furthermore, these studies provide evidence that there are differential gender effects after in utero exposure to Pb that can be detected in juveniles but also persist into adulthood. Additionally, at the KLH concentrations utilized, the balance of cell-mediated vs. humoral response differed among the two strains examined. The project was conducted during the course of one year and completed in 2000.

Publication/presentation information:


Additional sponsors: None