P-110  Delayed-Type Hypersensitivity (DTH) model in the cynomolgus monkey

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Although a T-dependent antibody response (TDAR) assay is generally recommended as the first-line immune function assay in nonclinical immunotoxicity evaluation, second-line assays such as delayed-type hypersensitivity (DTH) to measure cell-mediated responses can provide helpful additional information. In this study, male Cynomolgus monkeys were injected intramuscularly either once or twice with 1 mg Keyhole Limpet Hemocyanin (KLH) or twice with a commercially available tetanus vaccine (40 IU tetanus toxoid + 0.06 mg aluminum hydroxide). All animals were subsequently challenged by intradermal injections of the same antigen or aluminum hydroxide after 4, 6 and 8 weeks. Clinical reactions at the injection sites were scored 24, 48 and 72 h post challenge. Skin biopsies were taken on completion of the observation period after each challenge for standard histological examination and immunolabeling using CD3 (T lymphocytes), CD19 (B lymphocytes) and CD68 (macrophages) antibodies. Tetanus toxoid induced stronger clinical reactions than KLH, whereas aluminum hydroxide induced no clinical reaction. Perivascular mononuclear cell infiltrates, a histopathological finding consistent with a DTH reaction, were seen after all challenges with tetanus toxoid or KLH, but not with aluminum hydroxide. Immunohistochemistry evidenced the presence of T lymphocytes and macrophages within these infiltrates. These results suggest that tetanus toxoid adjuvanted with aluminum hydroxide can induce a consistent DTH response for use as a model of cell-mediated response in Cynomolgus monkeys.