Immunoregulatory Responses in Trimellitic Anhydride Occupational Sensitization

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Trimellitic Anhydrides (TMA) are widely used in the plastic and paint industries. Occupational exposure to air-borne TMA is known to be very sensitizing and can cause a number of respiratory health problems including asthma. Numerous industries currently utilize TMA for product production where worker safety is a concern. The immunological basis of TMA-mediated sensitization is not well understood. Allergen sensitization and subsequent disease development are often explained as a hampered Th1/TH2 balance and a deficiency in Treg activation. Th2 cells which produce 'pro-allergic' or type-2 cytokines like IL4, IL5 and IL13, involved in IgE production, eosinophil differentiation and migration that are involved in allergen sensitization. More recently, Th17 cells, producing IL17 (a pro-inflammatory cytokine) have been found to also play a key role in allergic sensitization and disease pathogenesis.

To date, there is no report investigating Th1/Th2 balance and/or Treg activation in TMA-workers. We hypothesize that an altered TH1/TH2 balance and deficient Treg activation will predict whether TMA exposed workers become sensitized or tolerant to TMA in the workplace. Presently, TMA workers are monitored as part of an immunosurveillance program, which depends on measurement of serologic TMA-specific IgG, IgG4 and IgE, atopic status, smoking history and other demographic characteristics. However, this type of program is hampered by demographic diversity, level of TMA exposure, atopic status and the lack of immune markers that could identify workers early on at risk for developing sensitization and subsequent occupational disease. The present study will involve a cohort of workers including TMA exposed/non-sensitized, TMA exposed/IgG sensitized, TMA exposed/IgG and IgE sensitized and TMA non-exposed/non-sensitized groups. Th1 and Th2 cytokine levels will be assessed in blood cell culture supernatant by ELISA and within cells by flow cytometry. Regulatory T-cells will be identified as CD4+CD25+Foxp3hi using flow cytometry. We anticipate that there will be a gradient of Treg cell activation across the spectrum of TMA non-sensitized (maximal Treg cell populations) to TMA sensitized symptomatic workers (minimal Treg cell populations).

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