

## COMPARISON OF THE IN VITRO AND IN VIVO EFFECTS OF NATIVE AND GAMMA-RAY-IRRADIATED BACTERIAL ENDOTOXINS

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**Introduction:** Previous studies have reported that the level of environmental exposure to endotoxin and other bacterial wall components is an important protective determinant for the development of atopic diseases in childhood. In this study we compared the immunomodulatory potential of wild-type lipopolysaccharide (W-LPS) and radio (<sup>60</sup>Co)-detoxified LPS (R-LPS) in a murine model of allergic airway inflammation and on human monocyte-derived dendritic cells (DCs).

**Methods:** Cages (feed and bedding) of six-week old female BALB/c mice were treated daily with 5 microgram W-LPS or R-LPS (both originated from *E. coli*) in the form of aerosol spray. After a 10-week treatment period mice were sensitized intraperitoneally and challenged intranasally with ragweed pollen extract (RWE). Inflammatory cell infiltration into the airways was assessed by the analysis of the bronchoalveolar lavage fluid. In our *in vitro* experiments human DCs were exposed to W-LPS or R-LPS, and after that their phenotypic changes were monitored by flow cytometry and their cytokine and chemokine secretion was detected by ELISA. In separated experiments W-LPS- or R-LPS-treated DCs were co-cultured with allogeneic CD3+ pan-T cells and IFN-gamma production by activated T cells was detected by ELISPOT.

**Results:** Significantly less severe allergic airway inflammation could be observed in mice kept in R-LPS-rich milieu than in those raised in W-LPS-rich or common environment. *In vitro* exposure of human DCs to R-LPS induced similar phenotypic changes and triggered similar release of IL-8, TNF-alpha, IL-6, IL-1beta, IL-10 and IL-12 as did the treatment with W-LPS. Neither W-LPS nor R-LPS induced endotoxin tolerance in our experimental conditions. However, in co-culture experiments DCs primed with R-LPS activated more IFN-gamma-producing T cells than those pretreated with W-LPS. This observation indicates a higher Th1-polarizing capacity of R-LPS-primed DCs compared to W-LPS-exposed ones.

**Conclusions:** Collectively, our data suggest that based on the lack of endotoxin tolerance development radio-detoxified LPS may be suitable for long-term treatments and prolonged exposure to it during the early period of life may provide a novel tool to prevent/decrease symptoms of pollen allergy.

**Oral presentation / Subject: academic nature.**