

## Induction of allergic contact dermatitis by astigmatid mite-derived monoterpene, $\alpha$ -acaridial

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Dust mites (*Dermatophagoides pteronyssinus* and *D. farinae*) are known to cause allergic reactions by the type I dust mite proteinaceous allergens (Der p I and Der f I). More recently, however, our group has identified  $\alpha$ -acaridial, a highly conjugated terpene from the house dust mite, *Tyrophagus putrescentiae*, as a novel class of non-protein allergen that induced positive skin reactions in atopic dermatitis patients. Here we show the mechanistic studies of the delayed-type hypersensitivity induced by  $\alpha$ -acaridial.

First, Balb/c mice, sensitized with  $\alpha$ -acaridial for 5 days, were challenged by repeated administration of the antigen on the ear skin. After 2 weeks, significant redness and swelling were observed locally at the challenge site, where CD4<sup>+</sup> T lymphocytes were predominantly mobilized. To address the possibility that  $\alpha$ -acaridial might be conjugated with protein and function as a hapten recognized by CD4<sup>+</sup> T lymphocytes, we next looked at its reactivity to proteins. When incubated with BSA in the phosphate buffer/acetonitrile mixture (pH 5.5) at 36°C, the free form of  $\alpha$ -acaridial absolutely disappeared after 30 hours. Furthermore, when incubated with butylamine or butanethiol,  $\alpha$ -acaridial reacted with the primary amine and thiol to form pyrrole and furan adducts, respectively.

These results emphasize the ability of  $\alpha$ -acaridial to react with Lys or Cys residues of proteins. Thus, the  $\alpha$ -acaridial conjugated proteins or their peptide fragments may activate specific CD4<sup>+</sup> T cells that mediate the delayed type hypersensitivity observed in atopic dermatitis patients.