

 ALLERGY

Crystal clear culprit

“
therapeutic
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The deposition of crystals of uric acid (a by-product of metabolism that is expelled by stressed cells) is known to trigger the neutrophilic inflammation associated with gout. Now, Lambrecht, Hammad and co-workers have shown that uric acid crystals can also promote T helper 2 (T_H2)-type immune responses and allergic airway disease in mice.

In previous studies, the authors had found that intraperitoneal injection of alum leads to uric acid release. As alum is commonly used as an adjuvant in mouse models of allergic airway disease, they speculated that

alum-induced release of uric acid might drive T_H2 -type responses in these models. In keeping with this, in a model of ovalbumin (OVA)-induced allergic airway disease, T_H2 -type inflammation was inhibited if mice were treated with uricase (an enzyme that metabolizes uric acid) during priming with OVA and alum. Furthermore, uric acid crystals were able to substitute for alum in this model, and mice primed with OVA and uric acid developed T_H2 -type allergic airway disease in a similar manner to mice primed with OVA and alum.

Strikingly, mice treated with uricase were also protected from T_H2 -type inflammation following intranasal administration of house dust mite (HDM) allergen, suggesting that endogenous uric acid might serve as a common trigger of allergic airway disease. In immunohistochemistry studies, increased levels of uric acid were associated with airway epithelial cells and alveolar macrophages after allergen challenge and, notably, increased concentrations of uric acid were detected in bronchoalveolar lavage fluid when patients with asthma were exposed to specific allergens.

Experiments with genetically manipulated mice indicated that uric acid-induced T_H2 -type inflammation is dependent on dendritic cells (DCs), but independent of the NOD-, LRR- and pyrin domain-containing 3 (NLRP3) inflammasome — despite the fact that uric acid crystals have been shown to promote neutrophilic inflammation through NLRP3 activation. Instead, uric acid crystals were found to activate DCs in a spleen tyrosine kinase (SYK)-dependent manner. Although the exact mechanisms by which uric acid interacts with DCs to promote T_H2 -type immune responses are still uncertain, this study suggests that therapeutic targeting of uric acid crystals may be beneficial to patients with asthma.

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ORIGINAL RESEARCH PAPER Kool, M. *et al.*
An unexpected role for uric acid as an inducer of T helper 2 cell immunity to inhaled antigens and inflammatory mediator of allergic asthma.
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