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Title: BNN27, a synthetic derivative of dehydroepiandrosterone, suppresses allergic airway disease

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Body: Neurosteroids comprise a family of endogenous steroid hormones mainly known for their role in neuronal development and survival. A member of this family, dehydroepiandrosterone (DHEA), exhibits anti-inflammatory effects. Although DHEA could be beneficial in allergy, long-term administration of this molecule may induce side-effects, as it metabolizes into other steroids such as androgens and estrogens. Thus, we tested the effects of a DHEA-synthetic-analog BNN27 that does not metabolize to steroids, on allergic airway inflammation and allergic immune responses. For this we used a well-established mouse model for allergic asthma. Our results demonstrate that administration of BNN27 significantly suppressed allergic disease and the immune responses that mediate it. This included suppressed airway hyperresponsiveness, decreased pulmonary eosinophilia, suppressed allergen-specific IL-4 and IL-13 production, as well as significantly decreased allergen-specific IgE. Moreover, allergic mice treated with BNN27 had increased numbers of CD3⁺ CD4⁺CD25⁺ Foxp3⁺ T regulatory cells and suppressive CD11c⁺ PDCA-1⁺ plasmacytoid dendritic cells. We also found that BNN27 suppressed Th2 responses in vitro. We conclude that administration of the synthetic neurosteroid BNN27 has a significant immunomodulatory effect and protects from allergic airway inflammation.