1. **TLR2 Agonist Enhances CD8+Foxp3+ Regulatory T cells and Limits Th2 Immune Response during Allergen Immunotherapy**
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Rationale: To investigate whether Dermatophagoides pteronyssinus (DP)-specific Allergen-specific immunotherapy (IT) can enhance CD8+ Treg populations, as well as whether Pam 3CSK4 increases CD8+ Foxp3+ Treg cells and suppress a mite allergen-induced Th2 immune response.

Methods: Fifty children with moderately persistent asthma and with sensitivity to DP.

Results: All asthmatic subjects who received DP IT had a significant improvement of asthmatic scores after 1 y treatment.
CD8+Foxp3+ cells in DP 2-stimulated PBMCs had a significant increase after 1 year of IT. Purified CD8+CD25+ T cells isolated after DP 2-stimulated PBMCs showed increasing expression of Foxp3 during IT.
PBMCs from asthmatic patients contained significantly greater numbers of CD8+CD25+IL-10+ T cells after 1 y of IT than before IT and greater numbers of granzyme B-expressing CD8+CD25+ T cells.
Freshly isolated PBMCs were cultured with DP 2 in the presence or absence of Pam3CSK4 for 5 d. The number of CD8+Foxp3+ T cells was significantly greater in nonatopic than in asthmatic subjects before IT without Pam3CSK4 stimulation. After Pam3CSK4 costimulation with DP 2, the numbers of CD8+Foxp3+T cells in the asthmatic group were much greater than with DP 2 alone. Pam3CSK4 cos-timulation also significantly increased the percentage of CD8+Foxp3+ cells in nonatopic children.
The percentage of TUNEL+CD4+CD45ROhi+ T cells increased after the addition of CD8+CD25+ Treg cells (but not after the addition of CD4+CD25+ Treg cells) to CD25+ -depleted PBMCs from control subjects and asthmatic patients.

Conclusions: Pam3CSK4 ameliorates the Th2 allergic immune response by boosting CD8+ Treg cell function and decreasing Th2 cytokines.