Immunomodulatory impact of the BanLec-Bet v 1 chimera and its variants on antigen-presenting cells

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Abstract text

Text: Employing suitable adjuvants and hypoallergenic isoforms of allergens is necessary for improving the efficacy and safety of allergen-specific immunotherapy. Banana lectin (BanLec), a mannose binding protein, was shown to have immunomodulatory potential, while a His-Thr-mutation at position 84 ($BanLec_{H84T}$) reduced its intrinsic mitogenicity. This study evaluated the immunomodulatory potential of BanLec in the context of allergens, by creating recombinant chimeras between the major birch pollen allergen Bet v 1a or its hypoallergenic isoform Bet v 1l and BanLec or $BanLec_{H84T}$.

Proteins were produced in *Escherichia coli,* purified, and tested for stimulation of Bet v $1_{142-153}$-specific TCR-transgenic Jurkat T cells harboring an IL-2 promoter driven luciferase. EBV-transformed B cells or MoDC were used as APC. Proteins were preincubated with APC and luciferase activity with the APC-Jurkat co-culture was used as proxy for allergen-specific T cell activation.

Dose-response determinations revealed that the Bet v 1a-BanLec chimera compared to Bet v 1a induced a similar degree of T cell activation at 500-fold lower concentrations. At low concentrations, only Bet v 1a-BanLec was able to activate allergen-specific T cells, regardless of the APC type. While BanLec and $BanLec_{HT84}$ led to low T cell activation in MoDC/Jurkat co-cultures (SI: 5.7±0.6), Bet v 1-BanLec induced a stronger signal (SI:27.5±0.4). The immunostimulatory capacity of Bet v 1-BanLec could neither be explained by the endotoxin content (similarly low in all preparations) nor by differences in Th1/Th2 cytokines produced by MoDC. Unlike the single molecules, Bet v 1a-BanLec induced upregulation of CD86 and HLA-DR on MoDCs, but did not lead to high levels of TNF-a or IL-6. Moreover, Bet v 1a-BanLec induced IL-10 secretion in both THP-1 macrophages and MoDC.

Our results highlight the potential of recombinant allergen chimeras to modulate allergen-specific immune responses by enhancing anti-inflammatory cytokines and allergen-specific T-cell activation, potentially inducing T-regulatory cells.

Conflict of Interest statement

Do you have any conflict of interest to declare?: Yes

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Affirmation

1. Consent to participate and present onsite: Yes

2. Consent to publication publication: Yes

3. Consent on treatment of contact details saved in this system: Yes