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Disruption of T-cell immunoglobulin and mucin domain molecule (TIM)-1/TIM4 interaction as a therapeutic strategy in a dendritic cell-induced peanut allergy model.

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Abstract

BACKGROUND: Recent reports indicate that dendritic cell (DC)-derived T-cell immunoglobulin and mucin domain molecule (TIM)-4 plays an important role in the initiation of T(H)2 polarization. This study aims to elucidate the mechanisms of peanut allergy mediated by microbial products and DCs and the relationship between peanut allergy and TIM4.

METHODS: Mouse bone marrow-derived DCs (BMDCs) were generated and exposed to cholera toxin (CT) or/and peanut extract (PE) for 24 hours and then adoptively transferred to naive mice. After re-exposure to specific antigen PE, the mice were killed; intestinal allergic status was determined.

RESULTS: Increased expression of TIM4 and costimulatory molecules was detected in BMDCs after concurrent exposure to CT and PE. Adoptively transferred CT/PE-conditioned BMDCs resulted in the increases in serum PE-specific IgE and skewed T(H)2 polarization in the intestine. Oral challenge with specific antigen PE induced mast cell activation in the intestine. Treating with Toll-like receptor 4 small interfering RNA abolished increased expression of TIM4 and costimulatory molecules by BMDCs. Pretreatment with anti-TIM1 or anti-TIM4 antibody abolished PE-specific T(H)2 polarization and allergy in the intestine.

CONCLUSION: Concurrent exposure to microbial product CT and food antigen PE increases TIM4 expression in DCs and promotes DC maturation, which plays an important role in the initiation of PE-specific T (H)2 polarization and allergy in the intestine. Modulation of TIM4 production in DCs represents a novel therapeutic approach for the treatment of peanut allergy.

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