J Clin Cell Immunol 2018, Volume: 9
DOI: 10.4172/2155-9899-C4-058

10th World Congress and Expo on
Immunology, Immunity, Inflammation & Immunotherapies
October 19-20, 2018 | New York, USA

Retrovirus-derived virus-like particles as tolerogenic vaccines for allergy treatment

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The rise of immune disorders in the last decades paved the way for the development of new therapeutic approaches such as tolerogenic vaccination. The rationale is to administer allergens in a specific formulation thus reinforcing allergen-specific Th1 and/or regulatory T cell responses. Among the different vector systems used to formulate allergens, we selected and designed a retrovirus-derived virus-like particles (VLP) to carry allergens into the core and display an inhibitory molecule on the surface using chimeric binding. Recombinant tolerogenic VLPs (tVLPs) with ovalbumin (OVA) as model antigen were produced and we investigated their regulatory activity on both human and murine dendritic cells (DCs). We showed that tVLPs downregulate the surface expression of costimulatory molecules (i.e. CD80, CD86) on DCs and induce a pro-tolerogenic cytokine secretion profile. The therapeutic efficacy against allergy was assessed in a murine model of OVA-induced food allergy. BALB/c mice sensitized to OVA were vaccinated with tVLPs and then challenged by OVA p.o administrations. tVLP vaccination significantly reduced the clinical signs of allergy and protected against anaphylactic reactions. Notably, we demonstrated that the induced protection is maintained over a 5 months period in vaccinated mice and was dependent on regulatory T cells. Altogether, our results support the proof of concept for the efficacy of a VLP-based tolerogenic vaccine against food allergy and the characterization of related mechanisms are under investigation.

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