Development of allergen-specific Foxp3+RORγt+ Treg cells during allergen-specific immunotherapy

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Allergen-specific immunotherapy (ASIT) is an effective treatment that can induce clinical and psychological benefit. It is widely accepted that the IL23/Th17/IL17 axis is critical in the development of skin-resident memory CD4+ T (TRM) cells homing to infected or inflamed skin has been well-characterized, in vivo tracking of antigen-specific CD4+ T cells during development of skin TRM cells in our allergen-induced mouse model. We observed that both DNFB sensitized and OVA sensitized CD4+ T cells infiltrated into the skin, very early at 6 h after DNFB and OVA challenge, respectively. On day 7, only antigen-specific CD4+ T cells were visualized at day 7, finally developing sessile skin-resident memory CD4+ T cells at day 30 in our live imaging. These results suggest that antigens-specific TRM cells involve long-term inflammatory responses in both antigen-specific and non-specific effector CD4+ T cells participate acute inflammation.

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Allergen-specific immunotherapy (ASIT) is an effective treatment that can induce clinical and immunological tolerance to pathogenic allergens for atopic dermatitis (AD). The main mechanism of ASIT therapy is to induce the allergen-specific regulatory T (Treg) cells. Recently, transcriptional and functional analyses of Treg cells have identified three specialized subsets based on FoxP3 expression: FoxP3+RORγt+, FoxP3+RORγt−FoxP3−, and FoxP3−RORγt+ Treg cells. FoxP3+RORγt+ Treg cells have immunosuppressive function in different pathological and in testinal related organs. In our study, we enrolled AD patients with subcutaneous ASIT against house dust mite (HDM), and allergen-specific Treg cells were analyzed in peripheral blood mononuclear cells to extract RNA and performed transcriptomic analyses. We observed that FoxP3+RORγt+ Treg cells were increased from 3 months through 12 months of ASIT treatment in comparison with vehicle-treated HDM mice. Furthermore, we identified IL-23 as an upstream regulator that stimulated CDK7 expression and glycolysis through p-akt-Hif1α signaling pathway. Together, our results showed that abnormal CDK7 expression induced by IL-23 in CD4+ T cells in psoriasis patients contributed to the enhanced glycolysis levels which lead to the imbalance of Th17/Treg cells. CDK7 inhibitor THZ1 may serve as an immuno-modulator for psoriasis therapy in the future.

Levels of plasma total IgE and D-dimer basophil FcεRI expression potential predictors of response to autologous whole blood injection in chronic spontaneous urticaria

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Background: The efficacy and autologous of whole blood injection (AWBI) in treating chronic spontaneous urticaria (CSU) is unclear, which may be explained by seeking appropriate markers to effectively predict the response of the affected patients. Objectives: To explore the possible mechanism of AWBI in treating CSU by investigating the correlation between IgE, D-dimer, anti-FcεRI IgG and basophil FcεRI expression and the clinical symptoms of CSU treated by AWBI Methods: Eighty patients with autologous serum skin test (ASST)-positive CSU were enrolled and randomly divided into AWBI treated group (receiving AWBI and antihistamine) and control group (only with antihistamine). Urticaria activity score (UAS7) and dermatology life quality index (DLQI) of the patients before and after treatment were compared and analyzed. Levels of plasma total IgE, D-dimer, and anti-FcεRI IgG of 30 AWBI group patients before and after treatment were compared with those of 25 healthy controls. The basophil FcεRI expression in the peripheral venous blood of the patients was also analyzed. Results: A better clinical response was observed in the AWBI treatedgroup than in controls. ASST+ CSU patients had higher concentrations of baseline plasma IgE, D-dimer and anti-FcεRI IgG, as compared to health controls. IgE and D-dimer were differentially expressed between AWBI responders and non-responders, displaying good diagnostic value in predicting therapeutic response to AWBI. Basophil FcεRI expression was significantly higher in AWBI responders, with obvious decline during AWBI treatment. Conclusion: This study supported the effectiveness of AWBI in CSU, with the changes of plasma total IgE and D-dimer and psychological burden. it is widely accepted that the IL23/Th17/IL17 axis is critical in the development of psoriasis; however, the pathogenesis of psoriasis is still not fully understood. Recent studies reported that mast cells increase and may be the main source of IL-17, IL-22 in psoriatic lesions, whether mast cells participate in psoriasis need to be addressed. We used an imiquimod-induced mouse model of psoriasis to investigate the role of mast cells. We found that mast cells were increased significantly and activated mast cells in their skin compared to control group, while the Mregrβ2 knockout mice treated with IMQ had decreased and less activated mast cells, with decreased IL-17, IL-22, IL-23 and TNFα levels. In vitro studies showed that imiquimod could activate Mregrβ2 in human mast cell and Mregrβ2 in mouse mast cell. These results suggested that mast cells participated in the development of psoriasis-like dermatitis via Mregrβ2 in mice, associated with the IL23/IL17 axis, which will help us understand the immunopathogenesis and provide new strategies for the prevention and treatment in psoriasis.

Mast Cells participate in an imiquimod-induced mouse model of psoriasis

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Psoriasis is a chronic, inflammatory, polygenic disorder that is associated with both a physical and psychological burden. It is widely accepted that the IL23/Th17/IL17 axis is critical in the development of psoriasis. While the pathogenesis of psoriasis is still not fully understood. The clinical manifestations of psoriasis are well-known, but the underlying mechanisms of the disease are not well understood. The role of mast cells in the development of psoriasis-like dermatitis in a mouse model is not well understood. In this study, we used an imiquimod-induced mouse model of psoriasis to investigate the role of mast cells. We found that mast cells were increased significantly and activated mast cells in their skin compared to control group, while the Mregrβ2 knockout mice treated with IMQ had decreased and less activated mast cells, with decreased IL-17, IL-22, IL-23 and TNFα levels. In vitro studies showed that imiquimod could activate Mregrβ2 in human mast cell and Mregrβ2 in mouse mast cell. These results suggested that mast cells participated in the development of psoriasis-like dermatitis via Mregrβ2 in mice, associated with the IL23/IL17 axis, which will help us understand the immunopathogenesis and provide new strategies for the prevention and treatment in psoriasis.