CDK7 inhibitor suppresses psoriasis inflammation via inhibiting glycolysis to modulate Th17/Treg balance

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ABSTRACTS | Adaptive and Auto-Immunity

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

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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 in these processes remain undeveloped. In this study, we adoptively transferred both DNFB sensitized (Red) and OVA sensitized (Green) CD4+ T cells to naive recipients, and challenged with DNFB and OVA, respectively, into the recipients’ ears. Then, we performed two photon intravital imaging to monitor the in vivo tracking of antigen-specific CD4+ T cells during development of skin TRM cells in our allergen-injected 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 (Red or Green) cells infiltrated into the antigen-challenged ear while non-specific CD4+ T cells were barely observed. Immune antigen-specific CD4+ T cells were also visualized in the skin 10 days after antigen challenge, in contrast to non-specific CD4+ TRM cells. Consistently, OVA-specific DO11.10 CD4+ T cells also showed similar properties in our adoptively transferred mouse model. In summary, both antigen-specific and non-specific CD4+ T cells infiltrated into skin at day 7, then 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 antigen-specific TRM cells involve long-term skin-specific immune memory which both antigen-specific and non-specific effector CD4+ T cells participate acute inflammation.

Levels of plasma total IgG and D-mannidase basophil FcεRI expressions 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 biomarkers to predict the response of the afflicted patients. Objective: To explore the possible mechanism of AWBI in treating CSU by investigating the correlation between IgG, D-mannidase, 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 (UAS) and other clinical symptoms were compared and analyzed. Results: A better clinical response was observed in the AWBI treated group than in controls. ASST+ CSU patients had higher concentrations of baseline plasma IgE, D-mannidase and anti-FcεRI IgG, as compared to health controls. IgE and D-mannidase were different in AWBI responders, with an obvious decline during AWBI treatment. Conclusion: This study supports the effectiveness of AWBI in CSU, with changes of plasma total IgG and D-mannidase as potential predictors of treatment response. A feasible mechanism of AWBI in treating CSU is through the reduced expression of basophil FcεRI.

There are two isoforms of BP180 in the mouse brain

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BP180 is a homedomain protein in the skin and other epithelial tissues. The extracellular domain NC16A of BP180 is the main target of pathogenic autoantibodies in bullous pemphigoid (BP). Anti-BP180 autoantibodies exist in both the sera and cerebrospinal fluids of patients with dermatitis herpetiformis (DH). Since these isoforms of BP180 have the NC16A domain, they are expected to be targets of anti-BP180 autoantibodies in BP patients with dermatitis herpetiformis. In conclusion, this study identified two isoforms of BP180 in the brain that are different in size from BP180 in the skin. Since these isoforms of BP180 have the NC16A domain, they are expected to be targets of anti-BP180 autoantibodies in BP patients with dermatitis herpetiformis.

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 IL-23/T17/IL-17 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, IL22 in psoriatic lesions, whilst mast cells participate in psoriasis need to be addressed. We used an imiquimod-induced psoriasis-like dermatitis, the phenotype of which closely resembles the one observed in psoriasis patients. We found that wildtype mice treated with imiquimod had significantly increased and activated mast cells in their skin compared to control group, while the MrgprB2 knockout mice treated with imiquimod had decreased and less activated mast cells, with decreased IL-17, IL-22, IL-23 and TNF-a levels. In vitro studies showed that imiquimod could activate MRGPRX2 in human mast cell and MrgprB2 in mouse mast cell. These results suggested that mast cells participated in the development of psoriasis-like dermatitis via MrgrpB2 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.