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Follicular T helper and Breg cell balance in Severe Allergic Asthma before and after Omalizumab therapy

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Background: Severe Allergic Asthma (SAA) is based on type 2 (T2-high) immune responses to allergens promoting type 2 T helper (Th2) cell cytokine responses and production of IgE antibodies. Omalizumab was the first biological drug licensed for clinical use in the management of IgE-mediated SAA. Despite, emerging evidence supporting the prominent role of follicular T cells (Tfh), Breg and Treg subsets, in the development and progression of SAA, no data is available on the impact omalizumab therapy.

Methods: Ten SAA patients monitored at the Respiratory Diseases Unit of Siena University Hospital and 10 healthy sex- and age-matched controls were enrolled in the study. Clinical and functional parameters were collected at baseline (T0) and after 6 months of therapy (T6). Cellular population analysis were determined through multi-color flow cytometry.

Results: SAA patients showed higher percentages of Th17.1, Tfh and Tfh2 while CD24hiCD27hi Breg cell, Treg and Tfr percentages were significantly lower than controls. Higher percentages of Tfh2 in patients with nasal polyps than in those without and in controls were observed. At T6, significant decreases of Tfh and Tfh2 than T0 were observed. A slightly significant increase in Teff was reported at T6 with respect to T0. ΔIgE levels in serum were correlated with ΔCD19+CD24+CD27+ Breg cell percentages (r=-0.86, p=0.0022).

Conclusions: Our data explored the changes of Tfh cells, Tregs and Bregs in severe asthma. The restoration of immunological imbalance in SAA patients after omalizumab is surely intriguing and represents a glimpse of light in the comprehension of immunological effects of treatment.

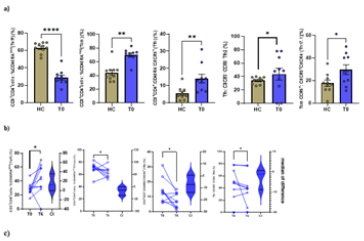

Fig.1 **a)** Gating strategy used to analyze markers of differentiation of T cell subsets. They are identified as CD4+CD45RA+ Cells (Teff) and CD4+CD45RA- T central memory cells (Tcm). Tcm were subsequently divided according to expression of CCR6. CD4+CD45RA-CCR6+ cells were classified as CXCR3+CCR4+ (Th17 double-positive), CXCR3-CCR4+ (Th17) and CXCR3+CCR4- (Th1-like Th17), whereas CCR6- cells were classified as CXCR3-CCR4+ (Th2) and CXCR3+CCR4- (Th1). CD4+CD45- cells were also used for the analysis of Tfh. In particular CD4+CD45RA-

Recent Publications

1. Bergantini, L., d'Alessandro, M., Cameli, P., Pianigiani, T., Fanetti, M., Sestini, P., & Bargagli, E. (2021). Follicular T Helper and Breg Cell Balance in Severe Allergic Asthma Before and After Omalizumab Therapy. Molecular diagnosis & therapy, 25(5), 593–605.

2. Bergantini, L., d'Alessandro, M., Cameli, P., Bianchi, F., Sestini, P., Bargagli, E., & Refini, R. M. (2020). Personalized Approach of Severe Eosinophilic Asthma Patients Treated with Mepolizumab and Benralizumab. International archives of allergy and immunology, 181(10), 746–753.

3. Yao, Y., Chen, C. L., Yu, D., & Liu, Z. (2021). Roles of follicular helper and regulatory T cells in allergic diseases and allergen immunotherapy. Allergy, 76(2), 456–470.

Biography

Laura Bergantini, born in Rome (27/07/1991), has her expertise in immunology of lung disorders with particular regards to severe asthma and immunology of lung rejection after transplantation. In these fields, she work in the evaluation of discriminatory pathways able to phenotyping different kinds of asthma and response to treatment. She started to work to these project during PhD and now, during post-doc fellowship. She worked between hospital and research center at the University of Siena. She also worked in Germany in MHH center of Hannover about lung transplant 3D cellular models. Nowadays She is author of more than 80 peer review articles and 15 of H index.

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