Trained immunity and tolerance during allergen-specific immunotherapy.

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Introduction

Allergen-specific immunotherapy (AIT) is based on allergen preparations' long-term administration, which mediates suppression of cellular and humoral effectors.

Aim

To analyze changes in the composition of systemic innate immune cell repertoire in the course of AIT.

Material and methods

Allergic patients received standard preseasonal subcutaneous AIT with allergoids to birch and/or grass pollens. We performed flow cytometric analysis of circulating ILC, NK cell, monocyte, and DC subsets at baseline (before

pollen season), three months (birch season), six months (grass seasons), and 12 months after the start of AIT in patients or in similar seasonal time-points in controls. We used classical analysis as well as the tSNE algorithm.

Results

We found a decrease of ILC2 and an increase of ILC1 after AIT. Besides, we observed dynamic changes in the composition of ILC caused by the induced expansion of CD127+CD25++ ILC1 cluster and development of CD127+CD25++c-Kit+ ILC3 clusters. Importantly, some of the effects in ILC subpopulations persisted after the 3rd year AIT. Next, we observed an increase in intermediate monocytes and reduced non-classical monocytes during the first year of AIT. Classical and intermediate monocytes presented significant heterogeneity in allergic patients, which was further reduced by AIT. Finally, an increase in pDCs and CD141+ mDCs was observed in allergic individuals, while CD1c+ mDCs were reduced in the first year of AIT.

Conclusions

Taking together, we showed that AIT induces changes in the composition and heterogeneity of systemic innate immune responses and brings them partly to the level observed in healthy individuals. Our study shows evidence of AIT-induced trained tolerance, opening a new window for monitoring AIT responses.

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