Alternative Activation of Macrophages During the Allergic Airway Inflammation Alters Antigen Presenting Capacities

C. Winkler¹,², H. Carstens¹, N. Moraw¹, M. Mueller¹, F. Schaumann¹, C. Faulenbach¹, J. M. Hohlfeld¹,²

¹Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany; ²Hannover Medical School, Hannover, Germany

Introduction

Macrophages (MΦ) undergo alternative activation (aa) in response to Th2 cytokines interleukin (IL)-4 or IL-13 and have been initially described in parasite infections. However, this cytokine microenvironment is also present during the allergic airway inflammation, but the impact of polarized macrophages in this context is poorly understood.

Aim: To characterize alveolar MΦ polarization during the acute airway inflammation with regard to their phenotype and function.

Methods

Macrophages and dendritic cells (DCs) were generated from human peripheral blood monocytes of atopic donors and aaMΦ were induced in the presence of IL-4. DCs and aaMΦ were stimulated with allergen and co-cultured with autologous CD4+ T-cells. Additionally human AMΦ were isolated from bronchoalveolar lavage (BAL) following segmental allergen provocation and co-cultured with autologous CD4+ T-cells in the presence or absence of allergen. T-cell proliferation was assessed by ³H-thymidine incorporation and alternative activation of human macrophages was further characterized by flow cytometric analysis of co-stimulatory surface markers (HLA-DR, CD86 and CD206) and expression of marker genes by rtPCR.

Results

Pulmonary MΦ are alternatively activated upon an acute allergic airway inflammation in mice, as determined by the induction of marker genes (Ym1, arginase and Fizz1). The polarization is persistent beyond the resolution phase of the inflammation, for more than 3 weeks.

Human monocyte derived MΦ from atopic patients upregulate Th2 promoting chemokines (CCL13, CCL18 and CCL23) on mRNA level in response to IL-4 (A) and also co-stimulatory molecules (CD86, HLA-DR) in contrast to naïve MΦ (B). Moreover, they induce specific T-cell proliferation (C), albeit to a considerable lower amount than DCs, generated in the same model (D).

Conclusion

The cytokine and chemokine milieu present during the acute allergic airway inflammation induces alternative activation of macrophages. These polarized macrophages are persistent and rather promote the ongoing Th2 immune response. Resolution might be decelerated due to release of chemotactic mediators and impaired phagocytic function and T-cell activation.

Contact

Email: carla.winkler@item-extern.fraunhofer.de

This work was funded by the Deutsche Forschungsgemeinschaft (SFB 587/B8).