Ruprecht-Karls-Universität Heidelberg

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Dissertations-Kurzfassung

Macrophages possess variable immune receptors

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Traditionally, antigen-specific immune recognition is thought to be solely restricted to lymphocytes. Recent evidence of T cell receptor (TCR) expression in neutrophil and eosinophil granulocytes, however, calls this concept into question.

This work demonstrates that subpopulations of human and murine monocytes and macrophages express TCRαβ and immunoglobulin (Ig) based variable (recombinatorial) immune receptors. These unexpected findings rely on combined evidence from (i) mRNA expression profiling, (ii) immunocytochemistry and immunoblot analyses, (iii) mass-spectrometry, (iv) genomic rearrangement assays and (v) in detail analyses of expressed immunoreceptor repertoires.

Consistent with VDJ rearrangement of the TCRαβ and the Ig heavy chain loci, I demonstrate individual-specific expression of diverse TCR and Ig repertoires in human and murine macrophages. *In vitro*, Th1/ Th2 cytokines and exposure to bacterial pathogens elicit expression of complex TCRαβ and Ig heavy chain repertoires in macrophages from healthy individuals indicating that normal macrophages have the capacity to respond to a variety of stimuli in a flexible fashion.
Moreover, specific engagement of the macrophage-TCRαβ stimulates secretion of the major monocyte chemoattractant MCP-1 and targeting of phagocytosis baits to the macrophage-TCRαβ facilitates the process of phagocytosis.

In vivo, analysis of freshly obtained carotid endarterectomy specimens from patients with severe carotid atherosclerosis consistently reveal the excessive presence of TCRαβ bearing macrophages that express highly restricted Vβ repertoires. Similar results are obtained for advanced coronary artery disease. These results provide proof of concept that the macrophage-TCαβ is implicated in chronic macrophage-driven inflammatory disease.

Collectively, this work demonstrates, for the first time, that macrophages, which are traditionally viewed as a pillar of innate (non-variable) immunity, possess variable immune receptors that may enable them to engage in flexible host defense.