Heterogeneous macrophage responses to dead cell clearance during development and inflammation

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Introduction: Macrophage responses to phagocytosis of dead cells has been extensively characterized during the inflammatory resolution. The elimination of dying cells is, nonetheless, an essential homeostatic mechanism that occurs through embryonic and postnatal development and in intact tissues in the adult. Tissue-resident macrophages are the main phagocytic cells that ensure this cell turnover in the absence of inflammation. However, the responses of tissue-resident macrophages to “homeostatic phagocytosis” still remain unknown. Moreover, whether tissue-resident macrophages modify their phenotype through mechanisms of cell plasticity upon “homeostatic phagocytosis” or whether subsets of them are programmed by ontogenic or environmental cues to phagocytize dead cells is still under debate.
Materials: In this study we analyzed the phenotypic features of different tissue-resident and inflammatory-recruited macrophages upon phagocytosis of dead cells. We also developed several in vitro strategies, using embryonic-derived macrophages and ER-HoxB8 immortalized myeloid progenitors, to characterize the diverse responses of macrophages to “homeostatic phagocytosis”.
Results: We show that ER-HoxB8-derived and embryonic-derived macrophages are good models to in vitro mimic the phagocytosis of apoptotic cells by tissue-resident macrophages. In addition, in vivo experiments using CX3CR1GFP reporter mice show that tissue-resident macrophages responses are influenced by the tissue microenvironment also in the presence of inflammatory stimuli.
Conclusions: Our results indicate that the phagocytosis of apoptotic cells in homeostasis is a mechanism of macrophage plasticity, highly influenced by the tissue microenvironment. In addition, our pioneer studies using different derived-macrophage approaches pave the way to develop novel techniques to study macrophage physiology in vitro.

Keywords : Macrophage; Innate Immunity; Phagocytosis; Heterogeneity; Plasticity
Authors :
References : , , ,

Authors

Noelia Alonso Gonzalez 1,

1. Institute of Immunology, University of Muenster, Muenster, GERMANY