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Metabolic regulation of macrophages in tissues

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Abstract

Macrophages are innate immune cells that provide host defense and have tissue-specific roles in the maintenance of organ homeostasis and integrity. In most cases macrophages keep us healthy but when their balanced response to damage or homeostatic signals is perturbed, they can drive chronic inflammatory responses and pathology. To fulfil their broad range of functions, macrophages adopt a plethora of activation states. Understanding their regulation and phenotypic heterogeneity is crucial because macrophages are critical in many diseases. Consequently, macrophages have emerged as attractive targets for therapy of diseases in which they determine disease outcome, such as cardiovascular disease, cancer and other Western killer diseases. Recent advances in the flourishing field of immunometabolism highlight that the metabolic profile of macrophages directly regulates their activation status and associated functions. In this short review, we summarize how recent research on the metabolic regulation of macrophages has vividly improved our understanding of macrophage activation. Most of our existing knowledge results from *in vitro* studies with murine bone marrow-derived macrophages which can't fully grasp the complexity of (micro)environmental control of macrophages in tissues. We therefore highlight current weaknesses and missing links in macrophage immunometabolism research and provide future directions to make the step from the well-controlled plastic *in vitro* cell culture systems to the complex *in vivo* tissue environment.

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