During the acute phase response, MK2 is differentially and cell type-dependently involved in the control of the acute phase response

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Abstract

Acute phase proteins (APPs) are essential components of the acute phase response (APR) triggered by pathogens, toxins, or other causes of inflammation. The primary goal of this response is to mitigate damage and initiate repair processes.

Regulation of APP production in hepatocytes, the major source of APP, is facilitated by cytokines released during the inflammatory process. MAPK-activated protein kinase 2 (MK2) plays a central role in regulating the production of several cytokines in myeloid cells; however, its role in the production of the APR remains unclear. Therefore, the role of MK2 in the APR was investigated in vivo using mice in which MK2 was specifically deleted in hepatocytes or myeloid cells after lipopolysaccharide injection.

Consistent with previous findings using constitutive MK2 deletion, myeloid cell-specific MK2 deletion supports the notion that MK2 promotes cytokine production. However, mice with hepatocyte-specific MK2 deletion suggest that in hepatocytes, MK2 contributes to the regulation of cytokine levels of several cytokines. Furthermore, the results suggest that the function of MK2 in regulating APP expression depends on the specific cell type and APP under investigation. For example, constitutive or myeloid cell-specific deletion of MK2 specifically leads to dysregulation of Hepcidin. Conversely, deletion of MK2 in hepatocytes predominantly leads to dysregulation of IL-1 receptor antagonist.

Taken together, these findings suggest that MK2 is not only involved in the control of the acute phase response at the cytokine level, but also has a direct influence on APP synthesis and the control of APR, depending on the cell type.