The role of nuclear factors as ?Find-Me?/alarmin signals and immunostimulation in defective efferocytosis and related disorders

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Efferocytosis as an apoptotic cell (AC) clearance mechanism facilitates the removal of dangerous and damaged cells, an important process in regulating normal homeostasis. Failure to correctly execute apoptosis and efferocytosis is associated with atherosclerosis, as well as chronic inflammatory and autoimmune disorders such as systemic lupus erythematosus (SLE). Effective and timely efferocytosis involves various molecules that act as ?Find-Me? signals or as alarmins to quickly allow identification by phagocytic cells. In recent years, most of these molecules have been investigated, but less attention has been paid to the nuclear molecules associated with efferocytosis of ACs and necrotic cells (NCs). These molecules have several functions including acting as alarmin signals for faster recognition of ACs, facilitating the cleanup of ACs and for maintaining self-tolerance. The same group of molecules is also implicated in several inflammatory and autoimmune diseases. Previous studies have shown that these molecules also serve as targets for pharmacological agents such as necrostatins, recombinant Fcnb, anti-histone, neutralizing antibodies, calbiochem, aminophylline, activated protein C, CD24IgG recombinant fission protein, and recombinant thrombomodulin. Thus, greater understanding of these molecules/pathways will enable developments in the treatment and/or prevention of various disorders, especially autoimmune diseases. Here, we review current knowledge about the mechanisms by which nucleic acids, histones, nucleosomes and monosodium urate microcrystals (MSU) can act as alarmins/?Find-Me? signals, how they might be stimulated in defective efferocytosis and their

function and importance as biomarkers for prognosis and treatment of atherosclerosis, inflammatory disorders and autoimmune diseases. © 2020 Elsevier B.V.

Auto-antigen

Chromatin

DAMPs

Free DNA

Immune tolerance

Macrophage clearances

Phagocytosis

Self-nucleic acid

advanced glycation end product receptor

CD24 antigen

complement component C1q

deoxyribonuclease

high mobility group B1 protein

histone

histone deacetylase

nuclear factor

nucleic acid

serum amyloid P

toll like receptor

urate

apoptosis

atherosclerosis

autoimmune disease

crystal

DNA RNA hybridization

efferocytosis

human

immunological tolerance

immunostimulation

nonhuman

nucleosome

phagocyte

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prognosis

protein function

Review

systemic lupus erythematosus