JLB JOURNAL OF LEUKOCYTE BIOLOGY

Inflammation, Extracellular Mediators, & Effector Molecules

Anti - C1q autoantibodies from patients with systemic lupus erythematosus induce C1q production by macrophages

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First published: 14 September 2016
https://doi.org/10.1189/jlb.3A1215-535R
Cited by:1

Abstract

Antibodies against C1q (anti - C1q) are frequently found in patients with systemic lupus erythematosus (SLE). The anti - C1q antibodies strongly correlate with the occurrence of lupus nephritis and low - circulating C1q levels. Previous studies have demonstrated that myeloid cells, i.e., dendritic cells and macrophages, are a major source of C1q. However, a direct effect of anti - C1q on C1q secretion by macrophages has not yet been established. In the present study, we investigated the C1q secretion profile of in vitro human monocyte - derived macrophages (HMDMs) obtained from healthy donors and from patients with SLE. The effect of SLE patient - derived anti - C1q bound to immobilized C1q (imC1q) and imC1q alone on HMDMs was investigated by C1q secretion levels, the expression of membrane - bound and intracellular C1q using flow cytometry and ImageStream^X technology, and testing the ability of secreted C1q to activate the classical pathway (CP) of the complement. Bound anti - C1q induced significantly greater C1q secretion levels as compared with imC1q alone or healthy donor IgG. The extent of C1q secretion by HMDMs correlated with IgG anti - C1q levels of patients with SLE but not of healthy controls. Furthermore, bound autoantibodies and imC1q induced continuous and de novo C1q synthesis as evident by the intracellular C1q content, which correlated with C1q secretion levels. Finally, secreted C1q was able to activate the CP, as reflected by C4b deposition. Interestingly, anti - C1q–dependent C1q secretion could also be observed in SLE patient - derived cells. In conclusion, our data indicate that imC1q - bound anti - C1q strongly stimulate the C1q production by HMDMs. Anti - C1q–induced C1q secretion might be an important immune - modulatory factor in SLE.

Citing Literature

Supporting Information