Anti-C1q Autoantibodies from Systemic Lupus Erythematosus Patients Induce a Proinflammatory Phenotype in Macrophages

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4408166
Author(s) Thanei, S.; Trendelenburg, M.
Author(s) at UniBasel Trendelenburg, Marten ;
Year 2016
Title Anti-C1q Autoantibodies from Systemic Lupus Erythematosus Patients Induce a Proinflammatory Phenotype in Macrophages
Journal J Immunol
Volume 196
Number 5
Pages / **Article-Number** 2063-74
Keywords Adult; Autoantibodies/*immunology; Autoantigens/immunology; Complement C1q/*immunology; Female; Humans; Inflammation/immunology; Lupus Erythematosus, Systemic/*immunology; Lupus Nephritis/immunology; Macrophages/*immunology; Male; Middle Aged; Phenotype
Mesh terms Adult; Autoantibodies, immunology; Autoantigens, immunology; Complement C1q, immunology; Female; Humans; Inflammation, immunology; Lupus Erythematosus, Systemic, immunology; Lupus Nephritis, immunology; Macrophages, immunology; Male; Middle Aged; Phenotype
Anti-C1q autoantibodies (anti-C1q) are frequently found in patients with systemic lupus erythematosus (SLE) and correlate with the occurrence of proliferative lupus nephritis. A previous study of anti-C1q in experimental lupus nephritis demonstrated an important role for FcgammaRs in the pathogenesis of lupus nephritis, suggesting a direct effect on phagocytes. Therefore, we developed an in vitro model to study the effect of SLE patient-derived anti-C1q bound to immobilized C1q (imC1q) on human monocyte-derived macrophages (HMDMs) obtained from healthy donors and SLE patients. HMDMs were investigated by analyzing the cell morphology, LPS-induced cytokine profile, surface marker expression, and phagocytosis rate of apoptotic Jurkat cells. Morphologically, bound anti-C1q induced cell aggregations of HMDMs compared with imC1q or IgG alone. In addition, anti-C1q reversed the effect of imC1q alone, shifting the LPS-induced cytokine release toward a proinflammatory response. FcgammaR-blocking experiments revealed that the secretion of proinflammatory cytokines was mediated via FcgammaRII. The anti-C1q-induced inflammatory cytokine profile was accompanied by a downregulation of CD163 and an upregulation of LPS-induced CD80, CD274, and MHC class II. Finally, HMDMs primed on bound anti-C1q versus imC1q alone displayed a significantly lower phagocytosis rate of early and late apoptotic cells accompanied by a reduced Mer tyrosine kinase expression. Interestingly, anti-C1q-dependent secretion of proinflammatory cytokines was similar in SLE patient-derived cells, with the exception that IL-10 was slightly increased. In conclusion, anti-C1q induced a proinflammatory phenotype in HMDMs reversing the effects of imC1q alone. This effect might exacerbate underlying pathogenic mechanisms in lupus nephritis.
Publisher AMER ASSOC IMMUNOLOGISTS
ISSN/ISBN 1550-6606 (Electronic) 0022-1767 (Linking)
URL https://www.ncbi.nlm.nih.gov/pubmed/26829984
edoc-URL https://edoc.unibas.ch/62490/
Full Text on edoc No;
Digital Object Identifier DOI 10.4049/jimmunol.1501659

PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/26829984
ISI-Number WOS:000372336300011
Document type (ISI) Journal Article