PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Cytokine dysregulation in macrophages of lupus-prone mice

ArticleInfo		
ArticleID	:	120
ArticleDOI	:	10.1186/ar-2001-66874
ArticleCitationID	:	66874
ArticleSequenceNumber	:	77
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2001–1–12 OnlineDate : 2001–1–12
ArticleCopyright	:	Biomed Central Ltd2001
ArticleGrants	:	
ArticleContext	:	130753311

Sylvie Fournel,[Aff1]

Aff1 CNRS, Strasbourg, France

Keywords

Apoptosis, cytokine, SLE

Context

In systemic lupus erythematosus (SLE), various autoantibodies recognize antigens that are modified and relocalized during apoptosis, suggesting that apoptotic cells may play a role in breakdown of tolerance and disease development. However, very little is known about intracellular signaling events induced by uptake of apoptotic cells. The authors have already reported that peritoneal and bone-marrow-derived macrophages from prediseased MRL/++ and MRL/lpr SLE-prone mice display a defect in lipopolysaccharide (LPS)-induced expression of several cytokines when compared with peritoneal macrophages derived from BALB/c mice. Therefore they investigated if these defects are present in other lupus-prone murine strains, and if apoptotic cells participate in these defects.

Significant findings

The defect in LPS-induced cytokine mRNA production was dependent on the presence of fetal bovine serum (FBS) and was not detectable if the MRL/++ mice peritoneal macrophages were cultured in FBS-free medium or in a medium complemented with delipidated FBS. This defect was found in 10 different lupus-prone strains. It was not observed in any of the 13 nonautoimmune strains tested. In the presence of FBS-treated apoptotic thymocytes, LPS treatment increased interleukin (IL)-1 mRNA production by macrophages derived from the BALB/c strain and, to a lesser extent, the MLR/++ strain. The defect in IL-1 mRNA production was not observed in the presence of FBS-treated viable thymocytes, suggesting that FBS-induced modifications of apoptotic cells were responsible for the defect. The authors conclude that FBS or apoptotic cells can reduce IL-1 expression in macrophages, and that this defect is a characteristic of lupus-prone mice.

Comments

Various mouse strains with different H-2 alleles and different genetic backgrounds can develop lupus-like disease. To date, a defect common to all strains has not been identified. The results provided in this paper identify a potential common defect. Nevertheless, some results in this paper are incomplete. First, it is mandatory to measure IL-1 protein levels, in addition to RNA levels. RNA levels, particularly for certain cytokines (eg TNFa), can be misleading since protein expression is regulated at the level of translation. Second, the authors failed to demonstrate that apoptotic cells could induce cytokine defects *in vivo* because this defect is obtained only in the presence of FBS. Regardless, these experiments provide valuable insights into the role played by apoptosis in SLE, warranting further investigation.

Methods

Lupus-prone mice, northern blotting, RNAse protection assays

References

1. Koh JS, Wang Z, Levine JS: Cytokine dysregulation induced by apoptotic cells is a shared characteristic of murine lupus. J Immunol . 2001, 165: 4190-4201.