

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

## Binding of anti-DNA antibodies on cell surface calreticulin

ArticleInfo		
ArticleID	:	104
ArticleDOI	:	10.1186/ar-2001-68034
ArticleCitationID	:	68034
ArticleSequenceNumber	:	61
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2001-6-11 Received : 2001-7-25 Accepted : 2001-7-25 OnlineDate : 2001-7-25
ArticleCopyright	:	Biomed Central Ltd2001
ArticleGrants	:	

Sylvie Fournel,<sup>Affl</sup>

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Affl CNRS, Strasbourg, France

## Keywords

Anti-DNA antibodies, calreticulin, SLE

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## Context

Systemic lupus erythematosus (SLE) is characterized by the presence of antibodies directed against nuclear components, including DNA. The pathogenicity of these anti-DNA antibodies in lupus disease is complex and involves several mechanisms, such as binding to extracellular antigens directly, immune complex formation and/or antibody penetration into living cells. The mechanism of anti-DNA antibody penetration seems to implicate binding to cell surface molecules. The authors investigated the mechanisms of antibody penetration and attempted to identify the cell surface molecules involved.

## Significant findings

Two anti-DNA antibodies (F14.6 and H9.3) bound to cultured cells and entered the cytoplasm. Antibody F14.6 entered the nucleus. A 50 kDa protein was shown to bind to F14.6 and H9.3 in an affinity matrix. The protein was identified as calreticulin and was present on the surface of a number of cell types. Finally, the authors demonstrated that four different anti-DNA antibodies can bind to calreticulin.

## Comments

Calreticulin is a cell surface protein newly implicated in anti-DNA antibody binding on cell surfaces. As is the case for other proteins implicated in antibody penetration of cells (e.g. heparan sulfate, collagen type IV, fibronectin, and myosin 1) the mechanisms by which calreticulin mediates this activity is not understood. The authors failed to demonstrate definitively that binding of calreticulin by

antibodies occurred at the cell surface (rather than in the endoplasmic reticulum following uptake), although soluble calreticulin inhibited subsequent antibody uptake in CHO cells. Surface calreticulin was not demonstrated in resting lymphocytes. Important controls were also not incorporated into the experimental design (e.g. evaluation of other monoclonal antibodies directed against non-nucleosomal components).

## Methods

ELISA, confocal microscopy, avidin-agarose affinity matrix, microsequencing

## Additional information

## References

1. Seddiki N, Nato F, Lafay P, Amoura Z, Piette J-C, Mazie J-C: Calreticulin, a potential cell surface receptor involved in cell penetration of anti-DNA antibodies. *J Immunol.* 2001, 166: 6423-6429.