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## Anti-DNA antibodies induce apoptosis

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## Keywords

Anti-DNA antibodies, apoptosis, SLE

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## Context

Anti-DNA antibodies (Abs) are important in the pathogenic development of systemic autoimmune diseases, in particular systemic lupus erythematosus (SLE). These Abs have also been described in some hematologic malignancies such as chronic lymphocytic leukemia (CLL). The major known pathogenic effect of anti-DNA Abs is the induction of an inflammatory response in kidneys due to their deposition. Cross reactivity of anti-DNA Abs with several membrane antigens may induce cellular dysfunction through either alterations in some cellular pathways or penetration of the Abs into living cells. DNA-hydrolyzing activity has also been observed in the presence of some anti-DNA Abs. More recently, the description that anti-DNA specific auto-Abs can trigger apoptosis in cultured mesangial and endothelial cells provides a possible clue to understanding anti-DNA Abs' deleterious effects. To gain insights into anti-DNA Ab-induced apoptosis, the authors studied the effect of anti-DNA Abs on various tumor cell lines.

## Significant findings

Anti-DNA Abs purified from SLE and CLL patient sera possessed DNA-hydrolyzing activity and showed cytotoxic activity on various tumor cell lines. The authors demonstrated that this cytotoxicity was due to the induction of apoptotic pathways. Correlation between the cytotoxicity and the penetration of Abs into cells was not clearly described. Anti-DNA Abs-induced apoptosis showed two distinct peaks during the course of incubation: one after 3-4 hours that is inhibited by YVAD-CHO (a caspase 1 inhibitor), and the second after 18-48 hours that is not inhibited by YVAD-CHO. The findings suggest two distinct apoptotic processes.

# Comments

In this paper, the description of anti-DNA Ab-induced apoptosis suggests another mechanism by which these autoantibodies may be pathogenic. However, several results presented in the paper are not entirely convincing. First, the study of anti-DNA Ab penetration into cells was not demonstrated by confocal microscopy, which permits localization of fluorescence in each part of the cell. Thus, one cannot conclude whether anti-DNA Abs induce apoptosis by acting directly on DNA or by binding to the cell membrane. Second, the CD95/CD95 ligand was not studied, and the study of this interaction may be important to the understanding of the apoptotic pathway used by anti-DNA Abs. In conclusion, these results are incomplete but raise important implications with regard to pathogenic autoantibodies.

## Methods

Immunofluorescence, measurements of apoptosis, DNA hydrolyzing activity

## Additional information

## References

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