

## Expression of p53 and Apoptosis in Discoid Lupus Erythematosus

**To the Editor:** We read the article by Zamolo et al (1), "Expression of p53 and Apoptosis in Discoid Lupus Erythematosus," with great enthusiasm. The authors clearly demonstrated p53 expression in the keratinocytes of discoid lupus erythematosus (DLE) lesions. Such a result hints at a role for the p53-induced apoptotic pathway in the pathogenesis of DLE.

Whether the presence of p53 positive keratinocytes results from an increase of the normal p53 protein or, alternatively, a non-functional mutant, is the question of critical importance. The authors' conclusions that p53 overexpression serves to activate apoptosis assumes that the form of p53 detected is functionally intact. However, mutated p53 would be unable to activate the apoptotic pathway.

Mutations of the p53 gene generally disrupt the function of the protein product, yet also stabilize it, such that it can then be detected by immunohistochemistry. Thus, the form of p53 expressed in neoplastic tissues, including skin lesions damaged by UVB radiation, is generally a non-functional, but stabilized mutant.

We suggest that the expression of p53 in DLE results from a mutation that both inactivates and stabilizes p53. Performing a series of polymerase chain reaction (PCR) experiments would reveal whether the form of p53 expression is mutant or wild-type. Logically, a non-functional mutant of p53 would not be able to activate apoptotic pathways. Thus, any discussion of how p53 trigger apoptosis should be preceded by a demonstration that the wild-type form of p53 is expressed in DLE.

Furthermore, we would like to suggest an alternative explanation for the expression of p53 in DLE. Several studies have proposed a role for polyoma viruses in the etiology of lupus. Specifically, the polyoma large T-antigen may bind to the chromatin of virally-infected cells, resulting in

the production of auto-antibodies against chromatin (2).

Furthermore, the large T-antigen binds to p53 (3). This interaction disrupts the ability of the cell to respond to DNA damage, but also stabilizes the wild-type p53 gene product (3-5). Thus, the binding of p53 by the large T-antigen may result in an accumulation of wild-type p53. Sequestration of wild-type p53 by T-antigen would render it inactive.

In summary, we speculate that the p53 expression reported by Zamolo et al (1) may result from polyoma virus infection in DLE. Certainly, the proposed role for polyoma viruses in the etiology of DLE merits further study.

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