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# LETTERS

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## NF-ATc1 levels are increased in murine and human lupus T cells: comment on the article by Kyttaris et al

*To the Editor:*

We read with interest the recent article by Kyttaris and colleagues (1), in which they reported their finding that lupus-prone MRL/*lpr* mice had increased levels of NF-ATc1 (also known as NF-AT2) in the cytoplasmic and nuclear fractions of freshly isolated lymphocytes, as compared with control lymphocytes from MRL/MpJ mice. They reported no increase in the expression of NF-ATc2 (also known as NF-AT1) in the lymphocytes of MRL/*lpr* mice and contrasted this finding to their observation of increased NF-ATc2 levels in the nucleus of T cells from patients with systemic lupus erythematosus (SLE) (2).

We previously reported markedly increased NF-ATc1 levels in CD4 T cells from pediatric patients with SLE as compared with age-, ethnicity-, and sex-matched controls (3). We also observed increased (although less markedly) levels of NF-ATc2 in lupus CD4 T cells compared with controls. This is consistent with the finding by Kyttaris et al in T cells from lupus-prone MRL/*lpr* mice.

NF-ATc2 is expressed constitutively in resting T cell cytoplasm (4,5), whereas NF-ATc1 expression is inducible (6) and up-regulated by NF-ATc2 (7). It has been suggested that NF-ATc1 is the NF-AT family member that is essential for effector T cell development and function (6). Thus, the findings by Kyttaris et al in a mouse model of lupus provide further support for our suggestion that increased NF-ATc1 levels in lupus CD4 T cells represent a more mature/effector T cell phenotype.

Jay Mehta, MD
*Albert Einstein College of Medicine*
*Bronx, NY*
Randy Q. Cron, MD, PhD
*University of Alabama at Birmingham*

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## Reply

*To the Editor:*

We agree with Dr. Mehta and colleagues that the up-regulation of NF-ATc1 in murine lupus lymphocytes signifies that lymphocytes in these mice display an activated phenotype. However, contrary to the findings by Mehta et al in pediatric patients with lupus (Mehta J, Genin A, Brunner M, Scalzi LV, Mishra N, Beukelman T, et al. Prolonged expression of CD154 on CD4 T cells from pediatric lupus patients correlates with increased CD154 transcription, increased nuclear factor of activated T cell activity, and glomerulonephritis. Arthritis Rheum 2010;62:2499–509), we did not observe a difference in the levels of NF-ATc1 protein in peripheral T cells between patients with SLE and control subjects. This discrepancy between the 2 studies could be attributable to small sample sizes, measurement of protein instead of messenger RNA in our study, different patient groups (adults versus children), or differences in disease activity or disease stage.

Similarly, we did not observe elevated levels of NF-ATc2 in resting T cells from patients with SLE (Kyttaris VC, Wang Y, Juang YT, Weinstein A, Tsokos GC. Increased levels of NF-ATc2 differentially regulate CD154 and IL-2 genes in T cells from patients with systemic lupus erythematosus. J Immunol 2007;178:1960–6). What we did observe was that dephosphorylation and nuclear migration of NF-ATc2 in T cells after activation were increased in patients with active SLE compared with control subjects or patients with quiescent disease. Therefore, we concluded that T cells from patients with active SLE display an overexcitable phenotype rather than an activated phenotype.

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Vasileios C. Kyttaris, MD
Zheng Zhang, PhD
Ourania Kampagianni, MD
George C. Tsokos, MD
*Beth Israel Deaconess Medical Center and Harvard Medical School*
*Boston, MA*

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## New evidence for a role of *MICA* in the pathogenesis of systemic lupus erythematosus: comment on the article by Yoshida et al

*To the Editor:*

We read with interest the recent article by Yoshida and colleagues (1), in which they reported that the frequencies of