Dr. Mahler replies

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*The Journal of Rheumatology* is a monthly international serial edited by Earl D. Silverman featuring research articles on clinical subjects from scientists working in rheumatology and related fields.
Dr. Mahler replies

To the Editor:

We thank Dr. Muro and colleagues for the thoughtful analysis of our study on anti-DFS70 (anti-dense fine speckled 70) antibodies in systemic autoimmune rheumatic diseases (SARD), disease controls, and apparently healthy individuals as measured by a novel chemiluminescent immunoassay (CIA). The data on patients with dermatomyositis (DM) presented by Muro, et al are interesting and complement our findings. Anti-DFS70 antibodies were found in 7/116 (6.4%) patients with DM. Although the prevalence in DM was not directly compared to a cohort of healthy individuals, based on previous data of 597 healthy hospital workers, Muro and colleagues concluded that anti-DFS70 antibodies are less prevalent in persons with DM compared to healthy individuals (6.4% vs 10.7%, respectively). It is important to point out that the 2 cohorts were tested with 2 different ELISA systems, the DM cohort with a commercial ELISA and the healthy individuals with a research assay. Of high interest, the prevalence of isolated anti-DFS70 antibodies (with no other SARD-related autoantibody) was even lower. In the DM cohort, 2/116 (1.7%) anti-DFS70-positive samples were negative for autoantibodies to Jo-1, PL-7, PL-12, EJ, KS, Mi-2, TIF1-γ, MDA5, and NXP-2. Of these, one (0.9%) was positive by immunoprecipitation, but the precipitating antibodies were not identifiable. These data are consistent with our finding on the low prevalence of isolated anti-DFS70 antibodies (with no other SARD-related autoantibody) and with previous studies. Anti-DFS70 antibodies have been reported in about 3% of patients with systemic lupus erythematosus (SLE)1, but usually accompanied by other SLE-associated antibodies such as anti-dsDNA, anti-SSA/Ro, or anti-Sm. In isolation, anti-DFS70 antibodies can be found in < 1% of patients with SLE2,3.

One significant variation between the data presented by Muro, et al and our data is the assay used to detect anti-DFS70 antibodies. In the study by Muro and colleagues, a commercial ELISA system was used. In contrast, our data were based on Quanta Flash® (DFS70, a novel CIA [research use only] that uses recombinant DFS70 coated onto paramagnetic beads and that is designed for the Bio-Flash® instrument (Biokit S.A.). The principles and protocols of the assay system have been described. Besides the technological difference, the assays also use different recombinant antigens.2,5 Although the 2 methods were compared in our previous study and the results were closely correlated, further studies using both the ELISA and the CIA are needed to analyze the prevalence of anti-DFS70 antibodies in various pathologies and geographic regions.

The followup data presented on anti-DFS70 antibodies in 4 patients with DM is of high interest and indicates that anti-DFS70 antibodies do not decrease during disease remission. In 3/4 patients, the anti-DFS70 antibody titers even increased during remission. In contrast, anti-MDA5 antibodies decreased in those patients. Muro, et al discussed the putative protective effect of anti-DFS70 antibodies that was noted in our study. This hypothesis is also in line with investigations suggesting that some auto-antibodies may serve as protective6 or indifferent or neutral effector7 autoantibodies. In patients producing anti-DFS70 antibodies, the presence and levels of the antibodies might be considered an expression and sign of immunological homeostasis. We agree that the findings are of high interest, and strongly emphasize that further longitudinal studies are needed to provide more insight. The effect of different treatments of patients with SARD on the titers of anti-DFS70 antibodies should be analyzed.

Anti-DFS70 antibodies have been historically associated with interstitial cystitis and atopic dermatitis, but they have also been described in various other diseases8. Although a distinctive clinical association remains unreported, anti-DFS70 antibodies have been proposed as a biomarker for the exclusion of SARD9,10. This suggestion is based mainly on the observation that anti-DFS antibodies are more prevalent in healthy individuals than in patients with SARD and that anti-DFS70-positive individuals did not develop SARD after clinical followup9.

The reasons underlying the observed relatively low prevalence in SARD are unclear, but may include the effects of therapeutic interventions (i.e., corticosteroids, immune suppression). Since antinuclear antibodies (ANA) and related autoantibodies are generally considered useful biomarkers for SARD, ANA testing on HEp-2 substrates outside a proper clinical framework may yield a sizable portion of ANA-positive individuals without consistent evidence of SARD,3,4 purportedly leading to inappropriate referrals to tertiary care specialists, as well as anxiety in patients and physicians, and perhaps inappropriate and potentially toxic therapies15. A clear understanding of the clinical relevance of the full spectrum of autoantibodies detected in a diagnostic laboratory becomes even more crucial because autoantibodies may precede the clinical onset of SARD by many years16.

The data presented by Muro and colleagues indicate that samples from patients suspected to have DM and with positive ANA should be tested for anti-DFS70 antibodies with other specific assay (i.e., ELISA or CIA) and the result should be included in the laboratory report. Isolated anti-DFS70 antibodies are rare in SARD, including DM2, and their presence may help to better classify patients with positive HEp-2 results by indirect immunofluorescence. The followup data might indicate that the monitoring of anti-DFS70 antibodies provides clinical value in the prediction of disease progression.

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