

Serine Proteases in Systemic Lupus Erythematosus: The Other Half of the Story

To the Editor:

The contribution by Trolldborg, *et al*¹ is a valuable addition to our understanding of disease, addressing half the question. Serine proteases do not function in isolation, but are also part of an enzyme-inhibitor interaction². Noting higher enzyme concentrations in their cross-sectional study of patients with systemic lupus erythematosus¹, direct correlation with nephritis and titers of anti-dsDNA, and inverse correlation with complement C3, the authors have demonstrated that serine protease levels appear to be markers of disease activity. It may also be worthwhile to assess whether their results reflect disease activity or alteration by the medications used in its treatment, as has been demonstrated for the major serine protease inhibitors, α -1-antitrypsin, α -2-macroglobulin, and antithrombin III^{2,3,4,5,6}. Their implication of a pathophysiologic involvement is an interesting speculation, especially if a moderating component is considered.

Serine protease inhibitor levels are also proportionate to disease activity⁷: We and others reported levels proportionate to α -1-antitrypsin directly, and α -2-macroglobulin and antithrombin III inversely^{7,8}. Serine protease inhibitors also have a significant immune modulation effect⁷, but it is unclear if this effect is related to the native molecule or to the complex it forms with serine proteases^{2,9,10}. In a relationship analysis of the levels, both components and their combination seem to be a fruitful area for future investigation.

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