

CORRESPONDENCE

SPECIFICITY OF ANTI-NEUTROPHIL CYTOPLASMIC AUTOANTIBODIES FOR PROTEINASE 3

To the Editor:

Niles et al<sup>1</sup> recently reported that patients with Wegener's granulomatosis have anti-neutrophil cytoplasmic autoantibodies (ANCA) that are specific for a 29-Kd neutrophil serine proteinase. They noted that ANCA with this specificity produce cytoplasmic indirect immunofluorescence microscopy staining of alcohol-fixed neutrophils (ie, are C-ANCA using the nomenclature adopted at the Second International ANCA Workshop held in The Netherlands, May 1989). We have shown that a second major category of ANCA (ie, P-ANCA) produces perinuclear staining of alcohol-fixed neutrophils, and most often have specificity for myeloperoxidase (MPO).<sup>2,3</sup>

Recently, Ludemann et al<sup>4</sup> reported data indicating that C-ANCA are specific for a serine proteinase that has biochemical properties like those of proteinase 3 (PR3), which is a neutrophil constituent that has been characterized by Kao et al.<sup>5</sup> Niles et al<sup>1</sup> also raised the possibility that their 29-Kd protein is identical with PR3, as did Goldschmeding et al.<sup>6</sup> We have used purified PR3 and monoclonal antibodies specific for PR3 (both produced by Dr John Hoidal) to show that the neutrophil serine proteinase with which C-ANCA react is in fact PR3.

As reported by Niles et al,<sup>1</sup> Goldschmeding et al,<sup>6</sup> and Ludemann et al,<sup>4</sup> using Western blot analysis, we observed the reactivity of some C-ANCA sera with an approximately 29-Kd fraction of neutrophil cytoplasm (29-Kd ANCA). MPO-specific P-ANCA (MPO-ANCA) did not react with the 29-Kd band, but did react with bands corresponding to the position of MPO in Western blot electrophoretograms.

We have previously used an enzyme-linked immunosorbent assay (ELISA) with MPO as antigen to demonstrate the specificity of

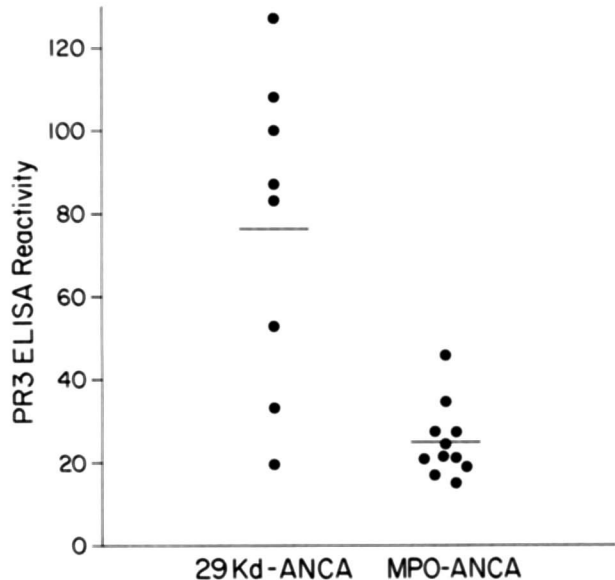


Fig 1. Graph comparing the PR3-reactivity of eight 29-Kd ANCA-positive sera to that of 11 MPO-ANCA-positive sera. The results are expressed as a percentage of a positive control serum. The horizontal lines are the group means.

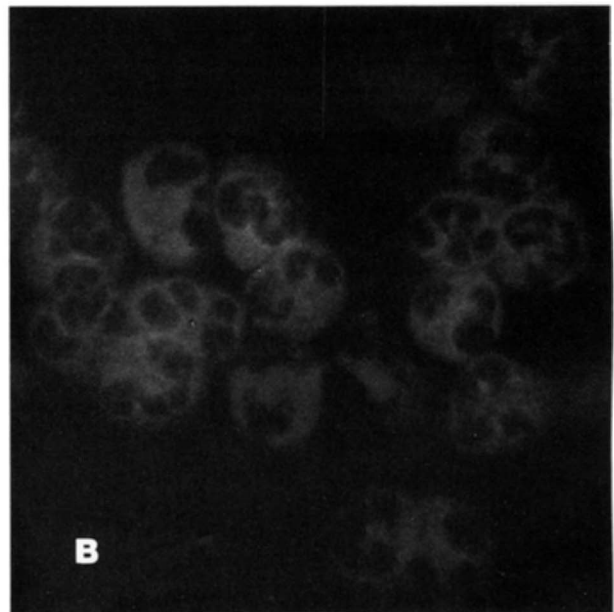
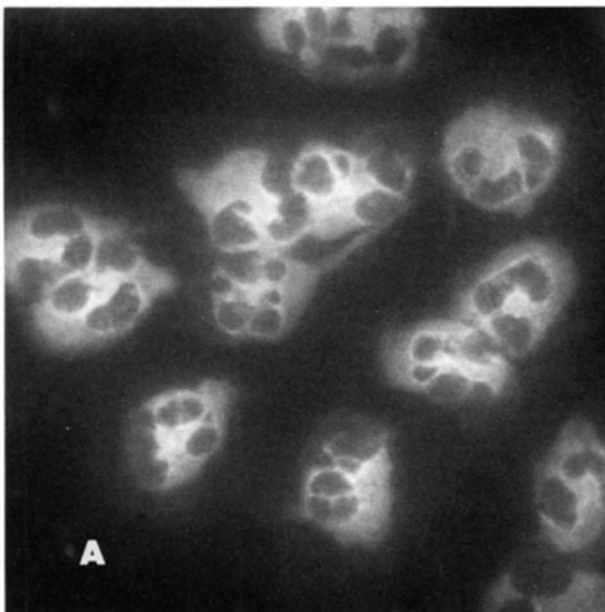


Fig 2. Blocking of 29-Kd ANCA staining with anti-PR3 but not with anti-MPO. (A) Alcohol-fixed neutrophils reacted sequentially with monoclonal anti-MPO, 1:800 29-Kd ANCA serum, and fluoresceinated anti-human IgG (20-second photographic exposure). (B) Alcohol-fixed neutrophils reacted sequentially with monoclonal anti-PR3, 1:800 29-Kd ANCA serum, and fluoresceinated anti-human IgG (60-second photographic exposure).





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## **Specificity of anti-neutrophil cytoplasmic autoantibodies for proteinase 3 [letter; comment]**

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