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SEQUENTIAL EPIOTOPE MAPPING OF THE MYELOPEROXIDASE ANTIGEN

Wynn DM and James JA. Oklahoma Medical Research Foundation and University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104.

A limited percentage of small-vessel vasculitis patients are shown to have a p-ANCA staining pattern revealing the presence of autoantibodies specific to proteins found in the azurophilic granules of neutrophils. Of these proteins, myeloperoxidase (MPO) seems to be the most commonly bound by p-ANCA, which suggests that these autoantibodies may in some way contribute to the propagation of vasculitic disease. Antibody responses to MPO have been found most frequently in patients with microscopic polyangiitis, crescentic glomerulonephritis, and in Churg-Strauss syndrome. In addition, anti-MPO antibodies have also been found in a wide variety of diseases ranging from rheumatoid arthritis to inflammatory bowel disease. Despite this, no specific causative role for these autoantibodies and vasculitis has yet been identified.

In this study, we seek to characterize the sequential anti-

genic determinants of MPO in patients with p-ANCA-positive vasculitis. We have screened p-ANCA-positive patient sera for reactivity with the maximally possible decapeptides of MPO on derivatized, polyethylene solid phase supports using a modified ELISA assay. Patient serum samples, shown to have p-ANCA by indirect immunofluorescence, were tested on INNOVA anti-MPO ELISA kits to identify patients with anti-MPO antibodies. Ten such patients were identified and were assayed on the decapeptide ELISA's to further establish what epitopes p-ANCA most commonly bound to on MPO. Six epitopes were found to be the most commonly bound by the ten patients at statistically relevant levels (four standard deviations above the normal mean). Epitope 1 (VLTPAQL-NVL) was bound by thirty percent of the patients, epitope 2 (EQDKYRTITG) by thirty percent of the patients, epitope 3 (YEDGFSLPYG) by thirty percent of the patients, epitope 4 (SARIPCFLAG) by thirty percent of the patients, epitope 5 (LPLVLGPTAM) by thirty percent of the patients, and epitope 6 (LPALNLSWR) by forty percent of the patients. This study shows that the anti-MPO response found in p-ANCA-positive patients bind most commonly at six sequential areas of the protein, a fact which may help evaluate the pathogenic potentials and potential etiological triggers of anti-MPO antibodies.