Autoantibodies against MPO and PR3

Neutrophil granulocytes or polymorphonuclear leukocytes (PMN) are phagocytotic blood cells representing an important component of the mammalian innate immune system. Upon opsonization and subsequent phagocytosis by PMN, microorganims are destroyed in the formed phagosome by a mechanism involving the production of reactive oxygen species and the secretion of proteolytic enzymes. Two important enzymes for this mechanism are myeloperoxidase (MPO) and proteinase 3 (PR3).

MPO is a heme containing enzyme composed of two identical subunits. Each subunit comprises a 64 kDa heavy and a 13 kDa light chain, which are formed by proteolytic processing of a common 80 kDa MPO precursor protein. MPO is stored in azurophilic granules, which fuse with and eventually release their content into the formed phagosome and the extracellular environment. MPO catalyzes the conversion of hydrogen peroxide to hypochlorous acid, a key step in the production of oxygen radicals leading to the oxidative degradation of microorganisms in the phagosomes. As an additional effect, hypochlorous acid produced in the extracellular environment is involved in the activation of proteases by inactivating protease inhibitors.

PR3 is a 29 kDa serine protease that is, like MPO, stored in azurophilic granules. In activated PMN, PR3 becomes secreted into both the phagosomes and the extracellular environment to destruct pathogens in the respective compartments.

Vasculitides are complex inflammatory autoimmune diseases of the blood vessels (vasculature) that appear to be associated with anti-neutrophil cytoplasmic antibodies (ANCA). Therefore, these diseases are also summarized as ANCA-associated vasculitides (AAV). In 1985, Woude *at al.* found an association between granulomatosis with polyangitis (GPA; formerly known as Wegener's granulomatosis) and a subgroup of ANCA, which give rise to a characteristic cytoplasmic pattern (cANCA) in indirect immunofluorescence (IIF) using ethanol fixed granulocytes. Follow-up work by Niles *et al.* (1989) identified PR3 to be the antigen in cANCA. In 1988, Falk and Jennette described a second subgroup of ANCA that appears to be associated with necrotizing and crescentic glomerulonephritis/renal vasculitis) and give rise to a perinuclear or atypic cytoplasmic pattern (pANCA) in IIF using ethanol fixed granulocytes. MPO was identified as the antigen in pANCA.

However, later findings identified autoantibodies against other proteins that also yield in cANCA or pANCA in IIF making its interpretation more ambiguous. One example is the bactericidal/permeability-increasing protein (BPI), which is another component of azurophilic granules and is preferentially detected in a cANCA pattern (Zhao *et al.* 1995). Therefore, the international consensus statement published by Savige *et al.* (1999, 2003) recommended additional enzyme-linked immunosorbent assays (ELISA) to identify autoantibodies against MPO and PR3.

Myeloperoxidase (MPO), proteinase 3 (PR3), and bactericidal/permeability-increasing protein (BPI) are purified from polymorphonuclear leukocytes of peripheral human blood.

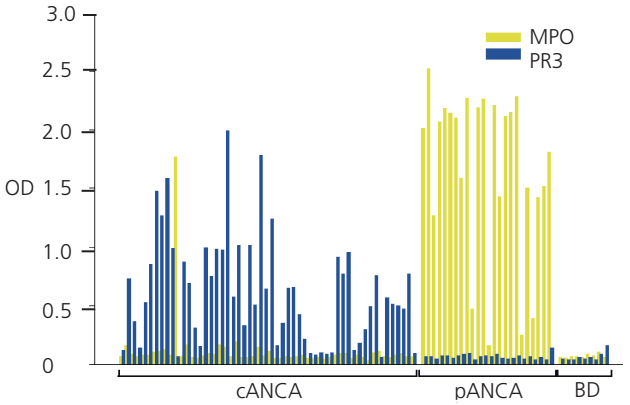

Figure: Analyses of patient sera with confirmed cANCA and pANCA pattern in IIF by ELISA for the presence of autoantibodies against PR3 and MPO, respectively. As a control, sera from blood donors (BD) were included. The MPO positive cANCA serum is a diagnostic anomaly found in Churg-Strauss-syndrome patients (R.-L. Humbel, personal communication).

Ordering Information		
18500 18501	Myeloperoxidase (MPO; non recombinant)	0.1 mg 1.0 mg
18600 18601	Proteinase 3 (PR3; non recombinant)	0.1 mg 1.0 mg
19200 19201	BPI (non recombinant)	0.1 mg 1.0 mg

References:
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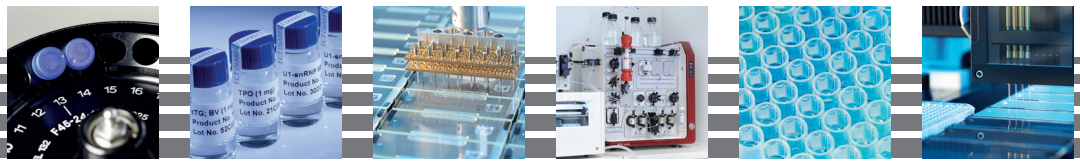

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