Antineutrophil cytoplasmic antibodies (ANCA) have become an established tool for the diagnosis of autoimmune systemic vasculitis and inflammatory disorders. In this clinical setting the major antigens are proteinase 3 and myeloperoxidase, and autoantibodies to these antigens from the azurophilic granules of neutrophils can best be tested by antigen-specific diagnostic devices like ELISA, line assays or in multiplex systems.

We have focused on establishing a manufacturing process for myeloperoxidase (MPO), which can be isolated from human peripheral blood polymorphonuclear cells.

MPO is the product of a single gene of 11 kb in size. Its initial translation product is an 80-kD protein, which following proteolytic removal of the 41 amino acid signal peptide, undergoes N-linked glycosylation with the incorporation of mannose-rich side-chains to generate an 89- to 90-kD enzymatically inactive apoproMPO. With the insertion of a heme, apoproMPO is converted to the enzymatically active proMPO. The removal of the N-terminal 125 amino acid proregion by proteolytic cleavage results in the production of a 72- to 75-kD protein, which undergoes a second proteolytic cleavage to generate the 467 amino acid heavy subunit (57 kD) and the 112 amino acid light subunit (12 kD) of MPO, which associate as a heavy-light protomer. Mature MPO has a molecular mass of approx. 150 kD and consists of a pair of heavy-light protomers whose heavy subunits are linked by a disulfide bond along their long axis. The mannose-rich carbohydrate and the two hemes are covalently bound to the heavy subunit.

MPO is involved in the oxygen-dependent microbicidal system of peripheral blood polymorphonuclear cells. It catalyzes the peroxidation of chloride into hypochlorite and its functional significance is twofold: (i) the generation of hypochlorite is important for the intracellular killing of phagocytosed microorganisms, and (ii) hypochlorite inactivates protease inhibitors and, as such, allows lytic enzymes released from neutrophils to degrade cells and other foreign material in the vicinity of neutrophils.

As the major target of p-ANCA immunofluorescence pattern MPO autoantibodies show high prevalences as well as clinical association with microscopic polyangiitis, idiopathic crescentic glomerulonephritis, Churg-Strauss syndrome, and classic panarteritis nodosa.

MPO autoantigen has been vigorously tested for assay performance parameters such as sensitivity and specificity. On the basis of convincing signal-to-noise ratio as well as superb lot-to-lot consistency the DIARECT antigen is available for your examination.