Neutrophil elastase (NE) is a serine protease released from the azurophilic granules in leukocytes (or neutrophils). Its primary role is to assist in the proteolytic breakdown and destruction of phagocytosed foreign pathogens as part of the normal immune response. However, secreted active NE has been implicated in contributing to a range of inflammatory disorders including chronic wounds, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF).

**NE-Tag Ultra**

NE Ultra is a novel biotinylated diphenyl phosphonate ProteaseTag® which targets NE, providing potent irreversible inhibition ($k_3/K_i = 4.08 (± 1.84) \times 10^6 \text{M}^{-1} \text{min}^{-1}$) similar to that provided by the currently available chloromethyl ketone inhibitor, MeOSuc-AAPV-CMK ($k_3/K_i = 6.68 (± 1.62) \times 10^6 \text{M}^{-1} \text{min}^{-1}$). NE Ultra binds covalently to the hydroxyl group of the catalytic serine residue, which is responsible for proteolytic activity in the active-site of NE. The use of NE Ultra rapidly results in complete and irreversible inhibition of Neutrophil Elastase. In contrast to MeOSuc-AAPV-CMK, NE Ultra displays an improved selectivity profile, increased stability in biological media and allows detection of NE in biological samples.

**Benefits of NE Ultra**

- Rapid inactivation of NE present in complex biological samples
- Irreversible inhibition means no reactivation of NE protease
- Low concentrations of NE Ultra are required to provide complete inhibition
- NE Ultra provides improved selectivity (Figure 1). Despite providing excellent inhibition of NE, MeOSuc-AAPV-CMK also completely abrogates the activity of the cysteine protease, Cathepsin B, showing its poor selectivity. In contrast, NE Ultra has no action against Cathepsin B remaining selective for NE
- NE Ultra also shows improved stability in the presence of 10% (v/v) serum (Figure 2), allowing further applications in biologically complex clinical samples
- The presence of a biotin reporter group allows detection of NE with the use of the avidin-biotin interaction
- Enables the detection of NE in both purified NE and in CF Sol samples, following electrophoretic. This indicates the successful application of NE Ultra as an activity-based probe (ABP) for the detection of NE in biological samples.