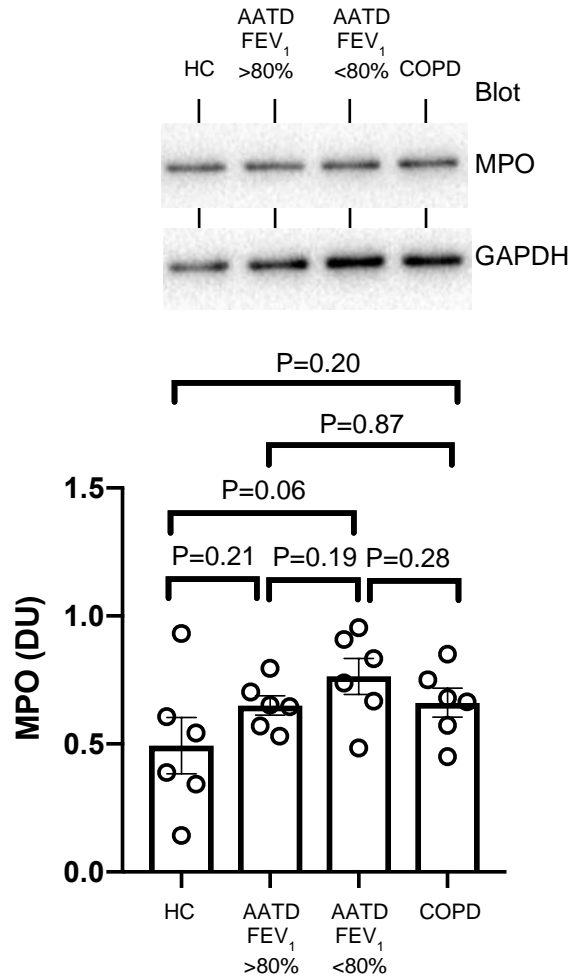


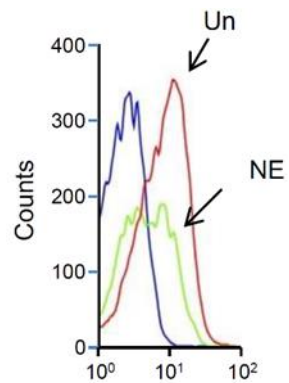
Supplementary Figure S1: AATD and healthy control neutrophils express equal primary granule content.

The aim of this experiment was to evaluate whether the observed increased level of primary granule exocytosis by AATD neutrophils was as a result of increased granule content within the AATD cell. However, by Western blot analysis of whole cell lysates, equal MPO expression in HC, AATD ($FEV_1 > 80\%$), AATD ($FEV_1 < 80\%$) and non-AATD COPD FEV_1 matched patients ($FEV_1 < 80\%$) was confirmed. This latter result eliminates disproportionate levels of granule content as the cause for increased degranulation by AATD cells (Supplementary figure S1).



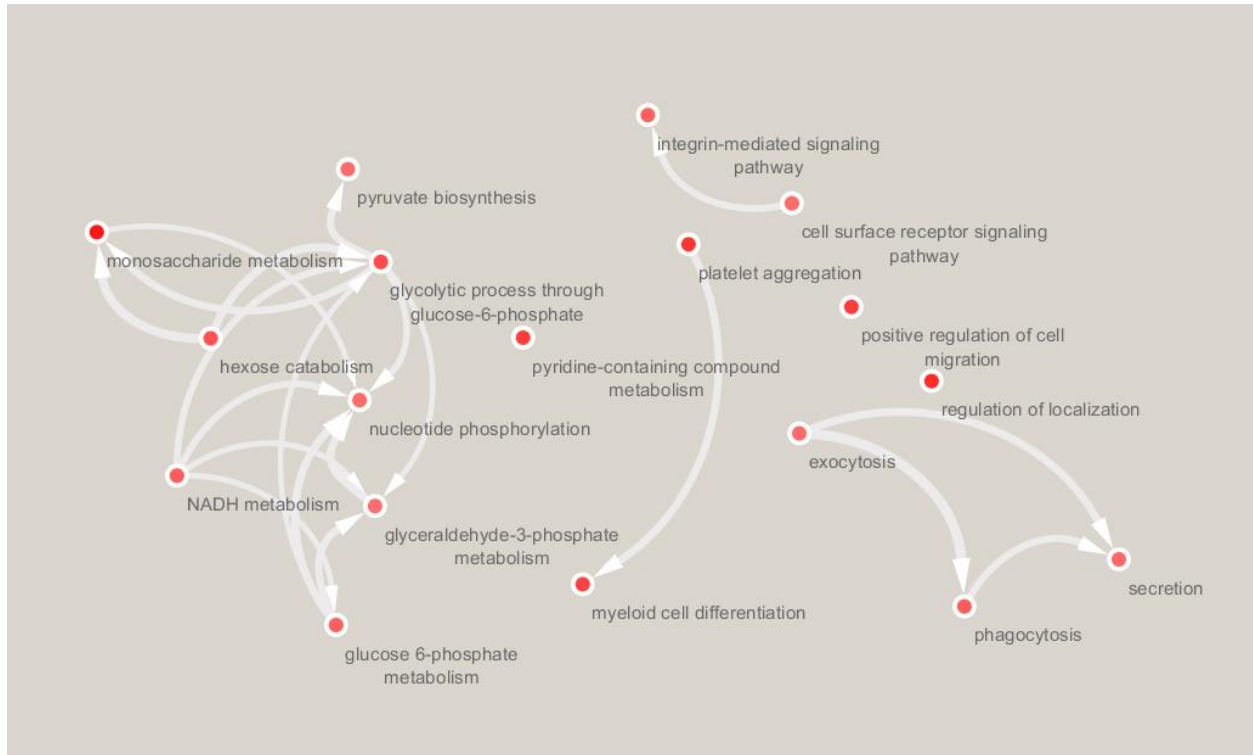
Supplementary figure S1 legend: AATD neutrophils illustrate equal expression of primary granule protein.

Neutrophils (1×10^7 cells per patient) were isolated from the peripheral blood of healthy controls (HC), AATD patients without obstruction (AATD FEV₁>80%), AATD patients with airways obstruction (AATD FEV₁ <80%) and patients with non-AATD COPD (COPD FEV₁<80%). Western blot and densitometric analysis of unstimulated neutrophil whole cell lysates demonstrated no difference in intracellular MPO levels between groups (all comparisons by unpaired t-test; n=6 subjects per group). Western blot of the same samples for GAPDH demonstrated equal protein loading indicative of equal cell numbers used per reaction.



Supplementary Figure S2: NE cleavage of PAR2

Flow cytometry analysis using a FITC-labelled anti-PAR2-antibody demonstrates reduced levels of plasma membrane PAR2 post NE exposure (100nM, 15min) compared to untreated cells (Un). Representative image from n=3 biological repeats. Isotype control presented in blue.



Supplementary Figure S3: The neutrophil PM proteome is modified by AAT augmentation therapy in vivo. Selected GO BP enrichment clusters for the dataset of proteins differentially expressed between day 0 and day 2 of AAT augmentation therapy in AATD individuals. GO analysis performed by GORILLA on DE proteins (fold change >1.5, $p \leq 0.05$) and redundant GO terms removed by REVIGO. Related GO terms are linked by lines and grouped according to similarity.