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Title: Quantitative proteomics on nasal lavage fluid from asthma phenotypes

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Body: Asthma is a complex disease composed of many phenotypes with different underlying mechanisms. In line with the united airways concept, identification of proteins in nasal lavage fluid (NLF) could reflect the proteome of the lung. This study aimed to explore differences in mechanisms between asthma phenotypes using quantitative proteomics on NLF. NLF was collected from 3 groups of asthmatics; aspirin intolerant asthma (AIA, n=9), multi-symptom asthma (MSA, n=9), and MSA with chronic rhinosinusitis (CRS, n=9) and a group of healthy subjects (n=9). Proteins extracted from NLF were quantified using tandem mass tag technology and a nano-LC MS/MS instrument. Pathway analysis was used to identify global proteome differences. In all, 474 proteins could be identified and quantified in at least 3 samples per group. In total, 93 proteins in AIA, 113 proteins in CRS and 75 proteins in MSA met the fold change cut off of 1.3 compared to healthy. Of these, 21 proteins were found in all asthma phenotypes, which could reflect common processes in asthma, while 33 proteins were unique to AIA, 56 to CRS and 26 to MSA. Analysis of the global proteomes revealed mechanistic differences between the phenotypes. CRS was more associated with epithelial associated conditions than AIA and MSA. AIA was more associated with carbohydrate metabolism than CRS and MSA, which had more proteins associated with cellular movement and signalling. Evidence of inflammatory processes can be found in different asthma phenotypes compared to healthy individuals. A comparison between asthma phenotypes revealed mechanistic differences. Quantitative proteomic analysis of NLF was thus capable of detecting relevant disease mechanisms in different asthma phenotypes.