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Title: High-throughput analysis of induced sputum from the U-BIOPRED study using novel proteomic and data mining approaches

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Body: RATIONALE: The U-BIOPRED consortium is an EU-wide collective of academics, pharmaceutical companies and other organisations working collaboratively to better understand severe asthma. The U-BIOPRED proteomics platform has been developed to discover novel protein biomarkers to enable disease stratification, and to enhance our molecular understanding of this disease. Using innovative sample processing, mass spectrometry and data-mining methodologies, we report here the most comprehensive quantitative proteomic analysis of human induced sputum to date. METHODS: Proteins from induced sputum were precipitated and dissolved in 50% trifluoroethanol, processed to peptides and analysed by LC-IMS-MS^e. An in-house pipeline was developed to enable the pre-processing and classification of LC-MS^e data and extract features independent of database searching. RESULTS: Analysis of samples from 119 U-BIOPRED volunteers allowed the absolute quantitation of >1500 proteins. Gene-set and pathway analyses have highlighted specific pathways enriched within the 'sputome'. Furthermore, we have developed an algorithm based on a robust bioinformatic approach for data extraction, alignment and normalisation of high-dimensional LC-MS^e datasets. These data-mining approaches have enabled us to identify spectral signatures that would have been missed using standard biased data processing and searching approaches. CONCLUSIONS: The application of novel sample analysis and data-mining methodologies, has allowed the most comprehensive proteomic analysis of human induced sputum to date, providing new insight into the profile of induced sputum in severe asthma.