Instability of sputum molecular phenotypes in U-BIOPRED severe asthma

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To the Editor:

The Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes (U-BIOPRED) project has described phenotypic differences of severe asthma using a systems biology approach. We obtained three molecular phenotypes termed transcription-associated clusters (TACs) using hierarchical clustering of differentially expressed transcripts between T2-high and T2-low [1]. TAC1 was characterised by receptors IL33R, CCR3 and TSLPR, with the highest enrichment of gene signatures for IL-13/type-2 (T2) inflammation with sputum eosinophilia; TAC2 by inflammasome-associated genes, interferon-α (IFN-α) and tumour necrosis factor-α (TNF-α)-associated genes with sputum neutrophilia; and TAC3 by metabolic and mitochondrial function genes with pauci-granulocytic inflammation. Given that sputum eosinophilia may vary with time in many asthmatic subjects [2, 3], we hypothesised that TAC status may also change with time.