SPUTUM AS A DIAGNOSTIC TOOL FOR THE MEASUREMENT OF LUNG INFLAMMATION IN ASTHMA

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BACKGROUND

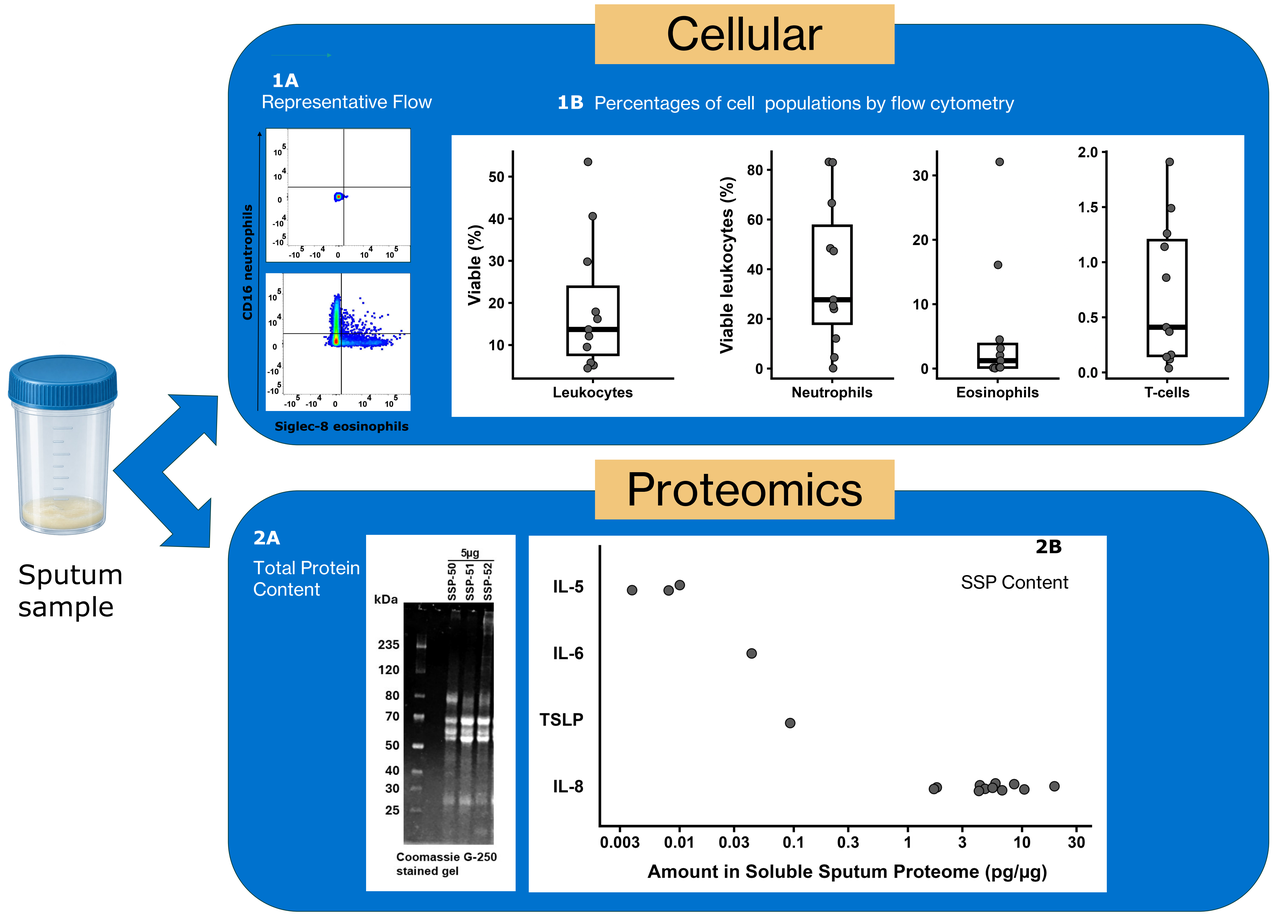
- Lung inflammation in asthma and COPD is heterogeneous, and blood biomarkers may not fully capture inflammatory status of a patient
- We developed a sputum-based test combining inflammatory cell phenotyping and cytokine measurements to characterize lung inflammation
- Cellular and proteomic targets of biologic drugs are measured

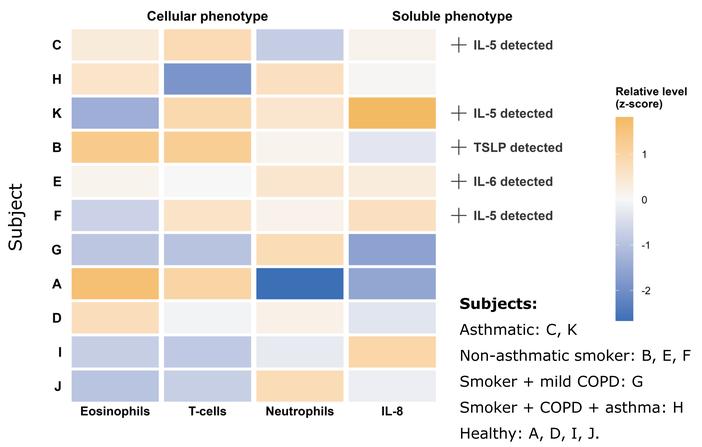
METHODS

- Sputum collected at home and shipped cold
- Processing to a cell suspension
- Cells analyzed by flow cytometry
- Proteomic analysis by ELISA
- Combined data analyzed using machine learning

CLINICAL IMPLICATION

- Sputum biomarkers of lung inflammation can suggest the treatment modality
- Cellular and soluble biologic drug receptors might inform treatment
- Sputum biomarkers of lung inflammation can suggest the optimal treatment modality
- Machine learning could improve understanding of disease phenotypes enabling more accurate diagnosis, prognosis, and personalized treatment strategies.





Cellular Legend
1A. Representative flow cytometry dot plots of neutrophil and eosinophil populations. **1B.** Box plots illustrating leukocytes (CD45+) as a percentage of all viable cells; neutrophils, eosinophils and T-cells as a percentage of all leukocytes for 11 subjects.

Proteomics Legend
2A. Gel showing total protein content in the soluble sputum proteome. **2B.** Cytokines (pg/µg) in the soluble sputum proteome of 11 subject sputum samples.

Inflammatory Profiles Legend
3A. Heat map illustrating normalized cellular and cytokine data. Select cytokines detected in samples shown by sample row.

Select drug related biomarkers detected in sputum

(TSLP, IL-4, IL-5, IL-13, IL-33, CD124, CRLF2)

TSLP/CRLF2

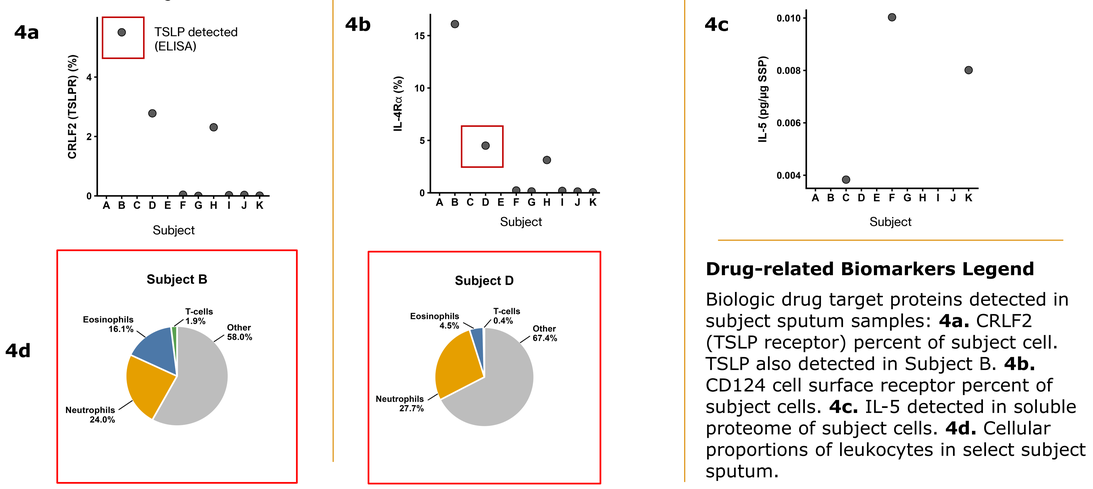
- Alarmin secreted by epithelium
- Cell surface receptor CRLF2
- Drug targets for tezepelumab and verkitug

IL-4R (CD124)

- Receptor subunit in IL-4R and IL-13R cell surface receptor
- Drug target for dupilumab

IL-5

- Cytokine in Th2 asthma and some COPD.
- Drug target for mepolizumab



Drug-related Biomarkers Legend

Biologic drug target proteins detected in subject sputum samples: **4a.** CRLF2 (TSLP receptor) percent of subject cell. TSLP also detected in Subject B. **4b.** CD124 cell surface receptor percent of subject cells. **4c.** IL-5 detected in soluble proteome of subject cells. **4d.** Cellular proportions of leukocytes in select subject sputum.

CONCLUSIONS

- These results suggest that longitudinal monitoring of lung inflammation may inform specific treatment targets or alert to emerging problems
- Commercial test is in development
- The test measures both cellular and proteomic features of lung inflammation using flow cytometry and ELISA to analyze a sputum sample collected by patients at home
- Select biologic drug targets were measured

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