Repeat Measurements of Complement proteins C3a and C5a in COPD patients

COPD - mechanism, Biomakers, Inflammation

T. Southworth1*, H. Richardson2, C. Pattwell3, L. Tan4, P. Deschatelets5, D. El Mehdi5, C. Vega5, C. Francois5, F. Gross5, D. Singh1

1 The University of Manchester, Division of Infection, Immunity and Respiratory Medicine, School of Biological Sciences, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, The University of Manchester and University Hospital of South Manchester NHS Foundation Trust - Manchester (United Kingdom),

2 ParamStat Ltd - Sandwich (United Kingdom), The Medicines Evaluation Unit - Manchester (United Kingdom),

3 Lisa Tan Pharma Consulting - Cambridge (United Kingdom),

4 Apellis Pharmaceuticals Inc - Crestwood, KY (USA)

Background: Complement proteins C3a and C5a are chemoattractants for neutrophils and macrophages, and may increase these cells in COPD lungs. Previous studies have shown that C5a is higher in COPD patients compared to controls and negatively correlates with FEV1, while C5a and C3a are both increased during exacerbations, making C3a and C5a potential therapeutic targets for COPD.

Aim: To compare C3a and C5a levels in blood and sputum samples from COPD patients and healthy subjects and to assess reproducibility in repeat samples for potential use as clinical trial biomarkers.

Methods: Plasma (22 COPD; 11 healthy) and sputum supernatants (13 COPD; 9 healthy) were assessed for levels of C3a and C5a. Eleven COPD
patients donated two additional plasma and sputum samples, which were used for repeat C3a and C5a measurements. Comparisons between COPD and healthy samples by Mann-Whitney or T-test. Bland-Altman and Intraclass correlation coefficient used to assess repeatability.

Results: Plasma C3a levels were significantly lower in COPD patients compared to healthy subjects; there was no difference in the plasma C5a levels, or sputum C3a and C5a. Sputum C3a and C5a values correlated well between the visits, with sputum C3a showing better repeatability. Plasma C3a levels were increased in repeat samples for all patients, while C5a levels were lower in 9 out of 11 patients.

Conclusions: Unlike previous studies, we were unable to show an increase in sputum C5a in COPD patients compared to healthy subjects. However, we have shown that sputum levels of C3a, and possibly C5a, remain consistent, suggesting that they could be useful clinical trial biomarkers for therapies targeting the complement system in COPD patients.