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Title: Induced sputum cytokines and chemokines and mechanistic pathways in adult asthma phenotypes

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**Body:** Background: Evaluation of induced sputum can be used to predict asthma severity or exacerbation Research hypothesis: Relate asthma visible properties to sputum cytokines to define new mechanisms for asthma. Methods: The Local Ethics Committee approved the study. Asthma phenotypes evaluated: early and late onset, premenstrual, atopic, exercise-induced, aspirin-sensitive, remitting/relapsing, near-fatal, brittle asthma, frequent exacerbator, smokers, comorbidities (obesity, chronic rhinosinusitis-CRS, nasal polyps, food allergy), corticosteroids (CS) responsiveness and lung function (fixed airway obstruction and fast FEV1 decline). Both sputum and serum were sampled outside an asthma exacerbation. Sputum induction and processing was performed according to the ERS recommendations. Sputum and serum cytokines were measured with the 27 Plex Human Cytokine Group I Bioplex (Biorad). Correlations were analyzed with SPSS 21 (One Way Anova). Results: 24 adult asthma patients, mean age 47.75±15.57 years old, 79% of them are females were enrolled. Many of the sputum and serum cytokine levels correlated, except for IL-9, IL-10 and IL-12. Correlations for sputum cytokines were IL-17, eotaxin and RANTES and smokers with asthma; IL-13 and MCP-1 and atopic asthma; IL-5 and IL-10 and asthma associated with CRS, IL-6 and fast FEV1 decline, IL-10 and CS responsive asthma, IL-2 and brittle asthma, VEGF and near-fatal asthma and IP-10 and frequent exacerbators. Conclusion: Several new pathogenetic mechanisms in asthma can be pinpointed by correlating the expression of cytokines in sputum and serum with asthma phenotypes.