

## Publication

### Relation between circulating CC16 concentrations, lung function, and development of chronic obstructive pulmonary disease across the lifespan : a prospective study

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Low concentrations of the anti-inflammatory protein CC16 (approved symbol SCGB1A1) in serum have been associated with accelerated decline in forced expiratory volume in 1 s (FEV1) in patients with chronic obstructive pulmonary disease (COPD). We investigated whether low circulating CC16 concentrations precede lung function deficits and incidence of COPD in the general population.; We assessed longitudinal data on CC16 concentrations in serum and associations with decline in FEV1 and incidence of airflow limitation for adults who were free from COPD at baseline in the population-based Tucson Epidemiological Study of Airway Obstructive Disease ([TESAOD] n=960, mean follow-up 14 years), European Community Respiratory Health Survey ([ECRHS-Sp] n=514, 11 years), and Swiss Cohort Study on Air Pollution and Lung Diseases in Adults ([SAPALDIA] n=167, 8 years) studies. Additionally, we measured circulating CC16 concentrations in samples from children aged 4-6 years in the Tucson Children's Respiratory Study (n=427), UK Manchester Asthma and Allergy Study (n=481), and the Swedish Barn/children, Allergy, Milieu, Stockholm, Epidemiological survey (n=231) birth cohorts to assess whether low CC16 concentrations in childhood were predictive for subsequent lung function.; After adjustment for sex, age, height, smoking status and intensity, pack-years, asthma, and FEV1 at baseline, we found an inverse association between CC16 concentration and decline in FEV1 in adults in TESAOD (4.4 mL/year additional FEV1 decline for each SD decrease in baseline CC16 concentration, p=0.0014) and ECRHS-Sp (2.4 mL/year, p=0.023); the effect in SAPALDIA was marginal (4.5 mL/year, p=0.052). Low CC16 concentration at baseline was also associated with increased risk of incident stage 2 airflow limitation (ratio of FEV1 to forced expiratory volume [FEV1/FVC] less than 70% plus FEV1 % predicted less than 80%) in TESAOD and ECRHS-Sp. In children, the lowest tertile of CC16 concentrations was associated with a subsequent FEV1 deficit of 68 mL up to age 16 years (p=0.0001), which was confirmed in children who had never smoked by age 16 years (-71 mL, p<0.0001).; Low concentrations of CC16 in serum are associated with reduced lung function in childhood, accelerated lung function decline in adulthood, and development of moderate airflow limitation in the general adult population.; National Heart, Lung, and Blood Institute and European Union Seventh Framework Programme.

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