Title	***6. Measurement of inflammatory markers in exhaled breath condensate in cystic fibrosis: feasibility and variability***
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Study design	Prospective study on feasibility and variability of inflammatory biomarkers in exhaled breath condensate (EBC).
Grant by	Region of Tuscany (Grant for Cystic Fibrosis)(1 year; E. 16.000)
Background and aims	There is increasing interest in the investigation of pulmonary inflammation by noninvasive means as measurement of inflammatory markers in exhaled breath condensate (EBC). Chronic neutrophilic airway inflammation is an important feature of cystic fibrosis (CF) lung disease. Interleukin-8 (IL-8), interleukin-6 (IL-6) and leukotriene B4 (LTB4), nitrotyrosine (3NO2-Tyr), reduced glutathione and abnormally low pH levels have been associated to airway inflammation in CF. Monitoring of inflammatory biomarkers may be important in patients with CF to measure disease activity and progression and to measure the short-term effects of interventions, as antibiotic treatment for pulmonary exacerbations and new antinflammatory drugs. The main purpose of our study is to assess the feasibility of EBC collection in subjects of different age and the intra-subject and inter-subject variability of EBC inflammatory biomarkers. We are also interested in assessing the levels of EBC biomarkers before and after the antibiotic treatment for a pulmonary exacerbation in patients with CF.
Inclusion criteria	Patients with CF, aged from 6 to 40 years, able to perform spirometry and healthy subjects of similar age.
Exclusion criteria	Patients with CF and: a) airway infection by Burkholderia cepacia complex; b) severe liver, kidney, central nervous system disease; c) respiratory failure with need of oxygen therapy.
Methods	Spirometry values, body mass index (BMI), presence of chronic airway infection by Pseudomonas aeruginosa and genotype will be recorded in patients with CF. EBC will be collected using a commercial device (EcoScreen, Jaeger, Germany). Subjects will breath tidally for 10-15 minutes: minute ventilation will be measured by a pneumotachograph and EBC collection will be stopped when a volume of 100 L will be expired. The pH will be measured immediately with a benchtop pH meter. IL-6, IL-8, LTB4, 3NO2-Tyr, glutathione, urea, K^+, Na^+ and Cl^- will be measured by mass spectrometry (HPLC – MS/ms Api 4000, Applied Biosystem). To assess the within-subject variability a second EBC sample will be collected 45-60 minutes and 24 hours after the first sample in healthy subjects and stable subjects with CF. EBC samples will be collected in CF patients at the start and end of an antibiotic treatment of a pulmonary exacerbation.
Expected results and anticipated output	To validate a protocol for the collection of EBC and the measurement of inflammatory biomarkers, which will be used for research purposes.
Start of recruitment	June 2008
End of experimental plan	December 2010
Pubblication on medical Journal	June 2011