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CBP AND PPARγ mRNAs AFTER CORTICOSTEROID OR FORMOTEROL THERAPY OF COPD PATIENTS

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Inhaled corticosteroids (ICS), which effectively switch off pro-inflammatory genes in asthma are ineffective in chronic obstructive pulmonary disease (COPD). We have previously reported increased cAMP response element binding protein (CREB) and activated (CREB-P) protein levels in cells isolated from induced sputum, during COPD therapy with formoterol/inhaled corticosteroid (F/ICS). Thus, our data pointed to the possible role of increased CREB–associated signaling in poor response to the therapy. In this study we assessed how similar therapy affects expression of two CREB-related nuclear signaling molecules, particularly CREB binding protein (CBP) which interacts with integrated upstream nuclear signaling (at pre-chromatin level) and peroxisome proliferator-activated receptor gamma (PPARγ) which negatively interfere with proinflammatory nuclear factor kappaB (NF-κB) for CBP binding. Twenty five patients with stable disease were subjected to sputum induction before and after F or Budesonide (ICS) b.i.d. 4 weeks therapy. Sputum samples were solubilized, intact cells were extracted using millipore filtration and centrifugation and total cellular RNA was extracted from isolated cells using qPCR-grade RNA isolation kit (Superarray, USA). First strand cDNA samples were prepared and amplified by thermal cycling on ABI 7900 Cycler with SYBR-green detection and appropriate controls (Superarray, USA). In patients treated with F, CBP mRNA was not altered due to the drug therapy, but PPARγ mRNA levels were increased by more than 2 fold ($P<0.01$). ICS therapy resulted in significant decrease of CBP mRNA (almost 70% decrease; $P<0.01$) and increased by more than 3 fold ($P<0.01$) mRNA of PPARγ. Since PPARγ is negatively correlated with proinflammatory signaling and altered CBP expression may result in its reduced recruitment to the transcriptional initiation complex on the promoter region of various genes, elevated levels of PPARγ mRNA and lowered CBP mRNA after therapy may reflect their involvement in nuclear anti-inflammatory signaling.