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Title: Elevated circulating CTLA-4 level in patients with COPD is related to systemic inflammation and disease severity

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Body: Objective: Cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) involved in down-regulation of T-cell response, T-cell homeostasis, which plays a role in COPD. The present study aimed to detect the serum level of CTLA-4 in COPD and its relation with systemic inflammation and lung function. Method: 42 COPD patients and 30 controls were recruited, serum was separated immediately and stored at -80° until analysis. Serum CTLA-4 and C-reactive protein (CRP) were analyzed by enzyme-linked immunosorbent assay. Results: The clinical characteristics and levels of CTLA-4, CRP of included subjects were listed in Table 1.

Characteristics of included subjects

	COPD (n=42)	Control (n=30)	P value
Age (year)	62±10	58±11	0.160
Sex (m/f)	28/14	20/10	0.626
Smoking (pack-years)	14.17±17.36	12.02±20.06	0.692
FEV1 (L)	1.98±0.72	2.67±0.63	0.000
FVC (L)	3.28±1.08	3.21±0.79	0.746
FEV1/FVC%	59.41±8.48	83.53±5.04	0.000
FEV1%predicted	85.71±23.06	115.80±16.27	0.000
CTLA-4 (pg/ml)	35.29±19.60	24.94±15.09	0.018
CRP (ng/ml)	19.06±5.72	15.46±5.99	0.012

The mean levels of serum CTLA-4 were significantly elevated in COPD patients when compared to controls (35.29±19.60 vs. 24.94±15.09 pg/ml, p < 0.05). Levels of CRP, were also increased in COPD patients

(19.06 ± 5.72 vs. 15.46 ± 5.99 ng/ml, $p < 0.05$). Regression correlation analysis showed serum CTLA-4 levels were inversely correlated with forced expiratory volume at 1 second (FEV1% predicted) ($r = -0.340$, $p = 0.028$), while positively correlated with CRP ($r = 0.434$, $p = 0.004$) in COPD group. Conclusion: Serum level of CTLA-4 is higher in COPD patients than controls, and are related with systemic inflammation and disease severity in COPD. These findings suggest circulating CTLA-4 maybe involved in COPD.