Levels of Autoantibodies against Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) are Elevated in the Sera of Pneumoconiosis Patients.

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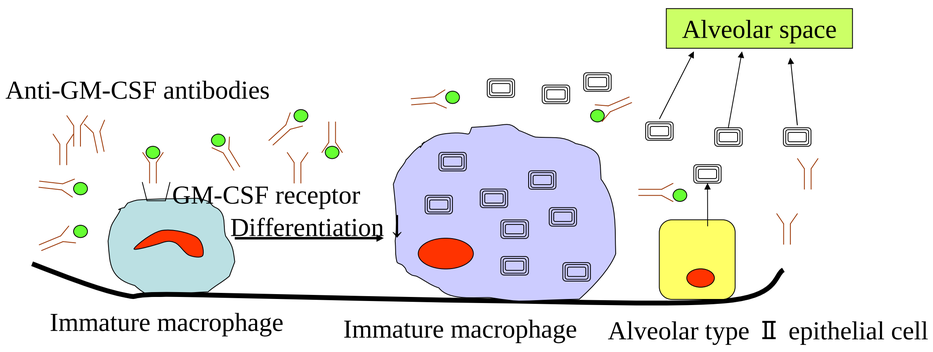
Abstract

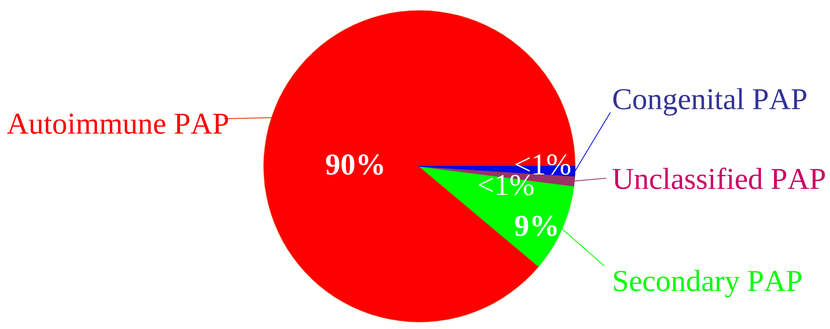
[Background] Pulmonary alveolar proteinosis (PAP) is a rare diffuse lung disease characterized by excessive accumulation of surfactant proteins in the alveoli and terminal bronchioles. Recent progress in the pathogenesis of PAP is the discovery of elevated levels of autoantibodies against GM-CSF in idiopathic PAP patients. Epidemiological studies have shown that about a quarter of PAP patients had the history of dust exposure.
[Objective] To examine the levels of anti-GM-CSF antibodies in the sera of pneumoconiosis patients.
[Methods] We obtained sera from 150 pneumoconiosis patients and 58 healthy controls, and measured the levels of anti-GM-CSF antibodies by enzyme-linked immunosorbent assay (ELISA).
[Results] The levels of GM-CSF antibodies were significantly elevated in the sera of pneumoconiosis patients compared with healthy controls (p<0.0001).
[Conclusion] Dust exposure may play roles in the generation of anti-GM-CSF autoantibody.

Background

Anti-GM-CSF Antibody

<Autoimmune PAP>





Autoimmune PAP and Dust Exposure

- A case of idiopathic pulmonary proteinosis accompanied with silicosis.
  (Hosokawa T, Yamahuchi E, et al. Respirology 2004; 9: 286-8)
- Twenty-six percent of autoimmune patients had the history of dust exposure.
  (Inoue Y, et al. Am J Respir Crit Care Med 2008; 177: 752-62)
- Pulmonary alveolar proteinosis in workers at an indium processing facility.
  (Lison D, et al. Am J Respir Crit Care Med. 2010; 181: 458-9)

Aim

To examine the levels of anti-GM-CSF antibodies in the sera of pneumoconiosis patients and a wide variety of other lung diseases.

Materials and Methods

Subjects

	n
Healthy controls (HC)	88
Pneumoconiosis (PC)	150
Interstitial pneumonia (IP)	16
Sarcoidosis (SAR)	52
Chronic obstructive pulmonary disease (COPD)	11
Bronchial asthma (BA)	22
Pulmonary mycobacterial infection (PM)	17
Lung cancer (LC)	12
Autoimmune PAP (PAP)	8

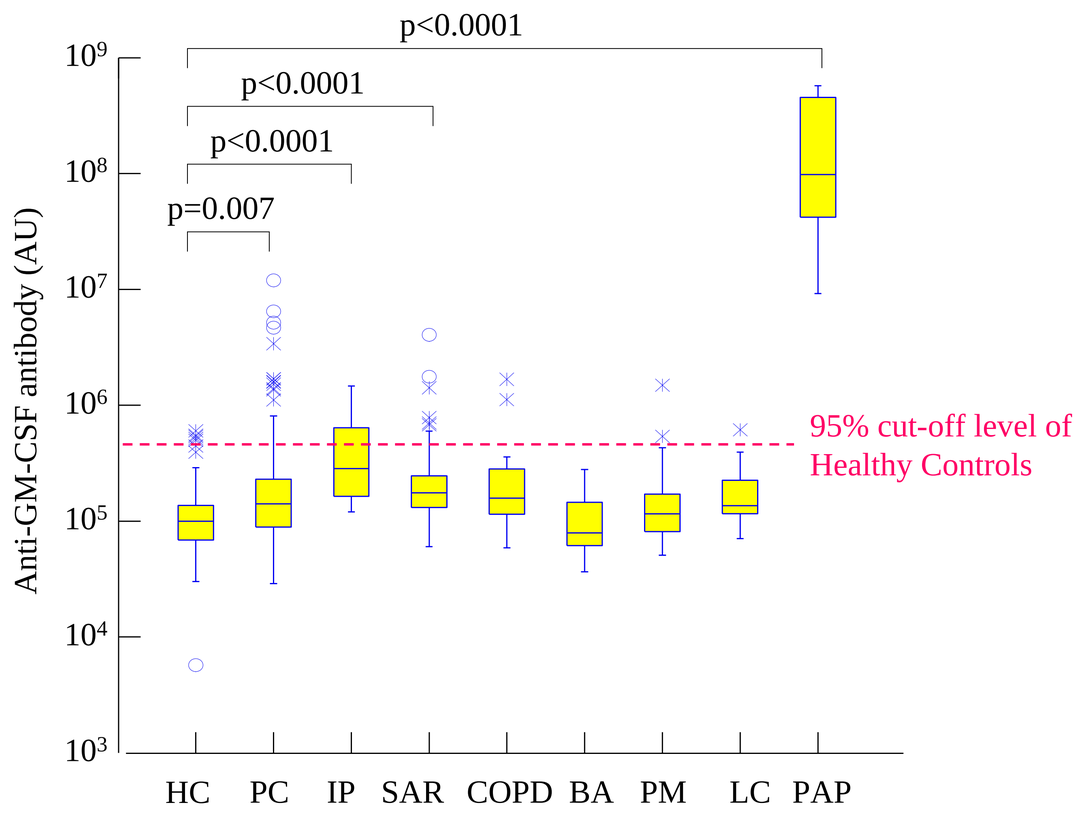
Measurements

- Levels of anti-GM-CSF IgG antibody in serum by enzyme-linked immunosorbent assay (ELISA).
- The concentration of sera pooled from four patients with autoimmune PAP and diluted 10,000 fold was defined as 10,000 arbitrary unit (AU) anti-GM-CSF antibody.

Results

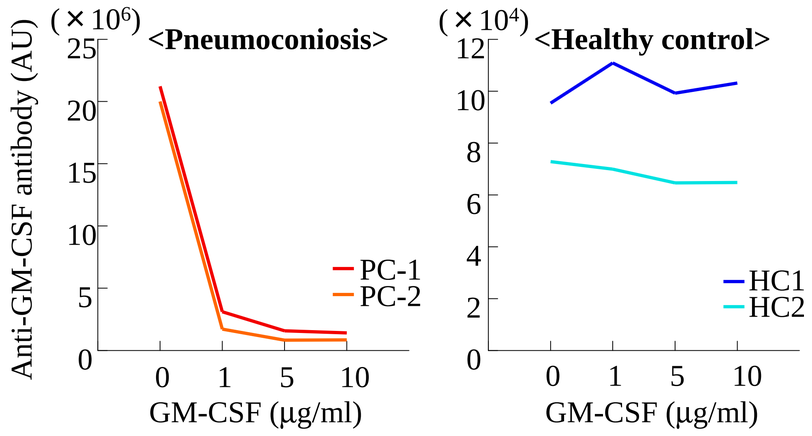
Anti-GM-CSF IgG Antibody Levels in Sera

(Mann-Whitney test with Bonferroni's correction)



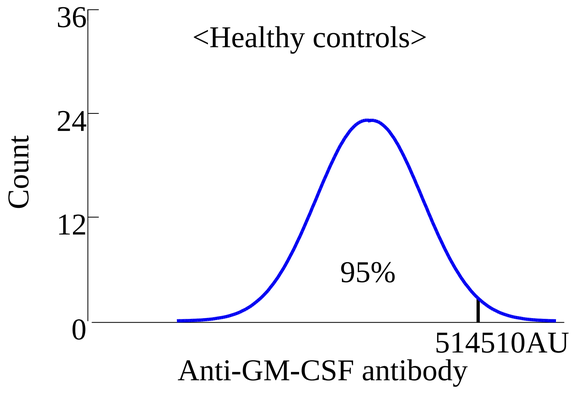
Inhibition Test by GM-CSF

To investigate whether the elevation of anti-GM-CSF Ab in some of pneumoconiosis patients is specific or non-specific, Ab levels were measured in the presence of various concentrations of GM-CSF.



Anti-GM-CSF Ab level { in pneumoconiosis : specific ; in healthy control : non-specific (background) }

Number of Sera above the 95% Cut-off Level of Healthy Controls



PC	16/150	(10.7%)
IP	5/16	(31.3%)
SAR	8/52	(15.4%)
COPD	2/11	(18.2%)
BA	0/22	(0%)
PM	2/17	(11.8%)
LC	1/12	(8.3%)
PAP	8/8	(100%)

Conclusion

- Some of the patients with pneumoconiosis have increased levels of specific anti-GM-CSF IgG antibody in serum.
- Dust exposure may play roles in the generation of anti-GM-CSF autoantibody.
- Dust exposure and PAP might be at least in part associated.
- Generation of anti-GM-CSF antibody may be ubiquitously accelerated in some immune-mediated respiratory diseases.