**Immunotoxicology of Silica: Silica activates regulatory T cell**

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Silica induces pulmonary fibrosis and also autoimmune diseases

Silica

Autoimmune diseases

Silicosis

Systemic sclerosis

Rheumatoid arthritis

(Caplan’s syndrome)

SLE

ANCA-related vasculitis/nephritis

Serum soluble Fas is elevated in SILICOSIS as well as autoimmune disease such as SLE

Soluble Fas mRNA is dominantly expressed in PMBC derived from SILICOSIS

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Silica activates regulatory T cell

→ will presented in Free Paper Program, 16:00~17:30, March 19th, 2012 at Coata Maya 5

Allergy and Immunotoxicology SC

in this session

Alteration of Fas and related molecules found in silicosis
SILICOSIS patients are divided into four groups according to immunological and respiratory factors.

Detection of alternatively spliced variant message of Fas gene in PMBCs from SILICOSIS.

mRNA expression of DcR3, function similar to sFas, is higher in PBMCs from SILICOSIS than that from healthy donors.

Although percentage of Fas-positive cells was not different between SILICOSIS and healthy donors, MFI of membrane Fas is lower in SILICOSIS.

Secret from cells, since lacking transmembrane domain.
Fas<sup>high</sup> lymphocyte is expresser of membrane Fas and Fas<sup>low</sup> is for soluble Fas

Patients with low membrane Fas MFI revealed higher titer of ANA in SILICOSIS

Expression of inhibitory genes for Fas-mediated apoptosis in PBMCs derived from SILICOSIS

Expression of inhibitory genes for Fas-mediated apoptosis in PBMCs derived from SILICOSIS

Reduced in SILICOSIS
- Senrin
- cFLIP/I
- DFF45/ICAD
- SURVIVINE

Enhanced in SILICOSIS
- CASPASE 3

Apoptotic pathway is continuously processing in SILICOSIS

Anti-Fas autoantibody was detected in 23.1% of SILICOSIS serum
Anti-Fas autoantibody detected in SILICOSIS serum is functional: Causin apoptosis on Fas-expressing myeloma cell line, but not in Fas-negative cell line.

Silica may activates responder T cell and also regulatory T cell

CD4+CD25+Foxp3+ regulatory T cell

Functional analysis of peripheral CD4+25+ fraction from healthy donors and silicosis
Chronic Activation

Excess Expression of CD95/Fas

Reduced Peripheral CD4+25+ fraction

Dysregulation of autoimmunity

Mesothelioma

Lung Cancer

Asbestos fibers: Mineral Silicate

Silica Particles

Enhancement of autoimmunity

Immunocompetent cells