

Immunotoxicology of Asbestos: Asebstos enhances regulatory T cell function

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Immunological Effects of Asbestos and Silica

Immune Suppression Mediated by Regulatory T (Treg) Cells

Regulatory T cells (CD4⁺CD25⁺) **Effector T cells (CD4⁺CD25⁻)**

Suppression

CD4⁺CD25⁻ (Treg) CD4⁺CD25⁺ (Tresp)

CD28 CTLA-4

B7 B7

APC MHC

● Tumor immunity
● Autoimmune disease

Foxp3: Forkhead box P3
CTLA-4: Cytotoxic T lymphocyte antigen 4
GITR: Glucocorticoid-induced tumor necrosis factor receptor

% Incorporation (x10³)

Ratio Treg:Tresp

MT-2 Cells May Have Originated from Treg Cells

MT-2

- was established from normal human cord leukocytes of a male infant by co-culturing with leukemic T-cells from a female patient with adult T-cell leukemia. (Miyoshi, I. et al., *Gann*, 72, 978-981 (1981))
- is human T cell leukemia virus type 1 (HTLV-1)-infected and immortalized CD4⁺ T cell line. (Chen, S. et al., *International Immunology*, 18, 269-277 (2005))
- expresses CD25 and Foxp3 at high level and is harbored the Treg-cell-like suppressive function.

Establishment of an Asbestos-induced Apoptosis-Resistant Sublines (MT-2Rsts)

Asbestos (Chrysotile-A or Chrysotile-B)
Low-dose (10 µg/ml)
Long-term (more than 8 month)

MT-2 original cells (MT-2Org) → chrysotile-induced apoptosis-resistant sublines (MT-2Rst): CA1, CA2, CA3, CB1, CB2, CB3

Suppressive Activity of MT-2 Cells on the Cell Division of TCR-stimulated Naive CD4⁺CD25⁻ T Cell

Responder T cell (Tresp): CD4⁺CD25⁻ T cells (1 x 10⁵) Irradiated MT-2 cell

● Stimulation: plate-coated anti-CD3 mAb (1 µg/ml) and soluble anti-CD28 mAb (1 µg/ml)
● Culture period: 3 days
● Proliferation assay: CFSE assay

■ Org ■ CB1

Non-divided cells (%)

Ratio Tresp:MT-2

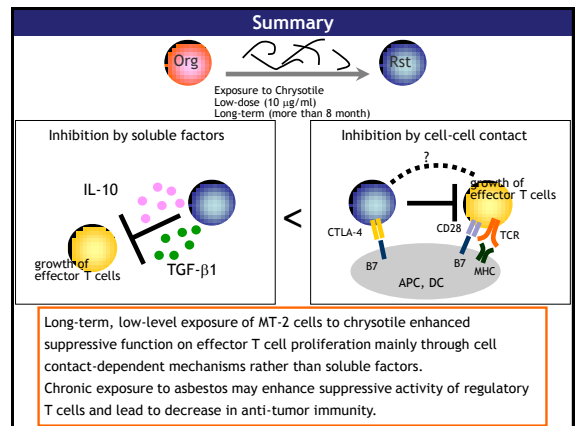
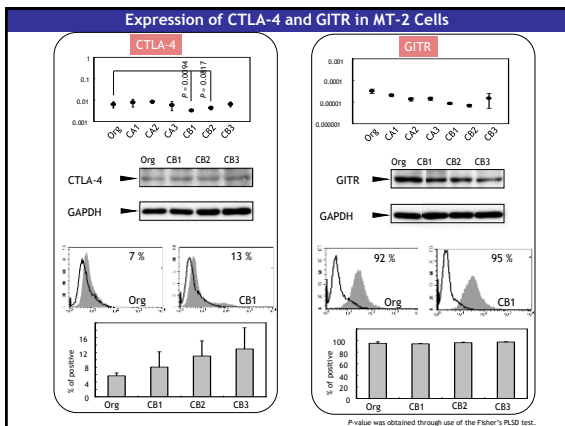
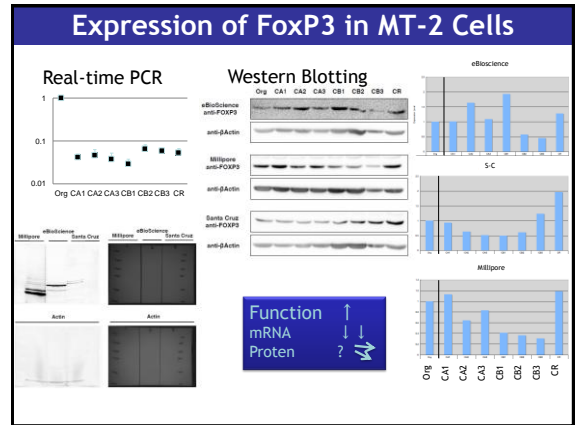
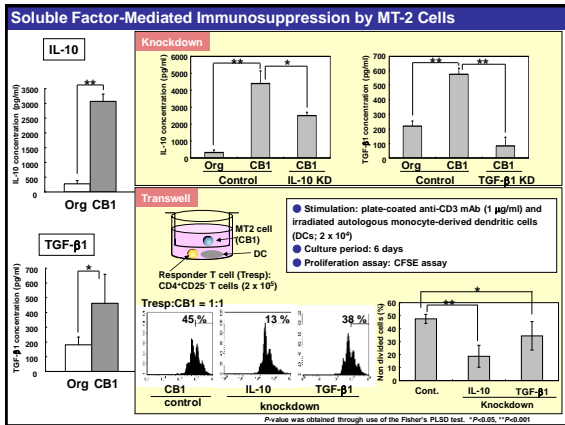
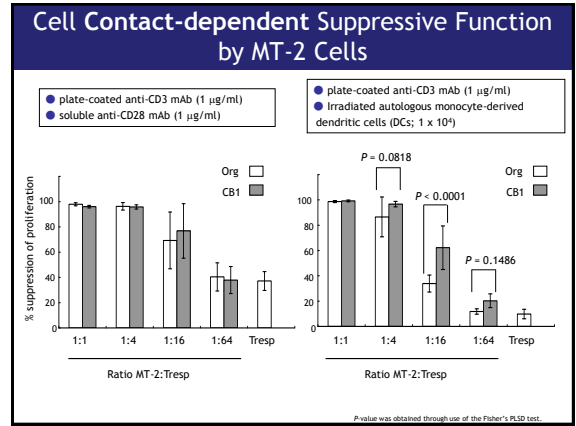
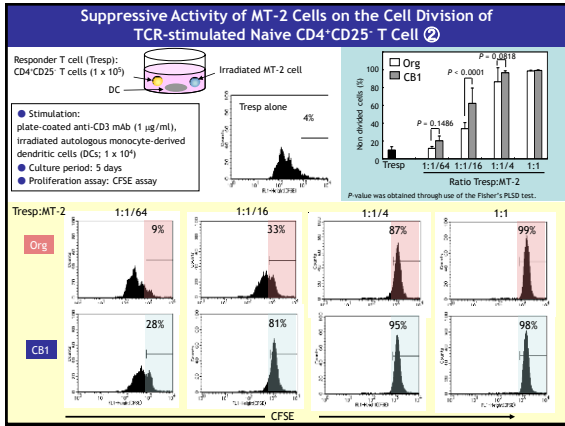
P-value was obtained through use of the Fisher's PLSD test.

Tresp:MT-2 1:1/64 1:1/16 1:1/4 1:1

Org 43% 75% 98% 98%

CB1 38% 83% 96% 95%

CFSE



Acknowledgements

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