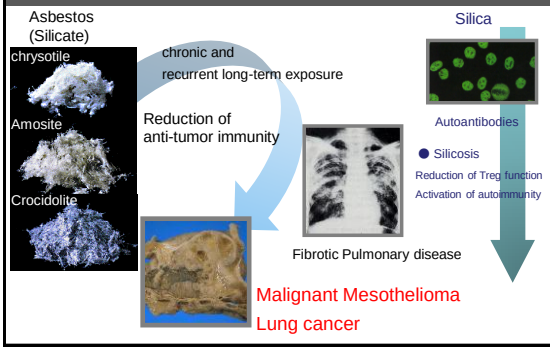
Immunotoxicology of Asbestos: Continuous exposure to asbestos to human T cell caused reduction of CXCR3, a chemokine receptor

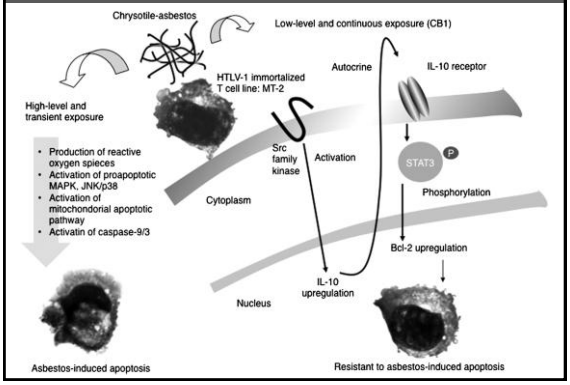
Maeda M[1,2], Otsuki T[1], Kumagai N[1], Matsuzaki H[1], Lee S[1], Hayashi H[1,3], T Kishimoto[4], Nishimura N[1]

[1]Department of Hygene, Kawasaki Medical School, Kurashiki, Japan
[2]Department of Biofunctional Chemistry, Division of Bioscience, Okayama University Graduate School of Natural Science and Technology, Okayama, Japan
[3]Deprtment of dermatology, Kawasaki Medical School, Kurashiki, Japan
[4]Okayama Rosai Hospital, Okayama, Japan

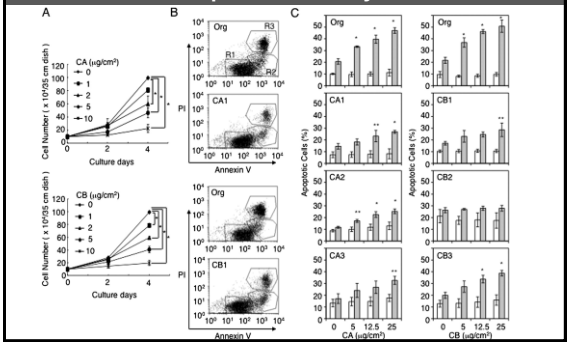
Immunological Effects of Asbestos and Silica



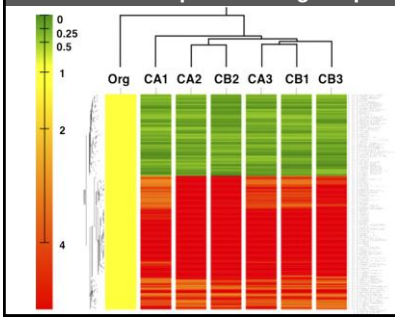
Transient and Continuous exposure of chrysotile B, an asebstos, onto HTLV-1 immortalized human polyclonal T cell line, MT-2



Original MT-2 (MT-2Org) cells acquire resistance to chrysotile-induced apoptosis by long-term and low-level exposures to chrysotile.

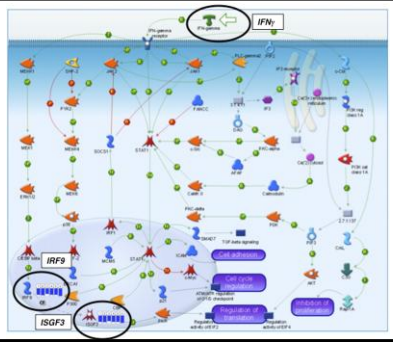


Clustering analysis of 139 genes reveals differences between MT-2Org and MT-2Rsts cells. Expression is scaled so that green represents low expression, and red represents high expression.

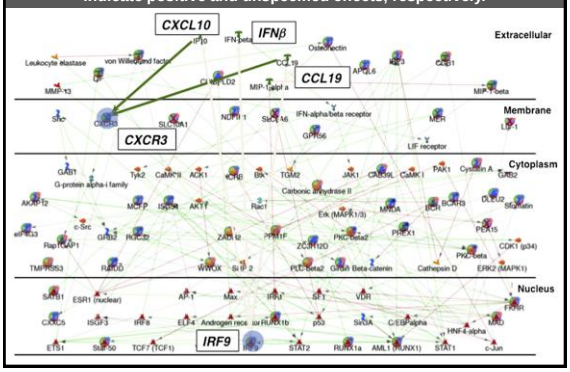


Org: original MT-2 cell line
CA1~3, and CB 1~3: Independently established sublines derived from orginal MT-2 line exposued more than 8 months to the chrysotile A (CA) or B(CB) showing resistance to the asbestos-induced apoptosis.

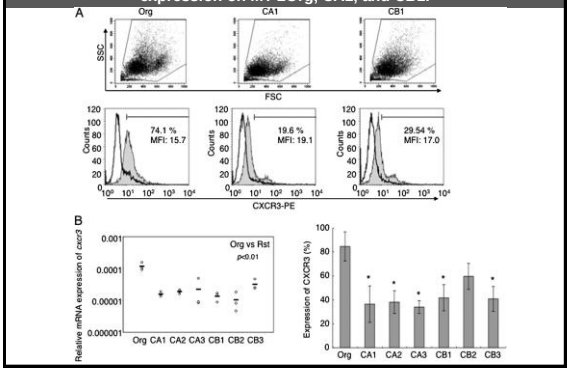
IFN-γ signaling canonical pathway analysis shows that the expression of IRF9 and ISGF3 is down-regulated in MT-2Rsts cells. Blue thermometers indicate down-regulation. Numbers indicate cell line names (2, CA1; 3, CA2; 4, CA3; 5, CB1; 6, CB2; 7, CB3).



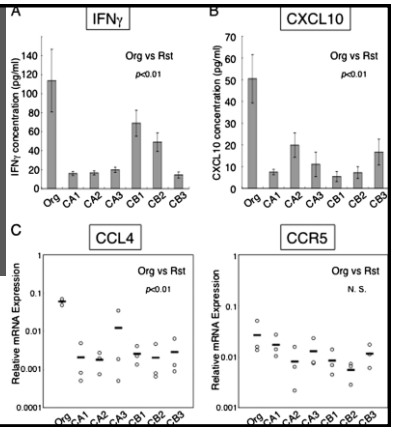
Network analysis indicates that down-regulation of CXCR3 is regulated by IRF9. Blue circles indicate reduced genes. Green arrows and gray arrows indicate positive and unspecified effects, respectively.



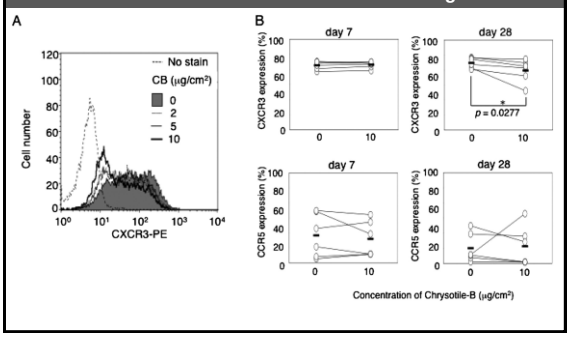
Chronic exposure to chrysotile inhibits the expression of CXCR3 in MT-2Rsts cells. (A) Representative FACS profiles of cell-surface CXCR3 expression on MT-2Org, CA1, and CB1.



Continuous exposure to chrysotile decreases Th1-type cytokine IFN-γ and chemokine CXCL10/IP10 production in MT-2Rsts cells.

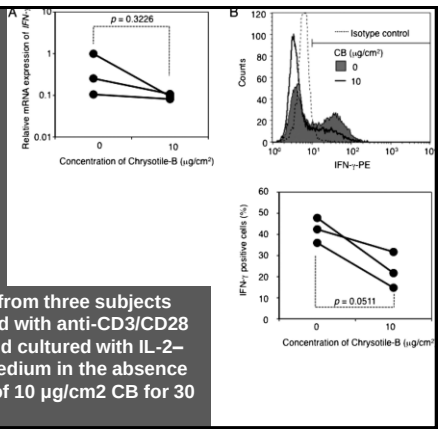


Chronic exposure to chrysotile reduces expression of CXCR3 in IL-2–cultured human CD4+ T cells. Peripheral CD4+ T cells from healthy donors were stimulated with anti-CD3/CD28 antibodies and maintained with IL-2–containing medium.

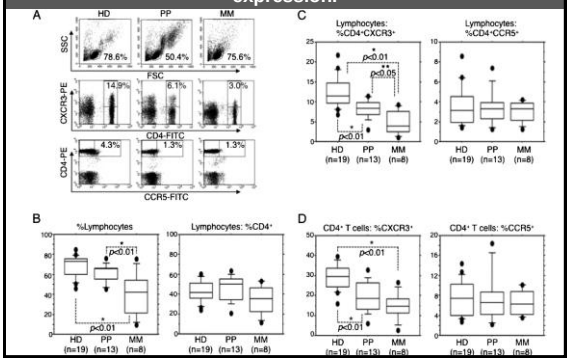


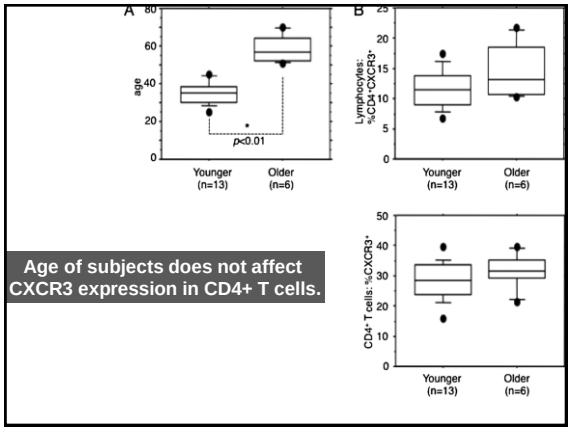
IFN-γ production in IL-2–cultured human CD4+ T cells from patients showing reduced CXCR3 expression by exposure to chrysotile.

CD4+ T cells from three subjects were activated with anti-CD3/CD28 antibodies and cultured with IL-2–containing medium in the absence or presence of 10 μg/cm2 CB for 30 days.



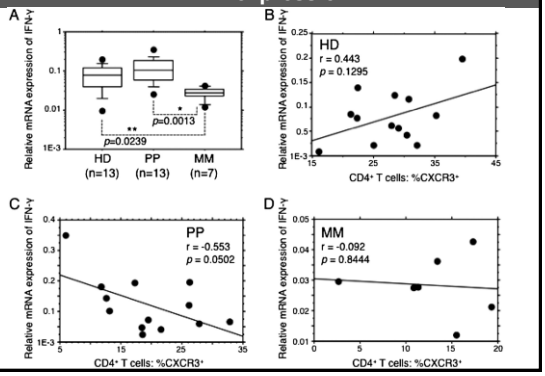
Peripheral CD4+ T cells in patients with pleural plaque (PP) or malignant mesothelioma (MM) show decreased CXCR3 expression.

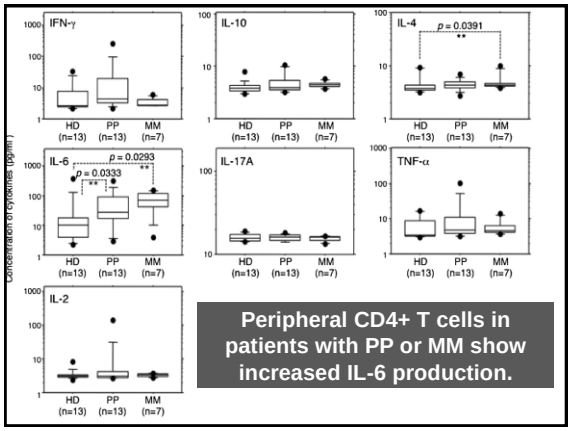




Age of subjects does not affect CXCR3 expression in CD4+ T cells.

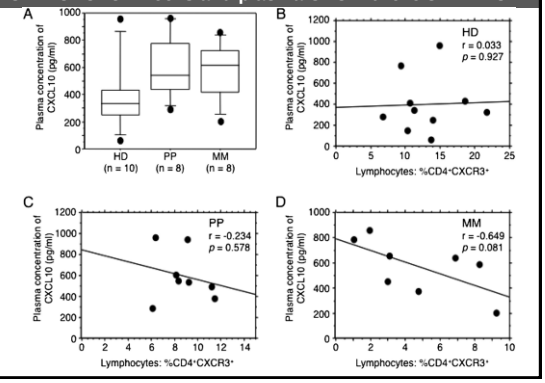
Peripheral CD4+ T cells in MMs show reduced IFN-γ mRNA expression.

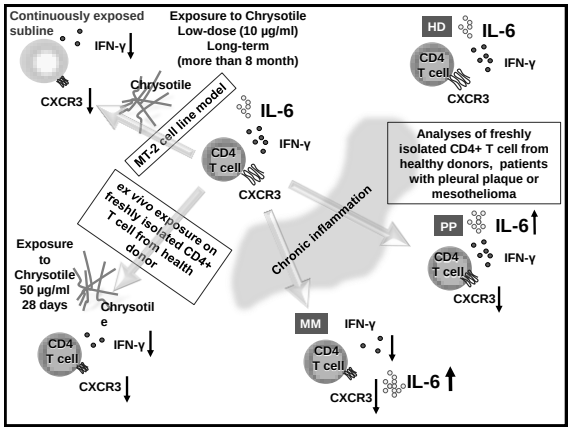




Peripheral CD4+ T cells in patients with PP or MM show increased IL-6 production.

Modest inverse correlation between the population size of CD4+CXCR3+ T cells and plasma CXCL10 levels in MMs.





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