The immunological effects of asbestos exposure on various lymphocytes such as the regulatory T cell (Treg), responder CD4+T helper cell (Tresp), CD8+cytotoxic T lymphocytes (CTL) and natural killer (NK) cells were investigated. Results show that asbestos exposure impairs anti-tumour immunity through enhancement of regulatory T cell function and volume, reduction of CXCR3 chemokine receptor in responder CD4+T helper cells, and impairment of the killing activities of CD8+cytotoxic T lymphocytes (CTL) and NK cells. These findings were used to explore biological markers associated with asbestos exposure and asbestos-induced cancers, and suggested the usefulness of serum/plasma IL-10 and TGF-β, surface CXCR3 expression in Tresp, the secreting potential of IFN-γ in Tresp, intracellular perforin level in CTL, and surface expression NKp46 in NK cells. Although other unexplored cytokines in serum/plasma and molecules in these immunological cells, including Th17, should be investigated by experimental procedures in addition to a comprehensive analysis of screening methods, biomarkers based on immunological alterations may be helpful in clinical situations to screen the high-risk population exposed to asbestos and susceptible to asbestos-related cancers such as mesothelioma.

557 CONTACT DERMATITIS AMONG WORKERS OCCUPATIONALLY EXPOSED TO FERRONICKEL ALLOYS


Introduction Many studies have shown that nickel and its alloys can be potential irritants and sensitizers among workers engaged in ferronickel alloy production, and provoke occupational contact dermatitis.

Objective To assess the prevalence of contact dermatitis focusing on allergic contact dermatitis in workers exposed to nickel while producing ferronickel alloys.

Methods A cross-sectional study included 103 male workers (mean age=49.1±10.1) employed as ferronickel smelters (duration of exposure 18.2±11.9) employed in 37 male office workers (mean age=46.7±10.6), employed in plants producing ferronickel alloys.

Results and discussion Skin rush during six months was registered in 20 (19.5%) exposed workers, and in 4 (10.8%) controls. The prevalence of skin changes, chronic rhinitis, conjunctivitis, and asthma was higher in exposed workers, but without statistical significance. Hand skin efflorescence due to non-occupational substances was present in 10 (9.8%) of exposed workers, and among 2 (5.5%) of controls. There was no significant difference concerning urticaria between two groups, and non-occupational nickel sensitisation (metal buttons, jewellery, etc.). Positive patch test by 5% NiSO4 was registered in 20 (19.5%) exposed workers and in 2 (5.4%) controls (p<0.05). Significant difference was found between the two groups concerning improvement of skin lesions after temporary elimination of workplace exposure. Positive elimination test was registered among 5 (4.9%) exposed workers with hand contact dermatitis.

Conclusion Our data confirmed that workplace nickel exposure can cause occupational allergic contact dermatitis among workers producing ferronickel alloys, and determined the need of preventive activities in order to decrease the pathogenic dermal effect of nickel.

638 EFFECTS OF IL-15 ADDITION ON THE SUPPRESSED INDUCTION OF CTL UPON EXPOSURE TO ASBESTOS

N Kumagai-Takei*, Y Nishimura, H Matsuzaki, S Lee, K Yoshitome, T Otukii. Department of Hygiene, Kawasaki Medical School, Kurashiki, Japan

Introduction Asbestos exposure can cause malignant mesothelioma and lung cancer. However, in contrast, its effect on anti-tumour immunity remains unclear. Our previous study reported that asbestos exposure suppressed the induction of CTL during mixed lymphocyte reactions (MLR), accompanied by the decrease in proliferation of CD8+ T cells. Recently, we reported that IL-2 showed a tendency to increase% granzyme B+ cells in the CFSE-positive CD8+ lymphocytes without proliferation upon exposure to asbestos. Therefore, we investigated whether IL-15 addition might improve the suppressed induction of CTL upon exposure to asbestos.

Methods For MLR, human PBMCs were cultured with irradiated allogenic PBMCs upon exposure to chrysotile B asbestos at 5 μg/ml for 7 days. After 2 days of culture, IL-15 was added at 1 ng/ml. After 7 days of MLR, PBMCs were collected and analysed for phenotypic and functional markers of CD8+ T cells with fluorescence-labelled anti-CD3, anti-CD8, anti-CD45RA, anti-CD45RO, and anti-granzyme B Abs using flow cytometry.

Result IL-15 didn’t recover the asbestos-caused decreases in% CD25+ and% CD45RO+ cells and increase in% CD45RA+ cells, but recovered the decrease in cell numbers of CD3+CD8+ cells and% granzyme B+ cells, in contrast to IL-2.

Discussion These results indicate that IL-15 is more effective on recovery from asbestos-caused suppressed induction of CTL than IL-2, although the interfered expressions of cell surface markers were not recovered even by addition of IL-15. Further study about the characteristics of CD3+CD8+granzye B+ cells induced by addition of IL-15 will contribute to clarification for the mechanism of asbestos-caused suppression in CTL induction and to finding out a clue to restore it.

640 EFFECT OF LONG-TERM EXPOSURE TO ASBESTOS ON FUNCTIONAL PROPERTIES OF HUMAN CD8+T CELL LINE

N Kumagai-Takei*, Y Nishimura, H Matsuzaki, S Lee, K Yoshitome, T Otukii. Department of Hygiene, Kawasaki Medical School, Kurashiki, Japan

Introduction The tumorigenicity of asbestos, which is thought to cause mesothelioma, has been clarified, whereas its effect on anti-tumour immunity remains unclear. In ICOH Congress 2015, we have reported the enhanced decrease in% perforin+ cells of stimulated CD8+ cells of the patients with malignant

Abstracts
EFFECT OF ASBESTOS ON FOXP3 EXPRESSION IN HUMAN T CELL LINE MT-2

1H Matsuzaki*, 1S Lee, 2M Maeda, 1N Kumagai-takei, 1K Yoshitome, 1Y Nishimura, 1T Otsuki. 1Department of Hygiene, Kawasaki Medical School, Kurashiki, Japan; 2Okayama University Graduate School of Natural Science and Technology, Okayama, Japan

Abstracts

Discussion Our result indicates that long-term exposure with asbestos suppressed FoxP3 transcription through the epigenetic modification, such as DNA methylation.

EFFECT OF SHORT-TERM EXPOSURE OF ASBESTOS ON HUMAN T CELL LINE MT-2

1H Matsuzaki*, 1S Lee, 2M Maeda, 1N Kumagai-takei, 1K Yoshitome, 1Y Nishimura, 1T Otsuki. 1Department of Hygiene, Kawasaki Medical School, Kurashiki, Japan; 2Okayama University Graduate School of Natural Science and Technology, Okayama, Japan

Introduction Asbestos fibres cause mesothelioma and lung cancer. We propose that asbestos suppress anti-tumour immune system in addition to transformation of mesothelial and lung epithelial cells. It is reported that asbestos induces apoptosis of epithelial cells through various processes such as, mitochondrial dysfunction, DNA damage, ER stress. On the other hand, we proposed that asbestos fibres affects on immune cells to attenuate immune response to tumour cells. We employed MT-2 cells as a model of Treg and maintained them with low concentration of asbestos for longer than 8 months. MT-2 cells exposed with low-concentration asbestos for long term showed higher viability after treatment with high concentration of asbestos than original MT-2 cells, and they were designated as MT-2Rst. However, it is still unclear how asbestos induces apoptosis of MT-2 cells and molecular basis of resistance of MT-2Rst cells to high concentration of asbestos.

Methods We analysed acute effect of asbestos on mitochondria using mitochondrial membrane potential indicator JC-1 dye and immunoblot analysis using antibodies recognising DNA damage markers.

Result It was found that asbestos fibres induced loss of mitochondrial membrane potential and phosphorylation of Histone H2AX, a marker protein of DNA damage.

Discussion These data suggest that asbestos fibres induces apoptosis of MT-2 cells through the mitochondrial dysfunction and DNA damage, and these apoptotic pathways are modified in MT-2Rst cells.

NANOTOXICITY OF TITANIUM NANOSHEETS FOR HUMAN IMMUNE CELLS

1Y Nishimura*, 2D Yoshoka, 1N Kumaga-takei, 1H Matsuzaki, 1S Lee, 1K Yoshitome, 1T Otsuki. 1Department of Hygiene, Kawasaki Medical School, Kurashiki, Japan; 2Department of Natural Sciences, Kawasaki Medical School, Kurashiki, Japan

Introduction The characteristic toxicity of nano-scaled materials, that is nanotoxicity, is a recent problem arising in association with nanotechnology. Titanium nanosheets (TNS) are known as 2D materials composed of titanium and oxygen with very thin structure and expected to be valuable for industrial usage. The present study examined the effect of exposure to TNS on human immune cells.

Methods Human peripheral blood mononuclear cells (PBMC) or magnetically isolated CD14+ monocyte or CD4+ T cells were cultured with TNS. Apoptosis was assayed by flow cytometry with annexin V staining. Intracellular...