TNF-α production in U-937 and THP-1 promonocytic cells following exposure to low dose γ-radiation and silicon dioxide

[1]**Trollip, A.P.**, [2]Ress, S. and [1]Abrahamse, H.

[1]Faculty of Health, University of Johannesburg, P.O. BOX 17011, Johannesburg, South Africa; [2]Department of Medicine, University of Cape Town, Cape Town, South Africa.

There is a high prevalence of pulmonary disease caused by *M. tuberculosis* and *M. kansasii*, in South African miners. In addition to the known contributing factors to this epidemic, underground miners are uniquely exposed to silicon dioxide (SiO_2) and low levels of α-radiation. Alveolar macrophages are the initial cells that defend against infection with *M. tuberculosis* and *M. kansasii*. U-937 and THP-1 are promonocytic continuous cell lines that are precursors of the monocyte/macrophage lineage, and given their homogenous nature, are ideal to study the interaction between promonocytes/macrophages, environmental mutagens and mycobacterial infection.

Differentiated U-937 and THP-1 cells were exposed to SiO_2 (0, 25, 100 and 500g/ml) and low dose radiation (0, 1, 3, 10Gy) and then infected with either *M. bovis BCG* or *M. kansasii*. Following 90 minutes of infection (day 0), at day 3 and again at day 5, supernatants were collected and the TNF-α cytokine assay was performed.

TNF-α was produced in both cell types, consistent with the descriptions in the literature (1,2). U-937 cells infected with *M. bovis BCG* showed decreasing TNF-α production with increasing SiO_2 concentrations, a finding also observed in U-937 infected with *M. kansasii*. However, U-937 infected with *M. kansasii* required more than 1Gy γ-radiation to produce similar amounts of TNF-α. THP-1 infected with *M. bovis BCG* released increasing amounts of TNF-α as SiO_2 concentrations increased on day 0. Thereafter, TNF-α release decreased. A similar pattern was observed with THP-1 cells infected with *M. kansasii*.

[1]Hass, R., Lonnemann, G., Mannel, D., Topley, N., Hartmann, A., Kohler, L., Resch, K., and Goppelt-Strube, M. (1991). Regulation of TNF-alpha, IL-1 and IL-6 synthesis in differentiating human monoblastoid leukemic U937 cells. Leuk Res. 15: 327-339.

[2]Savici, D., He, B., Geist, L. J., Monick, M. M., and Hunninghake, G. W. (1994). Silica increases tumor necrosis factor (TNF) production, in part, by upregulating the TNF promoter. Exp Lung Res. 20: 613-625.