Carcinogenic and Inflammatory Effects of Plutonium-Nitrate Retention in an Exposed Nuclear Worker and Beagle Dogs

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Purpose: Plutonium-nitrate has a moderately rapid translocation rate from the lung to blood stream. Previous studies have shown an unexpected retention of soluble plutonium in the beagles and human case studied here. The inflammatory responses that may be associated with long-term exposure to ionizing radiation were characterized. These pathways include tissue injury, apoptosis, and gene expression modifications. Other protein modifications related to carcinogenesis and inflammation and the various factors that may play a role in orchestrating complex interactions which influence tissue integrity following irradiation were investigated.

Materials and methods: We have examined numerous lung samples from a plutonium-exposed worker, a human control, and a variety of plutonium-exposed beagle dogs using immunohistochemistry and quantitative Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR).

Results: The exposed human showed interstitial fibrosis in peripheral regions of the lung, but no pulmonary tumors. Beagles with similar doses were diagnosed with tumors in bronchiolo-alveolar, peripheral and sub-pleural alveolar regions of the lung. The terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay showed an elevation of apoptosis in tracheal mucosa, tumor cells, and nuclear debris in the alveoli and lymph nodes of the beagles but not in the human case. In both the beagles and human there were statistically significant modifications in the expression of Fas ligand (FASLG), B-cell lymphoma 2 (BCL2), and Caspase 3 (CASP3).

Conclusions: The data suggests that FASLG, BCL2, CASP3 and apoptosis play a role in the inflammatory responses following prolonged plutonium exposure. Utilizing these unique tissues revealed which pathways are triggered following the internal deposition and long-term retention of plutonium-nitrate in a human and a large animal model.

USTUR-0351A-13