Low Dose Ionizing Radiation Modulates Immune Function
New Project Overview

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The immune system provides the first line of defense for exposures to environmental hazards. Protective immunity mechanisms using innate or adaptive responses are employed to mitigate acute challenges or amplify the readiness of the system to respond to future challenges. Some stimuli lead to amplified inflammatory reactions such as delayed hypersensitivity which is required for immunity to parasites and can also lead to adverse consequences such as contact dermatitis. Radiation exposure has the potential to aggravate hypersensitivity reactions as well as to suppress protective immunity. Ionizing radiation at high doses has long been recognized as highly effective in destroying cells of the immune system, particularly lymphocytes. Increased risk of infection follows radiation exposure and potentially reduces immune surveillance of tumor cells. However, in the past decade attention has been turned to the effects of radiation exposure below 1 Gy in the context of risk assessment and evidence has accumulated that doses in the 1 to 50 cGy range may actually be protective rather than deleterious.

In order to examine the effects of low dose ionizing radiation on the immune system we have chosen to examine an amplified adaptive cellular immunity response. This response is Type IV delayed-type hypersensitivity also called contact hypersensitivity. The agent fluorescein isothiocyanate (FITC) is a low molecular weight, lipophilic, reactive, fluorescent molecule that can be applied to the skin where it (hapten) reacts with proteins (carriers) to become a complete antigen. Exposure to FITC leads to sensitization which is easily measured as a hypersensitivity inflammatory reaction following a subsequent exposure to the ear. Ear swelling, eosinophil infiltation, immunoglobulin E production and cytokine secretion patterns characteristic of a “Th2 polarized” immune response are the components of the reaction. The reaction requires successful implementation of antigen processing and presentation by antigen presenting Langerhans cells, communication with naïve T lymphocytes in draining lymph nodes, expansion of activated T cell clones, migration of activated T cells to the circulation, and recruitment of memory T cells, macrophages and eosinophils to the site of the secondary challenge. Using this model our approach will directly quantify system function rather than relying only on indirect biomarkers of cell function.

We will measure the FITC-induced hypersensitivity reaction over a range of doses from 1 cGy to 2 Gy and test for a radioadaptive response with low dose priming followed by a large challenge dose. Key events will be examined at optimum low and high doses. These include Langerhans cell antigen processing and migration to lymph nodes, changes in lymph node architecture, estimation of expanded T cell clones in the skin and assessment of response polarization by measuring cytokine signatures and quantifying Th1 and Th2 cell numbers in the spleen.

We hypothesize that ionizing radiation will produce a biphasic effect on immune system function resulting in an enhancement at low doses and a depression at higher doses. We further hypothesize that this transition will occur in the dose range of 5 to 50 cGy and that a low priming dose of radiation will modulate a later challenge dose.

This is a new start and work in progress has been limited to optimization of methods and establishment of baseline values for the various endpoints prior to initiating radiation exposures.

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