DOE Final Report

Title: Defining a Possible Low LET Bystander Effect

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Summary: The principal objective of this research was to derive an understanding of the mechanistic bases for the recognition, processing, and consequences of ionizing radiation initiated damage to mammalian cells. In particular, to determine whether low linear energy transfer radiation at environmentally relevant low doses only initiates responses in directly hit cells. That is, is there a low dose, low LET bystander effect? Establishment of bystander effectiveness at low doses would abrogate simple extrapolations and may have significant implications for established radiation protection standards. The approach taken used a precision charged particle microbeam for known delivery of radiation of high or low linear energy transfer, in the form of alpha particles or protons, and broad beam particles along with a low LET X-ray source.

Four goals were set to establish and quantify relationships for clastogenic, cell cycle and molecular changes in hit versus bystander cells, where the tissue origin of the human cells used was varied to assess cell communication likelihood.

Eleven manuscripts, each of which deals with different aspects of bystander responsiveness have been published.

Results clearly establish that high LET radiations can induce bystander responses at low fluences which ensure that only a small fraction of cells are ever traversed by an energetic particle. Further, inter-cellular communication, leading to responses in non-hit cells, were recorded over distances approaching millimeters, in both cells in 2-D culture and in 3-D human cell model tissues. However, the thrust of these investigations, namely the establishment of a low dose, low LET bystander response remains uncertain. Whereas molecular responses were noted at low doses in some experiments, in no instance was there a clear manifestation of a deleterious change in the form of enhanced chromosomal damage in bystander cells after environmentally relevant low doses.

Significance: Current radiation protection guidelines assume a linear response to ionizing radiations down through doses where epidemiological studies provide very limited to no information as to the propriety of such assumptions. The bystander response is a non-targeted effect which might impact such guidelines. These studies while clearly affirming a bystander response for high LET radiations, do not provide such affirmation for environmentally relevant low dose, low LET radiations. Caution and further study are necessary before making judgements that could impact on current standards.

Publications

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