

Radiation Therapy Symposium: Introduction

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*On March 6, 2000 a joint symposium was organized by the *District of Columbia Section of the Society for Experimental Biology and Medicine and †Oxygen Club of Greater Washington, D.C.*

The topics presented in this mini-symposium encompassed the whole spectrum from basic research to clinical applications of different qualities of radiation. Dr. Usha Kasid's laboratory uses cellular, molecular, biochemical, and *in-vivo* approaches to study the role of Raf-1, a cytoplasmic protein kinase, in cell growth, proliferation, and cell survival. The potential role of Raf-1 in tumor response to ionizing radiation (IR) is investigated. Dr. Kasid showed that exposure of human carcinoma cells to IR activates Raf-1, stimulates the association of Ras with Raf-1, and downstream activation of MKK, MAPK, and AP-1. These findings suggested that Raf-1 is an effector of Ras in IR-stimulated MAPK pathway. The data from this lab suggest a basis for clinical investigation of radiation and antisense-raf oligodeoxynucleotide in cancer therapy. Dr. Mark H. Whitnall presented very interesting and promising data on the use of 5-androstenediol (AED) as a radioprotectant to enhance the immune function and promote survival following wholebody exposure to IR. It is known that acute exposure to IR causes failure of the hemopoietic progenitors to proliferate leading to death due to infection and

hemorrhage. Free radical scavengers and antioxidants are the common pharmacologic tools used to minimize injury by reducing reactive free-radical species and, in certain cases by acting as immunomodulators, cytokines can stimulate hemopoietic recovery. It has been shown that pretreatment with dehydroepiandrosterone and its metabolite AED, increases survival during bacterial and viral infections in un-irradiated animals. Dr. Whitnall is studying this family of steroids and their application as countermeasures to whole-body IR at doses that can cause death attributed to reduced immunity to infection. In contrast to free radical scavenger therapy, AED seems to be not cytotoxic. Dr. Martin W. Brechbiel's research focuses on investigating the challenging technology and the promising use of radiolabeled monoclonal antibodies in their clinical cancer therapy applications. These macromolecules localize and bind to malignant cells to selectively target, as well as deliver, either an imageable isotope or a localized radiation dose. Dr. Brechbiel discusses the pros and cons of the various emitters and the potential advantage of using α -emitting radionuclides in treating leukemias and lymphomas.

Raf-1 Protein Kinase, Signal Transduction, and Targeted Intervention of Radiation Response

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Raf-1, a cytoplasmic protein serine-threonine kinase, plays an important role in cell growth, proliferation, and cell survival. State-of-the-art cellular, molecular, biochemical, and pre-clinical approaches have been used in our laboratory to elucidate the role of Raf-1 in tumor

response to ionizing radiation (IR). Our data demonstrate that exposure of human carcinoma cells to IR results in tyrosine phosphorylation, membrane-recruitment, and activation of Raf-1 protein kinase. In addition, IR stimulates the association of Ras with Raf-1, and downstream activation