



# Evaluating Drug Effects on Radiation Efficacy and Toxicity

For years, SRI's radiobiologists have been exploring molecular mechanisms to selectively enhance the ability of radiation to kill tumor cells while protecting the surrounding normal tissue from radiation damage. We work with government agencies to study the effects of chronic exposure to radiation and evaluate materials that may be used to help protect against radiation damage. We also perform efficacy studies and GLP and non-GLP combination radiation toxicology studies to assist companies in the development of novel therapies. SRI's on-site gamma and x-ray irradiation facilities aid clients in the development of new experimental biological systems to treat diseases such as leukemia or for cutting edge stem cell research.

Because these studies are highly experimental in nature, we work closely with our clients to design experiments that will give the highest return on their investment. Variables, including the dosing regimen of the test compound, the sequence of exposure to drug and radiation, radiation dose, and length of monitoring period, are jointly defined before the final protocol is submitted to SRI's Institutional Animal Care and Use Committee (IACUC). While the general health, body weight, and survival are key statistics for radiation studies using animals, pathology is crucial to understand the differential effects drugs have on healthy and diseased tissues.

## EVALUATING DRUG EFFICACY

Currently, radiation therapy is widely used as either the sole approach to the treatment of some cancers or as an adjuvant therapy in parallel to surgery or chemotherapy. For years researchers have sought compounds that will selectively sensitize cancerous tissue to radiation. More recently, researchers have been investigating compounds that can be used to protect healthy tissues and possibly allow radiologists to increase the radiation dose or exposure time to affected areas.

SRI provides contract services to study a compound's effects on:

- Radiation-induced apoptosis. Mice are sacrificed 4-8 hours after irradiation and selected organs and/or jejunum harvested for crypt apoptosis assay (TUNEL).



*Bridging the drug development gap*

- Survival rate after acute radiation exposure. Mice are irradiated and body weight and survival are monitored for 4 weeks before sacrifice.
- Crypt survival and crypt stem cell proliferation using either BrdU or proliferating cell nuclear antigen(PCNA) assays.
- Radiation sensitization using human xenografts in athymic animals or syngeneic tumors in immunocompetent mice. Once implanted tumors reach a specified size, the animals are treated with a drug-radiation regimen. The tumor volume and animal body weights are measured throughout the study. The tumors are harvested for pathology and follow-on studies.

## RADIATION TOXICOLOGY

We perform GLP and non-GLP radiation toxicology studies as either stand-alone services or as part of a comprehensive development package. Throughout a study we perform weekly clinical examinations, including alterations in teeth, nose, eyes, perineum, gross motor and behavioral changes, and monitor body weights, and water and food consumption.

Depending on your needs, we can perform:

- Clinical pathology including hematology, serum chemistry, and urinalysis
- Blood collection for plasma analysis of test compound and pharmacokinetics of tissue distribution
- Assays for cytogenetic damage in bone marrow, peripheral blood, erythrocytes, and lymphocytes
- Organ weights
- Histopathology—for major tissues, including target tissue, organs with gross lesions, brain, heart, lungs, liver, spleen, GI, skin, ovaries/teste, lymph nodes, and kidneys
- Molecular biology-based studies in tissues:
  - Quantitative RT-PCR for specific genes
  - Protein expression analysis using either immunofluorescence or Western techniques
  - Customized assays to address mechanism of action of the candidate drug
- Colony forming unit measurements in spleen and gut
- Studies with late effects end points, such as radiation-induced cataractogenesis, that are dose dependent and may take as long as 30 weeks to develop
- Studies on the long-term effects of radiation on behavior and cognition

## FACILITIES

Our irradiation facilities have both a Pantak HF320 X-ray source and a Mark 1-68A 137Cs gamma emission source. These facilities are used for both in vitro and in vivo studies. In addition to whole-body animal irradiation, focal irradiation is accomplished by using specially designed holders. Animals are housed under veterinary care in a modern AAALAC-accredited facility. All our procedures and facilities are routinely audited and maintained under GLP regulations. SRI has an in-house model shop that can custom design and manufacture holders to our clients' specifications.

## You Make the Call

For further information, contact our Client Services Team:

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