Update on the 3rd International Workshop on Space Radiation Research

Two hundred investigators, students, and interested professionals from the United States, Sweden, Russia, China, Germany, Italy, Japan, and the United Kingdom participated in the 3rd International Workshop on Space Radiation Research and 15th Annual NASA Space Radiation Health Investigators’ Workshop held May 16-20, 2004 at Danfords on the Sound in Port Jefferson, New York. Sessions on Radiation Carcinogenesis and Genomic Instability; Non-Cancer Risks; Neurological Damage from Space Radiation; Molecular and Cellular Responses; Radiation Quality and Biological Studies of Shielding; Dosimetry, Physics, and Shielding; Biomarkers, Sensitivity, and Prevention; and Space Exploration Radiation Risk Assessment Roadmap attracted the researchers to the Workshop. Special sessions included an evening poster session and reception and a special session at the Brookhaven National Laboratory that included a tour of the NASA Space Radiation Laboratory.

William E. Burrows, Professor of Journalism at New York University and Director of its Science and Environmental Reporting Program, presented "The Survival Imperative: Using Space to Protect Earth" at the Workshop Dinner Banquet.

Sixty-seven oral talks and 55 posters were presented; a total of 125 abstracts were published in an abstract volume. Selected manuscripts will be included in a Proceedings published as a supplement to Radiation Research.
New Funding Opportunity
Research Opportunities Soliciting Ground-Based Studies for Radiation Biology and Radiation Shielding Materials - NRA-NNH04ZUU005N

NASA solicits proposals for ground-based research in space radiation biology and space radiation shielding materials. NASA will provide beams of high-energy heavy nuclei produced at the NASA Space Radiation Laboratory and the Alternating Gradient Synchrotron at the Department of Energy's Brookhaven National Laboratory for this research. These beams simulate the high-energy, high-charge (HZE) components of galactic cosmic rays that constitute the biologically most significant component of space radiation. This ground-based research program supports NASA's mission and the Exploration Systems Mission Directorate. Specific information is available at http://research.hq.nasa.gov/code_u/nra/current/NNH04ZUU005N/index.html.

Proposals will be accepted through November 19, 2004.

Closed Solicitation
NSCOR for Estimation of Solid Tumor Cancer Risks from Space Radiation - NNH04ZUU002N

Proposals were due August 13, 2004 for funding to establish a NASA Specialized Center of Research (NSCOR) to provide the basis for estimation of solid tumor cancer risks from space radiation. An NSCOR is a group of investigators (either geographically continuous or dispersed) who have complementary skills and work together to solve a closely focused set of research questions.

NRA-03-OBPR-07 Funding Announcement:
On August 2, 2004, NASA announced the selection of 19 researchers to conduct ground-based research in space radiation biology and space radiation shielding materials. This research will utilize beam facilities at the NASA Space Radiation Laboratory at the Brookhaven National Laboratory.

Selectee List, Space Radiation Shielding

Benton, Eric
Eril Research Inc
Space Radiation Shielding Testing using the NASA Deep Space Test Bed

Grukel, Eric
University of Kentucky
Synthesis and Analysis of Nanoparticle Composites for Space Radiation Shielding

Sudarshan, Tirumalai
Materials Modification, Inc
Novel Radiation Shielding and Structurally Efficient Materials for Space Missions

Wilson, John
Langley Research Center
Ebeam-Cure Fabrication of Polymer Fiber/Foam/Matrix Composites for Multifunctional Radiation Shielding

Zhong, Wei Hong
North Dakota State University
Hybrid Composites with Reactive Nano-matrix for Cosmic Radiation Shielding

Selectee List, Space Radiation Biology

Amundson, Sally
Center for Radiological Research, Columbia University
Functional Genomic and Signaling Responses to HZE Particle Radiation

Bailey, Susan
Colorado State University
HZE Radiation: Modulation of Genetic Effects by RNA Interference of NHEJ

Behravesh, Esfandiar
Universities Space Research Association
Evaluation of the Late Effects of Heavy-Ion Radiation on Mesenchymal Stem Cells

Braby, Leslie
Texas Engineering Experiment Station
Methods for Real Time Measurement of Dose and Charged Particle Spectrum

Britt, Anne
University of California
Arabidopsis as a Model for the Study of DNA Double Strand Break (DSB) Repair and DSB Induction by
NSRL - NASA Space Radiation Laboratory Campaigns I-III

Three experimental campaigns have now been completed at the NSRL and a fourth is underway. Good indicators of scientific progress at NSRL are the number of hours of experiments completed and the number of ion species (charge and energy) used by investigators. In its first-year of operation, NSRL surpassed the number of hours and ion beams used by the NASA Space Radiation Health Program in the previous 4 years. This milestone is a direct implementation of the strategy recommended by the National Research Council in their 1996 Report, *Radiation Hazards to Crews of Interplanetary Missions*, and indicates a four-fold increase in the rate of scientific research the goal of which is to ensure the safe exploration of space by humans in the future.

Ions accelerated in the first-year at NSRL are shown in the following table:

<table>
<thead>
<tr>
<th>Ion</th>
<th>Energy</th>
<th>LET (keV/µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe</td>
<td>1000</td>
<td>150</td>
</tr>
<tr>
<td>Fe</td>
<td>800</td>
<td>160</td>
</tr>
<tr>
<td>Fe</td>
<td>600</td>
<td>176</td>
</tr>
<tr>
<td>Ti</td>
<td>1000</td>
<td>107</td>
</tr>
<tr>
<td>Si</td>
<td>600</td>
<td>53</td>
</tr>
<tr>
<td>O</td>
<td>1000</td>
<td>15</td>
</tr>
<tr>
<td>O</td>
<td>600</td>
<td>17</td>
</tr>
<tr>
<td>C</td>
<td>290</td>
<td>13</td>
</tr>
<tr>
<td>P</td>
<td>1000</td>
<td>0.21</td>
</tr>
</tbody>
</table>

A summary of the NSRL Campaign to date is provided in the following table:

<table>
<thead>
<tr>
<th>NSRL Campaign</th>
<th>Dates</th>
<th>Science Hours</th>
<th># Experiments</th>
<th>Participating Scientists</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSRL-0 (commissioning)</td>
<td>July 7-23, 2003</td>
<td>158</td>
<td>12</td>
<td>33</td>
</tr>
<tr>
<td>NSRL-1</td>
<td>Oct. 25-Nov. 24, 2003</td>
<td>285</td>
<td>27</td>
<td>73</td>
</tr>
</tbody>
</table>
Beams used at individual NSRL campaign are listed in the following table:

<table>
<thead>
<tr>
<th>Campaign</th>
<th>Ions</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSRL-0</td>
<td>C(0.29 MeV/µ), Fe (1 GeV/µ), Ti(1 GeV/µ)</td>
</tr>
<tr>
<td>NSRL-1</td>
<td>Fe(0.8 GeV/µ), Fe (1 GeV/µ), Ti (1 GeV/µ), C(0.29 GeV/µ)</td>
</tr>
<tr>
<td>NSRL-2</td>
<td>Fe(1.0 GeV/µ), Fe(0.6 GeV/µ), Ti (1 GeV/µ), Si(0.6 GeV/µ), C(0.29 GeV/µ)</td>
</tr>
<tr>
<td>NSRL-3</td>
<td>Fe (1 GeV/µ), Fe (0.6 GeV/µ), Protons (1 GeV)</td>
</tr>
<tr>
<td>NSRL-4</td>
<td>Fe (1 GeV/µ), Fe (0.6 GeV/µ), Ti (1 GeV/µ), Si (0.6 GeV/µ), O(1 GeV/µ), O(0.6 GeV/µ), Protons (1 GeV)</td>
</tr>
</tbody>
</table>

Highlights in beam characteristics achieved are dose-rates below 0.1 rad/min and as high as 5000 rad/min, and beam-spot sizes from above 20x20 cm to below 1x1 cm. During NSRL-3 a new mixed-field capability to deliver fractionated proton and Iron exposures was demonstrated, which will be available for experiments by SpaceRad investigators in 2005. The mixed-field capability will allow scientists to mimic the low-LET background in deep space from frequent proton traversals of cells before or after the passage of much less frequent cell traversals of high charge and energy (HZE) ions.

Above: NSRL computer display of Bragg curve behind polyethylene absorber for a 0.75 GeV/u Iron beam.

Below: Streaks and clusters of γH2AX foci indicating the induction of DNA double strand breaks in human fibroblast cells by 1 GeV/u Titanium (LET = 107 keV/mm) beam at NSRL-3.
Space Radiation Biologists in Training

Eleven graduate students and post-doctoral researchers formed the first class of the Space Radiation Summer School held at the Brookhaven National Laboratory in Upton, New York. Gregory Nelson, Ph.D., Director, Loma Linda University Radiobiology Program, and Marcelo Vazquez, M.D., Ph.D., Medical Scientist, Brookhaven National Laboratory, served as Associate Directors of the Space Radiation Summer School. The three-week course, held June 1 through June 18, 2004, consisted of an extensive series of lectures on radiation physics, the space radiation environment, and radiobiology - plus hands-on laboratory and accelerator experiments performed in BNL's Medical Department and in the new NASA Space Radiation Laboratory at BNL.

The students and their affiliations were the following:

<table>
<thead>
<tr>
<th>Student</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vered Anzenberg</td>
<td>MIT/Mass General Hospital</td>
</tr>
</tbody>
</table>
The course included lectures, low- and high-LET laboratory activities, NSRL runs, planning and protocol discussion sessions, and a series of data collection and analysis. Initial lectures dealt with basic concepts of physics, dosimetry, radiobiology, space radiation, and accelerator operations. Students received extensive laboratory protocol instruction and the same BNL training to perform radiobiology experiments given to all investigators. During their second week of training, the students ran control experiments using gamma rays. During their last week, the students ran experiments in the NSRL using 1 GeV/n iron ions obtaining different endpoints discussed and analyzed with their instructors. Each student also wrote a beam time request proposal. In short, students learned - in a very short time - the what, when, where, how, and why of conducting radiobiology experiments at the NSRL.

SRHP Featured Investigator: Ann Kennedy

Ann Kennedy
Professor of Radiation Biology and
Richard Chamberlain Professor of Research Oncology
"An ounce of prevention is worth a pound of cure" might be considered the mantra of Ann R. Kennedy, whose investigations in radiation biology have taken her from using ionizing radiation to induce cancer in cells to using nutritive supplements to prevent its formation. Early in her career, she exposed cells to ionizing radiation in an attempt to understand the types of genetic damage that might lead to cancer. That piqued her curiosity about how to prevent cancer, leading to her work with protease inhibitors and, eventually, to the Bowman-Birk Inhibitor (BBI), a soy protein that has been a powerful cancer preventative in her laboratory and which has shown great promise in clinical trials.

After receiving an A.B. from Vassar College in Biology in 1969 and M.Sc. and D.Sc. in Radiation Biology from Harvard University in 1971 and 1973, Kennedy began her career in radiation biology at the Harvard School of Public Health. In 1988 she moved her laboratory to the University of Pennsylvania School of Medicine to continue her work with protease inhibitors.

Despite the fact that BBI (and the BBI Concentrate used as a cancer preventative) are derived from plants, the Food and Drug Administration required Kennedy to obtain - and ultimately granted to her - investigational new drug (IND) status for BBIC so that human trials could begin. The compound is now in a Phase III Trial for treatment of oral leukoplasia, a premalignant lesion, and in Phase I and II Trials for use in treatment of genitourinary and inflammatory diseases.

In 1997 Kennedy joined the NSBRI as a member of the External Advisory Council and has served as Associate Team Leader of the Radiation Team. Recently named Team Leader of the NSBRI's Immunology, Infection, and Hematology Team, she envisions extensive interaction with other NSBRI teams to develop countermeasures for space and radiation-induced biologic effects. Examples of such interaction include the use of BBIC to prevent/reduce muscle atrophy in the mouse hind limb suspension model system and its use as a countermeasure for muscle and bone loss in bed rest patients. Observations of the effects of BBIC on cytokines during mouse hind limb suspension have also been made.

Kennedy's NSBRI project, "Countermeasures for Space Radiation-Induced Myeloid Leukemia," evaluates nutritional supplements as countermeasures to protect against space radiation-induced leukemogenesis. These nutritional supplements include L-selenomethionine (SeM), vitamin C, vitamin E succinate, alpha-lipoic acid, Co-enzyme Q10 and N-acetylcysteine. Data obtained from her earlier NSBRI in vitro and animal studies have demonstrated that the nutritional supplements to be evaluated in this project are effective in preventing radiation-induced oxidative stress and in protecting cultured human cells against adverse biological effects induced by the types of radiation of most concern during space travel, i.e., highly energetic heavy charged particles (known as HZE particles) and protons.

The NSBRI investigation will determine the efficacy of a combination of these nutritional supplements as a countermeasure against space radiation-induced acute myeloid leukemia (AML) using the CBA mouse model system. Two, two-year animal experiments are planned to determine the effect of supplement combination on the development of AML in CBA mice exposed to radiation with HZE particles (1-GeV or 5-GeV/nucleon iron ions) or protons. Blood cell profiles will be monitored throughout the studies, and gene expression patterns (of the oxidation resistance gene (OXR1) in selected white blood cells, myeloperoxidase in the spleen and CD33 in the bone marrow) will be determined at the end of the studies.

In addition, several short-term animal and cell culture experiments will be performed to determine the effects of radiation treatment and nutritional supplementation on three selected surrogate endpoint biomarkers: the host bio-reduction capacity measured as plasma total antioxidant status, plasma protein carbonyl content, and OXR1 gene expression in selected populations of white blood cells. The results of this study are expected to provide critical information about the feasibility and mechanism(s) of nutritional supplements in increasing the resistance to space radiation-induced malignancy.

Dr. Kennedy's NASA research grant, "Mechanisms by Which Selenomethionine Protects Against Space Radiation Biological Effects," attempts to identify and characterize genes that are likely to be involved in radiation transformation induced by HZE particles and x-rays and the mechanism by which L-selenomethionine is capable of affecting radiation transformation induced by the different types of ionizing radiation.

Her hypothesis is that its ability to regulate the expression of genes involved in the repair of radiation-induced DNA damage will enable L-selenomethionine (SeM) to serve as a countermeasure for HZE particle radiation-induced adverse biological effects. In preliminary studies, treatment with SeM was shown to upregulate ATR and CHK2 gene expression. Upregulation of ATR and CHK2 gene expression may allow the cells to handle HZE particle-induced DNA damage in a particularly efficient manner, resulting in protection against the adverse biological effects associated with DNA damage caused by HZE particle radiation. Results indicate that treatment with 5 micromolar SeM significantly increases the level of ATR mRNA in HTori-3 cells with and without the radiation exposure. Treatment with 5
micromolar SeM also significantly increases the level of CHK2 mRNA in the irradiated HTori-3 cells.

In 1984 Dr. Kennedy received the Radiation Research Society Research Award "...in recognition of her outstanding contributions to our understanding of the quantitative and qualitative aspects of radiation-induced malignant transformation." She received a "MERIT" ("Method to Extend Research in Time") Award in 1987 from the NIH, which established the award system for grants involving research investigations that fulfill the mission and goals of the NIH. She served as a member of the Committee on Public Education on Radiation for the National Council on Radiation Protection from 1980-1986, and as a member of the Committee on the Biological Effects of Ionizing Radiation (BEIR V Committee) for the National Academy of Sciences from 1986-1989, and is currently a member of the National Council on Radiation Protection and Measurements. Selected publications follow. Two of the papers by Kennedy and her colleagues (Kennedy et al., Proc. Natl. Acad. Sci. USA, 1980 and Kennedy et al., Nature, 1984) served as a basis for defining the kinetics of radiation-induced malignant transformation. The data presented in these papers led to the hypothesis that the first event in radiation induced malignant transformation is a high frequency event, likely to be epigenetic in nature, while a later event in radiation induced malignant transformation occurs during division of an irradiated population of cells at a frequency expected for a mutational event. The later event leads directly to the malignant state. These studies suggest that radiation induces genetic instability in a large fraction of irradiated cells, with the instability resulting in an enhanced rate at which transformants subsequently arise in the irradiated population. These studies are widely considered to be the earliest studies in the area of research that is now known as radiation induced genomic instability.

Selected Publications