Fiscal Year:	FY 2012	**Task Last Updated:**	FY 06/04/2012
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Project Title:	NSCOR: NASA Specialized Center of Research on Radiation Carcinogenesis		
Division Name:	Human Research		
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Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
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Human Research Program Risks:	(1) **Cancer**:Risk of Radiation Carcinogenesis		
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Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Task Description:	The goal of this NSCOR is to provide the information required to develop a rational scientific basis for estimation of risks for carcinogenesis in humans from exposure to radiation during space flight. Previous results from this Program found an unexpectedly low RBE value for acute myeloid leukemia (AML) induction by 1 GeV 56Fe ions. Systematic cytogenetic analyses suggested both microdosimetric factors related to the track structure of 1 GeV 56Fe ions and biological factors could account for this observation. In addition, these studies found an unexpected increase in hepatocellular carcinoma (HCC) at doses as low as 0.1 Gy of 1 GeV 56Fe ions but very little, if any, increase following gamma-ray exposure. These data suggest that processes associated with expansion and progression of initiated cells may play a more prominent role in HCC. If this is the case, it is possible that there are qualitative differences as well as quantitative in the effects of HZE irradiations. To expand on these results and to address the overall goal of this NSCOR a series of coordinated activities will conducted in 5 Projects and 3 Cores aimed at: (1) providing quantitative animal tumorigenesis data on the relative effectiveness of specific HZE particles and SPE protons compared with gamma-rays in mouse models of AML and HCC; (2) providing a better understanding of the impact of radiation exposure on the processes involved in the initiation and in the progression of initiated cells toward the neoplastic phenotype; 3) delineating potential differences between low LET radiation and high LET radiation such as those encountered in space travel on these processes; 4) developing links between animal data and radiation-induced effects for AML in humans; and (5) developing biologically-based modeling approaches which are critical to link these biological effects to risks in humans. Program Overview: The Radiation Carcinogenesis NSCOR was initiated in June 2009 and builds upon results obtained in its predecessor, the Leukemogenesis NSCOR. The Radiation Carcinogenesis NSCOR consists of four projects supported by three cores. The projects and cores are briefly described below. Project 1. Dose response relationships for induction of AML and HCC as a function of radiation quality (project leader, Dr. Robert. L. Ullrich). This project is designed to compare the effects of irradiation with gamma-rays, select HZE particles, and protons on the induction of AML and hepatocellular carcinoma (HCC) using the C3H murine model. Project 2. Mechanisms of radiation leukemogenesis (project leader, Dr. Michael M. Weil). The goal of Project 2 is to better understand how radiation leads to AML in a murine model and to generate data for the development of a biologically based model that can be used to predict AML risks from various HZE or high energy proton exposures. Project 3. Pathogenesis of radiation-induced hepatocellular carcinoma (project leader, Dr. Robert L. Ullrich). The overall hypothesis of this project is that the dose response is likely to reflect both quantitative as well as qualitative differences in high LET effects. This overall hypothesis will be tested in 3 specific aims: 1. Quantify the frequency and progression of preneoplastic foci (including both hyperplastic and dysplastic foci) in livers of C3H/HeNCrl mice irradiated with either 137Cs gamma-rays or HZE ions. 2. Examine irradiated liver for evidence of increased oxidative damage and alterations in the regulation of inflammatory processes. 3. Determine tumorigenic effects following HZE and gamma-ray irradiation in murine models of hepatocellular carcinoma in which secondary “promoting” events play a significant role. Project 4. Molecular and cytogenetic targets in murine and human AML. (Project leader, Dr. Michelle Le Beau). This project is designed to develop a cytogenetic and molecular profile of human radiation-induced AML, leading to an understanding of the key events and genetic pathways involved in the pathogenesis of this disease. Core A (Core Director, Dr. F. Andrew Ray). The Biology Core facilitates the distribution of irradiated and control animals, tissues, cells, and other biological samples to investigators. This core is also responsible for conducting the irradiations required at the various sites for all projects. Core B (Core Director, Dr. Michael Story). The Genomics and Biostatistics core provides appropriate genomic analyses, innovative statistical modeling, simulations, and data analyses for the projects. Core C (Core Director, Dr. Robert Ullrich). The Administrative Core provides administrative, fiscal and management support for the Radiation Carcinogenesis NSCOR. This core also oversees the overall scientific conduct of the NSCOR and facilitates interactions between projects, core leaders and project investigators as well as interactions with the internal and external advisors.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This work will provide basic information on mechanisms of carcinogenesis as well as mechanisms specific to radiation-induced cancer.
	Annual Progress Report/ Robert L. Ullrich, PhD. Reporting Period: May 11, 2011-May 31, 2012. Program Overview: The Radiation Carcinogenesis NSCOR consists of four projects supported by three cores. The projects and cores are briefly described below. Details of progress for each project during this reporting period follow this description. Project 1. Dose response relationships for induction of AML and HCC as a function of radiation quality (project leader, Dr. Robert. L. Ullrich). This project is designed to compare the effects of irradiation with gamma-rays, select HZE particles, and protons on the induction of AML and hepatocellular carcinoma (HCC) using the C3H murine model. Project 2. Mechanisms of radiation leukemogenesis (project leader, Dr. Michael M. Weil). The goal of Project 2 is to better understand how radiation leads to AML in a murine model and to generate data for the development of a biologically based model that can be used to predict AML risks from various HZE or high energy proton exposures. Project 3. Pathogenesis of radiation-induced hepatocellular carcinoma (project leader, Drs. Robert L. Ullrich and Yongjia Yu). The overall hypothesis of this project is that the dose response is likely to reflect both quantitative as well as qualitative differences in high LET effects. Project 4. Molecular and cytogenetic targets in murine and human AML. (Project leader, Dr. Michelle Le Beau). This

project is designed to develop a cytogenetic and molecular profile of human radiation-induced AML, leading to an understanding of the key events and genetic pathways involved in the pathogenesis of this disease.

Core A (Core Director, Dr. F. Andrew Ray). The Biology Core facilitates the distribution of irradiated and control animals, tissues, cells, and other biological samples to investigators. This core is also responsible for conducting the irradiations required at the various sites for all projects.

Core B (Core Director, Dr. Michael Story). The Genomics and Biostatistics core provides appropriate genomic analyses, innovative statistical modeling, simulations, and data analyses for the projects.

Core C (Core Director, Dr. Robert Ullrich). The Administrative Core provides administrative, fiscal and management support for the Radiation Carcinogenesis NSCOR. This core also oversees the overall scientific conduct of the NSCOR and facilitates interactions between projects, core leaders and project investigators as well as interactions with the internal and external advisors.

Project 1

The first cohort of the non-irradiated controls reached 800 days on 11/12/2011. In addition, the first cohort of the Fe and Si irradiated animals also reached 800 days and euthanized on 11/12/2011. Remaining animals in each group are being analyzed histopathologically as they are euthanized.

Project 2

Project 2 in the Radiation Carcinogenesis NSCOR is focused on developing a biological model for radiation-induced murine acute myeloid leukemia (rAML) development and determining the effect of radiation dose and quality on each leukemogenic step. The murine model of radiation-induced AML is particularly well suited for this project because the molecular and cytogenetic events involved are becoming increasingly well characterized and AML susceptible and resistant mouse strains are available allowing the use of genetic approaches.

The critical initiating step in murine radiation-induced AML is the biallelic loss of the PU.1 tumor suppressor gene in a hematopoietic cell at the appropriate differentiation stage. The actual differentiation stage of target cell for leukemic transformation (leukemia-initiating cell) is unknown, though it is likely the hematopoietic stem cell (HSC), common myeloid progenitor (CMP) or granulocyte/macrophage progenitor (GMP). We have also found evidence of microsatellite instability (MSI) in radiogenic AMLs, though we don’t know if it is necessary for leukemogenesis. We are developing experiments that will identify the leukemia initiating cell, determine the mechanism(s) leading to PU.1 loss, and determine the role of microsatellite instability in radiation-induced AML leukemogenesis. Our progress over the past year in assay development and completing specific experiments is described below. To place the assays into their experimental contexts, please see last year’s progress report.

Apoptosis in Irradiated Hematopoietic Stem and Progenitor Cells from CBA and C57BL/6 Mice. Several hypotheses have been advanced to explain murine strain differences in susceptibility to radiogenic AML. One possibility is that radiation damaged leukemia initiating cells in susceptible strains are less likely to undergo apoptosis than those in resistant strains. The likely cells at risk for leukemogenic transformation are hematopoietic stem or progenitor cells (HSPC) so over the last year we have quantified apoptosis levels in HSPC cell subpopulations in irradiated CBA/CaJ and C57BL/6J mice.

Mice were irradiated to the whole body with 3 Gy of 137Cs gamma-rays at a dose rate of 1.17 Gy/min. Apoptosis in various bone marrow cell subpopulations was assayed at several post-irradiation time intervals. The irradiations were timed so that the bone marrow cells were always harvested at 11:00 A.M.. To avoid cage effects or day to day variation in the assay, mice for each time point were irradiated on at least two separate days and mice within a single cage were split among at least two time points. At varying times post-irradiation mice were euthanized by CO2 inhalation and their bone marrow cells were collected in RPMI 1640 (Hyclone Thermo Scientific, Logan, Utah). The cells were disaggregated and the cell suspension was treated for 3 minutes with ACK buffer (150 mM NH4Cl, 10 mM KHCO3, and 0.1 mM Na2EDTA) to lyse red blood cells. Cells were plated at approximately 1-2 x 10(6) cells per well in a 96-well plate in FACs buffer (PBS with 2% fetal bovine serum and 0.05% sodium azide) or 1 x 10(7) cells in FACs buffer per snap cap tube. Prior to immunostaining, non-specific antibody binding was blocked by addition of normal mouse serum and unlabeled anti-Fc gammaRIII antibody (clone 24.G2, eBioscience, San Diego, CA), except for wells in which labeled anti-Fc gammaRII/RIII was used, in which case just mouse serum was added. Staining with indirectly and directly conjugated antibodies was done in FACS buffer at room temperature followed by washing. Secondary streptavidin conjugates were added to the cells, incubated at room temperature in FACs buffer, and the cells washed. For assessment of apoptosis, Pacific blue-labeled Annexin V (BD Horizon, San Diego, CA) was added to each well and incubated for 20 minutes at room temperature prior to analysis. In addition, either propidium iodine (PI) or 7-AAD was added to each sample to analyze live verses dead cells. All flow cytometry was done using a Cyan ADP flow cytometer (Beckman Coulter, Fort Collins, CO). Data was analyzed using FlowJo (Tree Star, Inc, Ashland, OR) software. The bone marrow cells were immunophenotyped with anti-Fc gammaRII/III PE (clone 93), anti-ckit/CD117 APC-eFluor 780 (clone ACK2), anti-CD127-biotin and PE (IL-7R alpha, clone A7R34), anti-Sca1 APC (clone D7), anti-CD150 PerCP-eFluor 710 (clone mShad150), anti-CD90.1 APC –eFluor780 (Thy1, clone HIS51), anti-ckit FITC or eFluor 780 (clone 2B8), anti-CD135 PE (Flt-3, clone A2F10), (all from eBioscience), Mouse Lineage Mixture-biotin (Lin, Invitrogen, Camarillo, CA) and anti-CD34 FITC (clone RAM34, BD/Pharmingen).

Common myeloid progenitor cells (CMP) were identified as Lin- IL7R alpha- Sca1- ckit+ CD34+ Fc alphaRII/III lo; granulocyte macrophage progenitors (GMP) as Lin- IL7R alpha- Sca1- ckit+ CD34+ Fc alphaRII/III hi; megakaryocyte-erythroid progenitors (MEP) cells as Lin- IL7R alpha- Sca1- CD34- ckit+ Fc alphaRII/III lo and common lymphoid progenitors (CLP) as Lin- IL7R alpha+ Thy1- Sca1 lo ckit lo.

We initially defined hematopoetic stem cells (HSCs) Lin- IL7R- Sca1+ ckit+/hi CD34- CD150+ CD135+. However, it soon became clear that CBA hematopoietic cells lack Sca1 expression, an observation recently reported by Papathanasiou and colleagues (1). Therefore we modified the panel by inclusion of anti-CD48 (eBioscience) and defined HSC as Lin- IL7R- ckit+/hi CD34- CD150+ CD135+ CD48-.

For CMPs, GMPs, MEPs, and CLPs, between 500,000 – 1,000,000 total bone marrow events were collected per sample. Due to the rarity of the HSC population (predicted as 1:10,000-1:15,000), we collected approximately 10 million events per sample.

Task Progress:

The mice were irradiated with the maximally leukemic dose of 3 Gy and at various times afterwards their bone marrow cells were collected for simultaneous flow cytometric analysis of their differentiation stage and apoptosis status. Apoptosis levels were low for all of the subpopulations and did not differ consistently between the rAML sensitive CBA mice and the rAML resistant C57BL/6 mice. These results suggest that strain differences in susceptible to radiation-induced apoptosis do not account strain differences in susceptibility to rAML.

Chromosome 2 Engineered Mice. Previously we described the rationale and technology for making a panel of mice with chromosome 2 deletions. We isolated three correctly targeted ES cell clones and over the past year we tested one of these clones for germline competency (that is, a clone that generates chimeric founders that can father pups carrying the engineered allele). We found germline competency to be extremely low and have now begun to test the other two target ES cell clones. If one of these turns out to be suitable it will be irradiated and a panel of subclones with chromosome 2 deletions of varying sizes will be established. Selected subclones will be used to generate chromosome engineered mice that will be monitored for the development of AML.

Development of Additional rAML Mouse Models. We are developing or continuing to develop three additional mouse models to study the events involved in radiation leukemogenesis. As described in the previous progress report we are transgressing a green fluorescence protein (GFP) gene that is expressed in hematopoietic cells from C57BL/6-Tg(UBC-GFP)30Scha/J transgenic mice onto a CBA/CaJ background by repetitive backcrossing to the CBA/CaJ strain with selection for the transgene. The mice will be used to study the effects of irradiated stromal cells on leukemogenesis. We are currently on backcross generation N5.

A second mouse model we are constructing is a PU.1 R235C knock-in mouse. This knock-in should be particularly susceptible to rAML and will be useful in uncovering the events in addition to PU.1 activation that are required for radiation leukemogenesis.

At our last NSCOR external advisory panel meeting, we were directed to generate PU.1+/- Ddb2+/- knockout mice and follow them for leukemogenesis. The rationale for this experiment is that while a large deletion on chromosome 2 containing the PU.1 gene leads to AML, simply knocking out one allele of the PU.1 gene does not. This suggests that hemizygous loss of another gene in the deleted region contributes to leukemogenesis, perhaps by facilitating mutation of the remaining PU.1 allele. Ddb2, a DNA damage recognition gene involved in DNA repair, is in the region of chromosome 2 that is commonly deleted in rAML and consequently is a good candidate. If it facilitates the R235 mutation we would anticipate the mice would develop AML.

Development of an Assay for Rare PU.1 R235C Mutations. In order to determine when the PU.1 R235C mutation occurs during radiation leukemogenesis and the cells that are affected we need to develop an assay that can detect that mutation in one cell among many cells not carrying the mutation. We are developing an assay in which the wild type allele is removed from the DNA sample being assayed by digestion with a restriction endonuclease (BbvI) that recognizes the wild type allele but not the mutant allele. The mutant allele is further enriched by COLD-PCR techniques and identified by high-resolution melt analysis. We tested this approach with mixtures of DNA that contain known amounts of the mutant allele from an AML cell line. The assay can detect mutations that are present in the starting mix at <1%. The next step in assay development will be to perform the COLD-PCR step as small pool PCR which should give a detection sensitivity on the order of 2 mutant alleles in 105 wildtype alleles per 384-well plate.

Reference List

1. P. Papathanasiou, R. Tunningley, D. R. Pattabiraman, P. Ye, T. J. Gonda, B. Whittle, A. E. Hamilton, S. O. Cridland, R. Lourie and others, A recessive screen for genes regulating hematopoietic stem cells. Blood 116, 5849-5858 (2010).

Project 3

In the fall of 2010, 60 mice were irradiated for Project 3. Our original design was to perform serial sacrifice studies for liver tissue analysis at 6, 9, and 12 months after irradiation following 3 Gy of gamma rays or 0.1 Gy of 1 GeV Iron based on our previous studies. Surprisingly, we are observing liver tumors much earlier than expected. As a result we added a sacrifice time point at 3 months post irradiation. Based on our results we may add a 1 month time point.

We have added analysis of liver tumors in the main groups as well. These include livers from non-tumor bearing animals. Tumor and adjacent tissues in tumor bearing animals and in tumors that have metastasized are undergoing analysis. To date metastases have only been found in heavy ion irradiated mice. We have also begun to examine state-of-the art 3-dimensional imaging of tumors and surrounding stroma. Also we are exploring techniques for transplantation of hepatocytes into livers of other mice. With this technique clonal outgrowths can be identified and analyzed. This also allows us to examine effects of irradiation of the host liver on cells from donor.

Project 4

The overall goal of Project 4 is to develop a cytogenetic and molecular profile of human radiation-induced myeloid neoplasms (t-MN), and to elucidate the key events and genetic pathways involved in the pathogenesis of this disease. To this end, we proposed to profile the genetic alterations in radiation-induced t-MN by (1) Cytogenetic analysis; (2) High-density SNP array analysis of copy number alterations and loss of heterozygosity; (3) Gene expression profiling; (4) Analysis of promoter methylation; and (5) miRNA expression profiling. As described below, we have elected to replace some of the above technologies with transcriptome and whole genome sequencing.

Exposure to ionizing radiation is associated with the development of therapy-related myeloid neoplasms (t-MN). Several distinct clinical and cytogenetic subtypes of t-MN have been recognized and found to be closely associated various cytotoxic therapies, such as alkylating agents, anti-metabolites, and DNA topoisomerase-II inhibitors. However, the characteristics of t-MN that follow radiation therapy (RT) alone are not as clear. To characterize this subgroup of t-MN, we examined the clinical, epidemiologic, and cytogenetic characteristics of 72 cases of t-MN in patients who received RT alone for an antecedent disease at the University of Chicago.

Sixty-five (90%) patients had had a primary solid tumor, 5 had had a primary hematologic malignancy (4 Hodgkin lymphoma), and 2 had received RT for non-malignant disorders (acne; hydatiform mole). Prostate and testicular cancers were the predominant primary tumors (39%). Breast (21%) and gynecological cancers (18%, including ovarian, cervical, endometrial, and vaginal cancers) were also common. There were 36 women and 36 men; 51 patients were white (71%), 10 were African American (14%), 1 was an Asian American (1%), and race/ethnicity was unrecorded in the remaining ten patients.

The median time from diagnosis of t-MN to death was 0.9 years (95% confidence interval (CI), 0.6-1.2 years). Sixty-one patients had one or more clonal cytogenetic abnormality (85%) at diagnosis of t-MN; 11 (15%) had no detectable abnormality. Most common (39 patients, 54%) were loss or deletion of chromosome 5 (n=19), 7 (n=9), or both (n=11). Eleven patients (15%) had recurring balanced translocations previously reported in t-MN; 3 with inv(16), 4 with t(15;17), and 3 with t(21q22). Eleven patients (15%) had other clonal abnormalities. Survival according to cytogenetic subgroups was determined. Patients with a normal cytogenetic pattern or recurring balanced translocations survived longer (log rank, p=0.008). t-MN with clonal abnormalities of chromosome 5, 7, or both had a poor median survival of 0.6 years (95% CI, 0.3-1.0 years) compared to other cytogenetic groups. There was no association between age at diagnosis of t-MN and overall survival. We reviewed treatment records for 47 patients who received therapy for t- MN -- either supportive care, chemotherapy alone, or chemotherapy with hematopoietic cell transplant. There was a trend towards better survival with higher intensity treatment, but it was not statistically significant (p=0.065).

In summary, our analysis revealed that t-MN following RT alone bears clinical and cytogenetic similarities to alkylator-associated t-MN with frequent clonal abnormalities of chromosomes 5 and/or 7, relatively long latency of 5-10 years, and poor outcomes even with intensive therapy. However, some patients who develop t-MN after RT alone have recurring, balanced chromosomal translocations or normal karyotypes. These patients have a shorter latency, better response to anti-leukemia treatment, and longer survival. This work was reported at the 2011 annual meeting of the American Society of Hematology.

To determine the genetic profile for t-MN, we performed transcriptome sequencing on 22 patient samples, and SNP array analysis on 35 samples, half of which were characterized by -7/del(7q) (collaboration with Dr. Kevin White, University of Chicago). Given the high frequency of -7/del(7q), in radiation-induced t-MN, and the adverse prognosis associated with this cytogenetic subgroup, we focused initially on the analysis of this subgroup of t-MN. Copy number analysis identified a 2.17 Mb commonly deleted segment on chromosome band 7q22.1, containing CUX1, a lineage-determining transcription factor normally expressed in hematopoietic stem cells. In addition, CUX1 was disrupted by a translocation resulting in an out-of-frame, chimeric fusion transcript in one patient. Moreover, CUX1 was expressed at haploinsufficient levels in t-MN with a -7/del(7q). To test the tumor suppressor activity of CUX1, the Drosophila homologue, CUT, was knocked-down in Drosophila melanogaster hemocytes, which led to melanotic tumor formation and increased numbers of hemocytes (the Drosophila equivalent of myeloid leukemia). These data suggest that CUX1 is a conserved tumor suppressor associated with -7/del(7q). To extend this work to radiation-induced t-MN, we have identified 13 cases from the series described above for which we have cryopreserved leukemia samples (germline tissue is available in a subset of these cases). We have extracted DNA and submitted samples from 5 cases to the Beijing Institute for Genomics for whole genome sequencing, and anticipate receiving the raw data for analysis within three months. Our research plan for the next year is to analyze additional radiation-induced t-MN samples depending the results of the initial series, and to perform functional analysis of candidate genes identified from these analyses.

Core A: Irradiation and Tissue Acquisition. Core A personnel have irradiated all mice for project 1. Animals are monitored over an 800 day time period and moribund and tumor bearing animals are euthanized. All animals are removed for necropsy based on clinical signs and symptoms of AML or HCC, other tumors, or when moribund. When animals reach 800 days post-irradiation they are being euthanized and examined for tumors. The first of the non-irradiated controls group reached 800 days on 11/12/2011. The first cohort of the Fe and Si irradiated animals also reached 800 days and euthanized on 11/12/2011. Other groups will reach 800 days at various times throughout the next two years.

Core B: Genomics. Data Analytics: All genomic/epigenomic data can now be placed in a user accessible database from remote locations. As part of data integration probe alignments can now be performed across 7 gene expression platforms with miRNA platforms (Illumina, Exiqon) ready shortly. The next generation sequencing data analysis pipeline is also running, including Chip-seq, DNA-seq, RNA-seq and shRNA-seq are operational. Joint modeling (Xie et al, Stat in Med, 2010) is available for integration of DNA copy number variation (CNV) and gene expression. We could consider developing a Carcinogenesis database and placing it on the UTSW cluster. That cluster is available now for outside access. It consists of a 36 CPU cluster and 84 Tbytes of storage with tape backup. Various statistical tools reside within the database confines which would be available for users to interrogate data.

Leukemia Genomics: To date 12 CBA splenic tumors have been examined for CNV. A common deletion of 34 Mb has been identified with very little in the way of CNV in other regions of the genome. This 34 Mb region contains Pu.1 (Sfpi1) and some 20 other genes and one miRNA (miR-130a). There are also two zinc fingers, the MADD gene (MAP-kinase activating death domain) and DDB2 (DNA damage binding protein 2), a gene associated with DNA repair. It must be kept in mind that these are single copy losses and gene expression will confirm a gene dosage effect. Our early gene expression analysis showed that PU.1 as actually upregulated over 2-fold. This comparison was against CD34+ cells and it was suggested that at the annual review that these were not necessarily the most appropriate control cell to use. We are in the process of obtaining CD117+ cells, which the review panel suggested was a more appropriate control. In common with the human AML analysis we also see a 20-fold reduction in the EGR1 gene, however, with all of our gene expression analysis we await the appropriate control (CD117+). It was suggested by the external advisory panel that also examine miRNA in the leukemia cells generated from C3H mice. This is an expensive goal and it may require some re-budgeting or re-prioritization.

Hepatocellular Carcinoma Genomics: Samples for gene expression, CNV, miRNA and methylation are being acquired. We will await the capture of all samples before we begin the appropriate analyses. This will be in the next grant year.

Core C Administrative Core. Core C ordered all animals for irradiations described above and planned and coordinated the NSCOR annual meeting on September 24th and 25th.

Bibliography Type: Description: (Last Updated: 07/25/2021)

Abstracts for Journals and Proceedings	Weil MM, Ray A, Bacher JW, Bedford JS, Steffen LS, Ding L, Bielefeldt-Ohmann H, Genik PC, Yu Y, McCarthy M, Fallgren CM, Story MD, Ullrich RL. "The Radiation Carcinogenesis NSCOR." To be presented at the 23rd Annual NASA Space Radiation Investigators' Workshop, Durham, NC, July 8–11, 2012. Program and abstracts. 23rd Annual NASA Space Radiation Investigators' Workshop, Durham, NC, July 8–11, 2012. In press, as of June 2012. , Jun-2012
Abstracts for Journals and Proceedings	Weil MM, Ray A, Bacher JW, Story MD, Bedford JS, Le Beau MM, Ullrich RL. "The Radiation Carcinogenesis NSCOR." Presented at the 22nd Annual Space Radiation Investigators' Workshop, League City, TX, September 18-21, 2011. 22nd Annual Space Radiation Investigators' Workshop, League City, TX, September 18-21, 2011. http://www.dsls.usra.edu/meetings/radiation2011/pdf/7063.pdf , Sep-2011
Articles in Peer-reviewed Journals	Chen M, Xie Y, Story M. "An exponential-gamma convolution model for background correction of Illumina BeadArray data." Communications in Statistics - Theory and Methods. 2011 Sep;40(17):3055-69. http://dx.doi.org/10.1080/03610921003797753 , Sep-2011