Thursday, February 13, 2014
POSTER SESSION II: SPACE RADIATION — CANCER AND DEGENERATIVE
8:00 a.m. Expo Hall A1-A2

Todorova P. Gillam M. Gil del Alcazar C. Ilcheva M. Story M. Bachoo R. Burma S.
Deletions of Ink4, Arf, p53, or Pten Cooperate with HZE Particle-Induced DNA Double-Strand Breaks to Trigger High Grade Gliomas in Mouse Models **[#3011]**
We are using transgenic mouse glioblastoma models to understand the tumorigenic potential of an array of charged particles; we are also identifying the underlying genetic changes driving gliomagenesis and the cell types in the brain that are most susceptible to transformation by ionizing radiation.

Hyrciw G. Grygoryev D. Ohlrich A. Dan C. Lasarev M. Gauny S. Kronenberg A. Turker M.
Induction of Radiation Signature Mutations In Vivo with Charged Particles at Low Fluence **[#3025]**
The cancer risks from charged particles in the space environment are not well defined, particularly at low fluence. We show that fluence as low as 1 for Fe and Ti ions induces cancer-relevant mutations in the mouse, which argues against a lower threshold for mutations induced by these heavy ions.

Zhu J. Su F. Asaithamby A.
Suppression of Genome Instability in Response to Space Radiation is Mediated by Fanconi Anemia Pathway **[#3060]**
Fanconi anemia factors coordinate the processing of clustered DNA lesions to suppress cellular transformation in response to galactic cosmic rays exposure.

Witawat Jangiam W. J. Montree Tungjai M. T. Kanokporn Noy Rithidech K. R.
Inflammatory Responses and Aberrant Patterns of DNA Methylation in the Liver of Mice Exposed Whole-Body to Titanium (^{48}Ti) Ions **[#3091]**
We detected chronic inflammatory responses and aberrant patterns of DNA methylation in the liver of mice exposed to ^{48}Ti ions. Since these two biological endpoints are known to be linked to cancer induction, our findings suggest that exposure to ^{48}Ti ions during space flights may pose health risks.

Li Z. Hudson F. Z. Huang H. Wang Y. Murnane J. P. Dynan W. S.
A Genomic Stress Response as a Novel Mechanism Leading to Chromosomal Instability in Heavy Particle-Irradiated Cell Populations **[#3138]**
High charge and energy particles, a main component of cosmic rays, cause complex damage to living systems, which leads to both direct and indirect effects. One of these indirect effects is to compromise the accuracy of the DNA repair machinery, sensitizing cells to future genotoxic insults.

Grygoryev D. Dan C. Gauny S. Eckelmann B. Ohlrich A. P. Connolly M. Lasarev M. Grossi G. Turker M. Kronenberg A.
Autosomal Mutants of Proton-Exposed Kidney Cells Display Loss of Heterozygosity on Other Chromosomes **[#3214]**
Clarifying mechanisms that contribute to cancer risk from space radiation is critical. This study shows that proton-induced changes at autosomal loci can arise by a genome-wide incident that causes loss of heterozygosity generating mutations on multiple chromosomes.

Patel Z. S. Kidane Y. H. Huff J. L.
Radiation Quality Effects on Transcriptome Profiles in 3-D Cultures After Charged Particle Irradiation **[#3260]**
We use gene set enrichment analysis to evaluate the differential effects of low- and high-LET radiation on 3-D organotypic cultures and quantify radiation quality impacts on gene expression and cellular responses.

Porada C. D. Soland M. Moon J. Rodman C. Soker S. Walker S. J. Almeida-Porada G. Wilson P. F.
The Role of the Bone Marrow Microenvironment in Space Radiation-Induced Leukemogenesis **[#3278]**
Astronauts in deep space will be exposed to constant bombardment with radiation in the form of GCR and intermittent SPE. We examined the direct effects of SPE/GCR on primitive hematopoietic cells, and the indirect effects on hematopoiesis due to SPE-GCR-induced alterations in the marrow niche.

Moding E. M. Min H. D. Castle K. D. Lee C. L. Kirsch D. G.
An Extra Copy of p53 Suppresses Initiation of Kras-Driven Tumors but not Radiation-Induced Lymphomas **[#3288]**
To investigate the role of p53 in carcinogenesis following exposure to space radiation, we exposed mice with an extra copy of p53 to X-rays and iron ions. We observed that an extra copy of p53 suppresses initiation of oncogene-driven lung cancers and lymphomas but not radiation-induced lymphomas.

Werner E. Tang K. X. Wang H. Doetsch P. W.
The Role of Persisting Phenotypes on Radiation-Induced Genomic Instability **[#3187]**
Radiation-induced reactive oxygen species and p38 MAPK-driven responses have opposite effects on the expression of genomic instability in the progeny of exposed cells.

Ray F. A. Robinson E. Cornforth M. N. Bedford J. S. Goodwin E. H. Bailey S. M.
Development of a New Improved Biodosimetry Method for Measuring Previous Exposure to HZE Radiation **[#3198]**
We developed a technique to measure a type of chromosome damage that was previously difficult to measure, i.e. inversions, we found a robust dose response when human lymphocytes were exposed to HZE compared to low LET radiation. Improvements to increase the sensitivity even further are underway.

Sridharan D. M. Chappell L. Clunn D. Enerio S. Garbe J. Stampfer M. Pluth J. M.
Role of Age, Radiation Quality and Genetic Background on Levels of Surrogate Cancer Biomarkers **[#3311]**
One of NASA's primary goals is to improve the understanding of the carcinogenic process related to high LET exposures to better define risk.

Lee C.-L. Moding E. J. Castle K. D. Blum J. M. Min H. Rodrigues R. C. Williams N. Ma Y. Borst L. Kim Y. Kirsch D. G.
The Tumor Suppressor P53 Acts During Total-Body Irradiation to Decrease Hematopoietic Stem/Progenitor Cell Fitness and to Promote Lymphoma Development **[#3313]**
Exposure to ionizing radiation can cause acute toxicity and long-term side effects, such as radiation-induced cancer.

Rampersad R. Onaitis M.
Fractionated High LET Iron Irradiation Effects on K-RasG12D-Induced Tumor Progression **[#3317]**
The second project in the Duke NSCOR is to examine cell-of-origin of high-LET-induced lung cancer. We have found increased tumor progression at eight weeks after fractionated iron irradiation of mice expressing K-RasG12D in Type II cells.

Story M. D. Ding L. H. Park S. Minna J. D.
The Radioresponse of Normal Human Bronchial Epithelial Cells to Charged Particle Exposures of Increasing Mass, Energy and LET **[#3327]**
At the transcriptional level, HBEC cells respond roughly as a function of the LET of the incident particle. Furthermore, HZE particles initiate the carcinogenic process at very low doses. These transformed HBECs exist in an environment of oxidative stress; however, they are not oncogenic.

Lima F. Ding D. Goetz W. Wang A. J. Yu L. Baulch J. E.
High LET ^{56}Fe Ion Irradiation Induces Tissue Specific Changes in DNA Methylation in the Mouse **[#3329]**
The results of this study are the first to demonstrate in vivo high LET ^{56}Fe ion irradiation induced changes in DNA methylation in the mouse that are tissue and locus specific, and dose and time dependent.

Sasi S. P. Park D. Walsh K. X. Carrozza J. P. Jr. Yan X. Goukassian D. A.
Low Dose Space Radiation Affects Long-Term Survival of Bone Marrow Progenitor Cell Populations **[#3067]**
Our ten months-long studies showed that despite an initial 1H-IR-induced increase in the number of bone marrow progenitor cell populations, both 1H-IR and ^{56}Fe-IR have profound and long-lasting, >50% decreases in these cells up to 7–10 months. The function of the surviving fraction remains unknown.

Alwood J. S. Tran L. H. Kumar A. Limoli C. L. Globus R. K.
Effects of Heavy-Ion Irradiation on Ex Vivo Osteoblastogenesis, Oxidative Stress Response, and Cancellous Bone Microarchitecture **[#3296]**
We hypothesize that exposure to heavy-ion radiation damages osteoblast progenitors via oxidative stress and that damage may contribute to imbalanced bone remodeling during long-duration space travel beyond the protection of the Earth's magnetosphere.