

Cooperation and Coordination of the Previous DOE Low-Dose Program and Research at NASA

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Developing a Long-Term Strategy for
Low-Dose Radiation Research in the United States

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Introduction

- NASA collaboration with DoE radiobiology research is rooted in use of Lawrence Berkeley National Lab (LBL) BEVALAC facility for heavy ion experimentation in the 1980's.
 - NASA funded investigator's pursued experiments at LBL and NASA benefitted from DoE funded studies related to normal tissue toxicity in cancer therapy with heavy ion beams.
- The demise of the BEVALAC in the early 1990's led NASA to fund the construction of the NASA Booster Accelerator Facility (BAF) at DoE's Brookhaven National Lab (BNL).
 - NASA funded construction at cost of \$34.1 Million with annual operation costs from \$6 M to \$10 M dependent on number of users (beam hours).
 - BAF construction started in 1998 with completion in June of 2003.

MEMORANDUM OF UNDERSTANDING
BETWEEN
NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
AND
U.S. DEPARTMENT OF ENERGY
REGARDING
ENERGY-RELATED CIVIL SPACE ACTIVITIES

I. PURPOSE

This Memorandum of Understanding (MOU) establishes the role of the Department of Energy (DOE) in supporting the National Aeronautics and Space Administration (NASA) civil space mission and the process for defining and implementing activities between the two agencies.

II. BACKGROUND

NASA, the U.S. civil space agency, is responsible for defining, designing, developing, launching and operating the Nation's civil spacecraft and space-related facilities. DOE's civil space activities support the NASA civil space mission in the DOE mission areas of energy and energy-related research and development (R&D), fundamental science and environmental technology, and the advanced technology development capability which underlies these, as well as science, engineering, and mathematics education.

DOE, its National Laboratories, and NASA have worked together for over 30 years in space science and applications, exploration, and technology development. Presidential National Space Policy Directives encourage DOE to expand its role in several areas, such as space exploration, space-based global change observation, remote sensing, space launch technology, commercialization, and associated international cooperation. Close collaboration between NASA and DOE will enhance the effectiveness of programs in both agencies.

III. POLICY

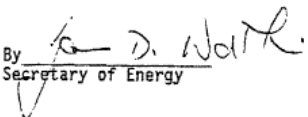
In areas consistent with NASA's civil space responsibilities and DOE's missions and capabilities, collaborative efforts between the two agencies will be pursued. This includes the following areas:

X. TERMINATION

This MOU may be terminated by mutual agreement of the NASA Administrator and the Secretary of Energy or by either party upon three months written notice to the other.

By 
Administrator
National Aeronautics and
Space Administration

Date: July 9, 1992

By 
Secretary of Energy

Date: July 9, 1992

INTERAGENCY AGREEMENT
BETWEEN the
OFFICE OF BIOLOGICAL AND ENVIRONMENTAL RESEARCH
U.S. DEPARTMENT OF ENERGY
And the
OFFICE OF BIOLOGICAL AND PHYSICAL RESEARCH
NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

I. PURPOSE

The purpose of this IAA is to establish formal scientific collaboration between the Office of Biological and Physical Research (OBPR) of the National Aeronautics and Space Administration and the Office of Biological and Environmental Research (OBER) of the U.S. Department of Energy. The major goals of this collaboration are: (a) to increase basic knowledge of living systems and their response to radiation exposure, (b) to increase the base and breadth of the group of scientists involved in radiation biology research, (c) to apply knowledge gained through collaboration to radiation protection and risk assessment, and (d) to exchange ideas and technology applicable to problems common to OBPR and OBER. Close collaboration between NASA and DOE will enhance progress in understanding and predicting the effects and health risks resulting from low-dose, low-fluence radiation.

II. SCOPE

The principal objective of this IAA is to establish collaborative science planning and joint funding of basic radiation research and technology relevant to common programs.

III. APPLICABILITY

This IAA applies to all activities between OBPR and OBER and is consistent with, and based upon, the Memorandum of Understanding (MOU) between NASA and DOE signed on July 9, 1992.

IV. BACKGROUND

The last decade has witnessed a revolution in our understanding of how cells grow and divide. Experiments on yeast, embryos, and cultured mammalian cells have molded seemingly disparate viewpoints into a unified philosophy of the cell cycle in plants, animals, and bacteria. A growing understanding of how deoxyribonucleic acid (DNA) is synthesized and chromosomes are replicated, of how the integrity of genetic information is preserved, and of how cell size and environmental signals regulate the cycle of growth and division, is providing hitherto unavailable insights into the mechanisms of processes vital to human health.

The human health outcome after exposure to ionizing radiation depends on a multitude of factors. Among the most important are physical characteristics of the radiation itself including dose, dose rate, and rate of energy deposition along a particle trajectory ("linear energy transfer" or LET). Biological factors include age or health status of the person at time of exposure, specific tissues or organs irradiated, etc. Thus the same dose delivered by different types of radiation may result in a different biological outcome, and by the same token, different individuals exposed to identical radiation fields may experience

Nature of DoE-NASA Cooperative Projects under IAA

The following cooperative efforts were identified by NASA OBPR and DoE OBER:

- Cooperative arrangements for funding of research that is consistent with the needs, merit and goals of the programs within OBPR and OBER;
- Cooperative arrangements for funding of research to increase the base and breadth of the group of scientists involved in radiation biology research;
- Cooperative arrangements for use of charged particle accelerators with capabilities for simulating radiation exposures;
- Joint sponsorship of workshops to identify specific research opportunities of interest to both OBPR and OBER; and
- Cooperative arrangements for exchange of technology, including biotechnology, of relevance within the context of this Inter-Agency Agreement.

Process and Focus

- From 2003 to 2010 NASA would consider proposals scored by a DoE peer-review panel in the “fundable range” for possible NASA joint funding with DoE.
 - Initial IAA developed by Dr.’s Marv Frazer and Noelle Metting (DoE) and Walter Schimmerling (NASA).
- Grants selected for joint funding would be managed by DoE with NASA transferring funds to DoE (\$ 1 M to \$ 2 M per year).
- An exception was DoE provided partial funding of two NASA Specialized Centers of Research (NSCORs) at UTMB (R. Ullrich) and UTSW (J. Minna).
- The NASA Space Radiation Initiative (SRI) started in 2003 in conjunction with operation of BNL NSRL Facility with over 50 Grants and 6 project grants at the peak, however NASA radiobiology funding was steadily reduced after 2010.
- The reduction of funds at NASA for radiobiology research after 2010 along with the end of DoE Low Dose Program solicitations eliminated opportunities for joint projects at that time.

Process and Focus- Continued

- The types of radiation and dose range of concern for NASA are quite different from DoE Low Dose or NCI (oncology) interests, however strong overlap occur on endpoints, science approaches and development of relevant model systems.
- NASA science interest in DoE Grants included:
 - Discovery of mechanisms of biological damage related to cancer development by radiation.
 - Systems biology models of cancer and other radiation risks.
 - Science of individual radiation sensitivity.
 - Development of experimental systems sensitive at low radiation exposure levels.
 - Biological countermeasures.
- Inter-agency process, included attracting DoE grantees to expand to the use of heavy ion beams at BNL as part of their science objectives.
 - However not a prerequisite for NASA interest.

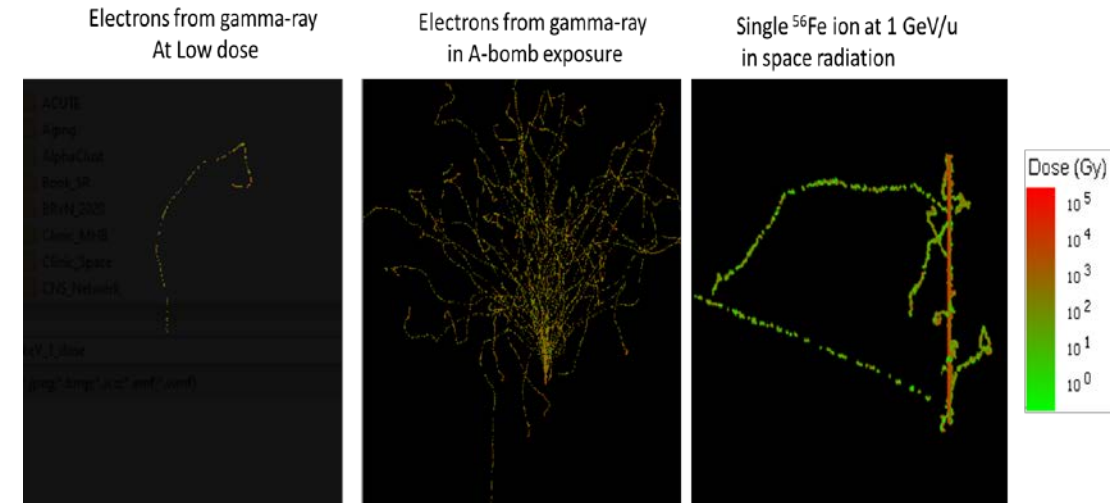
Jointly Funded Grants

PI last_name	Title	start_date	grant_number	solicitation
Balmain	Identification of Mouse Genetic Susceptibility to Radiation Carcinogenesis	10/1/03	DE-FG02-03ER63630	OSN 03-07
Redpath	Low dose suppression of neoplastic transformation in vitro	10/1/03	DE-FG02-03ER63648	OSN 03-07
Kohwi-Shigamastu	SATB1 deficiency accounts for high susceptibility to low dose radiation	10/1/02	LBNL 441B01	OSN 03-07
Green	Low Dose gamma irradiation potentiates secondary exposure to gamma rays or protons in thyroid tissue analogs	10/1/02	DE-FG02-03ER63448	OSN 03-07
Ford	Low Dose Response of respiratory cells in intact tissues and reconstituted tissue constructs	10/1/02	DE-FG02-03ER63438	OSN 03-07
Cornforth	Cytogenic response to low doses of ionizing radiation	10/1/02	DE-FG02-03ER63442	OSN 03-07
Ackerman	Effects of Low Doses of Radiation DNA Repair	10/1/02	PNNL 42699	OSN 03-07
Sutherland	DNA Damage clusters in low level radiation responses of human cells	10/1/02	BNL BO-113	OSN 03-07
Gridley	Mechanisms of Low Dose Radiation-Induce T Helper Cell Function	7/1/05	DOE2005_03	OSN-04-XX
Hall	Individual Genetic Susceptibility	10/1/03	DE-FG02-03ER63441	OSN 03-07
Engelward	Mechanisms of Low Dose Radio-Suppression of Genomic Instability	7/1/05	DOE2005_2	OSN-040XX
Wang	Proteomic and Biochemical Studies of Human Mesenchymal Stem Cells in Response to Low Dose Ionizing Radiation	7/1/05	DOE2005_06	OSN-04-XX
Cucinotta	Radiation Sensitivity and Processing of DNA Damage Following Low Doses of Gamma-Ray, Alpha Particles, & HZE Irradiation of Normal DSB Repair Deficient Cells	7/1/05	DOE2005_1	OSN-04-XX
Kohwi-Shigamastu	The Effect of Low Dose Ionizing Radiation on Epigenetic Changes in Chromatin	7/1/05	DOE2005_05	OSN-04-XX
Zimbrick	Transgenerational Effects of Chronic Low Dose Irradiation in a Medaka Fish Model System	7/1/05	DOE2005_07	OSN-04-XX
Jirtle	Imprinted Genes and Transposons: Epigenomic Targets for Low Dose Radiation Effects	7/1/05	DOE2005_04	OSN-04-XX

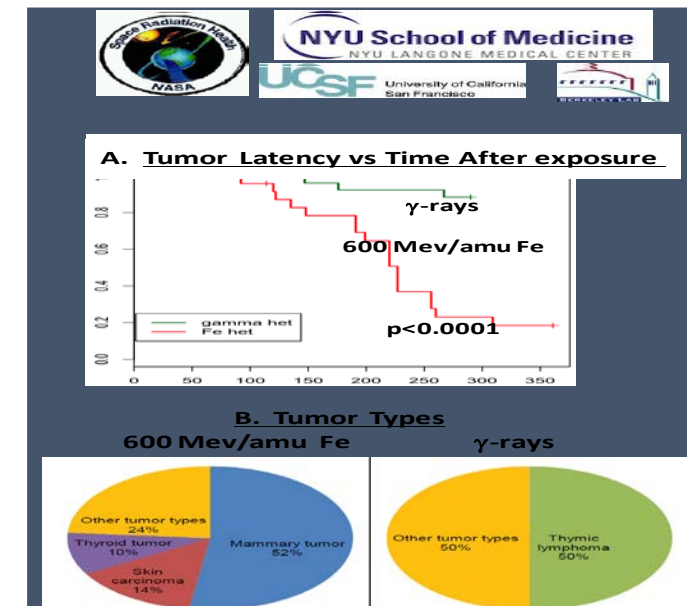
PI	Institute	Title	Year	DoE Solicitation
Woloschak, Gayle	Northwestern University	Radioprotectors and Tumors: Molecular Studies in Mice	2006	DE-
Cornforth, Michael	Texas, U of Medical Branch	Heritable Genetic Changes in Cells Recovered From Irradiated 3D Tissue Constructs	2006	DE-
Sutherland, Betsy	BNL	Mechanisms of Human Skin Responses to Low Radiation Doses and Dose Rates	2006	DE-
Amundson, Sally	Columbia University	Mechanistic and Quantitative Studies of Bystander Responses in 3-D Human Tissues for Low-Dose Radiation Risk Estimation	2006	DE-
Green-1, Lora	Loma Linda University	The Contribution of Tissue Level Organization to Genomic Stability Following Low Dose/Low Dose Rate Gamma and Proton Irradiation	2006	DE-
Dynan, William	GEORGIA RES INST., INC., MEDICAL COL. OF	Links Between Persistent DNA Damage, Genome Instability, and Aging	2008	DE-FG02-09ER64788
Boothman, David	UT SOUTHWESTERN MEDICAL CTR	Low Dose IR Activation of TGF-Beta 1-IGF-1-sCLU In Vivo: Mechanisms, Functions of a Changing Microenvironment	2008	DE-FG02-09ER64789
Spitz, Douglas	IOWA, UNIVERSITY OF	Mitochondrial-Derived Oxidants and Cellular Responses to Low Dose/Low LET Ionizing Radiation	2008	DE-FG02-09ER64801
Limoli, Charles	CALIFORNIA, UNIV. OF IRVINE	Neurodegeneration and Adaptation in Response to Low-Dose Photon Irradiation	2008	DE-FG02-09ER64798
Fornace, Albert	Georgetown University	A Metabolomics and Mouse Models Approach to Study Inflammatory and Immune Responses to Radiation	2008	DE-FG02-09ER64790
Cucinotta, Francis	NASA- Johnson Space Center	Systems Biology Model of Interactions Between Tissue Growth Factors and DNA Damage Pathways: Low Dose Response and Cross-Talk in TGFbeta and ATM Signaling	2008	DE-AI02-09ER64843
Globus, Ruth	NASA -Ames Research Center	Oxidative Stress and Skeletal Health with Low Dose, Low LET Ionizing Radiation	2008	DE-AI02-09ER64784
Goldstein, Lee	Boston University	Non-Invasive Early Detection and Molecular Analysis of Low X-ray Dose Effects in the Lens	2008	DE-FG02-09ER64797
Wu, Honglu	NASA- Johnson Space Center	Systematic Identification of Genes and Signal Transduction Pathways Involved in Radio-Adaptive Response	2008	DE-AI02-09ER64793

Science Highlights

- Cosmic rays are qualitatively different from gamma-rays or x-rays, however methods used to investigate the science is similar.
 - Epidemiology plays minimal role for astronaut risk and theoretical approaches based on experiments needed.
- The nature of complex DNA damage was advanced in several grants most notably Betsy Sutherland at BNL.
- The mechanistic basis for non-targeted effects (NTE) received extensive evidence in support of their important role at low dose:
 - Evidence that high LET radiation leads to detrimental NTEs, while low LET has beneficial NTEs in some contexts.
- Studies of several important genetic factors that lead to differences in radiation sensitivity for cancer and cataract risks.
- System biology approaches were advanced through several grants and special workshops jointly hosted by DoE, NASA, European Union (EU) and the Japan (RIKKEN).
 - Evidence on bio-molecular pathways involved in genomic instability and tissue controls on DNA damage responses, ROS responses, bioinformatic methods, etc.



Cosmic rays produce qualitatively different biological damage compared to from gamma-rays



Other Inter-Agency and International Activities

- Joint solicitation by National Cancer Institute (NCI) with NASA on genomic instability in the 1990s using a similar model at DoE-NASA activity.
- Other inter-agency activities include monthly across agency RADRAT team organized by NCI's Norm Coleman and infrequent joint workshops.
- Prospect of Heavy Ion therapy in USA suggests DoE-NCI and possible NASA activities.
- The European Union (EU) and DoE have a long history of joint workshops with DoE that has greatly suffered in the last decade with systems approaches a major causality.
 - NASA benefitted from EU research collaborations through interaction with DoE and also benefited in past from collaboration with research agencies in Japan and the European Space Agency.

Current Obstacles

- Recent changes at NASA include a shift in policy to allow higher radiation risks to astronauts, and has down-played the role of uncertainties in risk estimates.
 - In the past NASA has used estimate of Uncertainties in risks projections as part of operational radiation protection, which couples research to practical policies.
 - Cancer risk limit possible protects against non-cancer risks. However there is a proposal to have “waivable” limits for astronauts.
- Reduction in funding at NASA for radiobiology research after 2010 inhibits joint funding with other agencies.
- Role of internal DoE lab investigators is greatly reduced in last decade.
 - PI’s from LBL, BNL and Pacific Northwest Lab played an important role in earlier program, including research in support of NASA goals and interests.
- International collaboration with EU or others non-existent at this time.