Very few medical products exist to counter the variety of acute and long-term injuries that can result from nuclear or radiological attacks. In addition, there is currently no rapid means to detect the radiation dose that an individual may have received. The threat of nuclear or radiological attacks has grown in recent years, with increased activity of global terrorist organizations and a rise in illicit trafficking of radioactive materials. To expand the medical options available to prevent or treat radiation-induced injury, and thereby help minimize the terrorist threat, as well as develop effective countermeasures and biodosimetry triage tools, the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) established eight cooperative Centers for Medical Countermeasures against Radiation (CMCRs) in September 2005.

The CMCRs are intended to serve as multidisciplinary, extramural research centers comprised of academic, commercial, and government laboratories that are funded to: 1) move candidate countermeasures through the regulatory process into the national stockpile; 2) develop new techniques and devices to provide accurate dose assessment in a triage scenario; 3) conduct basic and translational research to identify new countermeasures; 4) develop and validate new animal models or in vitro assays to evaluate countermeasures or underlying biology; and 5) provide new or expanded education resources to improve expertise in radiobiology.

Each CMCR participates as a member of the CMCR network, which includes all CMCR awardees (principal investigators) as well as other NIAID-designated partners such as U.S. federal government laboratories and/or private companies. The CMCR network facilitates interactions among the awardees and assists in interactions with regulatory and public health organizations. The Centers network is governed by a CMCR Steering Committee, charged with coordinating and facilitating research activities for the overall program.

The CMCR program is designed for optimal research flexibility, synergy, and efficiency with the goal of rapidly developing effective countermeasures and/or biodosimetric tools for clinical use. The program is milestone based, and includes the flexibility to quickly redirect or replace research projects during the funding period. The Cooperative Agreement mechanism (U19) is used to support the work of multi-investigator teams with a scope of activities not possible with other funding mechanisms. Synergistic interaction with other Centers and the NIH will be a key feature. Each Center provides unique and complementary strengths in terms of technical potential and specific areas of investigation, and all Centers share responsibility for program development and resource coordination via the CMCR Steering Committee. When appropriate, and in accordance with NIH policies, project personnel are expected to collaborate; share novel reagents, assays, and animal models; and share both positive and negative results that would help guide the research and development activities of other CMCR network members.

Each CMCR consists of three components: (1) A minimum of three RO1-like research projects focused on mechanisms of radiation damage, biodosimetry to determine radiation dose received or countermeasure testing and/or development; (2) core facilities to support the research projects or to facilitate management of the CMCR and (3) short-term pilot projects. The projects and cores (except the Administrative and Pilot Project) for each CMCR are summarized below.
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University of Rochester – Rochester, NY
University of Rochester Center for Medical Countermeasures against Radiation
BRENNER, David

Locations

**Columbia University Medical Center, New York, NY**
University of Bern, Bern, Switzerland
New York University School of Medicine, New York, NY
Georgetown University, Washington, DC
Lovelace Respiratory Research Institute, Albuquerque, NM
Translational Genomics Research Institute, Phoenix, AZ

Key Personnel
Brenner, David
Garty, Guy
Formenti, Silvia
Amundson, Sally
Fornace, Albert J., Jr.
Smilenov, Lubomir
Guilmette, Raymond
Yao, Lawrence Y
Johnson, Gary
Bittner, Michael
<table>
<thead>
<tr>
<th>Name</th>
<th>CORE/Project</th>
<th>Activities</th>
</tr>
</thead>
</table>
| Formenti, Silvia (NYU)         | Rapid Automated High-Throughput Radiation Biodosimetry | ➢ understand the response of the high-throughput RABIT (Rapid Automated Biodosimetry Tool) biomarkers (micronucleus and Y-H2AX) for a variety of likely, but more complex, exposure scenarios  
 ➢ develop and assess 3-hour mononuclear micronucleus assay for the RABIT, taking advantage of in-vivo cell division and potentially removing the time-consuming step of stimulating in-vitro cell division  
 ➢ assess correlations between RABIT high-throughput assays and several more being developed and individual sensitivity to acute (early) radiation response |
| Amundson, Sally (Columbia)     | Radiation Biodosimetry Using Gene Expression Signs | ➢ develop gene expression signatures following complex exposure scenarios (partial-body exposure, internal emitters, low dose rate, and neutron exposure), develop gene expression signatures that provide a more accurate prediction of radiation injury response and outcome on an individual basis |
| Fornace, Albert (Georgetown)  | Rapid Non-Invasive Radiation Biodosimetry through Metabolomics | ➢ develop metabolomic signatures of radiation injury following low dose rate exposure, exposure to internal emitters, partial-body exposures and mixed gamma/neutron exposure  
 ➢ develop prognostic biomarkers to predict individual radiation sensitivity |
| Brenner, David (Columbia)      | CORE: Administrative                               | ➢ administer budget; coordinate travel and purchasing  
 ➢ establish and organize an Internal Advisory Committee and an External Scientific Advisory Group  
 ➢ facilitate collaboration between the various scientific cores and projects within the Columbia CMCR  
 ➢ facilitate collaboration between this and other CMCRs  
 ➢ organize annual retreat  
 ➢ coordinate patent applications  
 ➢ administer the pilot program  
 ➢ maintain Consortium website |
| Brenner, David (Columbia)      | CORE: Pilot Research Program                       | ➢ provide early stage support to foster innovative, exploratory, and developmental R&D projects, which have the potential to lead to practical products in the field of radiation biodosimetry |
| Smilenov, Lubomir (Lovelace)   | CORE: Irradiation Core                             | ➢ provide currently available services and facilities for highly protracted low dose rate irradiations for cells and mice, internal emitter mouse exposure, partial body mouse irradiations and neutron beam exposure simulating realistic scenarios  
 ➢ perform almost all the proposed irradiations and sample acquisition for the mice and ex vivo human blood irradiations |
| **Yao, Lawrence Y.**  
(Columbia) | **CORE: Fabrication** | - construct RABIT module for protein repair kinetics, rapid mBAND analysis and serum harvesting  
- customize precision shield for partial-body irradiations, IND-like neutron irradiation setup, micro-RT organ conformal irradiator and mouse housing for low dose rate studies |
| **Bittner, Michael**  
(Translational Genomics/ Univ. of Bern) | **CORE: Informatics and Biostatistics** | - provide general statistical support for the projects  
- conduct data viewing and analytical distribution testing to identify univariate trends among potential genomic or metabolomic biomarkers in cells as they react to radiation and to find independently informative, radiation damage biomarkers that may be used to gauge the level of severity of damage for a given individual exposed to a particular dose and type of radiation  
- conduct multivariate analysis to identify groups of genomic or metabolomic biomarkers that act collaboratively to carry out the cellular response to radiation  
- conduct random forests machine learning and self-organizing map analysis  
- provide contextual analysis to develop genomic or metabolomic biomarker panels that are specific for particular cell types, dose scenarios, or population subgroups  
- provide a common secure data-hosting facility so that the considerable amount of data to be shared can be readily exchanged |
CHAO, Nelson

Locations
Duke University, Durham, NC
University of Arkansas for Medical Sciences, Little Rock, AR
Wake Forest University Health Sciences, Winston-Salem, NC
University of North Carolina at Chapel Hill, Chapel Hill, NC

Key Personnel
Baldwin, Albert S.
Batinic-Haber, Ines
Bourland, J. Daniel
Brickey, Willie J.
Cline, J Mark
Chute, John
Dewhirst, Mark W.
Hauer-Jensen, Martin
Nevins, Joseph
Owzar, Kouros
Sempowski, Gregory
Ting, Jenny P-Y
Vujaskovic, Zeljko
Wang, Junru
Yoshizumi, Terry T.
| Chao, Nelson  
Centers for Medical Countermeasures Against Radiation |
|--------------------------------------------------|
| Chute, John  
(Duke)  
A Molecular Signature of Radiation Injury |
| ➢ Determine whether PB signatures of partial body irradiation can be identified and the accuracy of a total body radiation injury signature to predict the status of partially irradiated animals  
➢ Identify the molecular pathways altered by ionizing radiation injury in hematopoietic cells by applying high throughput computational methods  
➢ Test available drugs which modulate pathways altered by radiation as candidate mitigators of radiation injury in a validated murine radiation injury model |
| Hauer-Jensen, Martin  
(University of Arkansas for Medical Sciences)  
Somatostatin Analogs as Countermeasures against Intestinal Radiation Toxicity |
| ➢ Determine the relative importance of intestinal versus immune system dysfunction for the efficacy of SOM230 as a radiation mitigator  
➢ Determine the significance of somatostatin type-2 receptor (sst2) relative to the efficacy of SOM230 as a radiation mitigator  
➢ Assess the feasibility of combining SOM230 with a long-acting somatostatin analog for the purpose of improving logistics in a mass casualty situation  
➢ Determine whether the mitigating efficacy of SOM230 can be further enhanced by combination with another radiation mitigator, gamma-tocotrienol (GTS), which acts by an unrelated mechanism |
| Vujaskovic, Zeljko  
(Duke)  
Radiation Protection with SOD Mimetics |
| ➢ Determine the optimum dose of MnTnHex-2-PyP5+ given subcutaneously to non-human primates (NHP) starting 24 hours after radiation exposure that will achieve the most effective mitigation of lung injury.  
➢ Develop the optimal dosing regimen of oral formulation of MnTnHex-2-PyP5+ in mouse a model of radiation-induced pulmonary injury  
➢ Determine molecular mechanism of MnTnHex-2-PyP5+ mitigation of lung injury |
| Chute, John  
(Duke)  
Pleitrophin as a Mitigator of Radiation Induced Hematopoietic Syndrome |
| ➢ Determine the role of PTN in regulating hematopoietic stem cell self renewal and homeostasis  
➢ Determine if PTN can mitigate radiation-induced myelosuppression in vivo  
➢ Test the efficacy of PTN in mitigating human hematopoietic cell toxicity from radiation injury |
| Ting, Jenny  
(UNC)  
Inflammation and Radiation-Induced Lung Injury |
| ➢ Assess the use of TLR and NLR agonists as deliverable therapeutics for radiation-induced lung injury  
➢ Assess the mechanism by which MyD88 and NLRP3 serve as protective factors during lung radiation  
➢ Assess NLRP3 protection against dual exposure to irradiation and pathogenic virus and bacteria |
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<tr>
<th>Name</th>
<th>CORE:</th>
<th>Responsibilities</th>
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</table>
| Chao, Nelson       | Administration                      | - Provide overall strategic leadership for the RadCCORE program by providing scientific management and evaluation of each RadCCORE project and core  
                  | (Duke)                             | - Provide financial management for each RadCCORE project and core  
                  |                     | - Manage internal and external communications for the RadCCORE program                                      |
| Owzar, Kouros      | Biostatistics and Bioinformatics    | - Provide statistical expertise in study design and conduct of research projects conducted by RadCCORE investigators  
                  | (Duke)                            | - Provide support for the statistical analysis of molecular data from low dimensional candidate marker experiments, high-dimensional genome-wide experiments and cell assays  
                  |                     | - Provide statistical consulting and education                                                          |
| Sempowski, Gregory | Immune Monitoring                   | - Provide state-of-the-art, multi-color, fluorescence-activated cell sorting support for basic or translational research conducted by Duke RadCCORE investigators  
                  | (Duke)                            | - Provide targeted multiplex protein array profiling of biological samples, such as tissue culture supernatant and plasma, using BioPlex bead array reader (BioRad)  
                  |                     | - Provide T cell immune reconstitution monitoring in mice, humans and non-human primates               |
| Cline, Mark        | Primate Studies                     | - Facilitate rapid translational assessment of radiation effects and countermeasures by providing access to non-human primates to investigators in the consortium  
                  | (Wake Forest)                     | - Provide expertise in the clinical care and assessment of treatment responses in nonhuman primates, including acute and chronic outcomes  
                  |                     | - Provide support for consortium investigators using the unique strengths of core investigators (cognitive and behavioral studies, pathologic assessment of radiation-induced damage in brain, lung and other tissues) |
| Dewhirst, Mark     | Pilot Projects                      | - Solicit candidates for Developmental Research Projects by sending out requests for applications to RadCCORE members as well as by publishing the RFA on RadCCORE and NIAID CMCR websites and networking to other scientists within the field; meritorious application will be selected for support each fiscal year  
                  | (Duke)                            | - Provide monitoring of the Pilot Research Project during monthly RADCCORE meetings, and formal monitoring every 6 months by the Developmental Research Committee, by providing a written formal evaluation of the project, following review of progress reports provided by the pilot project principal investigator |
| Yoshizumi, Terry   | Dosimetry                           | - Provide physics support for irradiator users  
                  | (Duke)                            | - Develop an organ dose calculation method using Monte Carlo simulations  
                  |                     | - Provide mixed field neutron/gamma dosimetry support                                                    |
GREENBERGER, Joel

Locations
University of Pittsburgh, Pittsburgh, PA

Key Personnel
Bahar, Ivet
Bayir, Hulya
Brand, Rhonda
Cao, Shaonan
Catherine Corey
Dixon, Tracy
Doemling, Alexander
Epperly, Michael
Falo, Louis
Floreancig, Paul
Frantz, Marie-Celine
Gao, Xiang
Greenberger, Joel
Klein-Seetharaman, Judith
Lazo, John
Li, Song
Mustata, Gabriela
Normolle, Dan
Peterson, Jim
Shuai, Yongli
Star, Alexander
Stoyanovsky, Detcho
Wang, Hong
Wipf, Peter
Zellefrow, Crystal Ann
<table>
<thead>
<tr>
<th>Greenberger, Joel (UPitt)</th>
<th>Mitochondrial Targeting Against Radiation Damage</th>
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<tbody>
<tr>
<td><strong>Greenberger, Joel (UPitt)</strong></td>
<td>Mitochondrial Targeted Small Molecule Radiation Mitigators</td>
</tr>
<tr>
<td>➢ Determine whether an improved GS-nitroxide is a safe and effective radiation mitigator</td>
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<tr>
<td>➢ Determine whether (GS-NOS-I) XJB-5-133 and MCF-201-89 are effective radiation mitigators</td>
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<tr>
<td>➢ Determine whether p53/mdm2/mdm4 inhibitors BEB55 and BEB59 are effective radiation mitigators</td>
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<thead>
<tr>
<th>Kagan, Valerian E. (UPitt)</th>
<th>Mitochondria-targeted small-molecule inhibitors of cardiolipin peroxidation as radiomitigators</th>
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<tbody>
<tr>
<td>➢ Determine specific mechanisms defining development of CL peroxidation in cells and radiosensitive tissues of irradiated animals</td>
<td></td>
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<tr>
<td>➢ Develop and optimize small molecule inhibitors of cyt c/CL peroxidase complex and investigate mechanisms of their action to achieve maximized radiomitigating efficiency in cells and tissues</td>
<td></td>
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<tr>
<td>➢ Identify mechanism-based strategies and small molecules capable of regulating CL oxidizability and localization in mitochondria to limit its oxidation during irradiation induced apoptosis</td>
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<tr>
<th>Lazo, John (UPitt)</th>
<th>Identification of Radiation Mitigator Targets and Drugs using siRNA Protection Assays</th>
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<tbody>
<tr>
<td>➢ Optimize and deploy sentinel cells for use in detecting new drug targets and drugs to combat radiation damage and toxicity</td>
<td></td>
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<tr>
<td>➢ Interrogate druggable genome siRNA libraries and small molecule libraries for radiation damage mitigators</td>
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<tr>
<td>➢ Identify targets that interact synergistically with prioritized compounds</td>
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<tr>
<th>Bayir, Hulya (UPitt)</th>
<th>Radiation Damage Mitigation by Prevention of MnSOD Nitration</th>
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<tbody>
<tr>
<td>➢ Determine specific biochemical mechanisms modulating MnSOD activity in cells and tissues of irradiated animals</td>
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<tr>
<td>➢ Identify mechanism-based strategies and small molecules capable of regulating MnSOD activity in mitochondria as radiomitigators</td>
<td></td>
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<tr>
<td>➢ Develop and optimize small molecule SOD and combined SOD-antioxidant and SODcatalase/glutathione peroxidase (GPX) mimetic targeted to mitochondria</td>
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<thead>
<tr>
<th>Greenberger, Joel (UPitt)</th>
<th>CORE: Administrative</th>
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<tbody>
<tr>
<td>➢ Receive, process, and circulate pilot project applications</td>
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<tr>
<td>➢ Manage all projects and core budgets</td>
<td></td>
</tr>
<tr>
<td>➢ Coordinate, advertise, and oversee monthly CMCR Seminar Meetings</td>
<td></td>
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<tr>
<td>➢ Collect, collate, edit, and finalize CMCR Annual Reports</td>
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<tr>
<th>Greenberger, Joel (UPitt)</th>
<th>CORE: Pilot Projects</th>
</tr>
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<tr>
<td>➢ Manage pilot project applications by a highly efficient three-tiered approach in an effort to encourage new investigators to enter the field of radiation biology for drug development of radiation mitigators</td>
<td></td>
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<tr>
<td>Name</td>
<td>CORE:</td>
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| Wipf, Peter     | Innovative Medicinal Chemistry    | - Develop the concept that GS segment-conjugates are effective in delivering redox modulating, radioprotective nitroxides to mitochondria  
|- Generate JP4-039 analogues linked to NOS inhibitors such as AMT (i.e. GS-NOS-1), which will test the hypothesis of Project 1 that mitochondrial targeted small NOS inhibitors are effective alone and when used in combination with GS-nitroxides as radiation damage mitigators  
|- Establish the methodology to prepare nanoparticle conjugates of GS-nitroxide and GS-NOS-I as well as other combination therapeutics  
|- Provide Project 4 with novel hydrogen peroxide (H2O2) releasing small molecules  
|- Generate (TPP)-derived oximes, nitroxides, salen-Mn and porphyrin-Mn complexes for Project 1  
|- Provide a synthesis resource for all Projects and Cores that require medicinal chemistry optimization of new lead structures with desirable radioprotective and mitigative effects |
| Li, Song        | Smart Drug Delivery               | - Provide various types of tailor-designed lipidic formulations for different radiation mitigators suitable for topical or systemic applications  
|- Provide carbon nanotubes-based delivery systems for controlled and staged release of mitigators  
|- Provide tissue-specific delivery systems for targeted delivery of radiation mitigators |
| Wang, Hong      | Biostatistics                     | - Collaborate with project investigators on statistical aspects of the design and analysis of in vitro and in vivo experiments  
|- Develop efficient treatment selection designs to assess the toxicity and efficacy of novel radiation mitigation agents used individually and in combination  
|- Work with the Project and Core investigators to ensure that data collection and database development are appropriate for the requisite statistical analyses  
|- Review pilot project proposals, and provide statistical support to those that are funded by this CMCR  
|- Collaborate with investigators in writing and preparing progress reports, abstracts, manuscripts, and presentations |
| Epperly, Michael| Radiobiological Standardization   | - Carry out in vitro and in vivo testing for all five projects in the University of Pittsburgh CMCR Program |
| Bahar, Ivet (UPitt) | CORE: Chemoinformatics | - Contribute computational expertise to the hit-to-lead activities, library design, lead optimization and identification of potential mitigators of radiation damage at the CMCR  
- Provide computer-aided predictions of drug toxicity and metabolism  
- Identify target-mitigator interaction pathways and networks to correlate molecular functions to physiological processes that will help in designing safe and efficient mitigators of radiation damage |
GUHA, Chandan

Locations
Albert Einstein College of Medicine, Bronx, NY
Oregon Health & Science University, Portland, OR
Stony Brook University, Stony Brook, NY

Key Personnel
Alfieri, Alan
Chen, Emily I.
Fleming, William H.
Guha, Chandan
Imprey, Soren
Kuriand, Inwin
Nik, Sara
Sellers, Rani
Vaitheesvaran, Bhavapriya
Zhang, Hong
| Guha, Chandan (Albert Einstein) | Stem Cell-Based Therapies for Radiation-Induced Gastrointestinal Syndrome (RIGS) | ➢ Investigate Radiation-induced ISC injury and signaling pathways  
➢ Investigate whether acceleration of ISC regeneration could mitigate/protect RIGS in mice  
➢ Examine whether repair of the ISC niche by TLR activation and/or stromal cell-based therapies could mitigate RIGS in mice |
| Fleming, William H. (OHSU) | Endothelial Cell Derived Factors for Radiation-Induced Bone Marrow Syndrome | ➢ Define methods to augment hematopoietic recovery following bone marrow lethal doses of radiation  
➢ Determine the molecular mechanisms of hematopoietic regeneration and identify radioprotective factors by RNA-Seq screening |
| Guha, Chandan (Albert Einstein) | CORE: Administration | ➢ Provide a clearly delineated chain of command that involves the participation of a mix of senior scientists and administrators in the decision-making process, integrates their input into the governance of the CMCR and implements the CMCR strategic plan  
➢ Disseminate information regarding CMCR’s scientific findings and Core capabilities to the senior scientific, clinical and administrative leadership at Einstein  
➢ Provide a responsible and flexible support and oversight infrastructure to the CMCR program Cores and activities |
<p>| Guha, Chandan (Albert Einstein) | CORE: Pilot Project | ➢ Solicit and manage pilot projects in the following scientific areas: 1) elucidating cellular and molecular mechanisms relevant to radiation mitigation/treatment; 2) development of novel techniques and approaches for high throughput screening of radiation mitigators; 3) continued improvement of existing approaches for predicting risk of radiation toxicity, estimating host cytokine balances, and estimating genotoxicity; and 4) understanding and mitigating the pathophysiology of radiation related inflammation |</p>
<table>
<thead>
<tr>
<th>Name</th>
<th>CORE</th>
<th>Responsibilities</th>
</tr>
</thead>
</table>
| Sellers, Rani S.      | CORE: Histology and Comparative Pathology Core | ➢ Provide in vivo protocol design advice to the different members on the Program Project  
➢ Perform some of the histological and immunohistochemical methods needed for the specific experiments under study  
➢ Evaluate and consistently score histopathological and immunohistochemical findings to produce a histopathology report with interpretation of the findings  
➢ Provide photographic images of the histopathological and immunohistochemical data if required for the projects  
➢ Maintain a stock of common reagents and supplies required for the preparation of the samples and of the items required for use and maintenance of the fluorescence microscope for routine analysis |
| Chen, Emily           | CORE: Proteomics                          | ➢ Provide protocol design advice to different project investigators on the U-19 CMCR Project  
➢ Perform sample processing procedures necessary for mass spectrometry-based protein analysis  
➢ Perform LC-MS/MS analysis  
➢ Perform data analysis  
➢ Maintain mass spectrometers and computer clusters, and to purchase HPLC accessories and proteomic supplies required for sample preparation and analysis |
| Kuriand, Irwin        | CORE: Stable Isotope and Metabolomics      | ➢ Provide in vivo protocol design advice to the different members on the Program Project  
➢ Perform metabolite and flux profiling studies on tissues from radiation treated animals |
MCBRIDE, William

Locations
University of California, Los Angeles

Key Personnel
Bradley, Kenneth
Cacalano, Nicholas A
Cheng, Genhong
Dempsey, Paul
Gatti, Richard
Iwamoto, Keisuke S.
Jung, Michael
Jung, Mike
Kang, Mo
Loo, Joseph
McBrayde, William
Norris, Andrew
Pajonk, Frank
Rozengurt, Nora
Sayre, James W.
Schiestl, Robert H.
Whitelegge, Julian
Zawahir, Zahra
| McBride, William  
UCLA Center for Biological Radiation Mitigators |
|---|
| **Schiestl, Robert H.**  
Development of Novel Radiation Mitigators |
| ➢ Develop novel radiation mitigators with negligible toxicity  
➢ Characterize mitigators using a functional genomics assay in yeast  
➢ Determine radiation mitigation activity of novel lead compounds in vivo  
➢ Characterize the mitigators in animals |
| **McBride, William  
(UCLA)**  
Mitigation of Radiation Damage to the Immunohematopoietic System |
| ➢ Develop novel mitigators of radiation damage primarily to the immunohematopoietic system  
➢ Define the chemical and biological "signatures" that are responsible for the activity of radiation mitigators so that they can be chemically or biologically improved |
| **Cheng, Genhong  
(UCLA)**  
Mitigation of Radiation Damage by Mechanisms of Innate Immune Regulation |
| ➢ Define the innate PRR required for a productive mitigating response  
➢ Define the mechanism of crosstalk between innate mitigators and BM stem cells  
➢ Investigate the mitigating activity of infection by a live attenuated oral vaccine |
| **McBride, William  
(UCLA)**  
CORE: Administrative |
| ➢ Promote the most efficient use of the CMCR's resources  
➢ Promote the exchange of scientific ideas and data  
➢ Provide biostatistical support in terms of experimental design and analyses to ensure the generation of robust experimental and clinical data |
| **Gatti, Richard A.  
(UCLA)**  
CORE: Pilot Project |
| ➢ Provide pilot project research funding for 1-2 years to encourage established investigators who are not in the field of radiation research and young investigators who are just starting their career to contribute to the goals of the UCLA-CMCR  
➢ Provide funding to specific projects likely to yield radiation mitigators of interest to the CMCR Program as a whole  
➢ Encourage collaborative participation in the UCLA-CMCR by scientists outside of UCLA with products of interest to the CMCR |
| McBride, William (UCLA) | CORE: Mouse | ➢ Provide and maintain high quality immune competent, immune deficient, and transgenic mice at low cost for use in full and pilot research projects in the UCLA-CMCR, and for other CMCRs  
➢ Provide multiple models of normal tissue radiation damage  
➢ Provide expert advice on the design of radiation experiments  
➢ Provide assistance with the execution of animal irradiation experiments  
➢ Provide assistance with analysis and interpretation of results of animal experiments  
➢ Provide help in obtaining IACUC approval  
➢ Provide maintenance of IACUC compliance |
|------------------------|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Whitelegge, Julian P. (UCLA) | CORE: HTS and Proteomics | ➢ Provide high-throughput screening (HTS) capabilities for the 3 full projects and for pilot research projects in the UCLA-CMCR and for other CMCRs  
➢ Provide industrial-strength database for archival of HTS data and chemical Informatics data mining (CDD)  
➢ Provide expertise in structure-activity relationships and chemical synthesis for pharmacophore optimization  
➢ Provide state-of-the-art proteomics and mass spectrometry services for defining molecular signatures for classes of mitigators, and determination of mechanisms of action |
SWARTZ, Harold

Locations
Dartmouth Medical School – Hanover, NH
University of Florida, Gainesville, FL
Dana-Farber Cancer Institute, Boston, MA
Medical College of Wisconsin, Milwaukee, WI

Key Personnel
Angerhofer, Alexander
Brennan, Lisa
Demidenko, Eugene
Dong, Ruhong
Fanucci, Gail E.
Flood, Ann B.
Gladstone, David
Gougelet, Robert
Guinan, Eva
Gui, Jiang
Guinan, Eva
He, Xiaoming
Hyde, James
Lesniewski, Piotr
Ng, Andrea
Nicolalde, Roberto J.
Russell, Janice
Sidabras, Jason
Swarts, Steven G.
Swartz, Harold
Wilcox, Dean
Williams, Benjamin
Zaki, Bassem
| Principal Investigator | Biodosimetry Based on EPR Measurements of Teeth *In Vivo* | **Swartz, Harold**  
Physically-Based Biodosimetry for Triage after a Large Radiation Incident |
|------------------------|----------------------------------------------------------|---------------------------------------------------------------------|
| Williams, Benjamin     | Biodosimetry Based on EPR Measurements of Teeth *In Vivo* | ➢ Develop improved models and assessments of the potential impacts of personal and demographic factors on dosimetric performance  
➤ Complete additional advances in key aspects of the technology developed to make feasible a technique and an instrument that provides speed, accuracy, and ease of measurements  
➤ Develop and implement improved analytic models and procedures |
| (Dartmouth) Principal Investigator | | |
| Swarts, Steven         | *Ex Vivo* Analysis of Irradiated Finger/Toe Nails as a Biodosimeter System | ➢ Determine the molecular nature of the EPR signals observed in clipped and Irradiated nail  
➤ Determine the relationship between the use of clipped nails that are Irradiated after clipping and clippings from nails irradiated *In Vivo*  
➤ Determine the Importance of and, as necessary, develop methodologies to deal with Intrinsic demographic variables, nail disorders, and variations in the field (e.g. dirt, polishes, etc.) that potentially impact measurement  
➤ Establish methods for data acquisition, processing and output suitable for use by non-expert operators and ER managers under field conditions |
| (Univ. of FL) Principal Investigator | | |
| Swartz, Harold         | Biodosimetry Based on EPR Measurements of Nails *In Vivo* | ➢ Develop and optimize resonators that are capable of making measurements on human nails  
➤ Adapt, develop, and optimize a complete laboratory-based EPR nail dosimetry instrument, which is capable of making in situ measurements of human nails  
➤ Demonstrate that radiation-induced signals in nails can be detected and quantified *In Vivo* using the newly optimized resonators  
➤ Determine factors that affect the generation and stability of the radiation induced EPR signals in nails, including relationships, if any, to the mechanically induced signals  
➤ Develop the specifications and procedures for using the *In Vivo* Surface Resonator Array (SFRA) nail resonator in a complete field-deployable EPR dosimeter system that is capable of being operated by non-expert personnel |
<p>| (Dartmouth) Principal Investigator | | |</p>
<table>
<thead>
<tr>
<th>Name</th>
<th>Core Director</th>
<th>Core:</th>
<th>Responsibilities</th>
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| Swartz, Harold            | (Dartmouth) Core Director          | Scientific and Administrative            | To provide overall administrative and financial support and management for Dartmouth’s CMCR, including both its overarching and project-specific roles and responsibilities and other CMCR-wide activities such as the organization of the External Scientific Advisory Group (ESAG) which will meet annually.  
To provide biostatistical support and advice to the projects and advancement of statistical concepts that will be applicable for the general field of biodosimetry.  
To provide support and advice about human factors to advance the developments in the design and testing of the measuring devices—including requirements to accommodate the needs of human subjects in the design and the needs of non-experts in the operation of the instruments. |
| Flood, Ann                | (Dartmouth) Core Director          | Pilot Project                            | Facilitate the development of pilot projects  
Oversee and evaluate ongoing pilot projects                                                                                                           |
| Guinan, Eva               | (DFCI) Core Director               | In Vivo Irradiations with Patients Undergoing Radiation Therapy | Establish appropriate protocols that meet the goals of the projects and fully satisfy the requirements for experimental procedures involving human subjects  
Work with the personnel from the three projects to carry out the measurements in a safe and effective manner  
Test the operational capabilities of the instruments to be developed in the center for making the measurements by non-expert personnel |
| Hyde, James               | (MCW) Core Director                | Advanced Instrumental Development        | Develop advanced resonators that make it feasible for measurements in Vivo to be made at X-Band (9 GHz)  
Develop instrumentation to support in Vivo measurements at X-Band  
Improve resonators and bridges for measurements at L-Band (1.2 GHz)  
Support multi-frequency studies |
| Lesniewski, Piotr         | (Dartmouth) Core Director          | Instrumental Core                        | To enhance the ability of Project 1 (in Vivo tooth dosimetry) to reach its goals (40% effort)  
To enhance the ability of Project 2 (clipped nail dosimetry) to reach its goals (20% effort)  
To enhance the ability of Project 3 (in Vivo nail dosimetry) to reach its goals (40% effort)  
For each of these aims, there are 3 general subaims:  
Provide support of the operation of the hardware and software of the spectrometers, at all relevant sites  
Enhance the dosimetric capabilities by the development of improved resonators, microwave components, magnets, and software for operation and analysis  
Design, construction, and testing of a prototype instrument that is suitable for making measurements under field conditions with non-expert operators |
WILLIAMS, Jacqueline

Locations
University of Rochester, Rochester, NY

Key Personnel
Calvi, Laura
Chen, Yuhchyau
Fenton, Bruce M.
Finkelstein, Jacob N.
Hurley, Sean
Johnston, Carl
Kingsley, Paul
Lord, Edith M.
O'Banion, M. Kerry
Olschowka, John
Palis, James
Pentland, Alice
Ryan, Julie
Thurston, Sally
| **Williams, Jacqueline**  
**University of Rochester Center for Medical Countermeasures against Radiation** |
| --- |
| **Finkelstein, Jacob N.  
(Roch)** |
| **Mitigation and Modeling of Radiation Effects in Lung in the Context of Multi-Organ and Multi-Modal Injury** |
| ➢ Evaluate the efficacy of mitigation strategies for radiation-induced pulmonary toxicity in the context of multi-organ dysfunction  
➢ Establish a model of pulmonary and systemic radiation injury following internal radiation exposure and assess the efficacy of pulmonary mitigators on this response  
➢ Establish a pediatric model and assess the effectiveness of pulmonary mitigation after injury in this population  
➢ Establish a model of the effect of irradiation on the response of the lung to infectious challenge (secondary injury) and assess the efficacy of pulmonary mitigators on ameliorating this response |
| **O’Banion, M. Kerry  
(Roch)** |
| **Mitigation of Brain Inflammation and Cognitive Impairment after Radiation Injury** |
| ➢ In both adult and pediatric models, measure time- and dose-dependent indices of neuroinflammation and oxidative stress following whole body radiation exposure; relate them to changes in hippocampal neurogenesis and behavioral tasks that measure hippocampal-dependent learning and memory  
➢ Assess the efficacy of mitigating inflammatory changes and oxidative stress using three pharmacological interventions at selected radiation doses and time points in both adult and pediatric models  
➢ Examine brain inflammatory endpoints, neurogenesis, and cognitive changes following whole body irradiation combined with thermal burn (to explore hypothesis in setting of combined injury) |
| **Lord, Edith M.  
(Roch)** |
| **Mitigation of Radiation and Combined Injury to the Skin** |
| ➢ Investigate the effect of total body irradiation (TBI) and combined injury on trafficking and functionality of skin dendritic cells and assess the efficacy of mitigating agents to reduce injury  
➢ Investigate the effect of TBI and combined injury on skin barrier function, including ROS-mediated damage and inflammatory response and assess the efficacy of mitigating agents on injury  
➢ Determine if radiation exposure at a young age increases sensitivity to later secondary injury (as measured by a lower injury threshold, longer time to repair, poorer quality of repair) due to chronic defects in skin barrier function |
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<th>Name</th>
<th>CORE:</th>
<th>Main Objectives</th>
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| Palis, James (Roch)       | Mitigation of Bone Marrow Radiation injury | - Determine the effects of internal compared to external sublethal radiation on the stem, progenitor, and peripheral blood cell compartments  
- Determine the effects of combined internal plus external radiation exposure on the hematopoietic stem, progenitor and peripheral blood cell compartments  
- Assess the efficacy of mitigating agents directed at hematopoietic stem/progenitor cells (EUK-207) and through the marrow microenvironment (Homspera) to mitigate late radiation effects  
- Determine the sensitivity of the early postnatal hematopoietic system to radiation injury |
| Williams, Jacqueline P. (Roch) | CORE: Administration | - Provide administrative oversight, support, and evaluation of progress and fiscal performance of the projects and cores within the UofR-CMCR  
- Facilitate interactions within the University of Rochester Medical College, between other CMCRs in the network, NIAID, as well as with other agencies involved in the development of countermeasures for radiological and/or nuclear emergencies  
- Provide oversight of and assistance with radioactive materials and sources through the auspices of the University of Rochester’s Radiation Safety team  
- Provide facilities for the presentation and publication of data |
| Finkelstein, Jacob N. (Roch) | CORE: Pilot Projects | - Attract, support, and develop promising, nascent research that will augment the University of Rochester CMCR’s scientific goals |
| Fenton, Bruce M. (Roch)   | CORE: Imaging and Histology | - Provide central, standardized immunohistochemical methodologies, protocols, and imaging services that will be utilized by each of the four projects |
| Chen, Yuhchyau (Roch)     | CORE: Drug Translation and Development | - Facilitate each scientific project in the development of potential radiation mitigators for various organ systems, including lung, brain, skin, and bone marrow, each assessed in the context of a total body radiation exposure  
- Monitor the progress of testing radiation mitigators with respect to efficacy, safety, toxicology, pharmacokinetics, pharmacodynamics, and quality assurance |