NIAID Radiation and Nuclear Countermeasures Program

In 2004, NIAID was directed by HHS to develop a robust research program to accelerate the development and deployment of radiation/nuclear medical countermeasures (MCMs) for the Strategic National Stockpile.

Mission:
• Support early to mid-stage research to develop radiation/nuclear MCMs and biodosimetry devices.
• Provide funding opportunities:
  – Grants, collaborative agreements, contracts, inter- and intra-agency agreements

Research priorities:
• Drugs to treat or mitigate radiation injury 24hrs post-exposure
• Drugs to remove radioactive materials from the body
• Biodosimetry tools to determine levels of radiation exposure

NIAID Radiation and Nuclear Countermeasures Program

Mission Space

Acute Radiation Syndrome (ARS) & Delayed Effects of Acute Radiation Exposures (DEARE)
  • Hematopoietic, gastrointestinal, lung, skin, central nervous system, kidney, combined injury

Late Effects
  • Cardiovascular, immunologic, metabolic, cognitive, respiratory

MCM Mechanisms of Action
  • Anti-oxidants, anti-inflammatories, anti-apoptotics, growth factors, cytokines, proliferation and differentiation factors, cell-based therapies, etc.
Radionuclide Threats
- Am-241, Co-60, Cs-137, I-131, Ir-192, Po-210, Pa-238/239, Sr-90, U-235

Radionuclide MCMs include:
- Blocking agents
- Decorporation agents
- Enhancement of mucociliary clearance

Biodosimetry Markers, Methods & Devices

NIAID Radiation and Nuclear Countermeasures Program
Mission Space

NIAID Radiation and Nuclear Countermeasures Program Elements

NIAID Radiation and Nuclear Countermeasures Program Research and Product Development Opportunities

FDA approval - March 2015

**NIAID Radiation and Nuclear Countermeasures Program Achievements** - FDA approval - March 2015


Neupogen® Treatment Increases Survival in Irradiated Rhesus Macaques

Figure showing survival distribution function with irradiation days.


**NIAID Radiation and Nuclear Countermeasures Program Achievements** - FDA approval - November 2015

Neulasta® Treatment Increases Survival in Irradiated Rhesus Macaques

Figure showing survival distribution function with irradiation days.

FDA letter to proceed with first-in-human safety/PK evaluation of an oral radionuclide decorporation agent (Hydroxypyridinone – 3,4,3(1,2-HOPO)).

- Chelate radionuclides, promoting clearance and preventing tissue deposition
- Currently-approved drugs:
  - Ca and Zn-DTPA for transuranics; given IV
  - Prussian Blue removes radioactive cesium (Cs) and thallium (Tl); given orally, binds Cs and Tl entering GI tract

Abergel & Raymond, Hemoglobin 35(3): 276-290, 2011

NIAID Radiation and Nuclear Countermeasures Program Overview

EVALUATION OF >150 MCM CANDIDATES

- DECORP, 9
- PDSS, 74
- Biodosimetry, 24
- SBIR, 19
- APRR, 94
- CMBR, 108

FDA IND filed July 7, 2014

Grant, 68

EVALUATION OF >150 MCM CANDIDATES

Discovery and Development of Biomarkers for Acute and Delayed Radiation Injuries

- The objective is to identify and characterize biomarkers and/or techniques to predict radiation injury to specific organs and tissues of physiological systems
- The biomarkers should be linked to relevant clinical outcomes such as organ failure, other major morbidity and/or mortality, strictly related to the radiation exposure and stable for at least 24hr post-exposure
NIAID Radiation and Nuclear Countermeasures Program Biodosimetry Architecture

**Predictive Biodosimetry**
- Immediate triage

**Medical management**
- Dose estimation
- TBI vs PBI
- Specific tissue damage

**Risk assessment**
- POC devices
- Hematology
- OSL/EPR
- qPCR
- Biomarkers

**Cytogenetics**
- Micronucleus Assay

NIAID Radiation and Nuclear Countermeasures Biodosimetry Programs

**Predictive Biodosimetry R01 Grants (2012)**
- Dana-Farber Cancer Institute
- Fred Hutchinson Cancer Research Center
- Georgetown University
- Medical College of Wisconsin
- UCLA
- University of Rochester

**SBIR Grants (2009-present)**
- Microfluidic chips for detection of senescent cells
- Optically-based device for detection of miRNA biomarkers

**NIAID-NCI IAA (2005-present)**
- Gamma H2AX
- Metabolomics
- miRNA

**Columbia CMCRC U19 (2005-present)**
- Gene expression
- High throughput cytogenetics
- Metabolomics

NIAID: Bridging the “Animal Rule Pathway”

**Discovery, Research Development**

**NIAD RNCP**

**Licensure, Procurement, SNS**

**Government, Academic, Corporate Partnerships**

**Food and Drug Administration (CDER, CBER, and CDRH)**

**National Institute of Allergy and Infectious Diseases**

**NIH Extramural Research and Development Authority**
NIAID Radiation and Nuclear Countermeasures Program

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