Fiscal Year:	FY 2021	Task Last Updated:	FY 12/16/2020
PI Name:	Porada, Christopher Ph.D.		
Project Title:	Novel Microfluidic Biomarker Detection Platf Cosmic Rays Radiation, Using Mice with Hun	forms to Monitor In Vivo Ef nan Hematopoietic Systems	fects of Solar Particle Events and Galactic
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline Element/Subdiscipline:	TRISHTRISH		
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Organization Name:	Wake Forest Institute for Regenerative Medici	ine	
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Zip Code:	27157	Congressional District:	5
Comments:			
Project Type:	Ground	Solicitation / Funding Source:	2017 HERO NNJ16ZSA001N-TRIRT. Appendix C: Translational Research Institute for Space Health (TRISH) Research Topics
Start Date:	11/01/2017	End Date:	07/31/2022
No. of Post Docs:	1	No. of PhD Degrees:	0
No. of PhD Candidates:	3	No. of Master' Degrees:	1
No. of Master's Candidates:	1	No. of Bachelor's Degrees:	0
No. of Bachelor's Candidates:	1	Monitoring Center:	TRISH
Contact Monitor:		Contact Phone:	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 7/31/2022 per E.	Urquieta/TRISH (Ed., 10/20)/2021)
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Zenhausern, Frederic Ph.D. (University of Arizona) Almeida-Porada, Graca M.D., Ph.D. (Wake Forest Institute for Regenerative Medicine) Walker, Stephen Ph.D. (Wake Forest Institute for Regenerative Medicine) Langefeld, Carl Ph.D. (Wake Forest Institute for Regenerative Medicine) Wilson, Paul Ph.D. (University of California, Davis) Coleman, Matthew Ph.D. (University of California, Davis) Tepper, Clifford Ph.D. (University of California, Davis) Lacombe, Jerome Ph.D. (University of Arizona) Yang, Jianing M.D., Ph.D. (University of Arizona)		
Grant/Contract No.:	NNX16AO69A-T0103		
Performance Goal No.:			

We will use humanized immunodeficient (NSG) mice (huMice) whose hematopoietic system has been repopulated with human hematopoietic stem cells (HSC) from astronaut-age M/F donors. Using these huMice (3-4 months post-repopulation) as our experimental model, we will measure space radiation-induced human and mouse blood transcriptomic and proteomic changes using our low LET (linear energy transfer) photon-validated radiation biomarker detection panel and microfluidic-based detection platform. We will also test a promising curcumin-based nanolipoprotein (NLP)-based countermeasure that we have recently shown significantly improves human HSC proliferation and differentiation in vitro following low doses of high-energy proton and iron ions delivered at NASA Space Radiation Laboratory (NSRL). The huMice will serve as avatars allowing us to study in vivo responses and leukemogenic potential of human hematopoietic systems exposed to modeled space radiation. HuMice will be developed and matured at Wake Forest Institute for Regenerative Medicine (WFIRM) and transported to Brookhaven National Laboratory (BNL), as will HuMiX gut-on-a-chip populated with intestinal cells from healthy human donors (both sexes) of typical astronaut age. At NSRL, the huMice avatars and HuMiX chips will be exposed to mission-relevant doses of high-energy protons, intermediate and high LET ions, and the GCR (galactic cosmic radiation) simulator. HuMiX chips will be monitored for short-term human gastrointestinal (GI) cell biomarker responses, and the animals will be monitored for both short and long-term human and mouse biomarker responses, using our established low LET cesium-137 gamma radiation-specific protein biomarkers coupled to an ELISA-based microfluidic device that we will further optimize for International Space Station (ISS)/in-flight use. Biomarker responses measured in these devices will be validated using qPCR, RNASeq, Western blotting, and several traditional and molecular radiobiological techniques. We will serially monitor animals for short- and long-term blood-based biomarker responses and physiological radiation effects (specifically leukemogenesis). We will submit tissue/organ samples of huMice to the NASA Human Research Program (HRP) Shared Tissue Repository, and our biomarker datasets will be deposited into the NASA GeneLab database.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

During future missions beyond low Earth orbit (LEO), such as those planned to Mars and near-Earth asteroids, astronauts will face poorly defined health risks as a result of exposure to space radiation in the form of solar energetic particles (SEP) consisting primarily of protons and light ions, and galactic cosmic rays (GCR) ranging from high-energy protons to high-energy charged (HZE) nuclei. Although the intensity of the GCR heavy ion flux is fairly low, the relative biological effectiveness (RBE) of these high charge and energy (HZE) particles can be extremely high. Long duration spaceflight can result in the accumulation of radiation exposures that may produce significant short- and long-term untoward effects on human physiology, and that could potentially increase cancer morbidity/mortality in astronauts. Unfortunately, an incomplete understanding of biological effects resulting from exposures to this unique/complex radiation environment and the paucity of human epidemiological studies for these radiation types make it difficult to accurately estimate risks of carcinogenesis for various organ sites due to exposure to space radiation. It is well appreciated that the stem cell compartments of the hematopoietic and gastrointestinal (GI) systems constitute some of the most radiosensitive tissues of the body. Leukemias represent one of the most frequent radiogenic cancers and also exhibit the shortest latency periods. Ionizing radiation is also an established risk factor for colorectal cancer, and the Fornace group demonstrated exposure to HZE ions (1 GeV/n 56Fe ions) significantly enhanced the development and progression of intestinal tumors in Adenomatous polyposis coli (APC) mouse models. Compounding the carcinogenic risks that could arise from low to intermediate dose SEP/GCR exposures are numerous studies collectively demonstrating that extended spaceflight conditions deleteriously affect the immune system at multiple levels and impair astronauts' ability to respond to infection or immune challenge. Collectively, these findings illustrate an important need to use appropriate human hematopoietic and GI experimental models to precisely identify SEP/GCR radiation-induced effects, namely to better understand the genomic and epigenomic alterations responsible for low or high LET charged particle-induced carcinogenesis; identify appropriate molecular targets for effective countermeasure development; and provide more refined datasets for NASA's risk estimation modeling efforts. Herein, we are performing studies in humanized mice to enable omics capability for in-flight measurements of radiation/stress blood biomarkers (human) using RNASeq and microfluidic-based transcriptomic/proteomic biomarker detection platforms. We are also utilizing the Human-Microbial Cross-Talk model (HuMiX) gut-on-a-chip to perform the 1st studies monitoring the effects of simulated space radiation on the human GI tract. Based on exciting preliminary data, we will also examine the ability of the dietary supplement curcumin to prevent and/or mitigate the effects of space radiation on the hematopoietic and GI systems, and to determine the optimal working concentration for maximal radioprotective/radiomitigating effects. Given curcumin's poor water solubility, we are also performing studies to validate the ability of nanolipoprotein particles (NLP) loaded with curcumin (cNLPs) to serve as an effective countermeasure against the effects of SEP/GCR radiation in both the human hematopoietic and GI systems. Once validated as an effective countermeasure, we will also assess the stability of these cNLPs for long-term storage aboard ISS/long duration missions, suitability for lyophilization/resuspension for oral delivery. If successful, these cNLPs could readily be implemented as a dietary supplement during prolonged missions, protecting astronauts from the deleterious

The original aims of this project were to: 1) use mice with humanized hematopoiesis to define changes in radiation/stress blood biomarkers in response to mission-relevant doses of simulated space radiation; 2) use the innovative Human-Microbial Cross-Talk human gut-on-a-chip model (HuMiX) to perform studies defining the effects of mission-relevant doses of simulated space radiation on the human gastrointestinal (GI) tract; 3) validate the ability of nanolipoprotein particles (NLP) loaded with curcumin to serve as an effective countermeasure against the effects of simulated space radiation in both the human hematopoietic and GI models; and 4) assess the suitability of curcumin-NLPs as space radiation countermeasures.

During this third year of funding, we have made significant progress towards achieving these goals. During this time, we have:

• Performed H+, 56Fe ion, 16O, ?28Si, ?-ray, and simplified 5-ion galactic cosmic ray (GCR) simulator irradiations on both wild-type mice, as requested by TRISH (Translational Research Institute for Space Health), to provide an in vivo comparator/validation of the in vitro HuMiX human gut-on-a-chip system, and on NSG mice whose hematopoietic systems were first humanized by repopulation with human hematopoietic stem cells (HSC) isolated from the bone marrow of healthy, astronaut-age donors.

effects of space radiation on the hematopoietic and GI systems.

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 Londo manded motological allerations in small intention response to protocols and 56% in subs 100 and 26% enso. Lines Martinez, Ma		omics, and hematopoietic system for lineage alterations and DNA damage.
Task Progress: Proceeding the equipate to the second of the equipate to t		• Found marked histological alterations in small intestine in response to protons and both 160 and 56Fe ions.
• Humanized the hematopoint system of over 200 NSG mice, insulled RFI-macking p-CLaps, and implicited there mice within SNL-109. • Humanized the hematopoint is system of over 200 NSG mice, insulled RFI-macking p-CLaps, and mainted there mice within the abbreviated 200-2008 ma. All mice from NSL-109. • Have heap analyzing the various tissues from the 96 wild-type CS7B16 mice we indicated integring integring NSL-109. • Have heap analyzing the various tissues from the 96 wild-type CS7B16 mice we indicated integring integring and the oblity of our curcumin-balen NLP is to provide again the oblity of our curcumin-balen NLP is to provide again the oblity of our curcumin-balen NLP is to provide again the oblity of our curcumin-balen NLP is to provide again the oblity of our curcumin-balen NLP is to provide again the oblity of our curcumin-balen NLP is to provide again the oblity of our curcumin-balen NLP is to provide again the oblity of our curcumin-balen NLP is to provide again the oblity of the presentitive species from the microbiome in the 11MbK system appears to provide our degree of protection agains the obletrons offects of again radius (in the torus of the provide market) between the species of the curculation is to be in MKK system appears to provide our degree of protection agains the obletrons offects our species from the microbiome in the 11MbK system appears to provide our degree of protection agains the obletrons offects our species from the microbiome in the 11MbK system appears to provide our curcumine bale in NFK and the CVLP is our book market by the NFT and CCR mathine in the OVLP is our book market by the NFT and CCR mathine in the OVLP is our book market by the the transfer of the market by the interval to the analysis are abared by bot NFT and CCR mathine in the OVLP is our book market by the interval to the intereval to the interval to the interval bale indignore an		• Discovered that exposure to Mars mission-relevant doses of protons and 56Fe ions leads to disruption of the epithelial barrier of the small intestine, as assessed by immunofluorescent staining for Claudin-3.
• I lare began analyzing the various tissues from the 96 wild-type C2BU6 mice wei module (SFP) and GCR induction exert on the various tissues organ systems of the body and the ubility of our currum-laden NLPs to protect against these flacts. • Task Progress: • We have found that pre-treatment of the wild-type mice with CNLPs uppents to reduce the amount of apoptosis seen in the small institution. FORWING expression is supplied antimized bacterial apocies have been incorporated into the MANK both, This new optimized system with a simplified microbione was expressed to various insubiring NSRL-10°C and wild be returning for NSRL 20°C. • Have now that the presence of representative species from the microbione in the MANK system appears to provide rome degre of provide matcelly better protection against all varieties of ions tested than simply giving currently biological statistic basis for the softwartantic basis for the softwartantic basis for the softwartantic basis of the MOSC currently have been being the profession and have solven that current advector the softwartantic basis of the MOSC model packaged in NLPs is far more effective, and indices transcriptomic charges that differ markedly from, than currentin abstem of the tore, mystem and the impectine more of themone transological indication, as we observed in our		• Humanized the hematopoietic system of over 200 NSG mice, installed RFI-tracking p-Chips, and irradiated these mice during NASA Space Radiation Laboratory (NSRL)-19C and the abbreviated 20A/20B run. All mice from NSRL19A have now been sacrificed and tissues are being analyzed. Mice from NSRL 19C are being sacrificed and analysis has begun.
•We have found that pre-treatment of the wild-type mice with CNLPs appears to reduce the amount of apoptosis seen in the small instation Following exposure to SEP/GCR malation. Task: Progress: •The HaMix gut-on-a-chip platform has been further optimized and limited bacterial species have been incorporated institu HMMX chip. This new optimized type: the wild a simplified microbiome was exposed to various ions during DNRL -VCC and will be returning to KNRL 20C. •Have now above that the presence of representative species from the microbiome in the HMIX system appears to reduce the degree of practicutions against SEP and GCR malation. Further attales are now underway to define the mechanise basis for these observations. •Have shown on LIP can mediate protection against SEP and GCR malation in vivo, at omics level. •We have bown that the presence of representative species from the microbiome in the HMIX system appears to generate a wealth of data on the collular-molecular pathways that are altered by both SEP and GCR radiation and the impact that DIX is far more clearch and microbiome. •Have shown that the PCM DP provide markedly heter protection against all Parameters whown that carcennin adhebition (Dix is far nord Ferlow, and induced); using human fibrobiase. •We have shown for the first time ever, that the exposure of mice harboring human hematopoictic systems to GCR malation (SEP and GCR) on the impact and the used to repeptide NOG mice charboring burnes performancelly from, that carcennin adhebition (Dix is far nord Ferlow, and induced) carcelly clinical hematophabigets has performinarily concluded this is due to induction of finams hematopoical and provide states performinarily concluded the system stareston the malageneoty of the specens to roughly 30 times		• Have begun analyzing the various tissues from the 96 wild-type C57BI/6 mice we irradiated during NSRL-19B by both immunohistochemistry and multi-omics approaches to define the effects that solar energetic particles (SEP) and GCR radiation exert on the various tissues/organ systems of the body and the ability of our curcumin-laden NLPs to protect against these effects.
Task Progress: • The Hulding gut-on-schip platform has been further optimized and limited hascrid species have been incorporated into the Huldin X bin, Thin in ow optimized system with a simplified microbiome was exposed to various ions during NSRL-19C and will be returning for NSRL 20C. • Have now value degree of protection against Heb addetrivies effects of space radiation. Further studies are now underway to define the mechanistic basis for these observations. • Have shown eNLPs can mediate protection against SEP and GCR radiation in vivo, at omics level. • Have shown eNLPs can mediate protection against Meb addetrivies of the microbiome was exposed to various ions during with the explorate observations. • Have shown eNLPs can mediate protection against SEP and GCR radiation in vivo, at omics level. • Have shown eNLPs can mediate protection against Meb addetrivies and have shown in the correct height hydroxy but are stated by volts SEP and GCR radiation and the impact the XPLP and MBOS contenting in Junna flow/bases. • Have shown, for the first time ever, that the exposure of mice harboring human themstopoictic systems to GCR radiation (66r ions, fins far, ofter ions now being leaded) leads to enlagement of the splaces to ronghly 30 times the conclude this is due to induction of human hematopoictic systems to GCR radiation (64re) in the mains three on the main theoret down and the insplace and the main protection of protection against far differ markedly from, than curcumin suspended in DMSO. • We have shown, for the first time ever, that the exposure of mice harboring human themospoictic systems to GCR radiation (64re) in one three of human thematopoictic and (10 respect wall have addiate) of protection against far differ markedly from, than curcumin markedly addiated (10 respect wall		• We have found that pre-treatment of the wild-type mice with cNLPs appears to reduce the amount of apoptosis seen in the small intestine following exposure to SEP/GCR radiation.
• Have now shown that the presence of representative species from the microbiom in the HuMX system appears to provide some degree of protection against the deterious effects of space radiation. Further studies are now underway to define the mechanistic basis for these observations. • Have shown ncNLPs can mediate protection against EB and GCR radiation in vivo, at omics level. • We have shown that CPL Pprovide marketible better protection against at larvieties of ions tested than simply giving curcumin in DMSO (dimethylsulfoxide), using human fibroblasts. • We have shown, that cevel.(DP provide marketible) better protection against at larvieties of ions tested than simply giving curcumin in DMSO. (dimethylsulfoxide), using human fibroblasts. • We have shown, for the first time ever, that the exposure of mice harboring human hematopoietic systems to GCR madiation of thram hematopoietic systems to GCR madiation of forman hematopoietic systems to GCR madiation of forman hematopoietic and provide on proor progress to-date has enabled us to begin rigorously testing out hypotheses rule or uprior studies in which human IISC were exposed to these same ions in vitro and then used to eropopulate NSG mice. Extensive analyses are underway to define that are rule and GCR statistical and supported at comport our bypothesis that exposure to space radiation at Mars mission-relevant desses, produces marked deficients effects on a study which accurantical orden and support our phyloshesis that exposure to the deleterious effects of space radiation during prolonged missions beyond to Ore from the deleterious effects on a study which euroaminister counterneasure that can protect astromatis from at least some of the deleterious effects of space radiation during prolonged missions beyond to Ore form that curcumin in this response. • We have shown, for th	Task Progress:	• The HuMix gut-on-a-chip platform has been further optimized and limited bacterial species have been incorporated into the HuMiX chip. This new optimized system with a simplified microbiome was exposed to various ions during NSRL-19C and will be returning for NSRL 20C.
• Have shown cNLPs can mediate protection against SEP and GCR radiation in vivo, at omics level. • We have shown that the cNLPs provide markedly better protection against all varieties of ions tested than simply giving curcumin in DMSO (dimethystalitoxido), using human fherolasts. • Have generated a wealth of data on the cellula/molecular pathways that are altered by both SEP and GCR radiation and the import that cNLPs (and DMSO-curcumin Jhave on these alternations, and have shown that curcumin delivered packaged in NLPs is far more effective, and induces transcriptomic changes that differ markedly from, than curcumin suspended in DMSO. • We have shown, for the first time ever, that the exposure of mice harboring human hematopoietic systems to GCR radiation (56Fc ions, thus far, other ions now being tested) leads to enlargement of the spleens to roughly 30 times the normal size (in several mice; not all). Immunohistology cause we observed in our prior studies in which human HSC were exposed to these same ions in vitro and then used to repopulate NSG mice. Extensive analyses are underway to define the nature of the malignancy. Our progress to-date has arealided us to begin ingrouxly testing our hypotheses regarding the effects of space radiation of these same ions of the deleterious effects on both defines human spheres. Foundeers, marked deletrinos effects on both defines human spherement (curcumine) and the subsequence of the solution in the spleres to dark is area easy to administer courremeasure that can protect antennation (the first of this with and has also begun to sheld (big to nume courtemesaure that can protect antennation the sequence) or space radiation and being testems. And the rowolate on the cellular on delivered within multiple tissues as a result of deprotements of the analysin and to iminitized SP and GCR and the testem of the s		• Have now shown that the presence of representative species from the microbiome in the HuMiX system appears to provide some degree of protection against the deleterious effects of space radiation. Further studies are now underway to define the mechanistic basis for these observations.
+ We have shown that the eNLPs provide markedly better protection against all varieties of ions tested than simply giving currumin in DNSO (dimethylativitic), using human fibroblasts. + Have generated a wealth of data on the cellular/molecular pathways that are altered by both SEP and GCR radiation and the impact that eNLPs (and DMSO-curremnin) have on these alterents, and have shown that curcumin delivered packaged in NLPs is far more effective, and induces transcriptionic changes that differ markedly from, than curcumin suspended in DNBO. • We have shown, for the first time ever, that the exposure of mice harboring human hematopoietic systems to GCR radiation (S6F ions, thus far, other ions now being tested) leads to entappoint opticitie systems to GCR radiation (S6F ions, thus far, other ions in vitro and then used to repopulate NSG mice. Extensive analyses are underway to define the nature of the malignaney. Our progress to date has enabled us to begin rigorously testing our hypotheses regarding the effects of space radiation (SEF and GCR) on the human hematopoietic and G1 systems, and has provided compelling evidence to support our hypothesis that exposure to space radiation at Mars mission-relevant doses, produces marked detectives effects on both of these tharman systems. These data have also supported our premise that a novel formulation of a romologied mission beyond Low Earthed within multiple tissues as a result of exposure of a living organism to "any rubation and the signing to exposure of a living organism to "any rubation and the role played by the gut microbiata in this response. Bibliography Type: Description: (Last Update! 07/01/2025) Arricles in Peer-reviewed Journals Almeida-Pornda G, Antla AJ, Pernda CD. "Therapeutic mesenchymal stronal cells for immunotherapy and		Have shown cNLPs can mediate protection against SEP and GCR radiation in vivo, at omics level.
Have generated a wealth of data on the cellular/molecular pathways that are altered by both SEP and GCR radiation and the impact that cULPs (and DMSO-curumin) have on these alterations, and have shown that curumin delivered packaged in NLPs is far more effective, and induces transcriptomic changes that differ markedly from, than curcumin delivered in DMSO.• We have shown, for the first time ever, that the exposure of mice harboring human hematopoietic systems to GCR radiation (S6Fe ions, thus far, other ions now being tested) leads to entaphologists has preliminarily concluded this is due to induction of human hematological malignancy, as we observed in our prior studies in which human HSC were exposed to these same using our hypotheses regarding the effects of space radiation (SFP and GCR) on the human hematopoietic and G1 systems, and has provided compliancy exists on underway to define the nature of the malignancy.Our progress to date has enabled us to begin rigorously testing our hypotheses regarding the effects of space radiation of the some of the deleterious effect of space radiation during prolonged missions beyond Low Earth of the scheman systems. These data have also supported our premise that a novel formulation of ar eardly available dietary supplement (curcumin) may have the ability to serve as an easy to exposure of a living organism to ?-ruy radiation and to simulated SFP and GCR antidition, and it is beginning to provide mechanistic clues regarding the means by which curcumi-NLPs mediate their protocitic veffect. Our newly formulated HuMX chip is performing well, and it has begun providely availed set of veffect. During a vealth of rigor set as an easy of exposure of a living organism to ?-ruy radiation and to simulated SFP and GCR antidation in this response.Bibliography Type:Description: (Last Update: 07/01/2025)Articles in Peer-reviewed Journ		• We have shown that the cNLPs provide markedly better protection against all varieties of ions tested than simply giving curcumin in DMSO (dimethylsulfoxide), using human fibroblasts.
•We have shown, for the first time ever, that the exposure of mice harboring human hematopoietic systems to GCR radiation (56F ions, thus far, other ions now being tested) leads to enlargement of the spheres to roughly 30 times the normal size (in several mice; not all). Inmunohistogic exam by clinical hematopathologists has preliminarily concluded this is due to induction of human hematological malignacy, as we observed in our prior studies in which human HSC were exposed to these sum constraints and the nused to repopulate NSG mice. Extensive analyses are underway to define the nature of the malignancy. Our progress to-date has enabled us to begin rigorously testing our hypotheses regarding the effects of space radiation (SEF and GCR) on the human hematopoietic and GP systems, and has provided compelling evidence to support our hypothesis that exposure to space radiation at Mars mission-releaved to every available dietary supplement (curcumin) may have the ability to serve as an easy to administer countermeasure that can proteet astronauts from at least some of the deleterious effects of space radiation and their portological pathways that are altered within multiple tissues as a result of exposure of a living organism to ?-myradiation and to simulated SEP and GCR or radiation, and it is beginning to provide mechanistic cluse regarding the means by which curcumin-NLPs mediate their protective effects. Our newly formulated HuMIX chip is performing well, and it has begun providing a wealth of information (the first of is kind) on the response of the human hematopical straign and the role played by the gut microbiotia in this response. Bibliography Type: Description: (Last Updated: 07/01/2025) Articles in Peer-reviewed Journals Mineida-Ponda G, Atala AJ, Pornda CD. "Therapeutic mesenchymal stromal cells for immunotherapy and for gene and drug deliver		• Have generated a wealth of data on the cellular/molecular pathways that are altered by both SEP and GCR radiation and the impact that cNLPs (and DMSO-curcumin) have on these alterations, and have shown that curcumin delivered packaged in NLPs is far more effective, and induces transcriptomic changes that differ markedly from, than curcumin suspended in DMSO.
Bibliography Type:Description: (Last Updated: 07/01/2025)Bibliography Type:Description: (Last Updated: 07/01/2025)Articles in Peer-reviewed JournalsAlmerida-Porada G, Atala AJ, Porada CD. "Therapeutic mescnehymal stromal cells for immunotherapy and for gene and rug delivery." Mol Ther Methods Clin Dev. 2020 Mar 13/16/20424. <u>https://doi.org/10.3380/fgene.2021.812188. PMID: 35111205; PMID: 3511120</u>		• We have shown, for the first time ever, that the exposure of mice harboring human hematopoietic systems to GCR radiation (56Fe ions, thus far, other ions now being tested) leads to enlargement of the spleens to roughly 30 times the normal size (in several mice; not all). Immunohistology exam by clinical hematopathologists has preliminarily concluded this is due to induction of human hematological malignancy, as we observed in our prior studies in which human HSC were exposed to these same ions in vitro and then used to repopulate NSG mice. Extensive analyses are underway to define the nature of the malignancy.
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