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Authors: Beheshti, Afshin, Miller, Jack, Kidane, Yared, Berrios, Daniel, Gebre, Samrawit G., et al.

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COMMENTARY

NASA GeneLab Project: Bridging Space Radiation Omics with Ground Studies

Afshin Beheshti,[a] Jack Miller,[b] Yared Kidane,[a] Daniel Berrios,[c] Samrawit G. Gebre[a] and Sylvain V. Costes[d,1]

[a] *Wyle Labs, NASA Ames Research Center, Moffett Field, California, 94035;* [b] *Lawrence Berkeley National Laboratory, Berkeley, California, 94720;* [c] *USRA, NASA Ames Research Center, Moffett Field, Calfornia 94035; and* [d] *NASA Ames Research Center, Space Biosciences Division, Moffett Field, California 94035*

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Accurate assessment of risks of long-term space missions is critical for human space exploration. It is essential to have a detailed understanding of the biological effects on humans living and working in deep space. Ionizing radiation from galactic cosmic rays (GCR) is a major health risk factor for astronauts on extended missions outside the protective effects of the Earth's magnetic field. Currently, there are gaps in our knowledge of the health risks associated with chronic low-dose, low-dose-rate ionizing radiation, specifically ions associated with high (H) atomic number (Z) and energy (E). The NASA GeneLab project (https://genelab.nasa.gov/) aims to provide a detailed library of omics datasets associated with biological samples exposed to HZE. The GeneLab Data System (GLDS) includes datasets from both spaceflight and ground-based studies, a majority of which involve exposure to ionizing radiation. In addition to detailed information on radiation exposure for ground-based studies, GeneLab is adding detailed, curated dosimetry information for space-flight experiments. GeneLab is the first comprehensive omics database for space-related research from which an investigator can generate hypotheses to direct future experiments, utilizing both ground and space biological radiation data. The GLDS is continually expanding as omics-related data are generated by the space life sciences community. Here we provide a brief summary of the space radiation-related data available at GeneLab.

INTRODUCTION

There is a need in the radiation biology community for data on the effects of exposure to chronic low-dose radiation. Acquisition of low dose-rate ionizing radiation data is possible only at a small number of facilities worldwide (*1–8*).

NASA's GeneLab Data Systems (GLDS) (https://genelab.nasa.gov/) houses a library of omics datasets with associated detailed, curated dosimetry information that has been steadily growing since 2015 (Fig. 1). This repository is helping to bridge the gap between radiation studies performed on Earth and biological experiments conducted in space since the early 1990s. In this commentary, we provide a brief summary of the content of the repository in terms of species, radiation quality and dosimetry method, as well as the types of omics data being collected. We also provide comparisons of dose and dose rates for samples irradiated in ground studies versus spaceflight experiments.

Most of these studies were funded by the NASA Human Research Program, which has supported numerous ground-based studies with high-linear energy transfer (LET) radiation

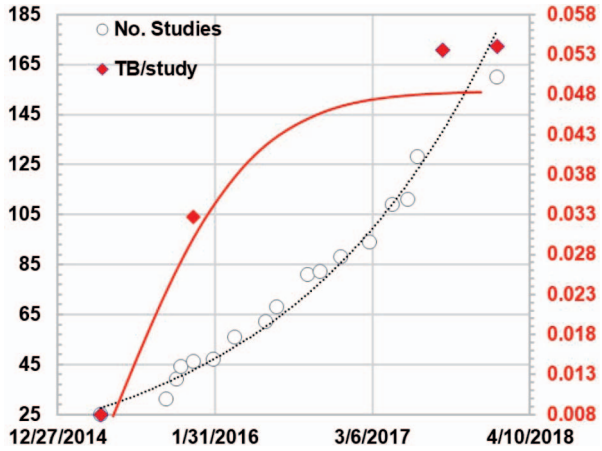

FIG. 1. The number of datasets on GeneLab over time. A scatter plot representing the number of datasets on GeneLab (left-side y-axis) that increase over time starting from the creation of GeneLab in 2014. The right-side axis and red data points represent the number of terabytes (TB) per study for the datasets on GeneLab. The lines represent exponential fits to the data.

[1] Address for correspondence: NASA Ames Research Center, Space Biosciences Research Branch (SCR), Moffett Field, CA 94035; email: sylvain.v.costes@nasa.gov.

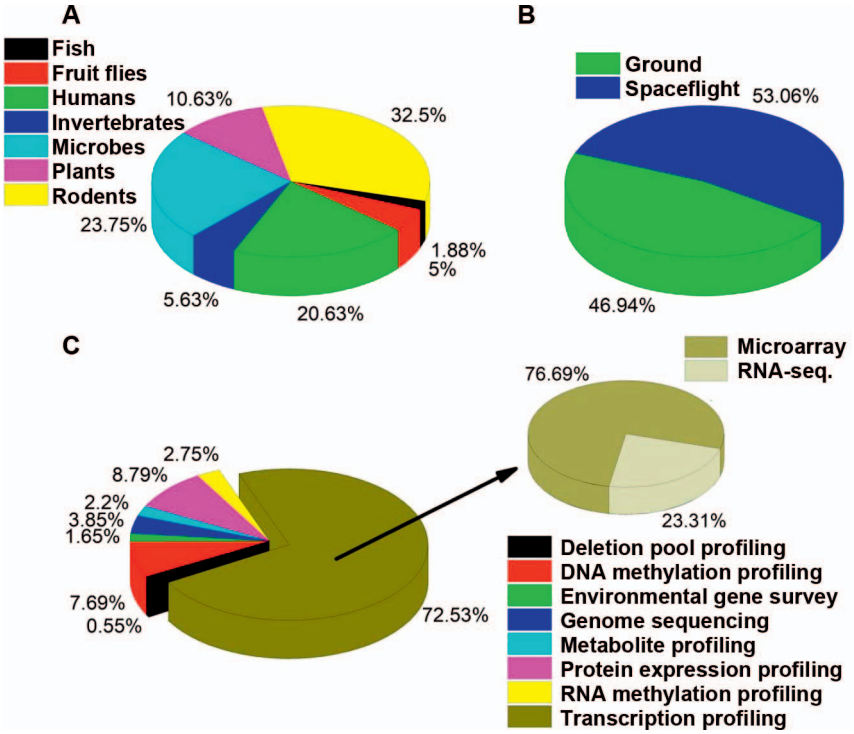

FIG. 2. The type of data available on GeneLab. Panel A: By organism. Panel B: The number of ground and spaceflight experiments Panel C: By type of assay.

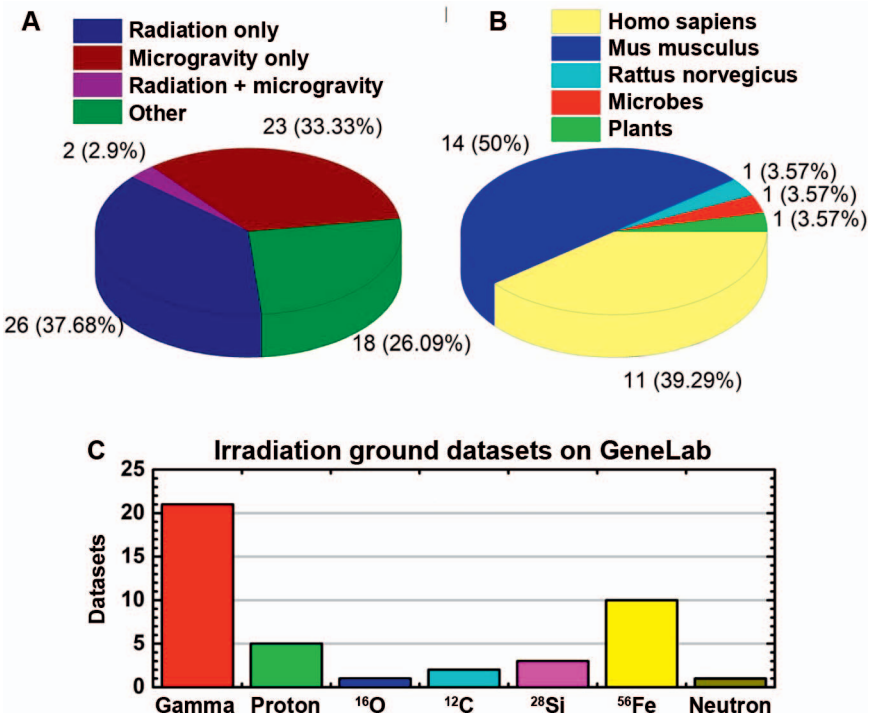

FIG. 3. The distribution of ground studies on GeneLab. Panel A: The type of data on GeneLab associated with ground studies. Panel B: The organism distribution of radiation ground study datasets available on GeneLab. Panel C: The number of datasets associated with different ionizing radiation available on GeneLab.

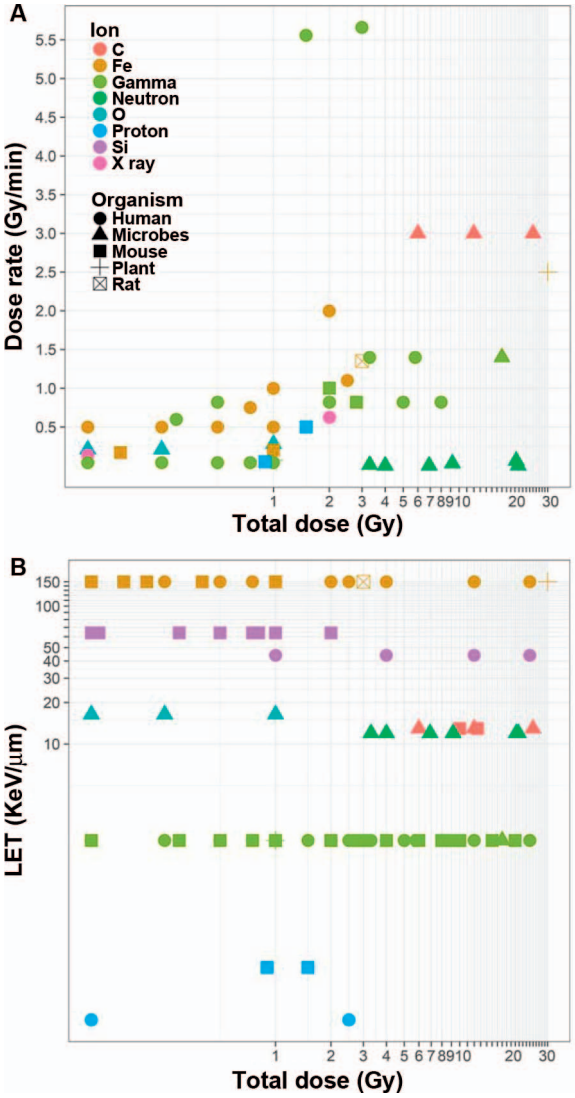

FIG. 4. Distribution dose rate, dose and LET for ionizing radiation ground studies on GeneLab. Panel A: Distribution of dose rate (Gy/min) vs. total dose (Gy) for all radiation ground studies available on GeneLab. Some GeneLab radiation datasets have missing dose-rate information due to the lack of information available from the investigator. Panel B: LET (KeV/µm) vs. total dose (Gy) for all radiation ground study datasets on GeneLab.

generated at the NASA Space Radiation Laboratory (NSRL; Upton, NY) (*3*), with the U.S. Department of Energy's Low Dose Radiation Research Program providing primarily low-LET data and the NASA Space Biology Program providing primarily data from specimens flown in space.

There is a diverse set of space-related omics data available on GeneLab, with a total of 157 datasets as of February 2018. These entries include data from a wide variety of different organisms including: rodents, human cells, plants, microbes, invertebrates, drosophila and fish (Fig. 2A). Fifty-three percent of the datasets were gathered from spaceflight experiments and 47% from ground-related space studies (which includes radiation studies done at NSRL) (Fig. 2B). The current datasets have employed various assays with 73% being transcriptional profiling, and 77% of the transcriptional profiling using oligonucleotide microarray techniques (Fig. 2C). Note that the latest trend shows a growing fraction of transcriptional profiles employing RNA sequencing techniques (currently 23%), which is also reflected by the increasing size per datasets in recent years (Fig. 1, red diamonds). Investigators with published or unpublished omics data related to space research are encouraged to join our effort by contributing their datasets (https://genelab.nasa.gov).

RADIATION GROUND STUDIES CURRENTLY IN GENELAB

Sixty-nine GeneLab datasets represent ground (Earth-based) space research, with 28 specifically investigating radiation effects and the majority of these were conducted at NSRL (Fig. 3A) (*3*). Investigations of simulated microgravity comprise the remainder of the ground experiments (*9–17*), together with a small number studying atmospheric pressure (*18*), exercise/nutrition (*19*), specimen freezing (*20*), genotype (*21–28*), hypergravity (*9, 29–31*), sample analysis protocols (*32*), temperature (*9, 33, 34*) or time points (*35*). The majority of the ground-based radiation experiments were performed using mice (Fig. 3B). *In vitro*, human tissue or cell experiments comprise most of the remaining experiments, with one study each on radiation effects on microbes, plants and rats. Gamma-radiation exposure experiments comprise the majority of the radiation datasets available in the repository (Fig. 3C), largely for comparison to HZE radiation. Proton and ^{56}Fe-radiation experiments (*28, 36–42*) comprise the majority of simulated space radiation-related GeneLab datasets, with a few experiments related to ^{16}O (*43*), ^{12}C (*44*), ^{28}Si (*45*) and neutrons (*46*) (Fig. 3C).

The GLDS also contains extensive information on parameters characterizing the ionizing radiation employed, with most datasets including the following information: ion, total dose, dose rate, LET and energies associated with the radiation. The distribution of dose rates versus total dose (Fig. 4A) illustrates the wide range of radiation-related datasets, from low doses (0.1 Gy) to high doses (30 Gy), with dose rates ranging from 0.001 Gy/min to 5.66 Gy/min. Typically, microbes and plants were exposed to higher total doses, while the majority of the rodent research used doses between 0.1 Gy and 3 Gy (with some gamma experiments done at higher doses). The LET for these experiments ranged from 0.24 keV/µm to 150 keV/µm (Fig. 4B). Since GeneLab relies on the investigators to provide these metadata, not all datasets have complete metadata: there are 13 datasets with missing dose-rate information. It is critical for all investigators submitting data to GeneLab to provide as much information as possible about irradiation conditions to avoid such issues. GeneLab is actively working to gather missing information.

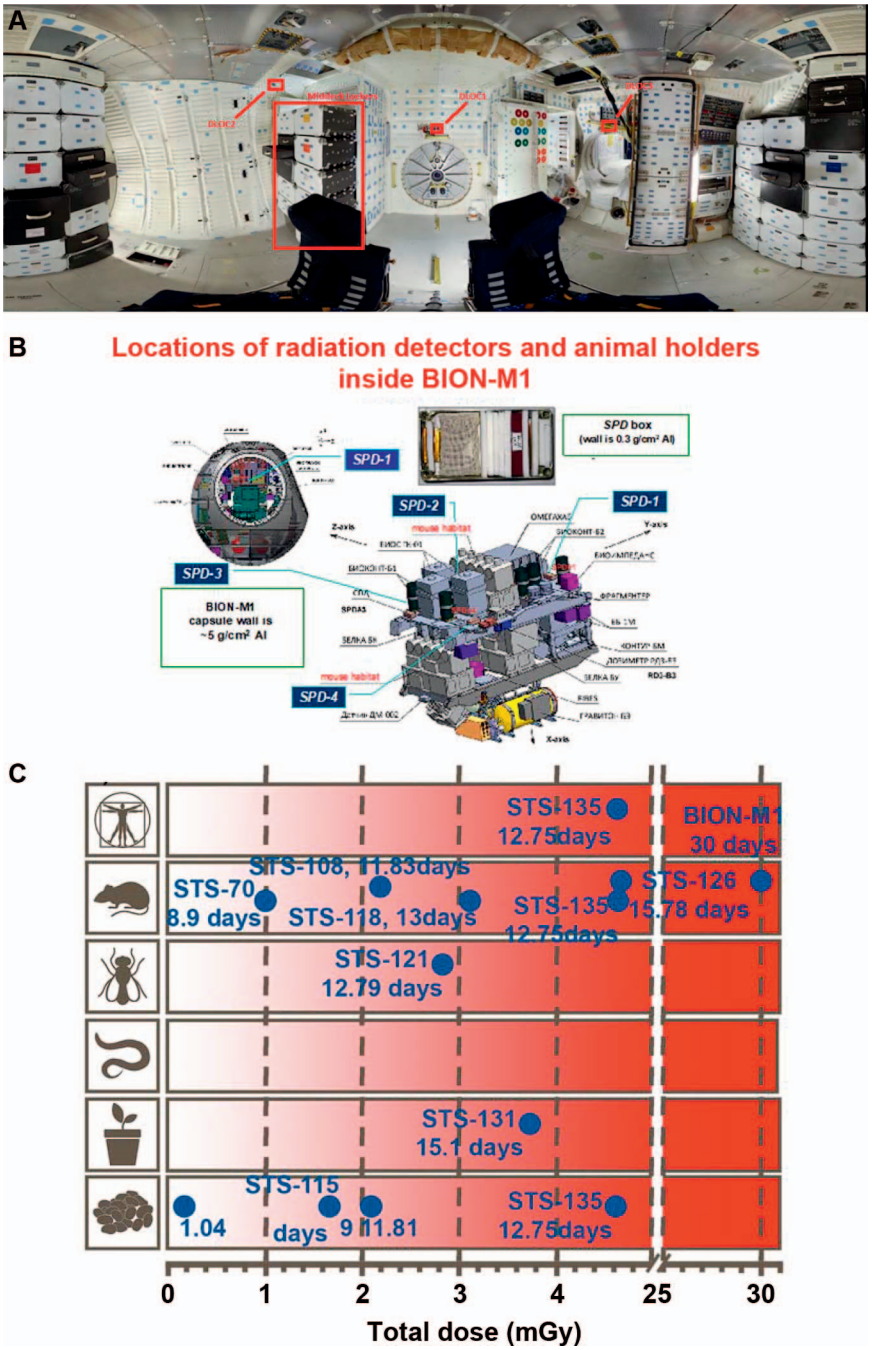

FIG. 5. Summary of spaceflight datasets available on GeneLab. Panel A: Image of the placement of the dosimeters on the space shuttle missions. Panel B: Image of placement of dosimeters on BION-M1 mission. Panel C: Distribution of total dose absorbed (mGy) per spaceflight mission for each organism. This includes both space shuttle missions (STS) and BION-M1 missions. The mission number and time in space is provided next to each datapoint.

SPACE RADIATION DOSIMETRY

GeneLab has recently begun documenting the absorbed radiation dose received by samples flown in space for experiments primarily testing the effects of microgravity (i.e., only incidentally examining space radiation effects). To date, omics data are available for experiments conducted on three types of vehicles that have carried samples into space: the ''Space Shuttle'' (or Space Transportation System, STS), free-flying satellites (BION, FOTON) (*47, 48*) and the International Space Station (ISS). The dosimetry measuring techniques varied from vehicle to vehicle and, for ISS, from module to module. Because the primary purpose of on-board dosimetry on crewed vehicles is to monitor astronaut health and, on free flyers, whole-environment monitoring, biology experiments typically

have not flown with ''dedicated'' dosimeters (i.e., dosimeters integrated into experiment platform housing). Therefore, doses to which study samples are exposed frequently must be interpolated and/or extrapolated from nearby dosimeters. Both passive and active dosimetry have been used on these vehicles. For STS, three passive dosimeter packages were fixed in locations on the shuttle middeck, where biological samples were located (Fig. 5A). In the case of BION (*47, 48*) (Fig. 5B) and ISS, both passive (thermoluminescent dosimeters, TLDs or plastic nuclear track detectors, PNTDs) and active (solid state, tissue equivalent proportional counters) were used. Two qualities of radiation were considered: low-LET (photons and electrons) and high-LET (charged nuclei). For passive dosimeters, TLDs are sensitive to low-LET charged particles ($<$10 keV/μm) and PNTDs to high-LET ($>$10 keV/μm). Active dosimeters are sensitive to a wider range in LET and, depending on the detector, can provide time resolution, LET spectra and some particle identification. By integrating the dose from the time-resolved data over the duration of the experiment, the total absorbed dose can be calculated. Depending on the configuration of dosimeters in the vicinity of the samples, absorbed dose may be reported as averaged with other detectors, or individually.

Taking into account the wide variety of dosimetry scenarios, we have chosen to report the ''lowest common denominator'' data: the data that are common to most if not all dosimeters, whether passive or active. Therefore, each omics dataset in the GeneLab repository with samples flown in space has a corresponding metadata set, which includes the exposure duration, and the average, minimum and maximum absorbed dose received, broken out into low- and high-LET charged particles (when LET resolution is available). The duration of the exposure is defined as the time a sample was in space and biologically active, i.e., when the sample has returned to Earth or when it is chemically fixed or frozen in space.

It is important to note that the absorbed doses we provide in these metadata are an approximation, due to several limiting factors. On factor is that there is known contribution of sensitivity in charge and LET for each detector being used. For example, even though TLDs detect low-LET radiation, the detected dose also includes some contribution from charged nuclei depending on the charge and speed of the nuclei traversing the detector. Similarly, active detectors, even if tuned to specific energies and charges, can still have trace doses from low-LET particles and neutrons. In addition, reported dosimetry does not take into account the additional shielding provided by the sample enclosure. For low-energy particles or low-LET, this hardware could have significant attenuating effect and would be unique for each mission and experiment. Therefore, in addition to the radiation metadata for individual datasets, GeneLab also reports dosimetry measurements for all detectors available for each mission, in a ''reference information'' section of the GeneLab database. A glance at these data show that there is a wide range of total absorbed dose over the various spaceflight experimental environments (Fig. 5C). For example, rodents flown on the BION-M1 missions (*49–51*) received the largest dose of ionizing radiation (30.2 mGy), while the rodents on-board STS missions received doses only in the range of 1–4.7 mGy. GeneLab is currently assembling all the dosimetry information for the ISS-related datasets and will have it available in the near future. Our goal in providing these data is to facilitate more detailed analyses of these kinds of environments by other investigators in the context of known radiation response measured in ground studies.

SUMMARY

The goal of GeneLab is to provide users with a data repository and analytical and visualization tools for molecular signals relating to a host of factors known to influence biological response, including radiation dose, dose rate and quality. Standardizing the dosimetry information in the entire repository is an essential first step towards accomplishing this task, and we hope the radiation biology community shares in our excitement about this new source of information and will visit the database often.

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