NASA GeneLab platform utilized for space radiation dosimetry biological response compared to radiation ground studies

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GeneLab Database (>200 data sets)

**All GeneLab Datasets**

- fish: 10.63%
- fruit flies: 5.63%
- human: 32.5%
- invertebrate: 20.63%
- microbes: 1.88%
- plant rodents: 5%

**Specific Ground Radiation GeneLab Datasets**

- Radiation only: 2 (2.9%)
- Microgravity Only: 14 (50%)
- Radiation + Microgravity: 23 (33.33%)
- Other: 11 (39.29%)

**GeneLab Data Types**

- deletion pool profiling: 76.69%
- DNA methylation profiling: 23.31%
- environmental gene survey: 72.53%
- genome sequencing: 8.79%
- metabolite profiling: 3.85%
- protein expression profiling: 3.85%
- RNA methylation profiling: 1.65%
- transcription profiling: 1.65%

**Irradiation Ground Datasets On GeneLab**

- Gamma: 10 datasets
- Proton: 5 datasets
- $^{16}$O: 2 datasets
- $^{12}$C: 1 dataset
- $^{28}$Si: 1 dataset
- $^{56}$Fe: 1 dataset
- Neutron: 1 dataset

Beheshti et al., Radiation Research 2018
Radiation Dosimetry for STS samples (ISS to follow)

Beheshti et al., Radiation Research 2018
Space Environment

2½ Years, 2,600 X-Rays

Americans on average absorb the radiation equivalent of at least 7 chest X-rays each year.

Space missions, outside of Earth's protective atmosphere and magnetic field, expose astronauts to many times more.

MILLIREM:

<table>
<thead>
<tr>
<th>Source</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEST X-RAY</td>
<td>8 to 50</td>
</tr>
<tr>
<td>AVG. YEARLY RADON DOSE</td>
<td>200</td>
</tr>
<tr>
<td>U.S. AVG. YEARLY DOSE</td>
<td>350</td>
</tr>
<tr>
<td>PET SCAN</td>
<td>1,000</td>
</tr>
<tr>
<td>1 YEAR IN KERALA, INDA</td>
<td>1,300</td>
</tr>
<tr>
<td>U.S. NUCLEAR WORKER LIMIT PER YEAR</td>
<td>5,000</td>
</tr>
<tr>
<td>APOLLO 14 (9 DAYS)</td>
<td>1,140</td>
</tr>
<tr>
<td>SHUTTLE 41-C (18 DAYS)</td>
<td>5,600</td>
</tr>
<tr>
<td>SKYLAB 4 (84 DAYS)</td>
<td>17,800</td>
</tr>
<tr>
<td>MARS MISSION TOTAL</td>
<td>130,000</td>
</tr>
</tbody>
</table>

TRIP TO AND FROM MARS (1 YEAR): 80,000
CN MARS (1.5 YEARS): 30,000
FROM SOLAR FLARE: 20,000

Credits: NASA
The Goal of this work and GeneLab Datasets Utilized for Analysis

- Ground datasets will be compared to both *in vivo* and *in vitro* datasets from samples flown to the ISS and on shorter shuttle missions.
- From this analysis we will be able to associate distinct biological signatures associating specific ions to specific biological response to radiation exposure in space.
Gene Set Enrichment Analysis to Compare all Datasets

Gene Ontology (GO)

- Auto-Annotate GO Clusters
- Use Normalized Enrichment Scores (NES) for downstream analysis

FDR < 0.05 GO pathways utilized

Create new GO network based on Annotated GO Clusters
Clustering of GO GSEA Terms Based on Normalized Enrichment Scores (NES)
Clustering of Pathways with Dose

All Go Terms

Annotated Go Terms
The Annotated GO Pathways will Subcluster into Logical Groups

Two possible explanations for this specific signature to ground studies:
1. This is a signature associated with deep space radiation, since all spaceflight samples are only experiencing doses at LEO
OR
2. This signature is only relevant to ground studies and has no relevance to the biology observed in space.
Example Annotated Pathways Known to be Impacted by Space Irradiation

Regression Splines

Annotated GO Pathways
Muscle Related Pathways

Single Ion Data

Annotated GO Pathways
Cell Cycle

Single Ion Data
Trends as a function of dose with annotated GO pathways

Cluster 1: RNA processing, telomere lengthening, and mitochondrial pathways

Cluster 2: Developmental Pathways

Cluster 3: Calcium Signaling and Actin Binding

Cluster 4: Immune, Inflammation, muscle, and lipid related pathways

Cluster 5: photoreceptor and synapse pathways

Cluster 6: amino acid and ribosomal pathways

Cluster 7: drug response and catabolic process pathways

Cluster 8: Mitotic and Cell Cycle Related Pathways

Cluster 9: hydration related pathways

Single Ion Data

Regression Splines
Summary and Future Work

Summary:
• This technique and results can be used to determine what pathways to filter out from ground experiments to provide relevance to actual space radiation exposure
• Help identify unique signatures associated with spaceflight

Analysis left to do:
• Add predictions and potentially modeling to predict impact on pathway regulation in deep space
• Add LET, Energy, and Dose Rate information to analysis