Building Better Biosensors for Exploration into Deep-Space, Using “Humanized” Yeast

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As we plan manned missions to Mars & beyond, it’s essential that we understand the deep-space environment.

Limitations in culturing human cells, human homology, and flight-history make yeast an ideal biosensor.
Leveraging technical “know-how” from BioSentinel

- 2y successful storage of desiccated yeast, growth media, & metabolic dye under spaceflight conditions
- 6 completed campaigns at the NASA Space Radiation Lab at Brookhaven National Labs + 5 runs at Loma Linda University’s proton facility (including 2 solar particle event simulations)
- Measured significant sensitivity of yeast cells to 10 cGy & lower doses of high LET particles (1 GeV Fe & H etc.) which are relevant doses in long duration deep-space missions
- The build of the entire payload enclosure containing yeast cells in fluidic cards, including a LET spectrometer coupled with the spacecraft and all functional elements of the BioSentinel payload, will be completed by Summer 2018
- One copy of BioSentinel will fly to the ISS & a second copy on the SLS-EM-1 mission (2019)
We can model effects of deep-space radiation on human cells, using yeast as a proxy.

- Replaced 414 yeast genes w/ human homolog
- ~50% rescue
- Even higher when matched into gene models!

Viability
Assays

DNA Repair

Measure ability of human gene to repair DNA damage induced by *space-like radiation

Using a built-in direct repeat recombination assay described in Manthey et al. 2017

Molecular Response

Assess molecular responses to *space-like radiation using Next Generation Sequencing

RNA-seq described by Hateley et al. 2016 (Bhattacharya lab)
How Measuring viability & metabolics of “humanized” yeast in response to space-like radiation

- **1st:** Yeast cells expressing human DNA repair protein were able to partially rescue loss of viability in response to ionizing radiation.
- **2nd:** DNA repair in response to radiation-induced DNA damage
- **3rd:** Molecular response to low-dose “space-like” radiation via alamarBlue metabolic assay & RNA-seq
The Direct Repeat Recombination assay measures repair of a spontaneous DNA double-strand break induced by “space-like” radiation.

Deep space ionizing radiation causes double strand breaks (DSBs) in DNA.

The Direct Repeat Recombination assay is a simple way to measure DNA DSB repair in yeast.

After a radiation induced DNA DSB in yeast, the process of homologous recombination repairs the break.

This results in cells that were previously unable to grow in histidine “minus” media (his-) cells to become HIS+ and now able to grow in such media.
Future Directions & Significance

**Completed initial run @ NASA’s Brookhaven National Laboratory** for radiation sensitivity to high energy Fe

Will **knockout or over-express** yeast genes identified in RNA-seq analysis, then **swap in human genes**, to better understand **molecular response to cosmic radiation**

**Leverage BioSentinel science, engineering & hardware** towards future missions to prepare humans for long-term deep-space travel
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