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

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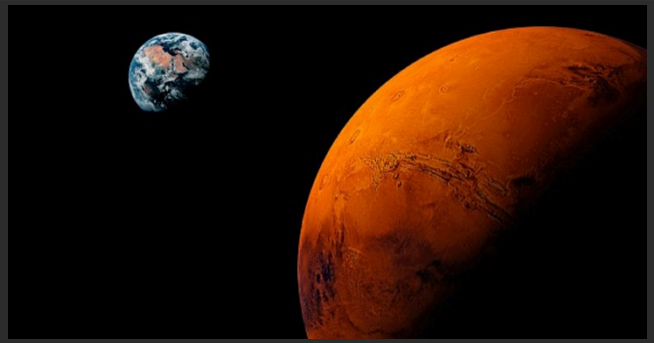
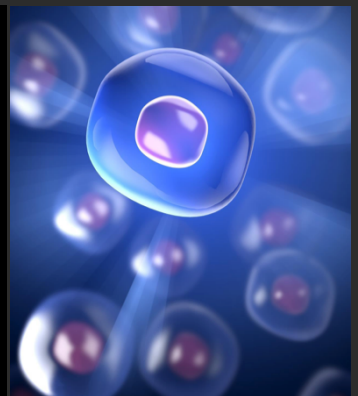
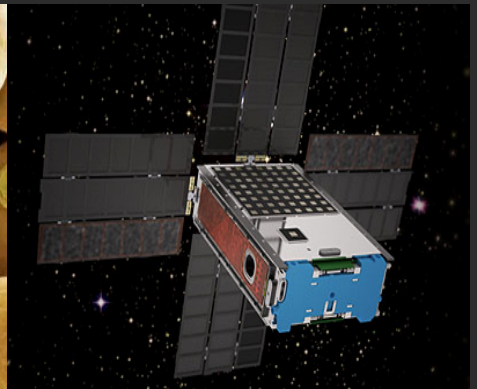
Why?

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

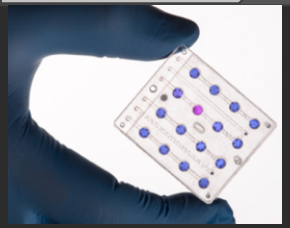
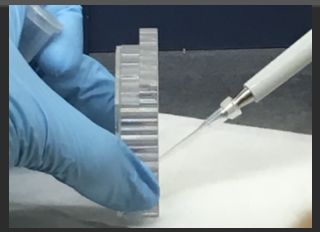
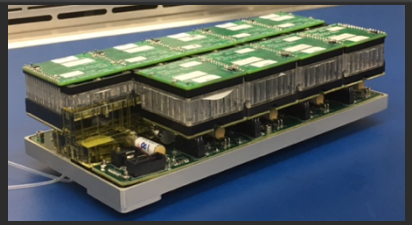
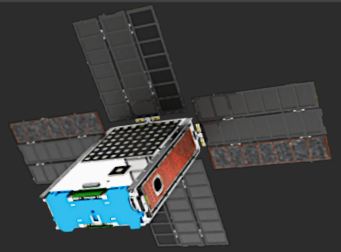


Limitations in culturing human cells, human homology, and flight-history make yeast an ideal biosensor





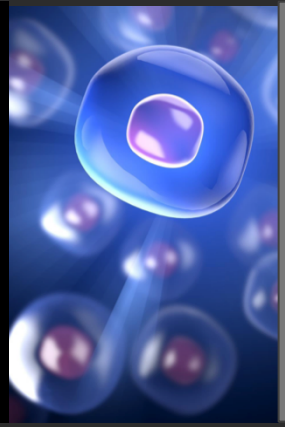
Experience Leveraging technical “know-how” from BioSentinel

- 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)*

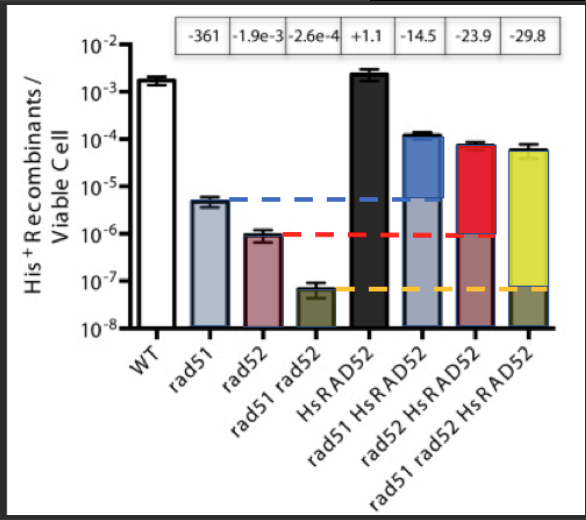
How?

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!

Kachroo et al. Science 2015



Viability Assays

Test response of our "humanized" yeast to *space-like radiation

**Gamma rays at ARC, 250 MeV protons at Loma Linda Univ, high LET particles (e.g. 1 GeV Fe etc.) at BNL – BioSentinel team*

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

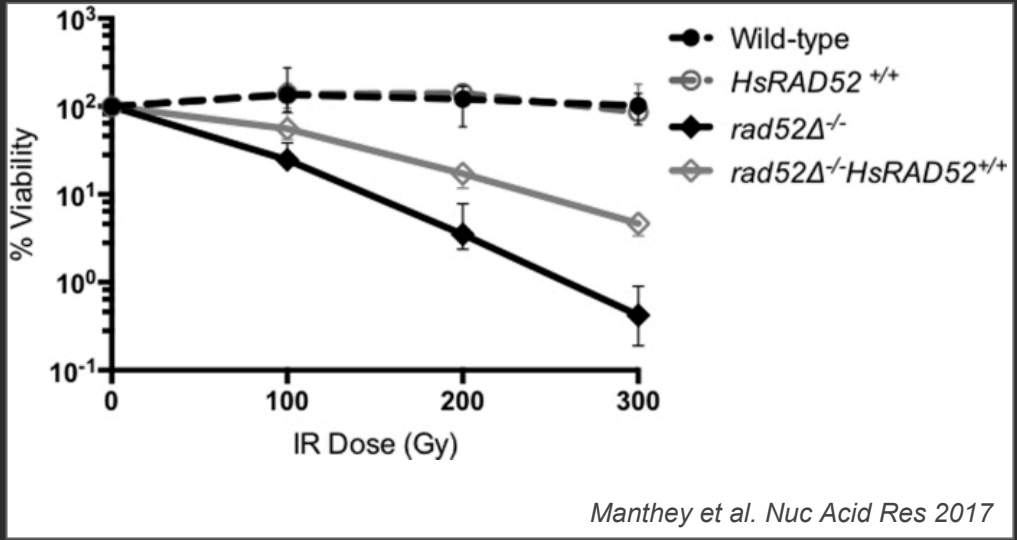
Molecular Response

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

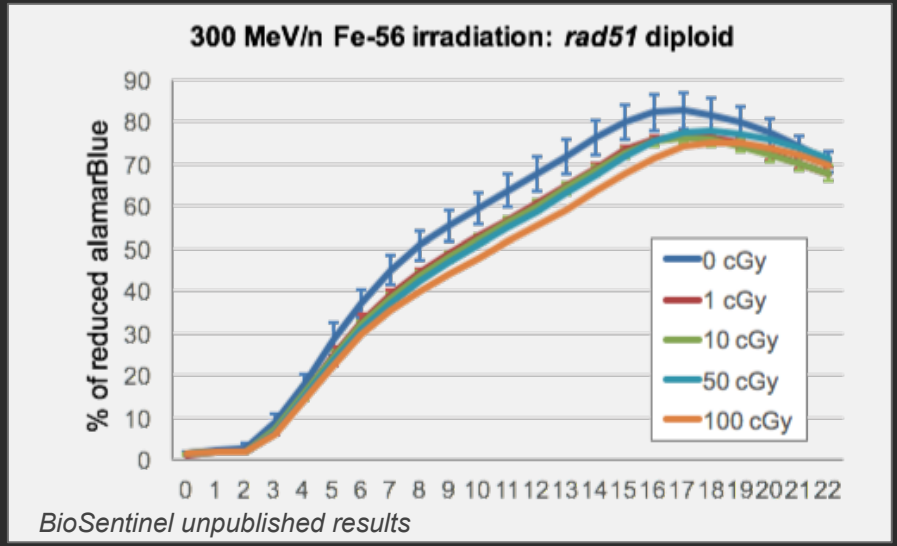
RNA-seq described by Hateley et al. 2016 (Bhattacharya lab)

How

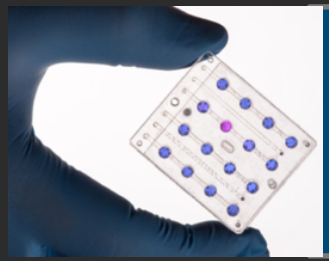
Measuring viability & metabolics of “humanized” yeast in response to space-like radiation



Manthey et al. Nuc Acid Res 2017



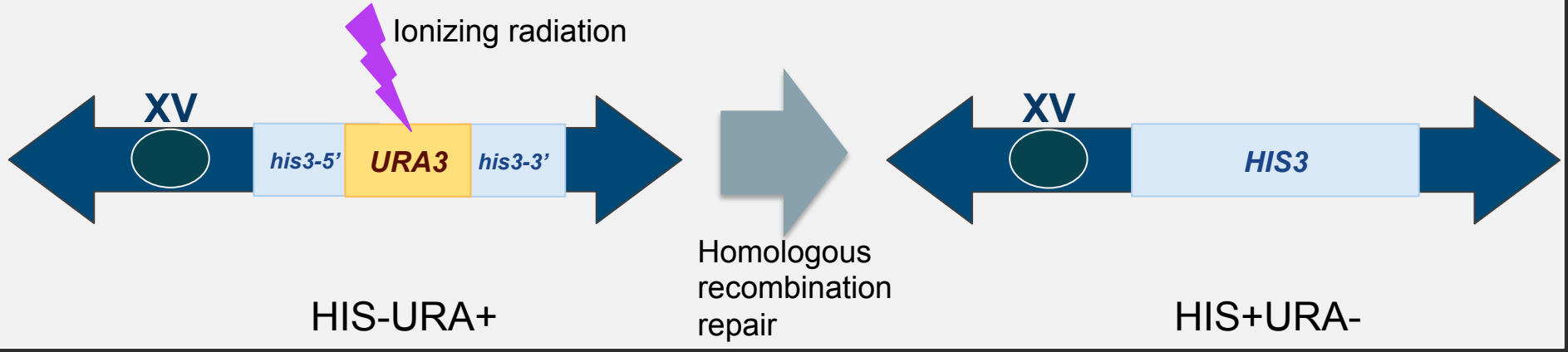
BioSentinel unpublished results



- **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

How?

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*

Acknowledgements

BioSentinel Team

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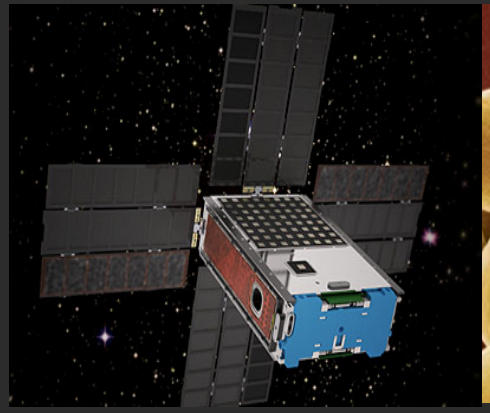

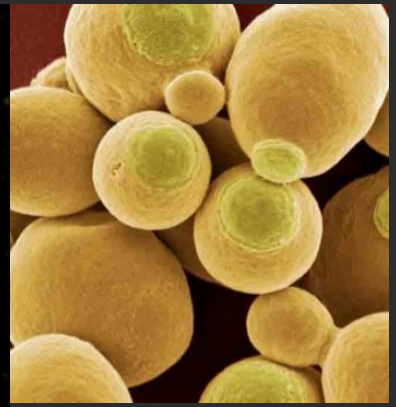

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