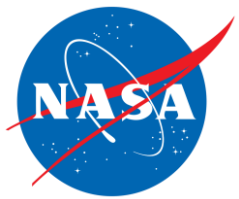




# Using DNA damage to investigate the individual variability of human sensitivity to ionizing radiation

*E. Pariset\**, S. Malkani, V. Gomez Gonzalez, Alejandra Lopez Macha, Ivan G. Paulino Lima, E. Cekanaviciute, and S.V. Costes

NASA Ames Research Center, Space Biosciences Branch  
Human Research Program HRP #NNJ16HP24I



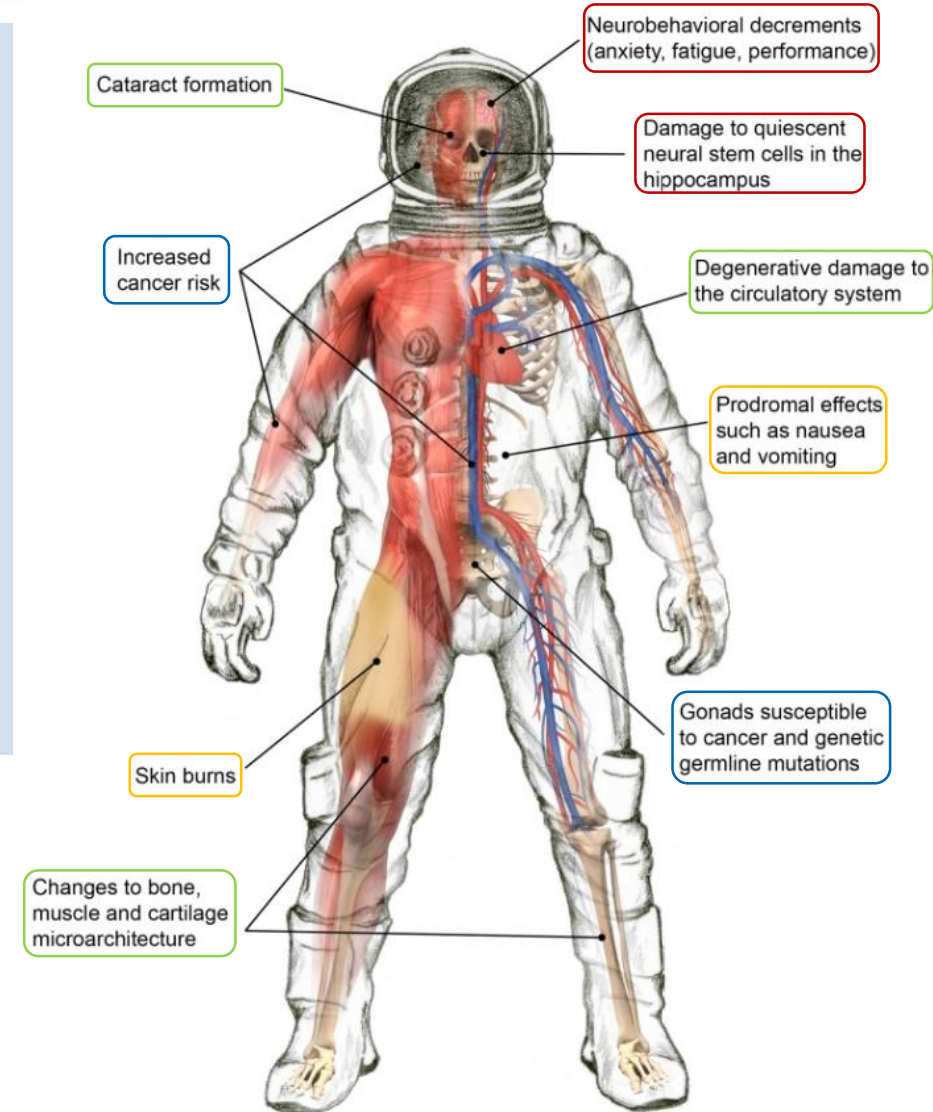
# Space Radiation Risks

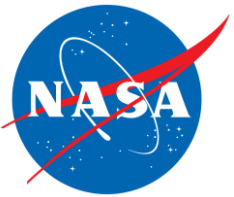
One of the 5 Hazards of Human Spaceflight (NASA's Human Research Program)



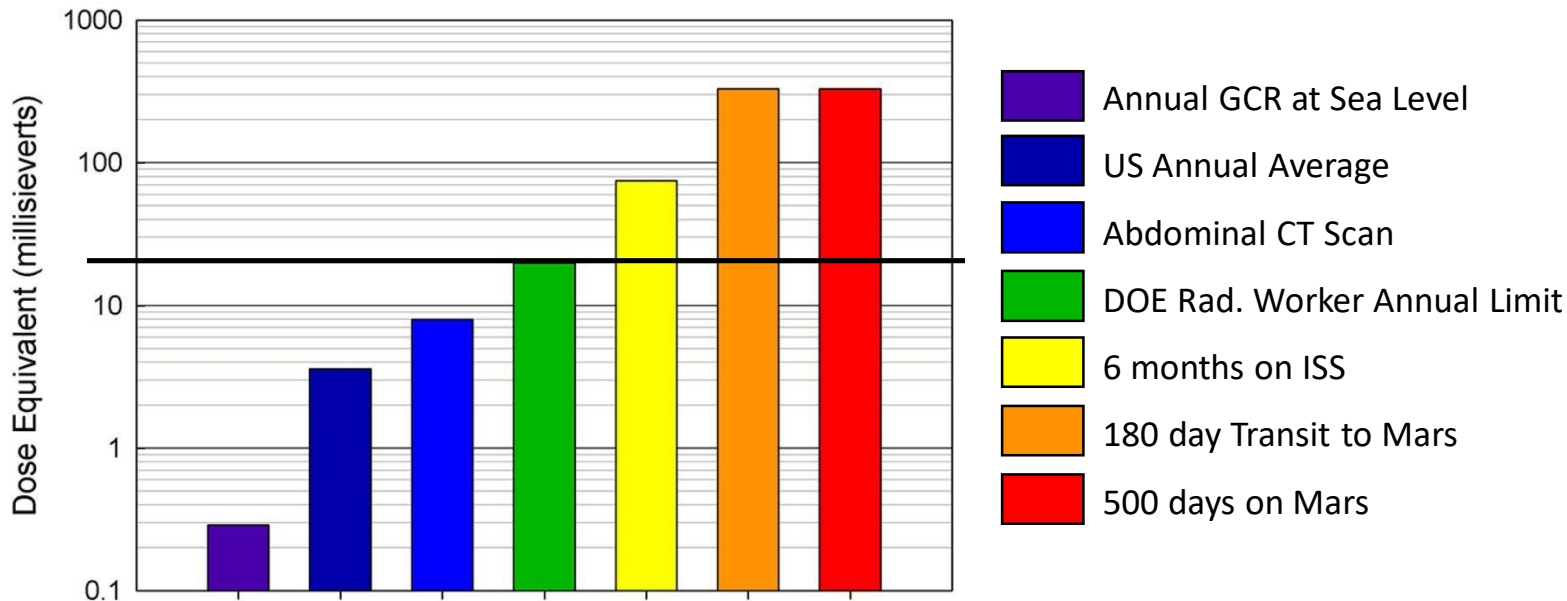
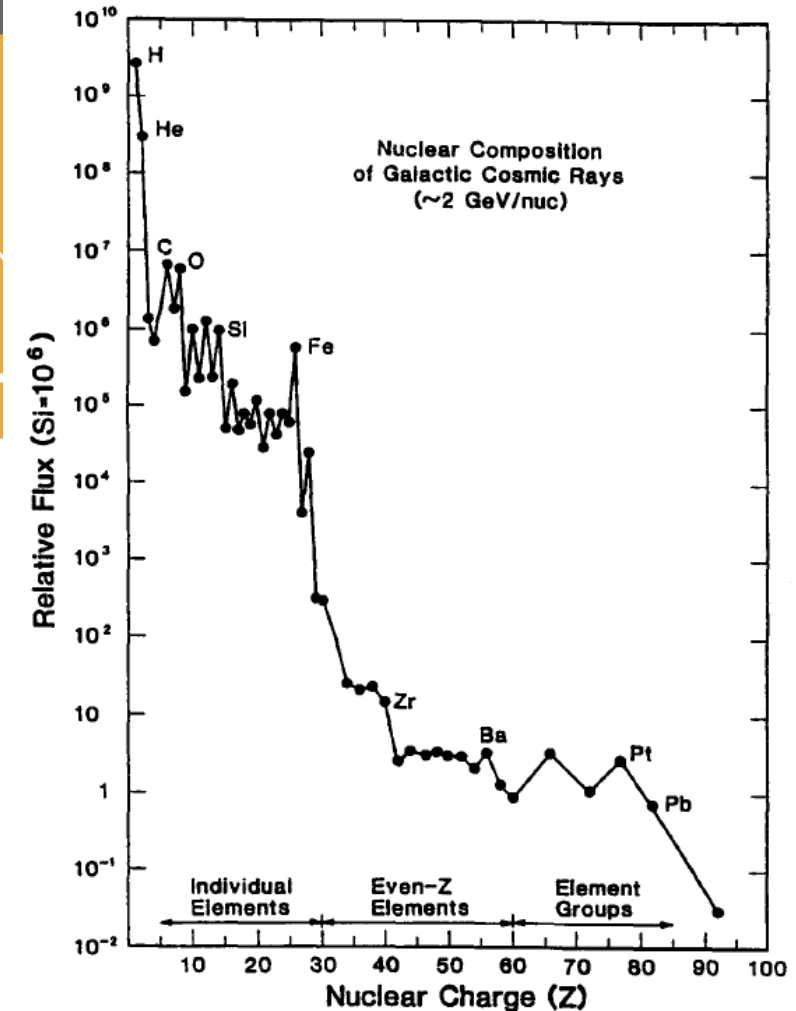
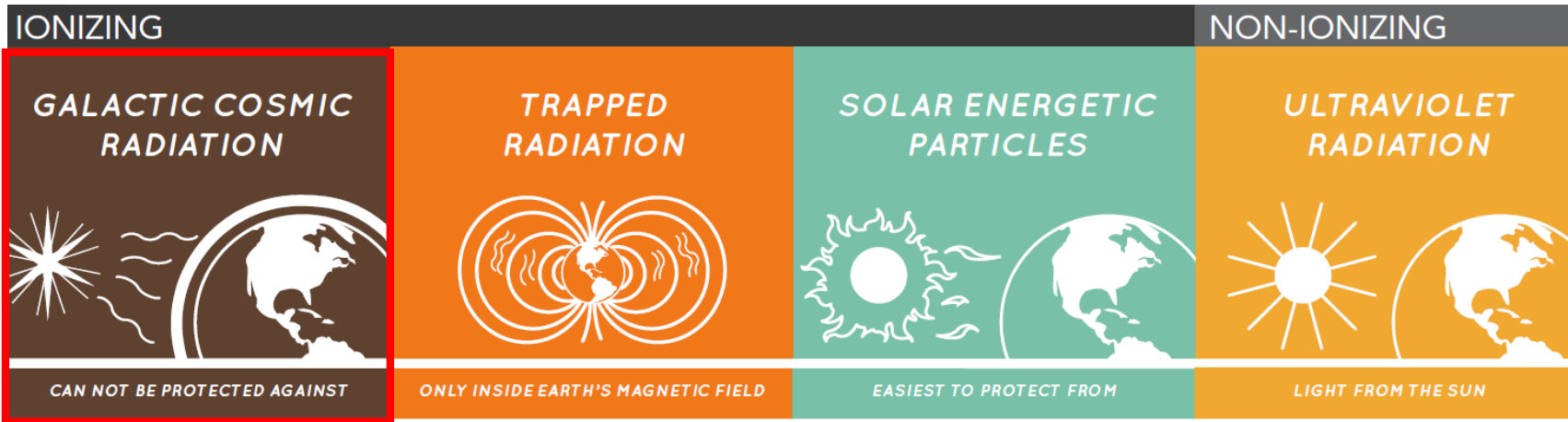
## Health Risks from Space Radiation:

- Increased risk of cancers
- Acute and late central nervous system effects
- Degenerative tissue effects
- Acute radiation risks



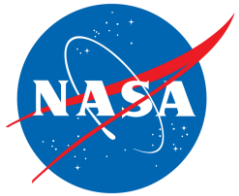


# Hazardous Components of Space Radiation

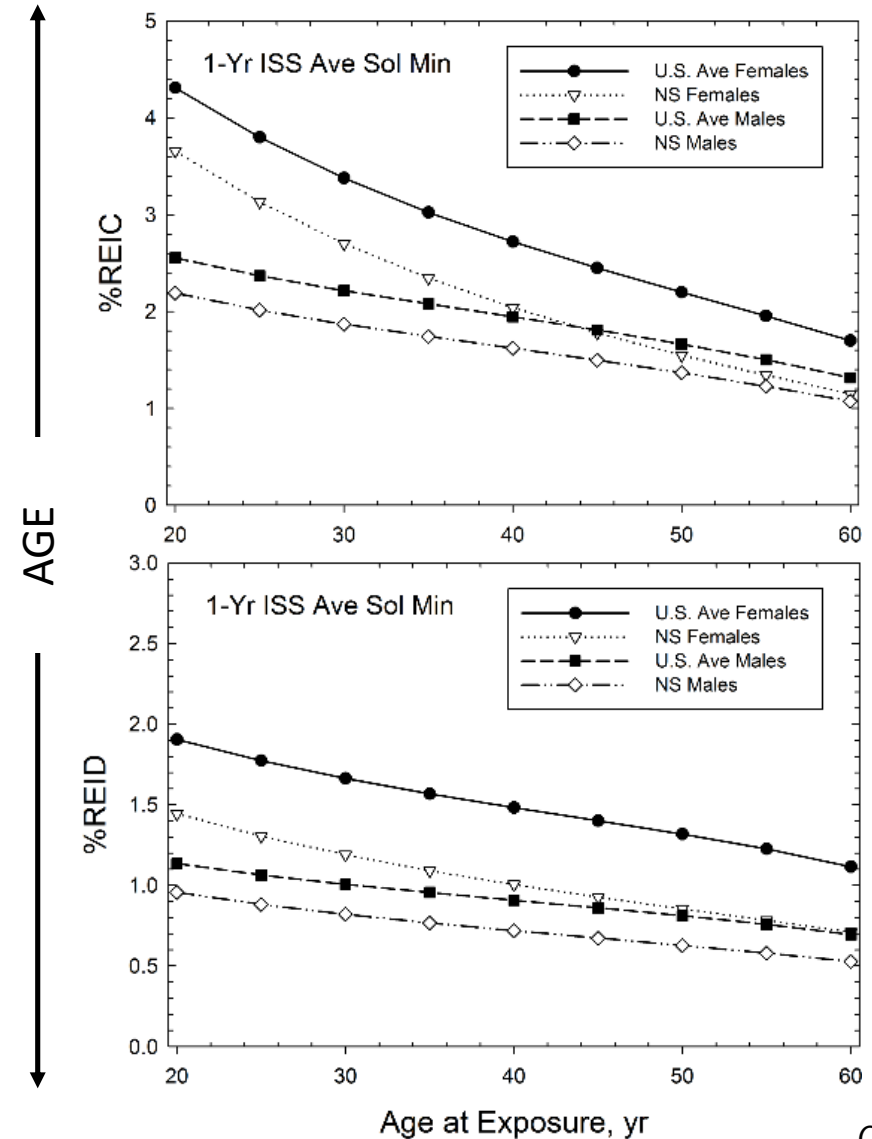
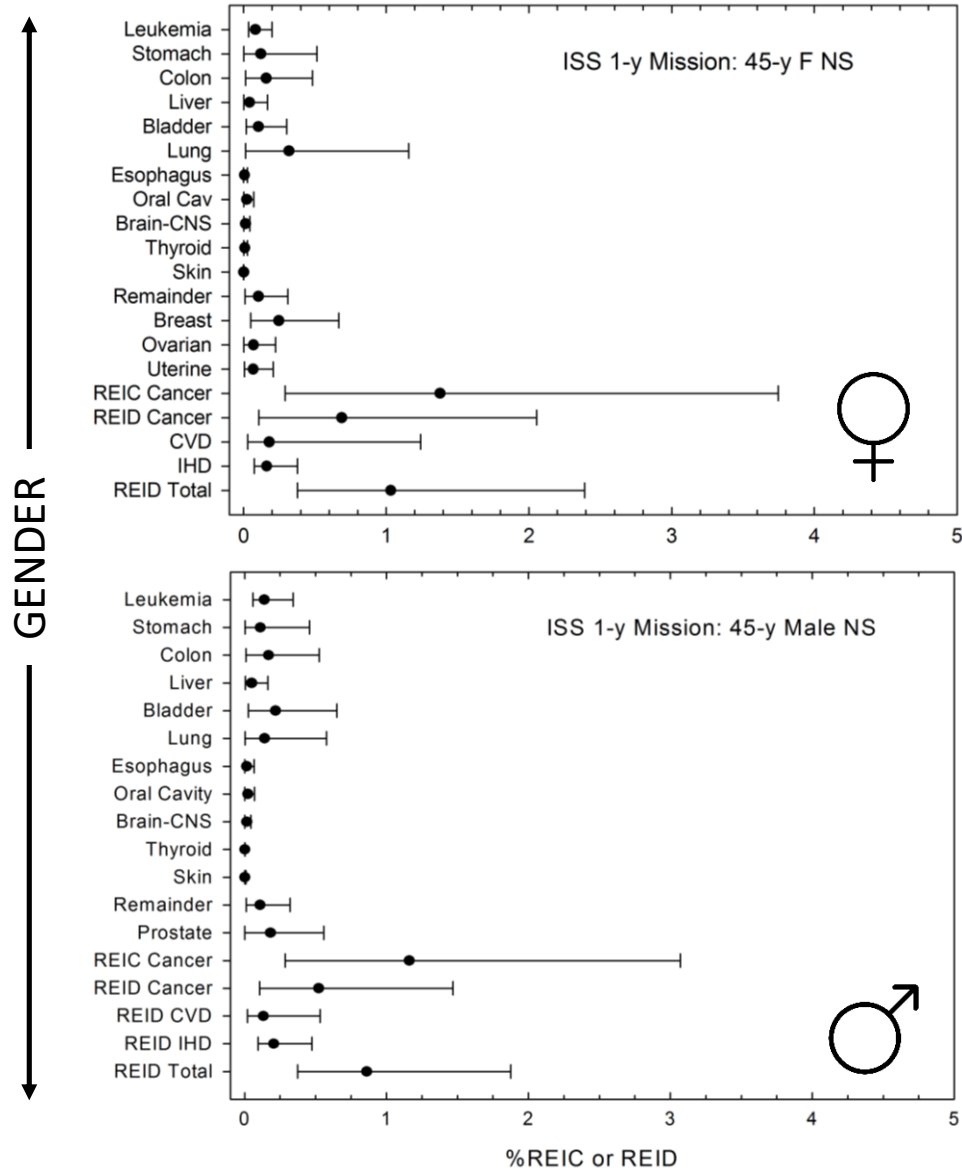


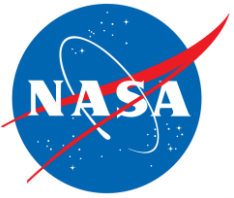
Hassler et al., Science, 2014

Mewaldt, Adv. Space Res., 1994

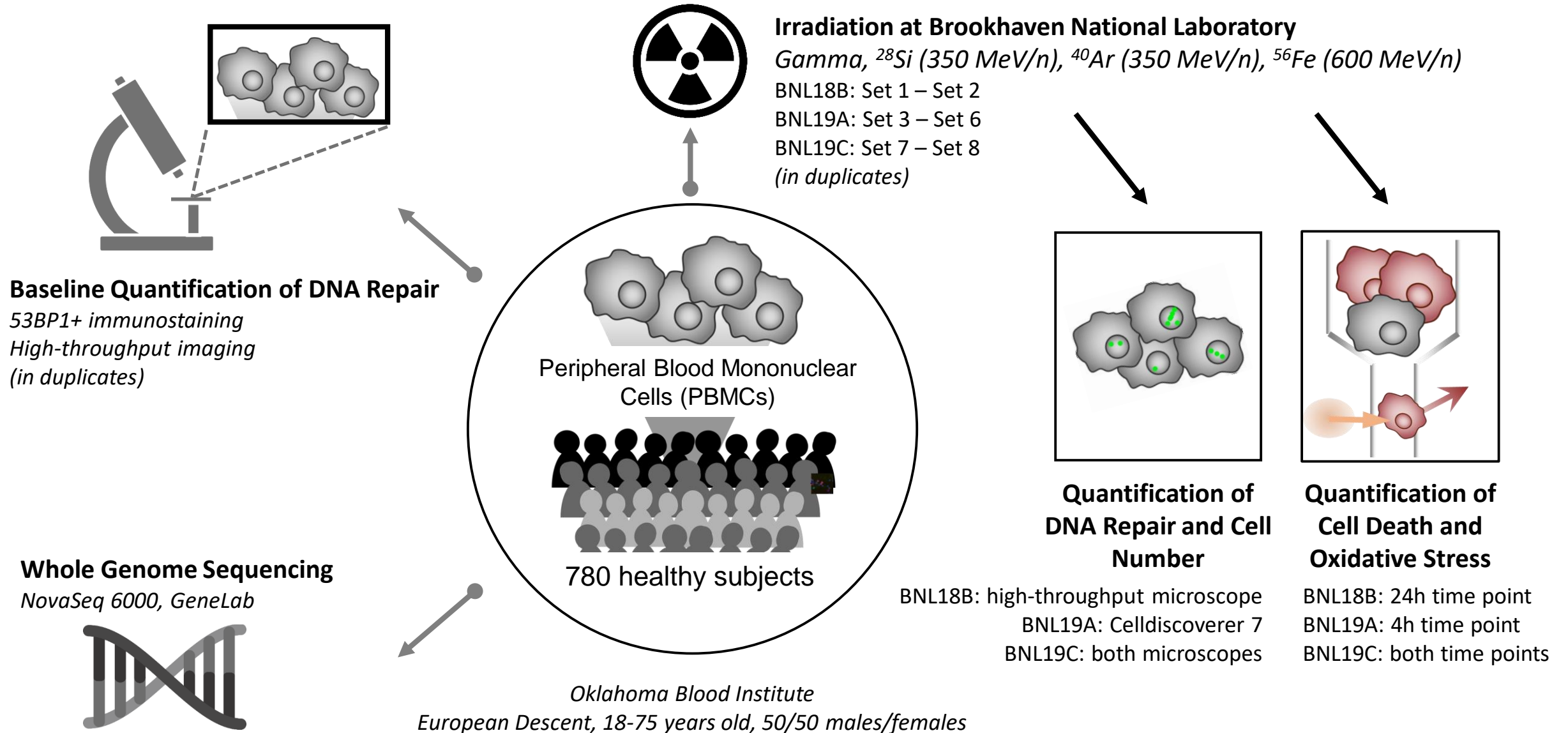


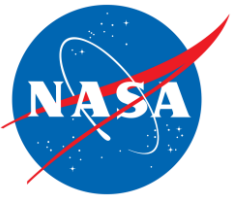
# Predicting Individual Radiation Sensitivity



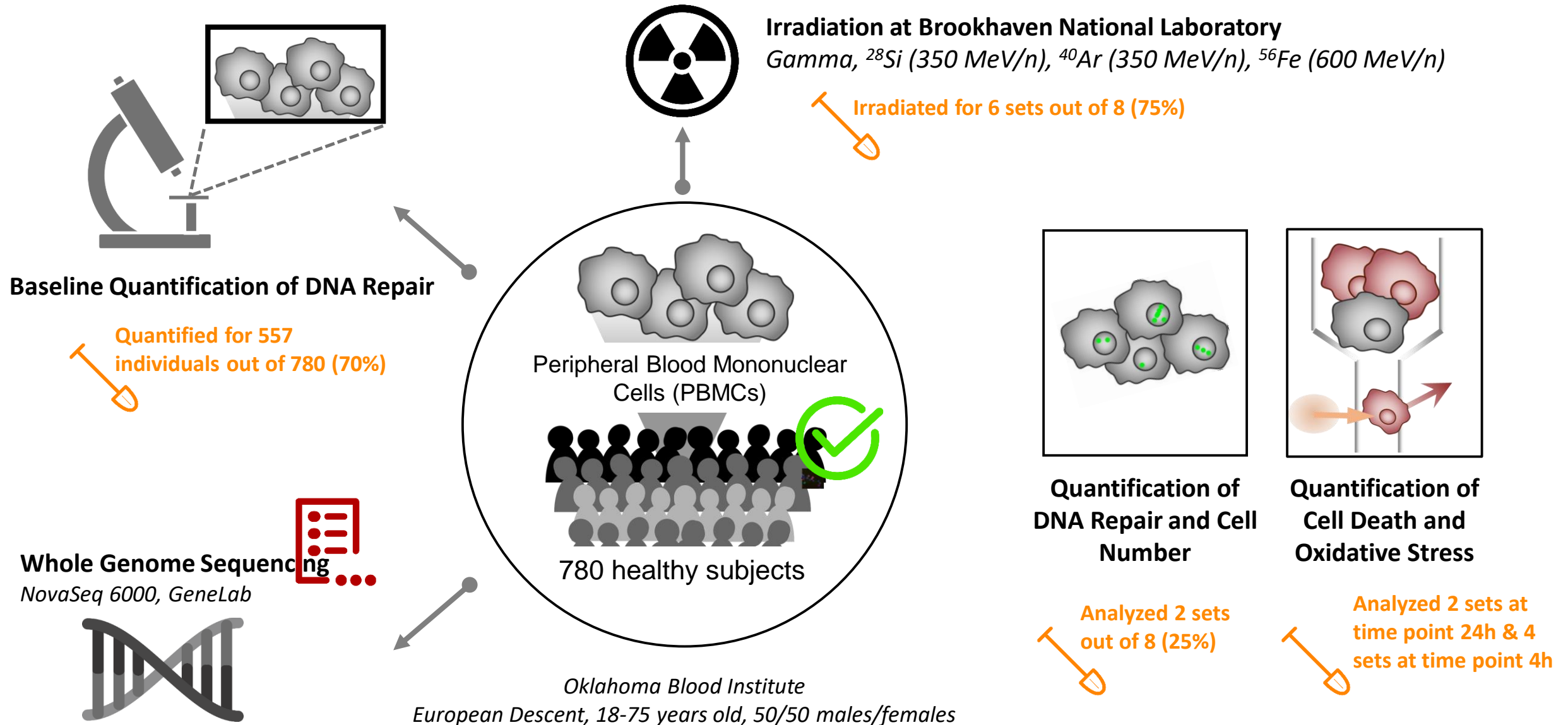


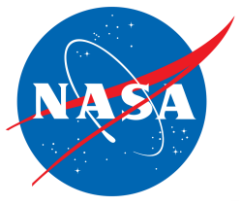
# Investigation in a cohort of 780 human donors



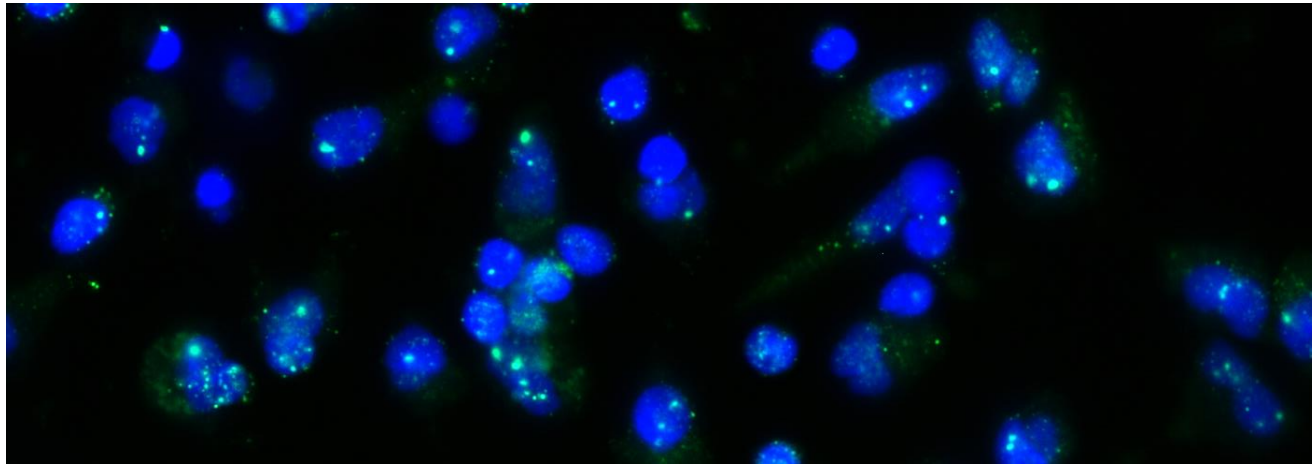


# Preliminary Results

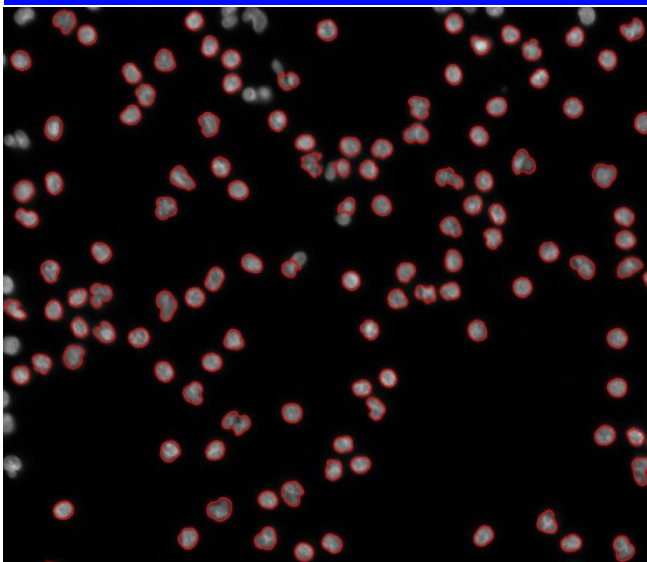




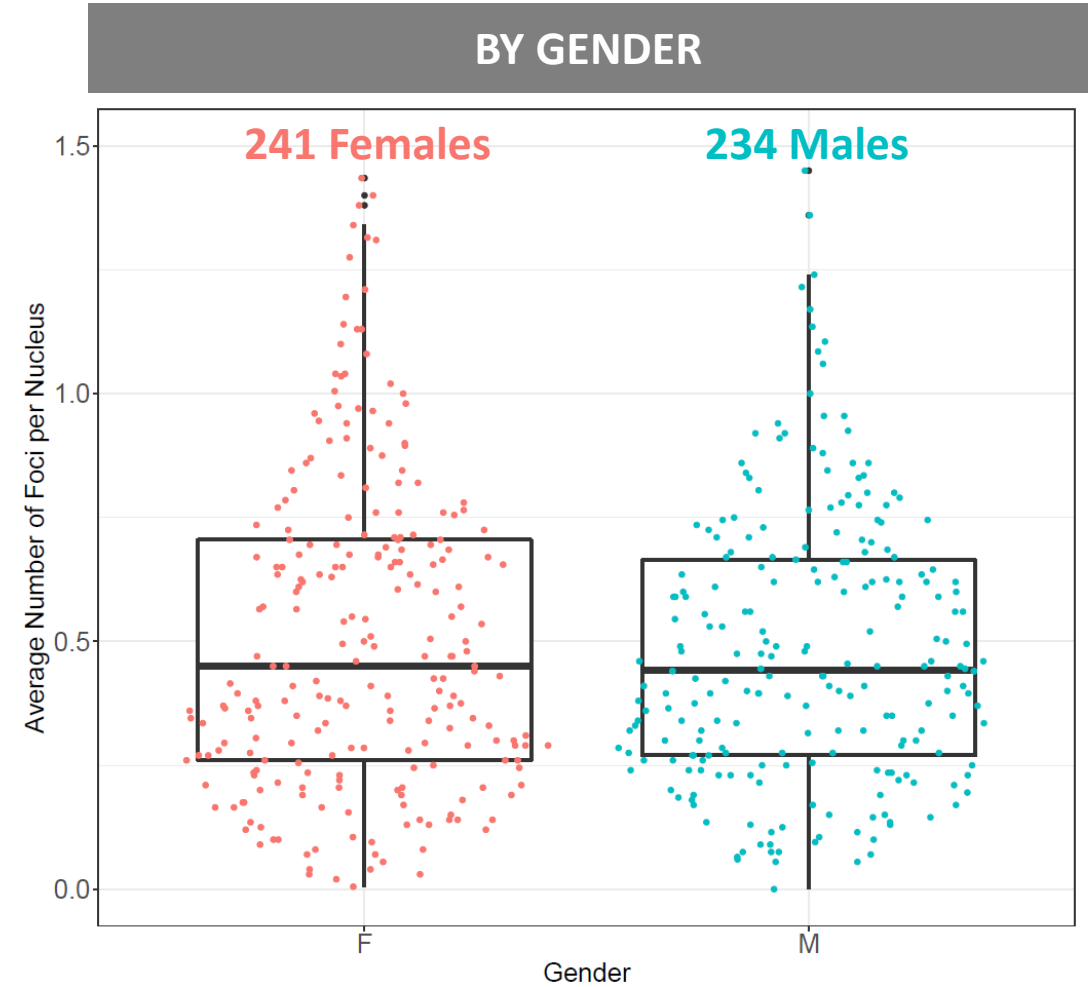
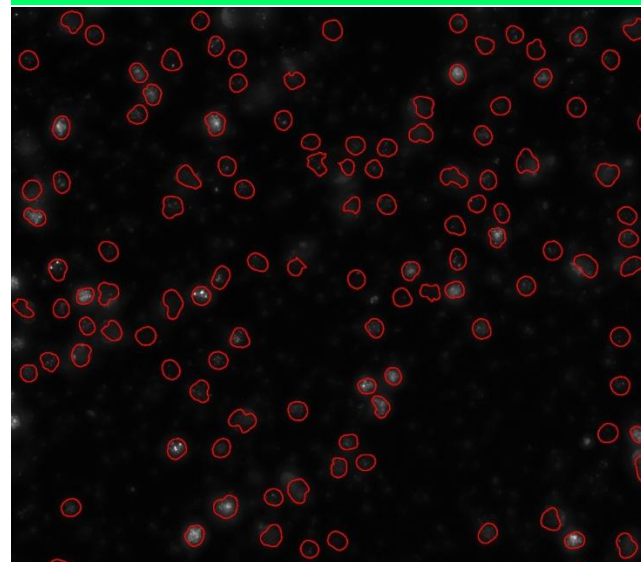
# Individual Variability in Baseline Level of DNA Damage

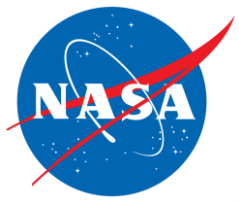


Nuclei Detection (DAPI)



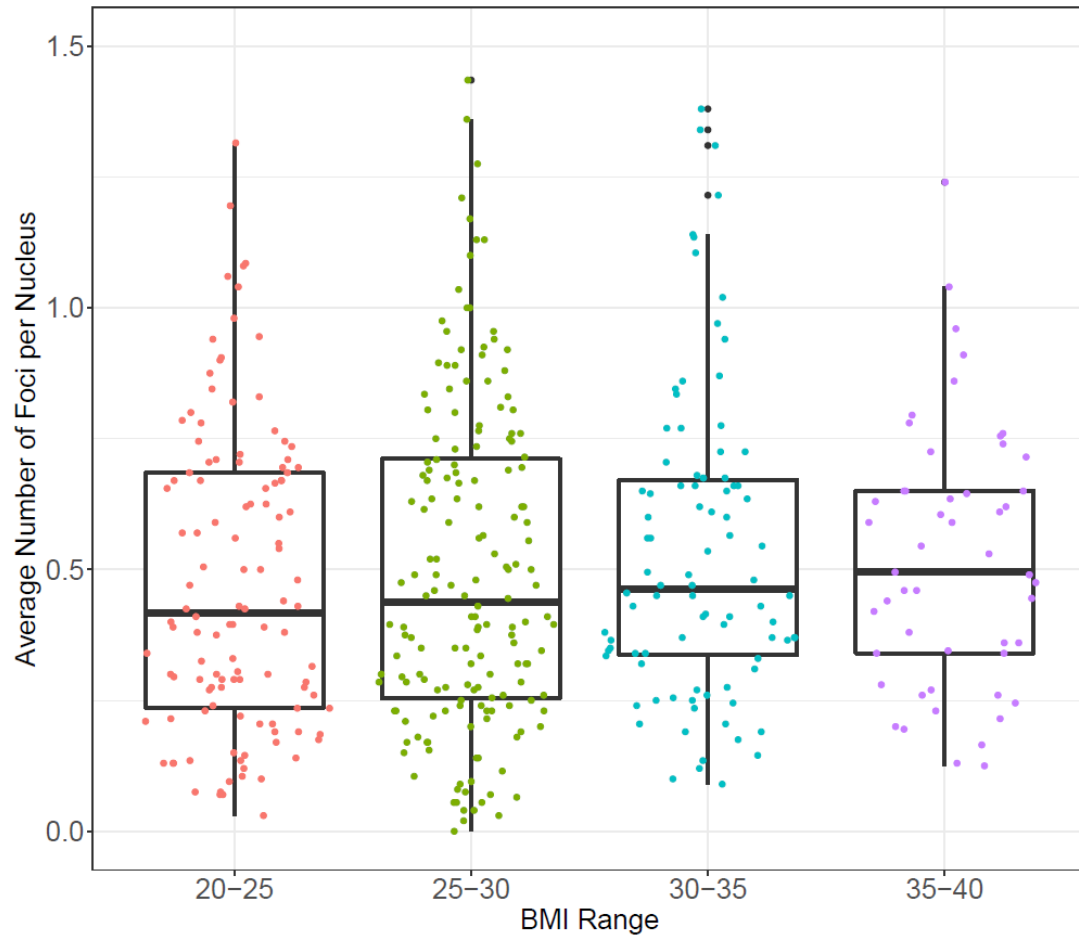
Foci Detection (FITC)



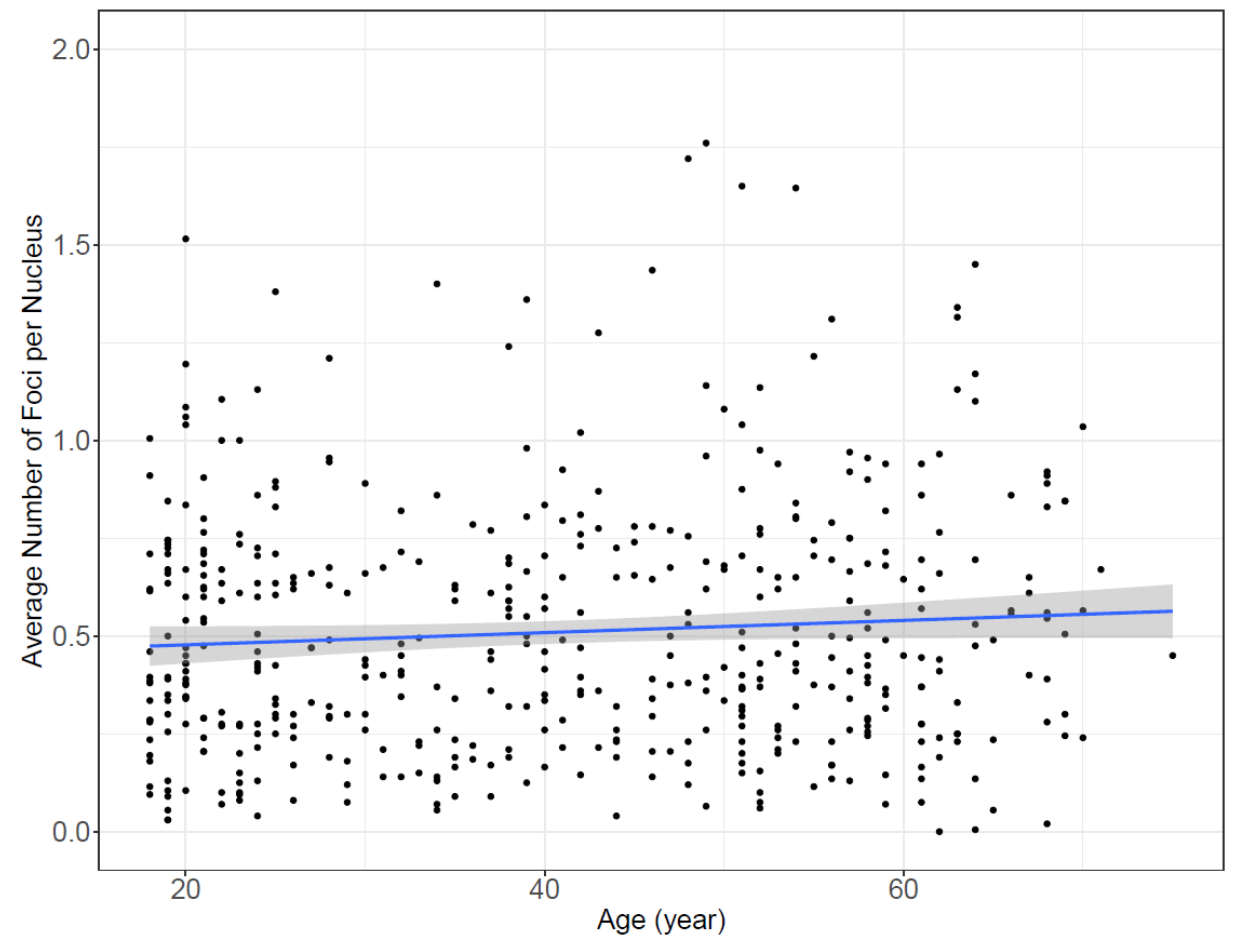


# Influence of Demographic Variables on the Baseline Level of DNA Damage

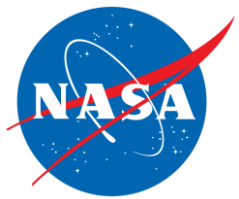
## BODY MASS INDEX



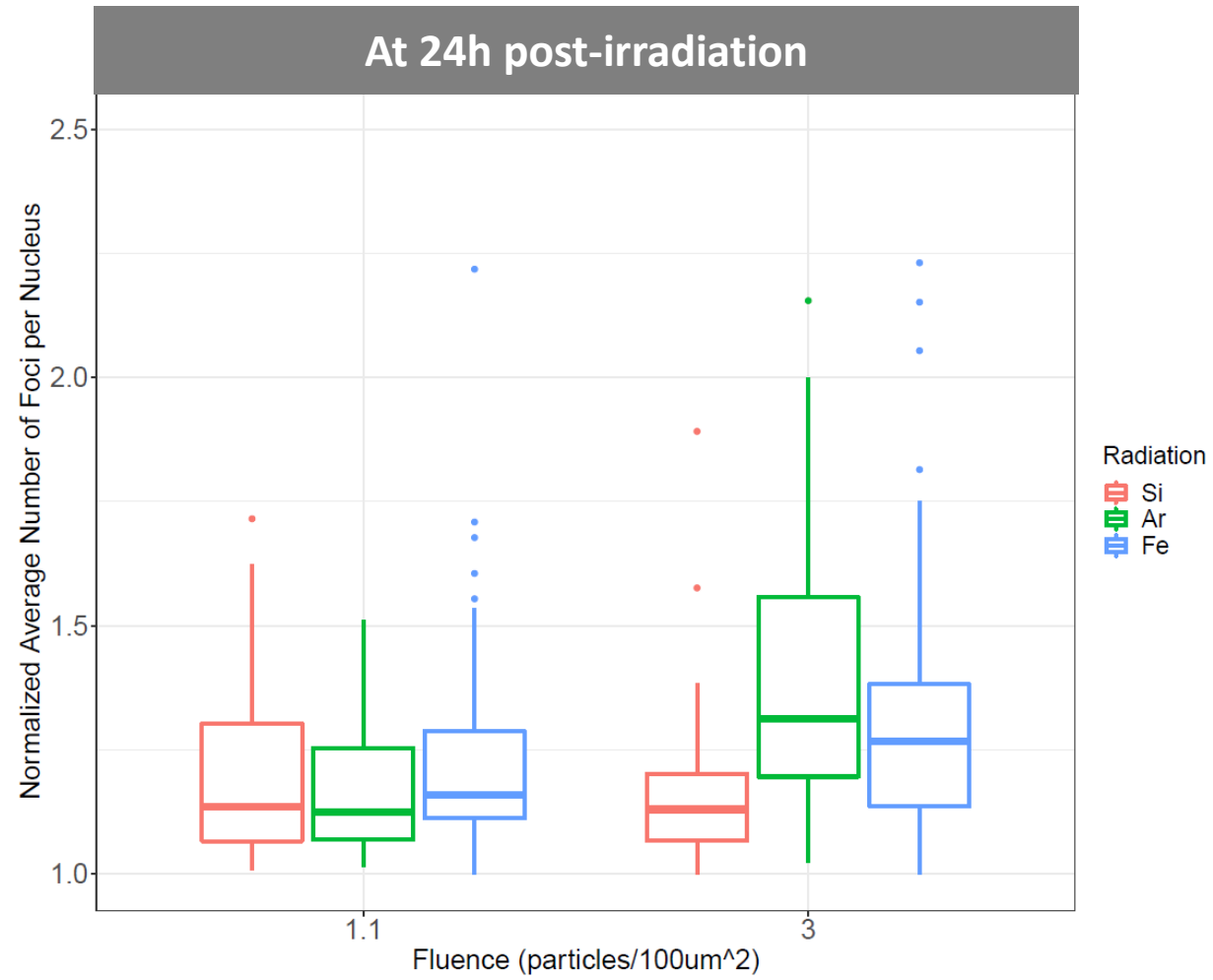
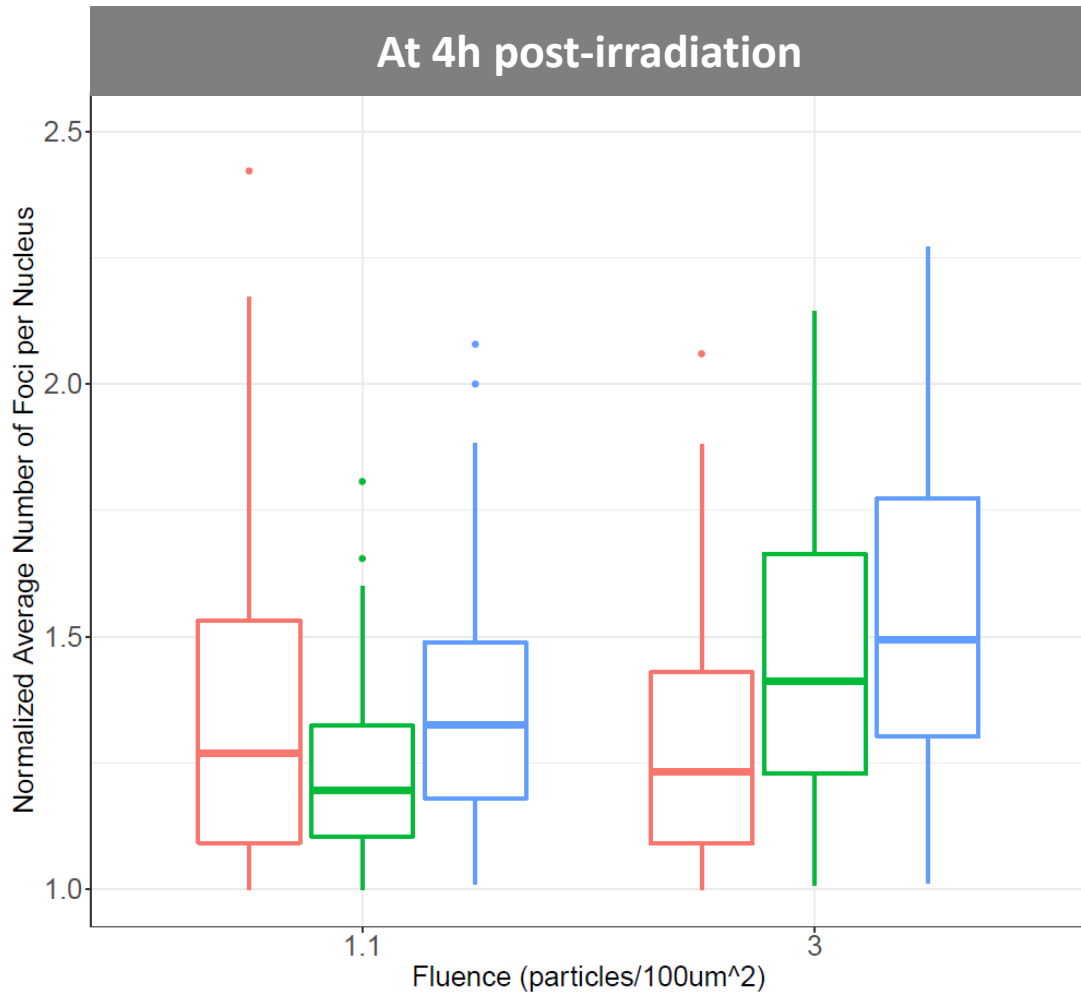
## AGE

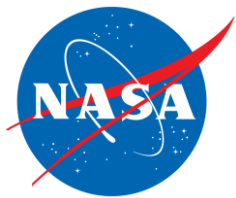






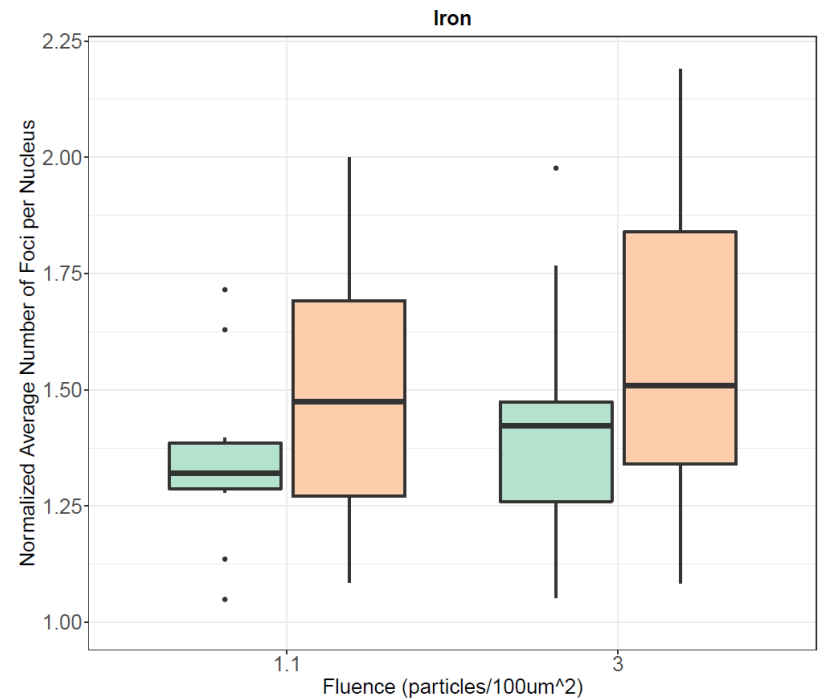
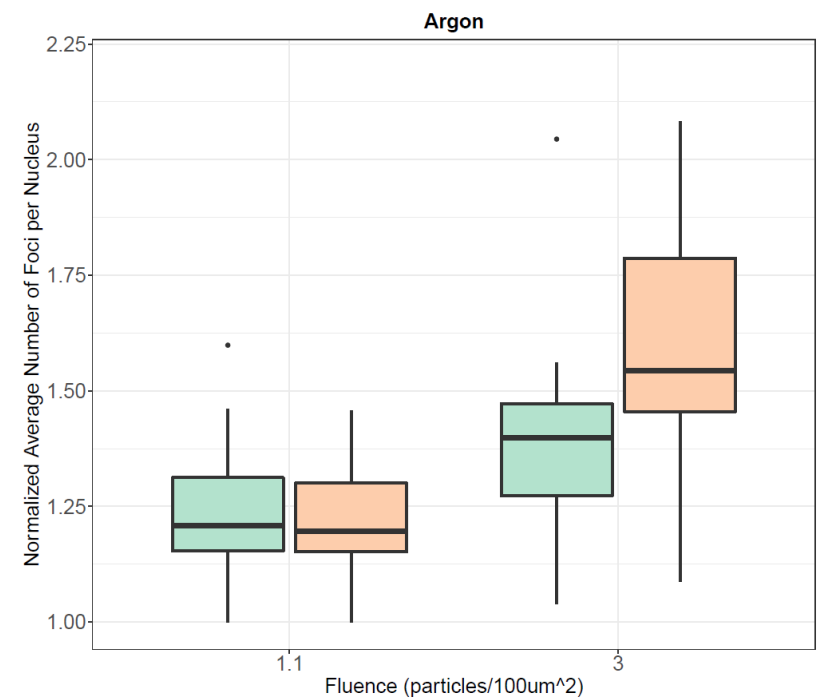
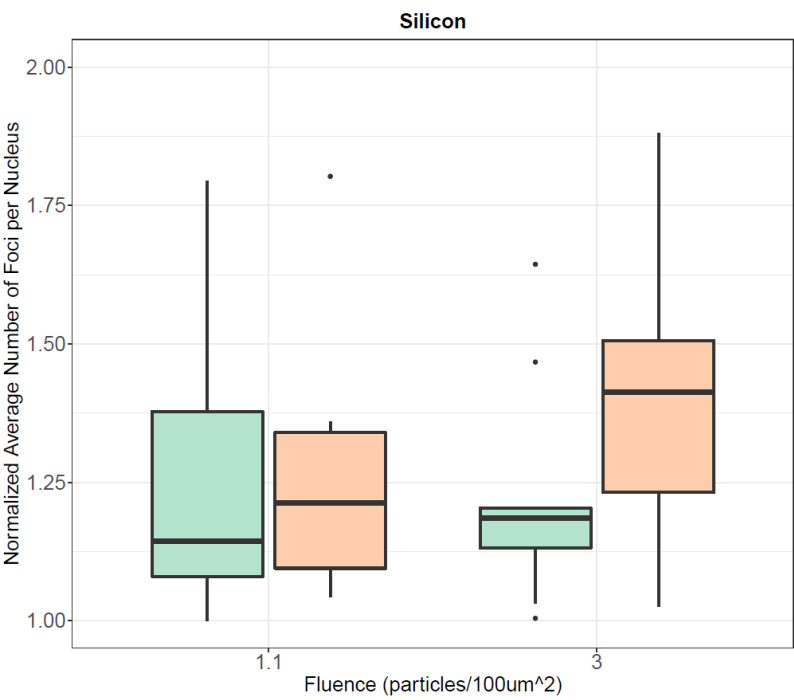
# Radiation Response: DNA Damage



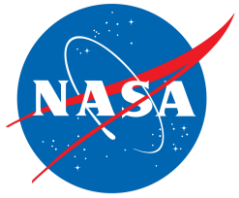


# Radiation Response for Extreme Baselines

*Selection of the 10 “highest baselines” and the 10 “lowest baselines”, based on the average number of foci per individual, without irradiation*



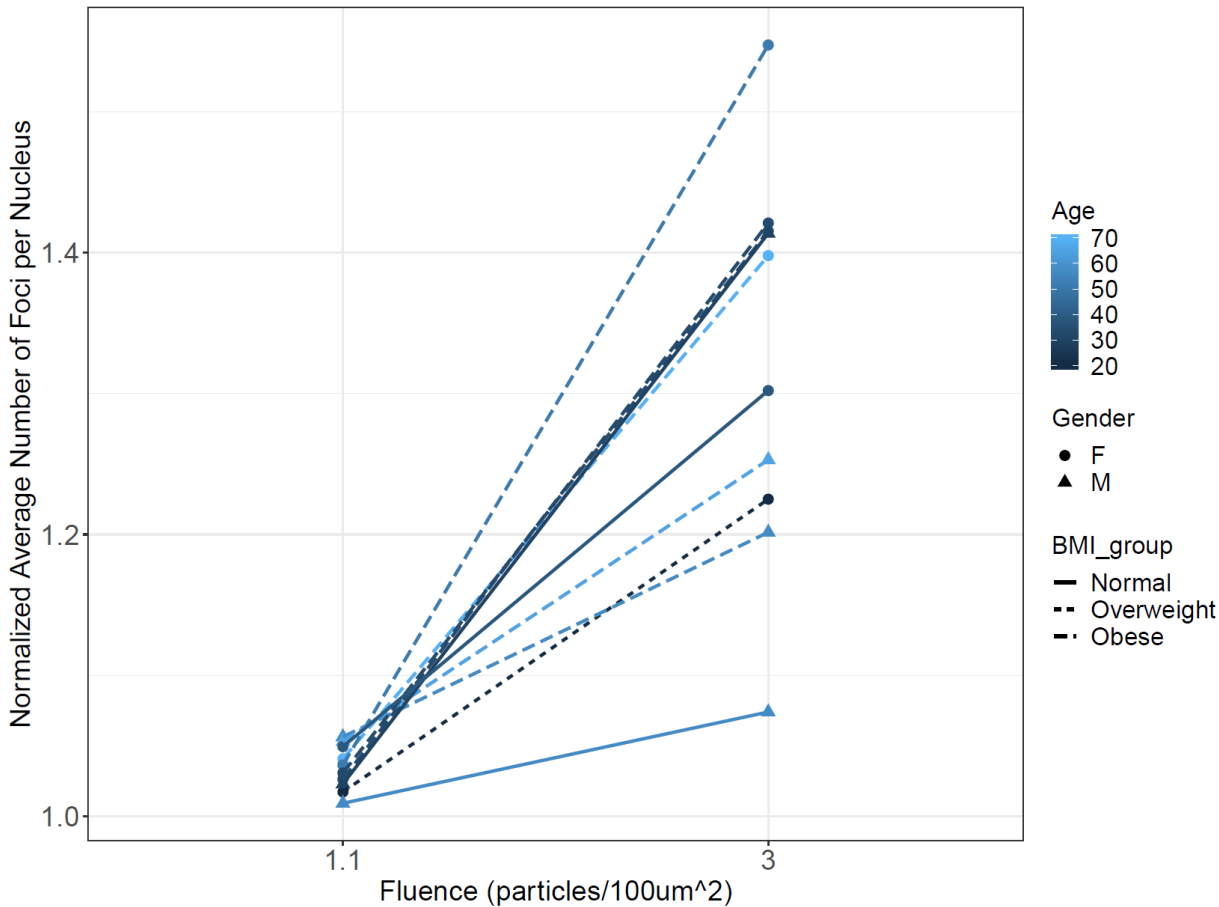
➤ Individuals with low number of foci at baseline seem to be more responsive to radiation



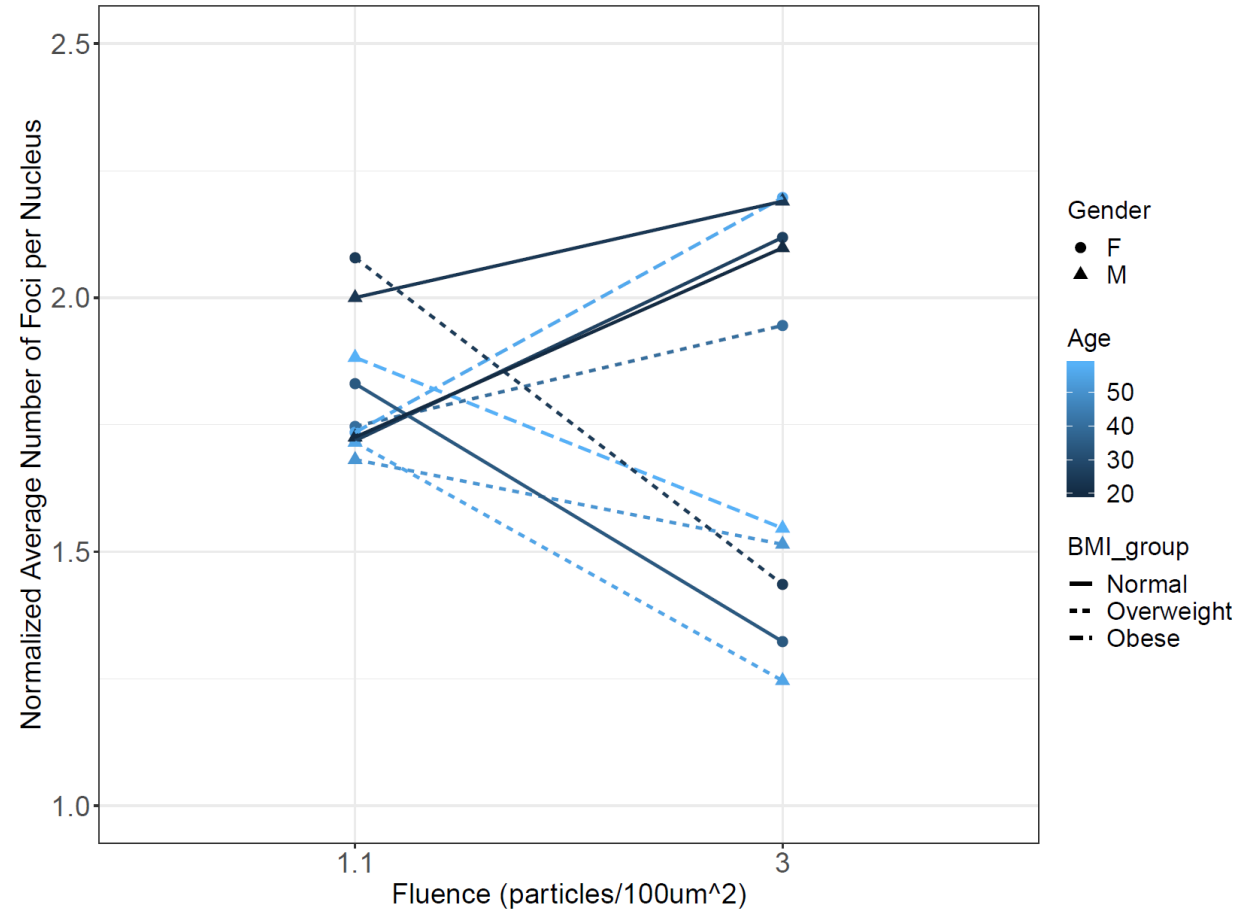
# Identifying Extreme Responders

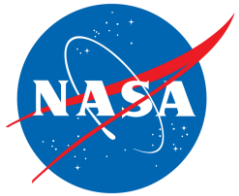
*Selection of the 10 “highest responders” and the 10 “lowest responders”, based on the level of DNA damage at Fluence 1*

Fe: top 10 resistant

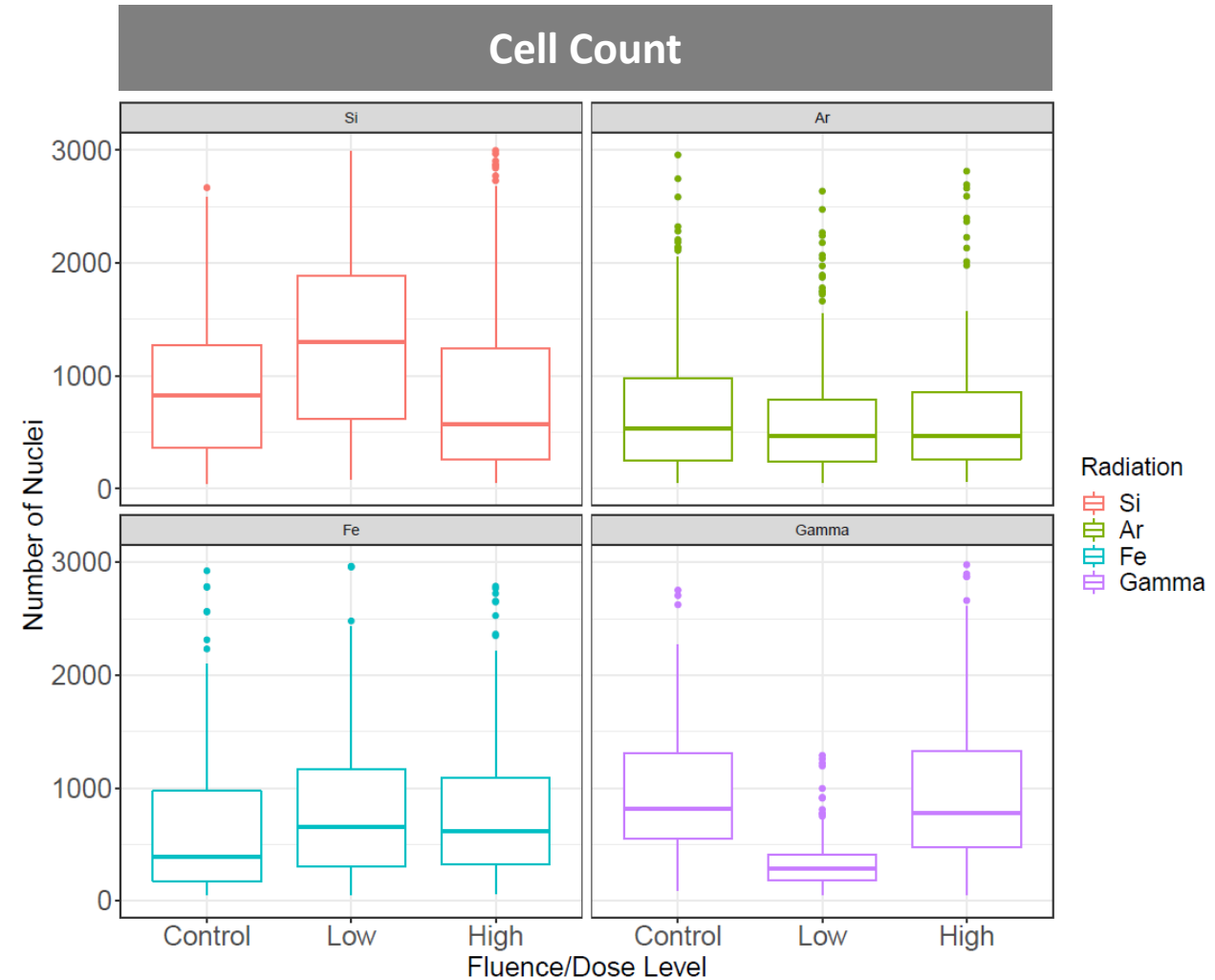
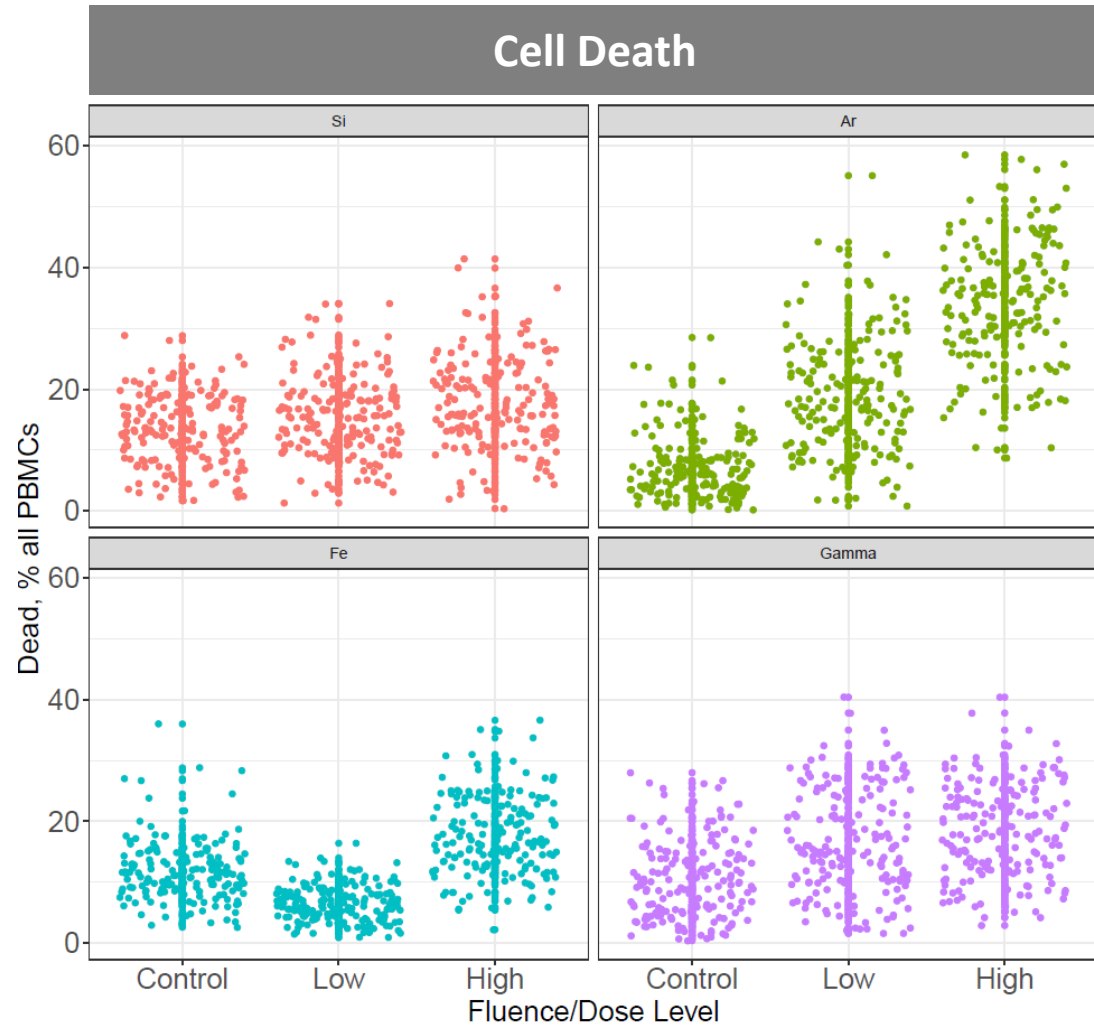


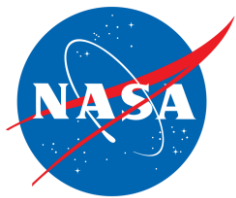
Fe: top 10 sensitive





# Additional Radiation Response Phenotypes





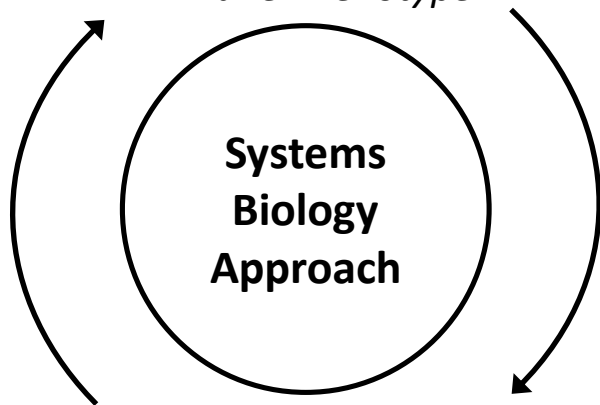
# Perspectives: Systems Biology Analysis

## Multiple Potential Predictors:

*Genotype*

*Secreted Factors*

*Immune Phenotype*



## Multiple Outputs of Radiation Sensitivity:

*DNA damage*

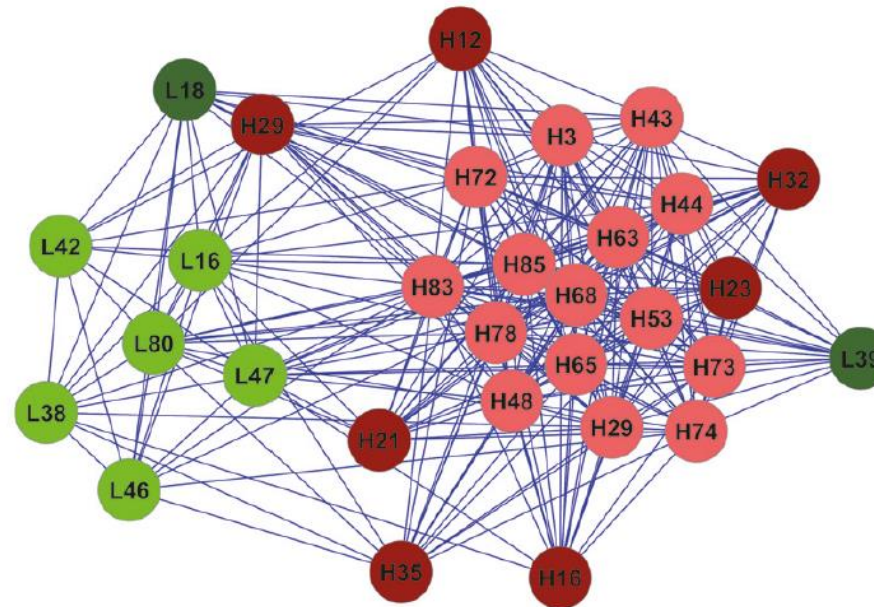
*Cell death*

*Oxidative Stress*

Example of Systems Biology strategy for the prediction of seroresponse to TIV vaccination<sup>1</sup>:

*The node size encodes the titer response score*

*The length of connecting edges encodes the distance between subject signatures*



<sup>1</sup>Marchetti et al., Hindawi, Exploring the Limitations of Peripheral Blood Transcriptional Biomarkers in Predicting Influenza Vaccine Responsiveness, 2017

# Thank you

## COLLABORATORS:

- **LBNL:** Gary Karpen, Jian-Hua Mao, Antoine Snijders
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  - **INSERM-FRANCE:** François Paris
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