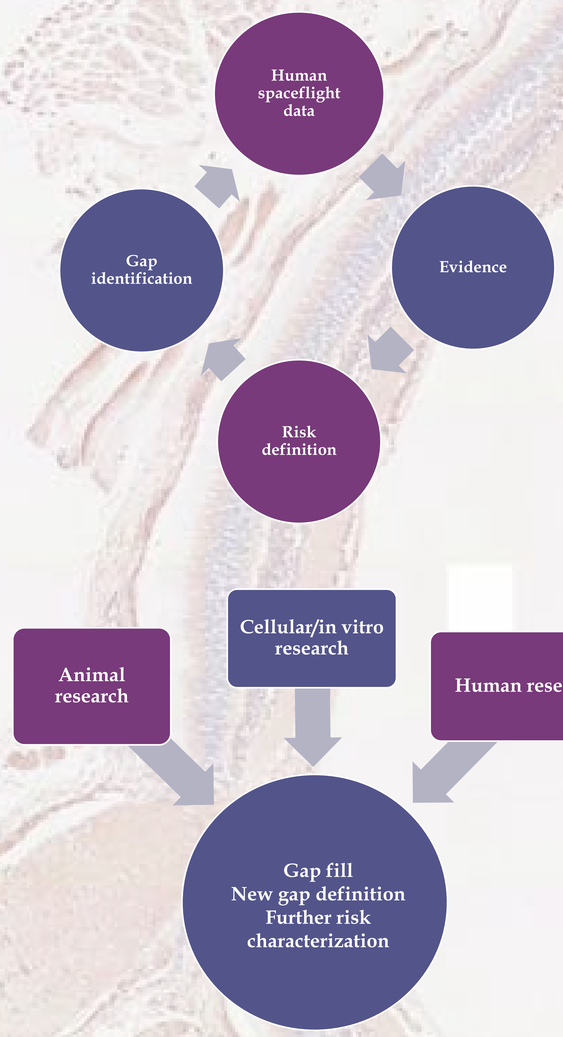
CONTRIBUTION OF SPACEFLIGHT ENVIRONMENTAL FACTORS TO VISION RISKS

***Susana Zanello*[1]**

[1]Universities Space Research Association, Houston, Texas, USA

INTRODUCTION

The recognition of a risk of visual impairment and intracranial pressure increase as a result of spaceflight has directed our attention and research efforts to the eye. While the alterations observed in astronauts returning from long duration missions include reportable vision and neuroanatomical changes observed by non-invasive methods[1], other effects and subsequent tissue responses at the molecular and cellular level can only be studied by accessing the tissue itself. As a result of this need, several studies are currently taking place that use animal models for eye research within the HHC Element. The implementation of these studies represents a significant addition to the capabilities of the biomedical research laboratories within the SK3 branch at JSC.

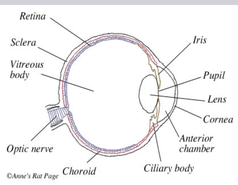


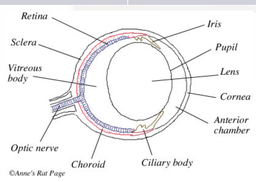
THE RODENT EYE AS A STUDY MODEL

The rodent eye has many similarities to the human eye, and both rats and mice have historically been used as models of human eye disease, aiding in the identification of disease genes, elucidation of mechanisms of disease, as well as in the assessment of therapeutic treatments. In addition, experimental conditions (i.e. induction of intraocular pressure increase, inflammation, light damage) are used to create conditions analogous to a disease state.

The following table summarizes notable similarities and differences between the human and the rodent eye:

HUMAN EYE	MOUSE EYE	RAT eye
Diurnal	Nocturnal	Nocturnal
	Larger cornea and lens (60% axial length) and less accomodation	
	Rods make up more 97% of phtotorreceptors	
	Smaller number of retinal ganglion cells (RGC)	
	Lower visual acuity	Lower visual acuity
Blue, green, red cones	Blue and green cones	Blue and green cones
		Highest degree of vascularization
Contains a fovea	No fovea, but peak cells density is in center of retina	No fovea, but peak cell density is in center of retina
Similar signaling between cell types	Similar signaling between cell types	Similar signaling between cell types





CURRENT VISION RESEARCH BASED ON TISSUE SHARING ANIMAL PROJECTS

RADIATION EFFECTS ON THE RETINA AND INVESTIGATION OF THE READIOADAPTIVE RESPONSE

Objective: to investigate whether gamma radiation provokes deleterious effects in the mouse retina and to evaluate whether exposure to a low priming radiation dose elicit protective responses that ameliorate the effects of a high challenge dose
Parent project and co-investigator(s): Radioadaptive response, Dr Honglu Wu (NASA-JSC)
Experimental design:

C57BL6J mice, male, 7 weeks-old

- CONTROL (C)
- LOW DOSE (LD, 50 mG)
- HIGH DOSE (HD, 6 Gray)
- LOW + HIGH DOSE (LHD) [24 hrs between priming and challenge; 4 hrs after challenge for collection)

Tissue collections at 4 hr, 1, 3, 7 and 14 days

Main findings: early oxidative and cellular stress response gene expression is induced at early time points (4 hr), but return to baseline levels at subsequent time points. Similar degree of induction is observed in LD and LHD treatments. Phenotypically, retinal thinckness is reduced in irradiated animals and the reductions appears to be additive.

EFFECTS OF SPACEFLIGHT ON THE MOUSE RETINA

Objective: to investigate whether spaceflight, with its contribution of various environmental factors, elicit gene expression and histological changes suggesting damage and stress exposure.
Parent project and co-investigator(s): Mouse Immunology Effect of Space Flight on Innate Immunity to Respiratory Viral Infections, Dr Rich Boyle (NASA-ARC)
Experimental design:

STS-133 Discovery
Duration: 12 days, 19 hours

Non-infected, BALB albino mice

FLIGHT	AEM (Animal Enclosure Module)	Vivarium
•R+1 •R+5 •R+7	•R+1 •R+5 •R+7	•R+1 •R+5 •R+7

Main findings: spaceflight induces oxidative and cellular stress responses in the mouse retina, affecting the expression of several genes associated with a the trigger of a protective response (upregulation of antioxidant enzymes, induction of autophagy and cell survival genes). This response is reversible upon return to Earth, as well as the oxidative stress induced DNA damage. Evidence also found supporting circadian rhythm disruption that gradually reverses after landing.

EFFECTS OF SPACEFLIGHT ON THE MOUSE RETINA- II

Objective: similar to the above, but on a different mouse strain (B57BL/6J), which is not susceptible to light-induced retinal degeneration.
Parent project and co-investigator(s): STS-135 space flight's effects on vascular atrophy in the hind limbs of mice (PI R Midura), Dr Rich Boyle (NASA-ARC)
Experimental design:

STS-133 Atlantis
Duration: 13 days

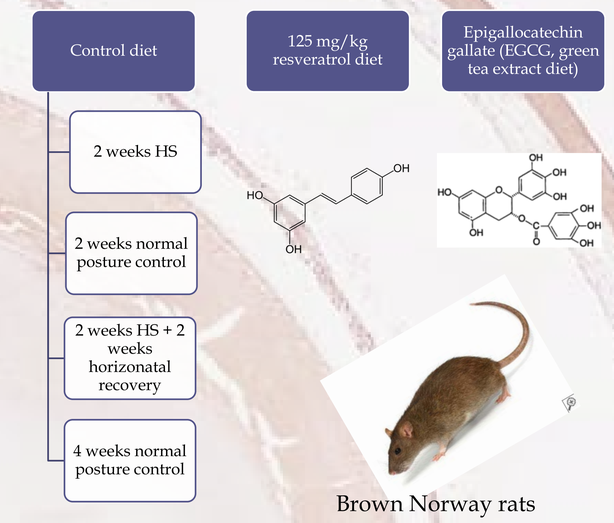
Non-drug control C57BL female mice

Flight AEM

Main findings: analysis in progress

HINDLIMB SUSPENSION (HS) AS AN ANALOG MODEL OF OCULAR ALTERATIONS ASSOCIATED WITH CEPHALAD FLUID SHIFTS:

Objective: to investigate whether HS and the associated cephalad fluid shift leads to adverse cellular effects in the retina involving oxidative and cellular stress, cell death and hypoxia.
Parent project and co-investigator(s): Exercise and hindlimb suspension in rats, Dr Stephen Always (West Virginia University-NASA Space Act Agreement)
Experimental design:



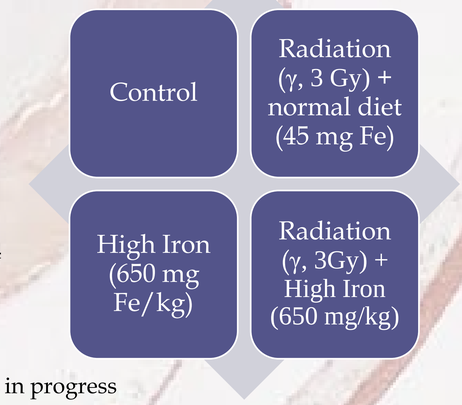
Brown Norway rats

Main findings: analysis in progress

COMBINED EFFECTS OF GAMMA RADIATION AND HIGH DIETARY IRON ON OXIDATIVE DAMAGE AND ANTIOXIDANT STATUS IN RAT EYES

Objective to investigate the combined effects of gamma radiation and iron overload on rat eye structures.
Parent project and co-investigator(s): Combined effects of iron overload and radiation on various organ systems (Dr Sara Zwart, USRA-NASA JSC)
Experimental design:

Sprague Dawley rat, 4 week experiment

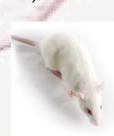


Main findings: analysis in progress

EFFECTS OF LUNAR DUST ON THE RAT CORNEA

Objective: investigate oxidative stress and cell death/survival in rat corneas exposed to lunar dust.
Parent project and co-investigator(s): Effects of lunar dust exposure in the respiratory tract (Drs Chu-Wing Lam, John James)
Experimental design: Fisher rats exposed to a low and high dose of lunar dust (from Apollo missions)

Lunar dust



Fisher rat

- Control
- Low dose (20 mg/m^3)
- High dose (60 mg/m^3)
- Collections at 1 day, 7, 30 and 90 days after exposure

* This work is pending funding

ACKNOWLEDGEMENTS

This work is funded by NASA HRP. I am thankful for the valuable assistance of the following investigators who provided technical help when "time and hands ran short": Corey Theriot, Chris Westby and Ginger Wotring, and James Fiedler for statistical analysis.