Fiscal Year:	FY 2006	**Task Last Updated:**	FY 02/08/2006
PI Name:	Hall, Eric J Ph.D., D.Sc.		
Project Title:	Mechanisms of Ocular Cataracts		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
Joint Agency Name:		**TechPort:**	No
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Human Research Program Risks:	(1) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	10032	**Congressional District:**	15
Comments:			
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No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
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The only non-cancer degenerative effect so far unequivocally observed in astronauts is the early onset of ocular cataracts. Previous studies have shown that mice haplo-insufficient for Atm develop cataracts earlier than wild type animals exposed to either gamma rays or high energy Fe ions. At a large x-ray dose (4 Gy) the Atm heterozygotes developed vision impairing cataracts 10 or more weeks early than the wild-type counterparts. At a lower dose x-ray dose (0.5 Gy) the Atm heterozygotes developed a low grade cataract, while the wild-type did not. We can conclude from this study that (a) Vision impairing cataracts appear earlier in Atm heterozygotes than in wild-type animals; the acceleration by 10 weeks is an appreciable fraction of the life-span of the animal. (b) At lower doses, low grade cataracts appear in Atm heterozygotes where none appear in wild-type animals. For animals exposed to 0.325 Gy of high energy Fe-59, cataracts again appeared earlier in the Atm heterozygotes and the acceleration is similar to that seen for

Task Description:	x-rays. Also, at this dose, vision impairing cataracts occur in Atm heterozygotes, but not in wild type animals. These earlier studies indicated that the susceptibility to cataractogenesis shown by Atm heterozygotes is much greater than for cell killing in cells grown in culture from the same animals, suggesting that errors in differentiation, not cell killing, is the mechanism for cataract formation. When dividing cells in the pre-equatorial region of the lens epithelium are damaged by radiation, they differentiate into fibers that are not translucent as they accrete at the posterior pole of the lens. We now have available mice heterozygous for Mrad9, for the BRCA1 and BRCA2 genes, as well as animals that are heterozygous for pairs of genes believed to be in the same DNA repair pathway, for example Atm/Mrad9, Atm/BRCA1. We propose to irradiate these animals carrying these various genetic deficiencies to a fluence of Fe-59 ions corresponding to one particle traversal per cell nucleus, and score the appearance of cataracts over the life-time of the mice. Data from these experiments will (a) Shed light on the genetic factors that control the susceptibility to radiation induced cataracts, and (b) Identify further sub-groups in the population that are radiosensitive to cataractogenesis. AT heterozygotes comprise 1 to 3% of the US population, RAD9 polymorphisms occur with a similar frequency, while 1 in 250 women carry a BRCA mutation. The combination of these genes, and others that may be identified in the future, add up to a small but significant group of individuals that would develop cataracts earlier and of a higher grade than normal individuals following exposure to high energy heavy ions. Laboratory experiments involving cytological and cytopathological endpoints are designed to elucidate the mechanisms of cataractogenesis in wild type and Atm heterozygous animals in an attempt to understand why the small difference in cell killing due to haploinsufficiency for the Atm protein translates into a large and important difference for cataract formation.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	Please note that this is a new grant for the FY 2006 year. The investigator will provide a task progress at the time of the one year anniversary of the grant. If you need more information, please contact the Task Book Help Desk at taskbook@nasaprs.com.
Bibliography Type:	Description: (Last Updated: 10/26/2023)