Biological effects of ultra-low radiation exposure

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Research group

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Principal Scientist – Bruce Power

Research interests:

- Low-dose radiobiology
- Diagnostic imaging
- Cancer therapy

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Funding

Bruce Power industrial support
- 2015: $85,000
- 2016-2020: $1,000,000 ($200,000 per year)

NSERC discovery
- 2015-2020: $190,000 ($38,000 per year)

Mitacs Accelerate
- 2015-2017: $330,000

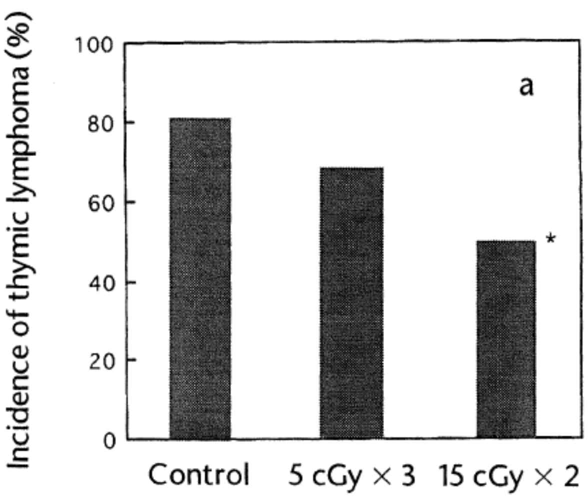
NSERC CRD
- 2016-2020: $1,000,000 ($200,000 per year)

Rationale

- Ionizing radiation is ubiquitous and all living organisms on earth
- There is increasing concern over radiation exposure from medical diagnostic procedures
- The effects from these exposures still remains largely unknown
- Limited epidemiological data exists in the low-dose region (< 100 mGy)
- There is growing evidence to suggest that low-dose radiation may provide beneficial effects to living systems
- SNOLAB provides a unique environment to examine the effects of ultra-low background radiation exposure

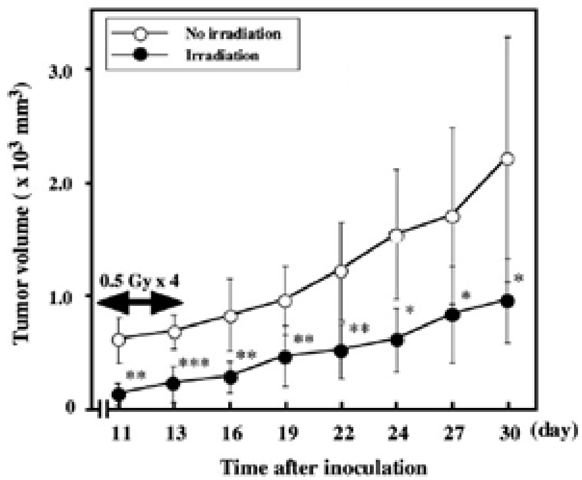
Low-dose and cancer

Reduction in cancer incidence



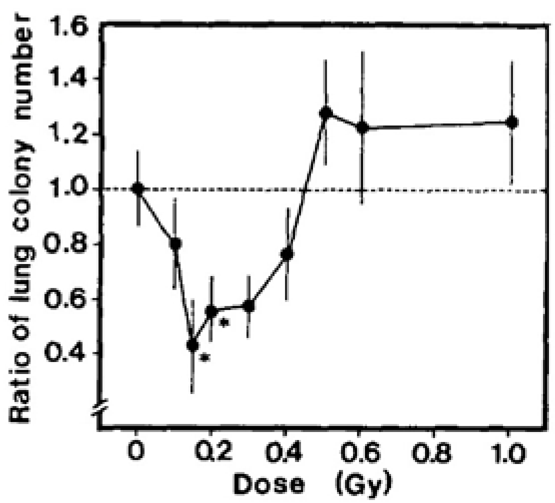
Ishii *et al* 1996

Decrease in primary tumor growth



Kojima *et al* 2004

Reduction in tumor metastases

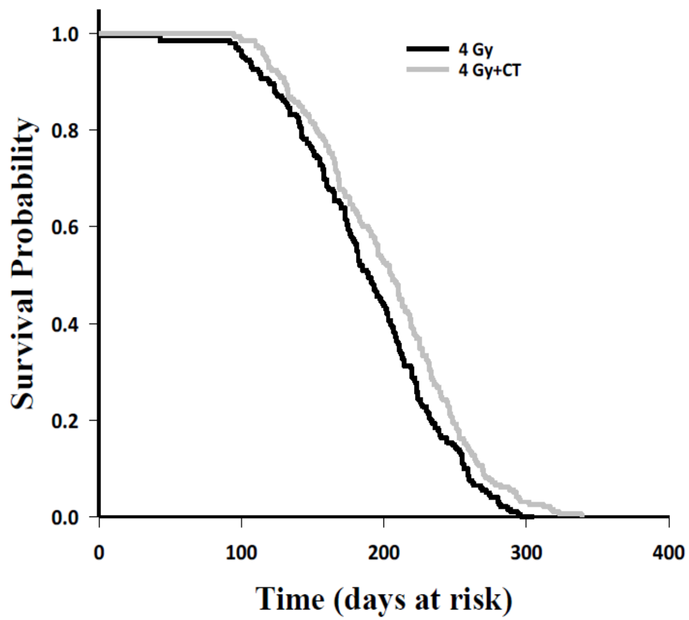


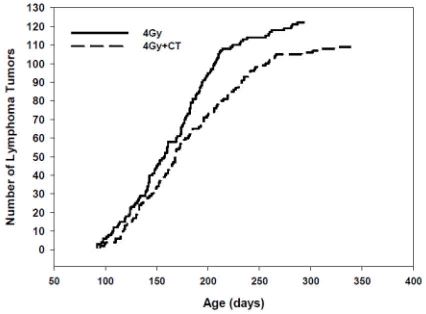
Hosoi and Sakamoto 1993

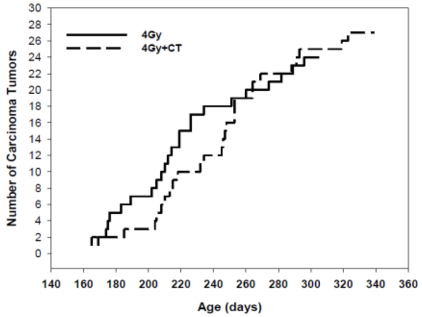
Diagnostic imaging

CT Scan

- Increased mean survival time
- Increased latency of lymphomas and carcinomas







Phan *et al*

PET Scan

- Reduction in kidney disease

Table IV. Number of *Trp53+/–* mice with tissue-specific lesions

Treatment	Kidneys	Bladder	Heart	Reproductive organs
Control	32	3	0	28
10 mGy γ-rays	23	6	0	20
10 mGy PET	15[a]	0	0	27
4 Gy γ-rays	25	0	0	38
10 mGy PET + 4 Gy γ-rays	32	0	0	36

[a] $P < 0.021$ relative to unirradiated control mice.

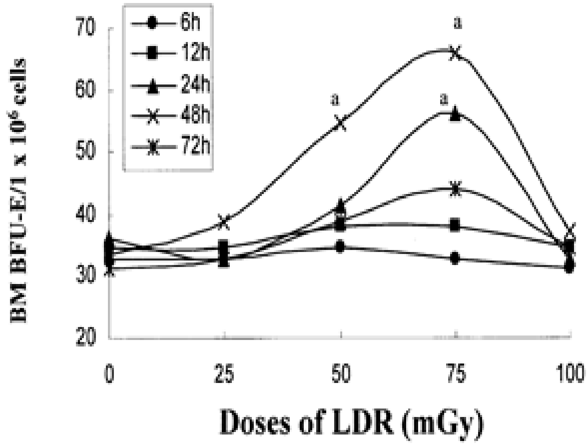
Taylor *et al* 2014

Growth stimulation

Increased body size in amphibians irradiated during embryogenesis (Stark *et al* 2015)

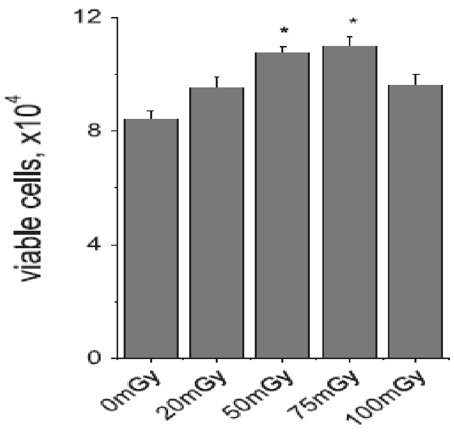
Increased plant size when seeds irradiated (Miller and Miller 1987)

Bone marrow hematopoietic progenitor cells



Li *et al* 2004

Cultured mesenchymal stem cells

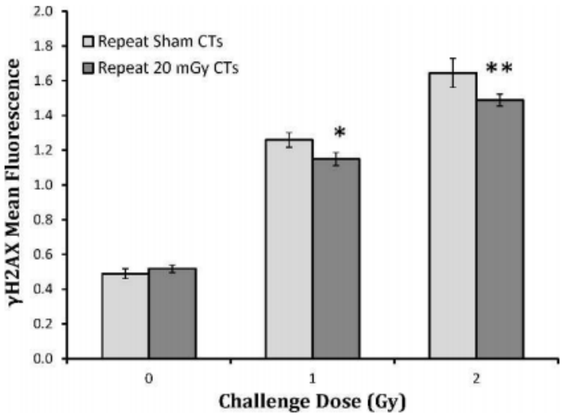


Liang *et al* 2011

Adaptive response

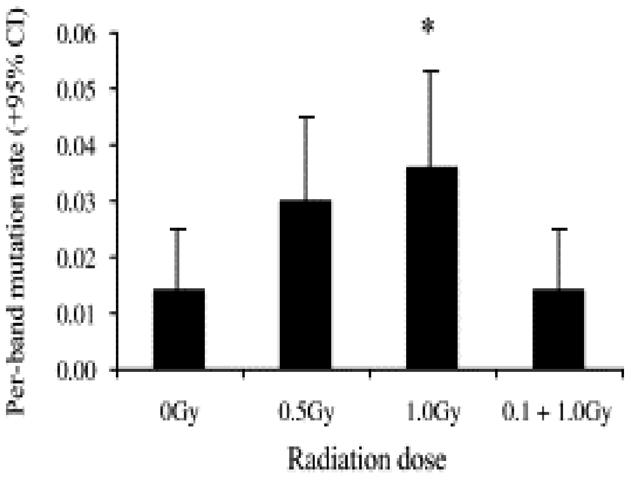
Low-dose radiation exposure can protect against a future high-dose exposure

DNA DSB formation



Phan *et al* 2012

Mutation rate



Somers *et al* 2004

Hypothesis and Objectives

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Hypothesis:

Natural background radiation is essential for life and maintains genomic stability in living organisms

Prolonged exposure to ultra-low radiation environments will be detrimental to biological systems

Objectives:

1. Establish a functional biological research laboratory within SNOLAB
2. Examine the effects of incubation in SNOLAB compared to surface control laboratory using 2 simple model systems
   - Cell culture – C3H 10T1/2 cell line
   - Whole organism – Lake Whitefish embryonic development

Low background results

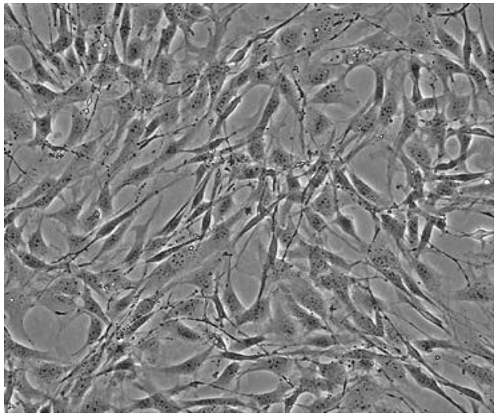
1. Removal of natural background radiation impairs growth. Growth rates are restored once radiation is artificially reintroduced. Demonstrated with:
   - Paramecium shielded with lead (Planel *et al* 1976)
   - Blue-green algae (*Synechococcus lividus)* shielded with lead (Conter *et al* 1983)
   - Yeast (*Saccharomyces cerevisiae*) shielded with lead/cadmium (Gajendiran and Jeevanram 2002)
   - Bacteria (*Deinococcus radiodurans)* grown in Waste Isolation Pilot Plant (WIPP) (Smith *et al* 2011)
   - Mouse lymphoma L5178Y cells shielded with lead (Taizawa *et al* 1992)
   - Mouse lymphoma L5178Y cells shielded with iron (Kawanishi *et al* 2012)

Low background results

2. Removal of natural background radiation reduces repair capacity towards induced damage. Demonstrated with:
   - Survival fraction in yeast (*Saccharomyces cerevisiae*) shielded with lead/cadmium (Gajendiran and Jeevanram 2002)
   - Background/induced mutation rate in Chinese hamster V79 cells grown in Gran Sasso Underground Laboratory (LNGS) (Satta *et al* 2002)
   - Micronuclei formation and ROS scavenging in human lymphoblastoid TK6 cells grown in LNGS (Carbone *et al* 2010)

C3H 10T1/2 cell line

- Mouse embryonic stem cell line
- Pre-carcinogenic
- High spontaneous transformation rate
- Sensitive to low-dose ionizing radiation



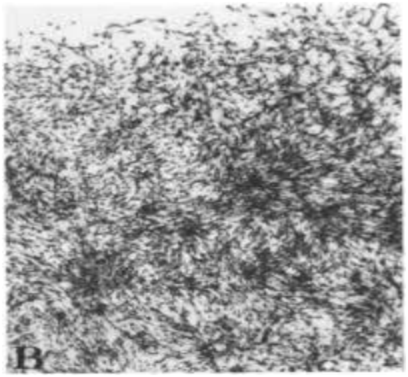
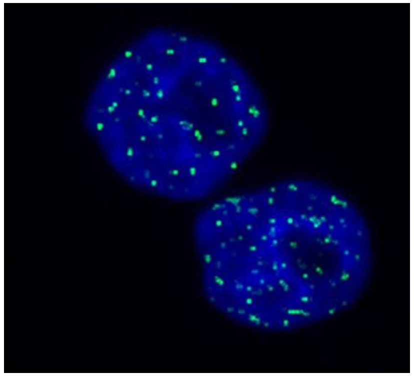
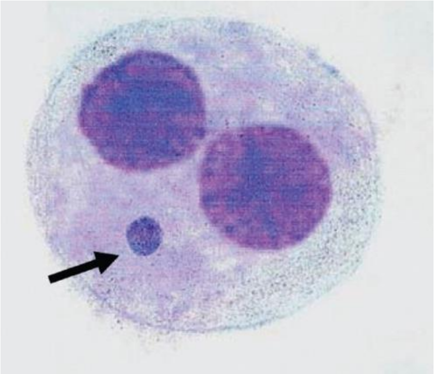
Previous findings:

A single low-dose of radiation (1 mGy to 100 mGy) can decrease transformation frequency below spontaneous levels (Azzam *et al* 1996)

Chronic adapting low-doses of radiation (0.1 Gy, 0.65 Gy or 1.5 Gy) can protect against an acute challenge dose of 4 Gy (Azzam *et al* 1994)

C3H 10T1/2 cell line

Radiobiological endpoints

Transformation frequency	DNA DSB formation	Micronuclei formation
		

C3H 10T1/2 cell line

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- Cells will be cultured within SNOLAB and the surface control lab
- Glove box incubators enable matching conditions by controlling air, temperature and pressure
- Cells will be cultured for multiple passages and at periodic intervals tested for:
  - Spontaneous transformation frequency
  - Background levels of DNA DSBs and micronuclei
- The dose-response for induced damage will be examined in low-background adapted cells

Lake Whitefish

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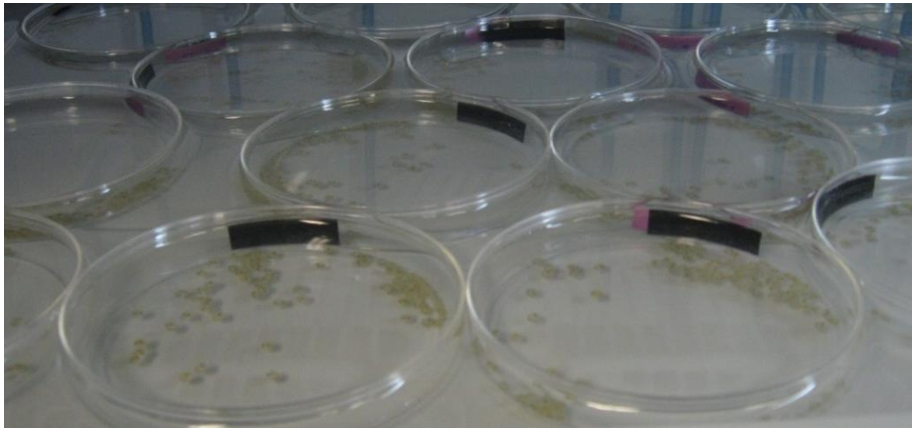
Good model organism for examining radiological effects

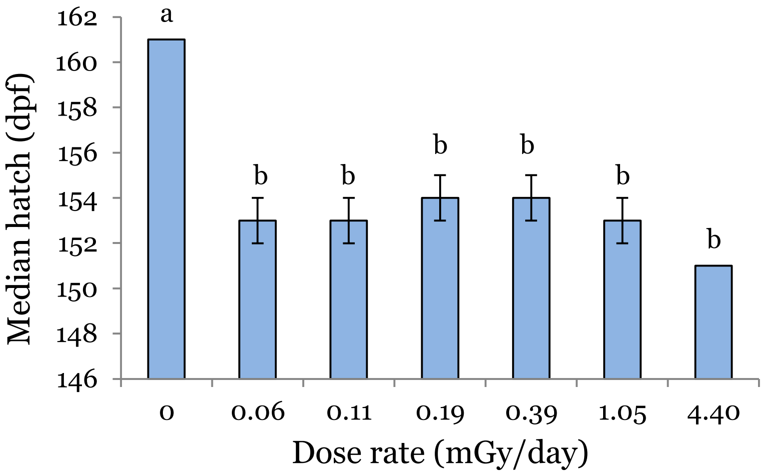
- Embryogenesis one of the most sensitive life stages to radiation
- Long development period (> 200 days)
  - Extended low-dose chronic exposures
  - Accurate targeting of specific development stages
- Can accurately quantify growth efficiency
- Easy to raise and low maintenance

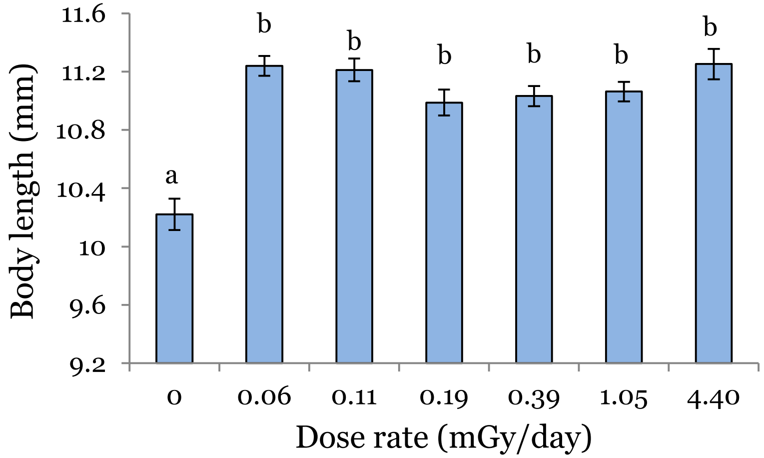


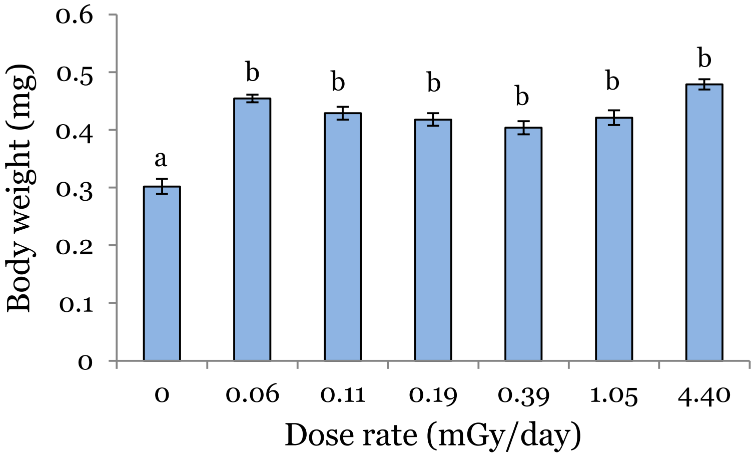
Lake Whitefish

Chronic low dose ^{137}Cs gamma ray exposure

- Accelerated development – earlier time to median hatch
- Stimulated growth – larger body length and weight







Lake Whitefish

- Lake Whitefish embryos will be reared within SNOLAB and the surface control lab
- Embryos will be raised from fertilization to hatch within standard refrigeration units
- At multiple stages, embryos will be analyzed for
    - Mortality
    - Development rate
    - Size
    - Growth efficiency
- The response to acute thermal or chemical stress will be examined in low-background adapted embryos