Investigating the biological effects of sub-natural background radiation exposure

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TRISEP
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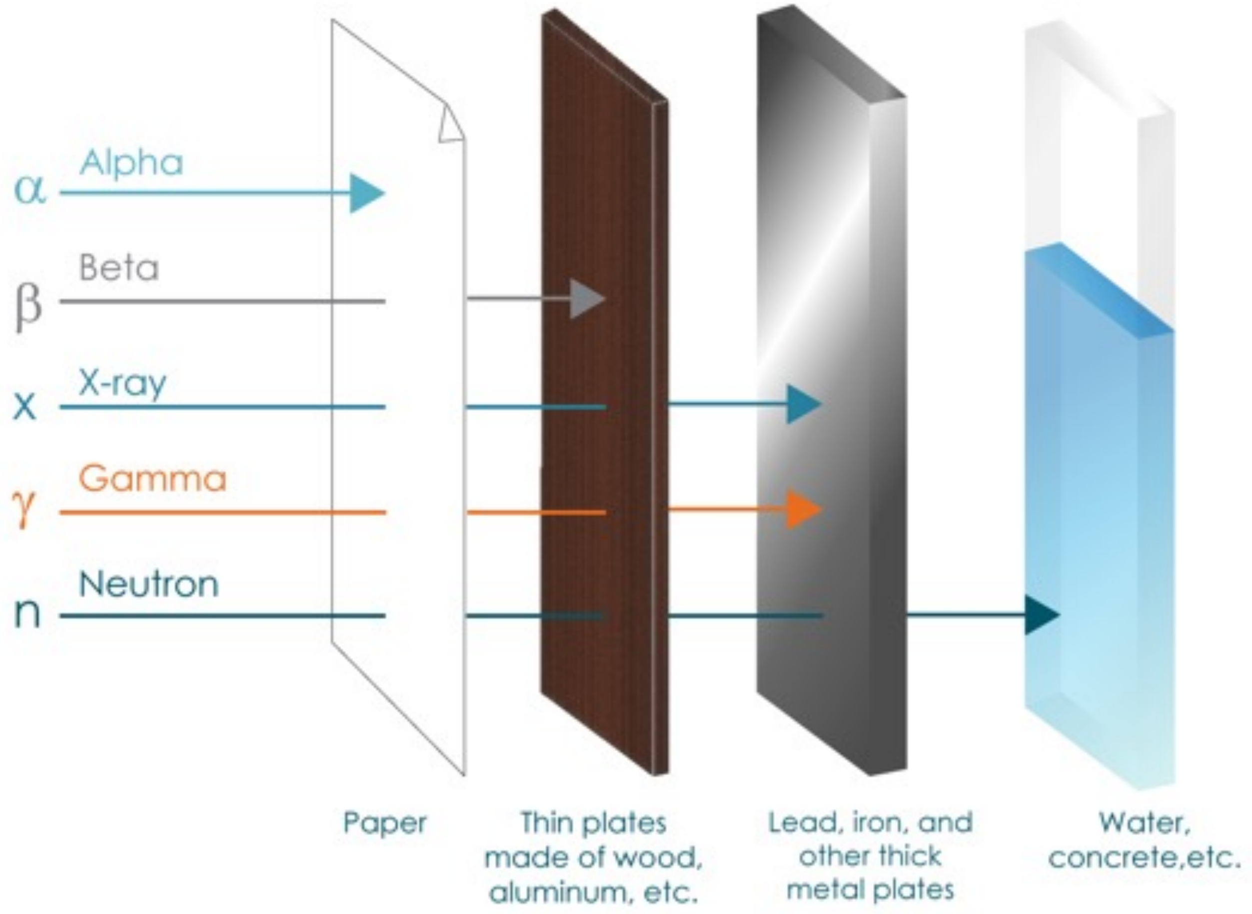
Outline

1. Sources of radiation
2. Biological effects
3. Sub-NBR research

Types of radiation



Radiation terminology

Activity:

The rate of decay of a sample

Units: Becquerel (Bq) or Curie (Ci)

1 Bq = 1 decay/s

Absorbed dose:

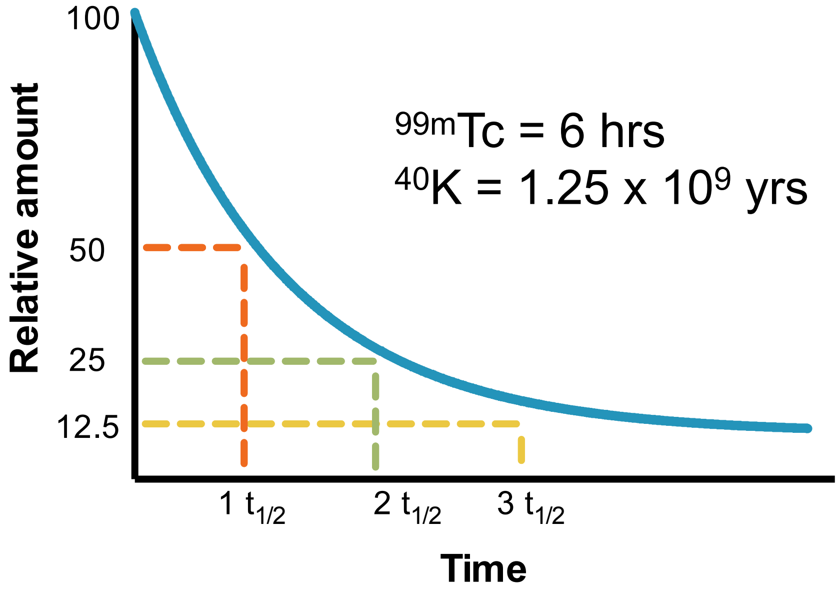
The amount of energy deposited per unit mass

Units: Gray (Gy), Sievert (Sv), Rad

1 Gy = 100 Rad = 1 J/Kg

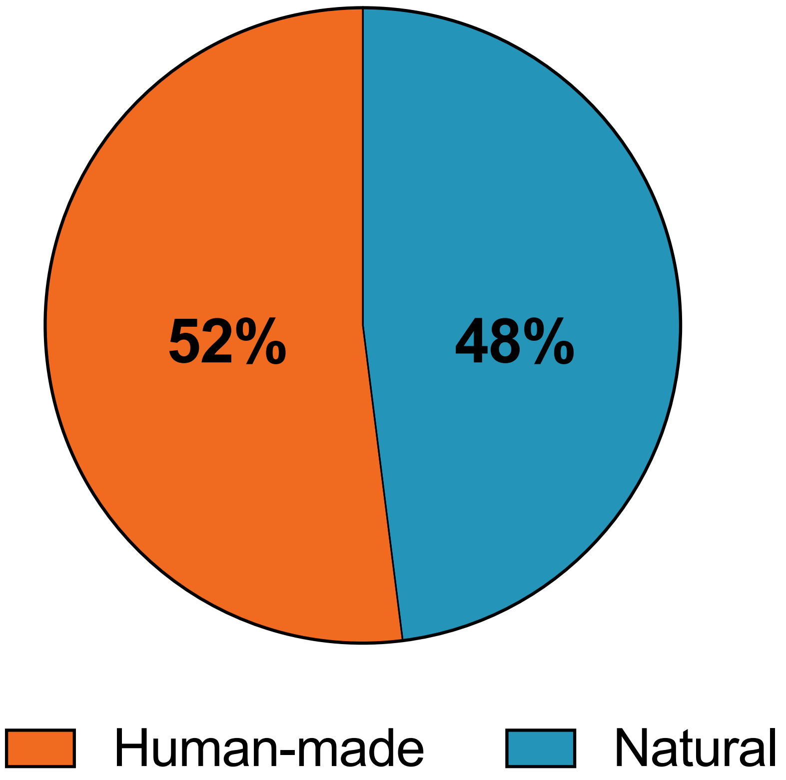
Half-life ($t_{1/2}$):

The time for an isotope to decay to half of its initial amount

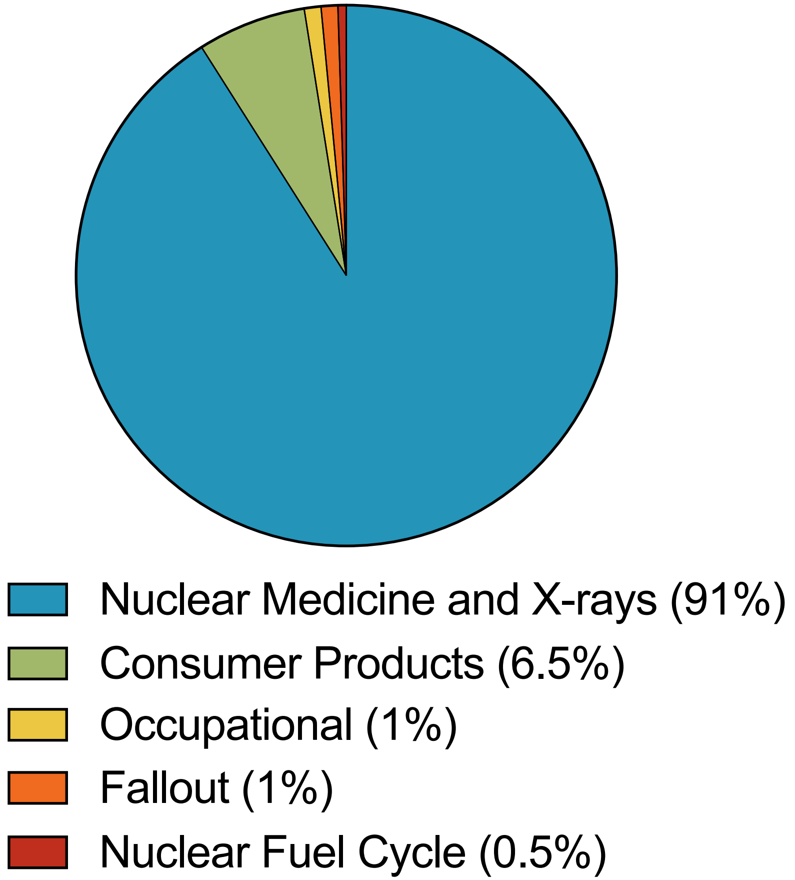


Background radiation

Annual ~ 6 mSv



Human made sources



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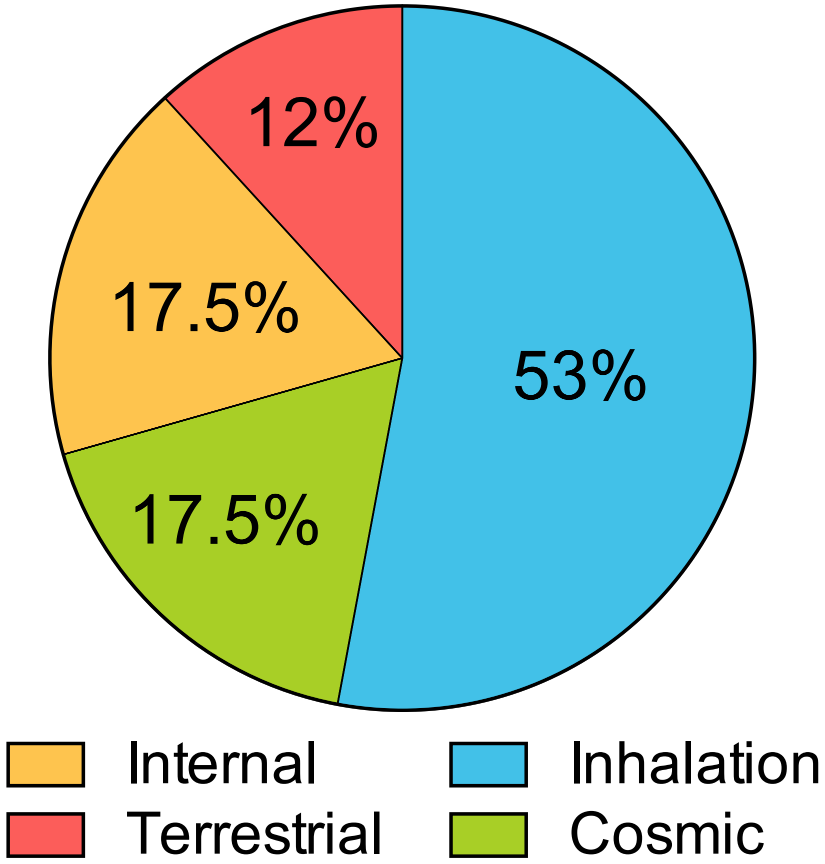
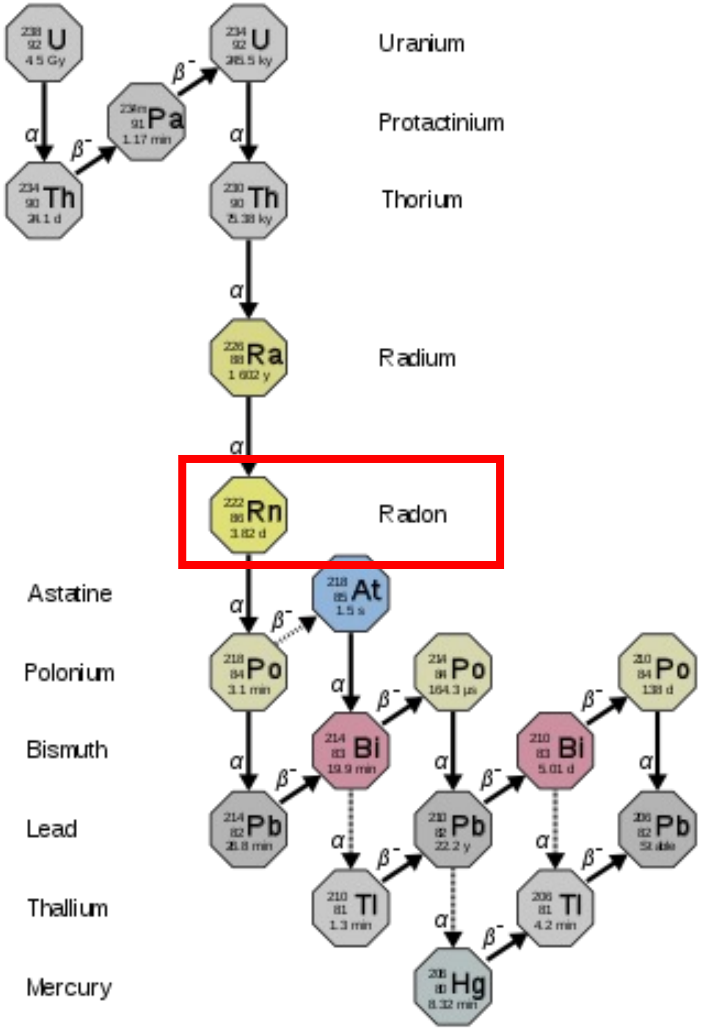
Natural background



Natural background

Location	Annual dose (mSv)
World Average	**3**
Guarapari, Brazil	Up to 175
Ramsar, Iran	Up to 100
Kerala, India	Up to 35
Yangjian, China	Up to 25
U.S. Rocky Mountain States	6–12
U.S. Gulf States	0.8–1.2
Evacuated land near Chernobyl	1–10
Evacuated land near Fukushima	<10

Radon gas



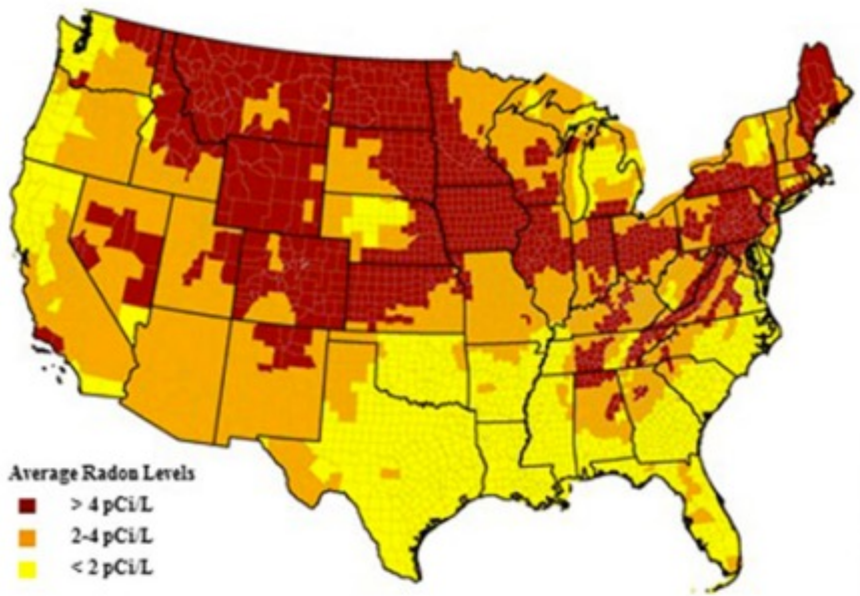
- Alpha emitter
- Dose to lung
- Lung cancer risk
- Health Canada guidelines = 200 bq/m^3

Radon decay products (RDP)

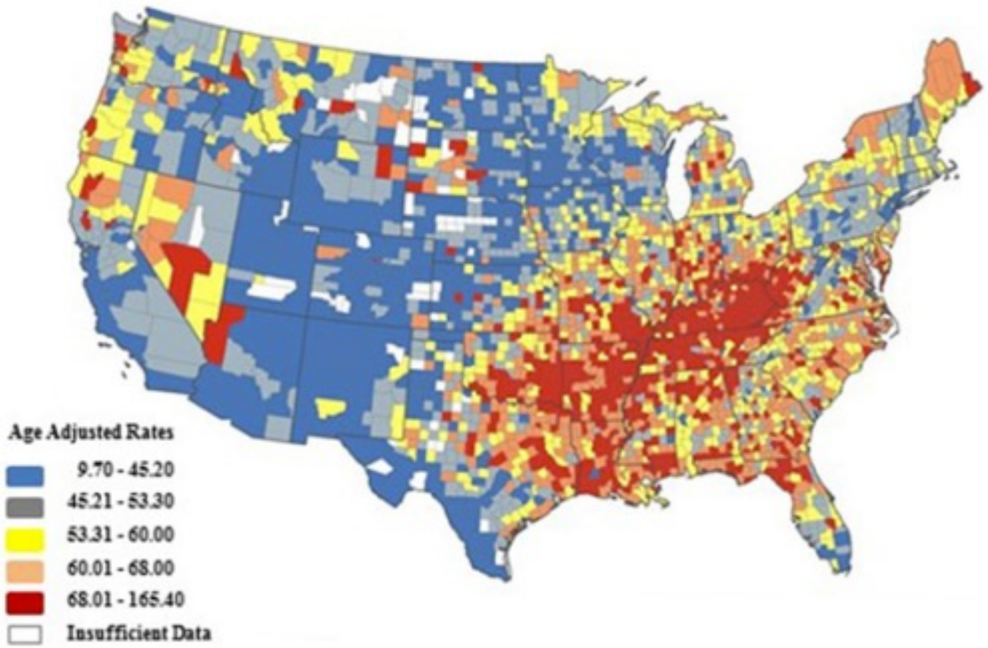
Radon gas

Second leading cause of lung cancer?

Radon levels



Lung cancer rates



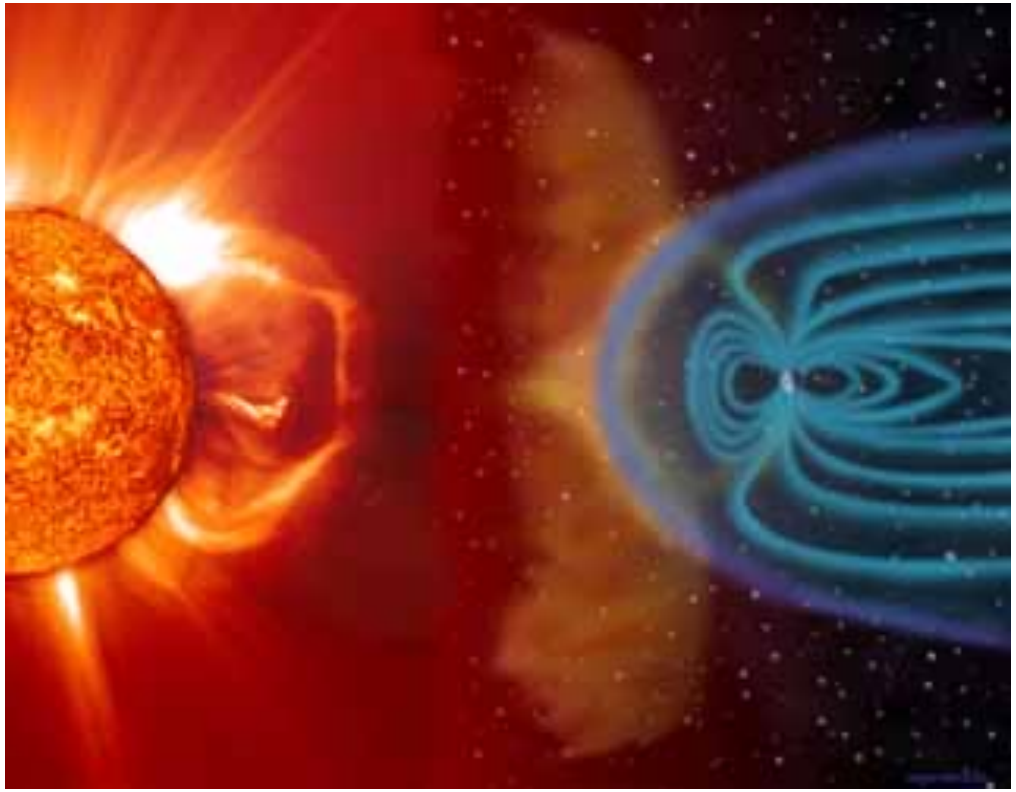
Cosmic

Galactic cosmic rays

- Protons (90%)
- Alpha particles (9%)
- Heavy nuclei (1%)

Secondary particles

- Muons
- Protons
- Neutrons
- ^{3}H, ^{14}C

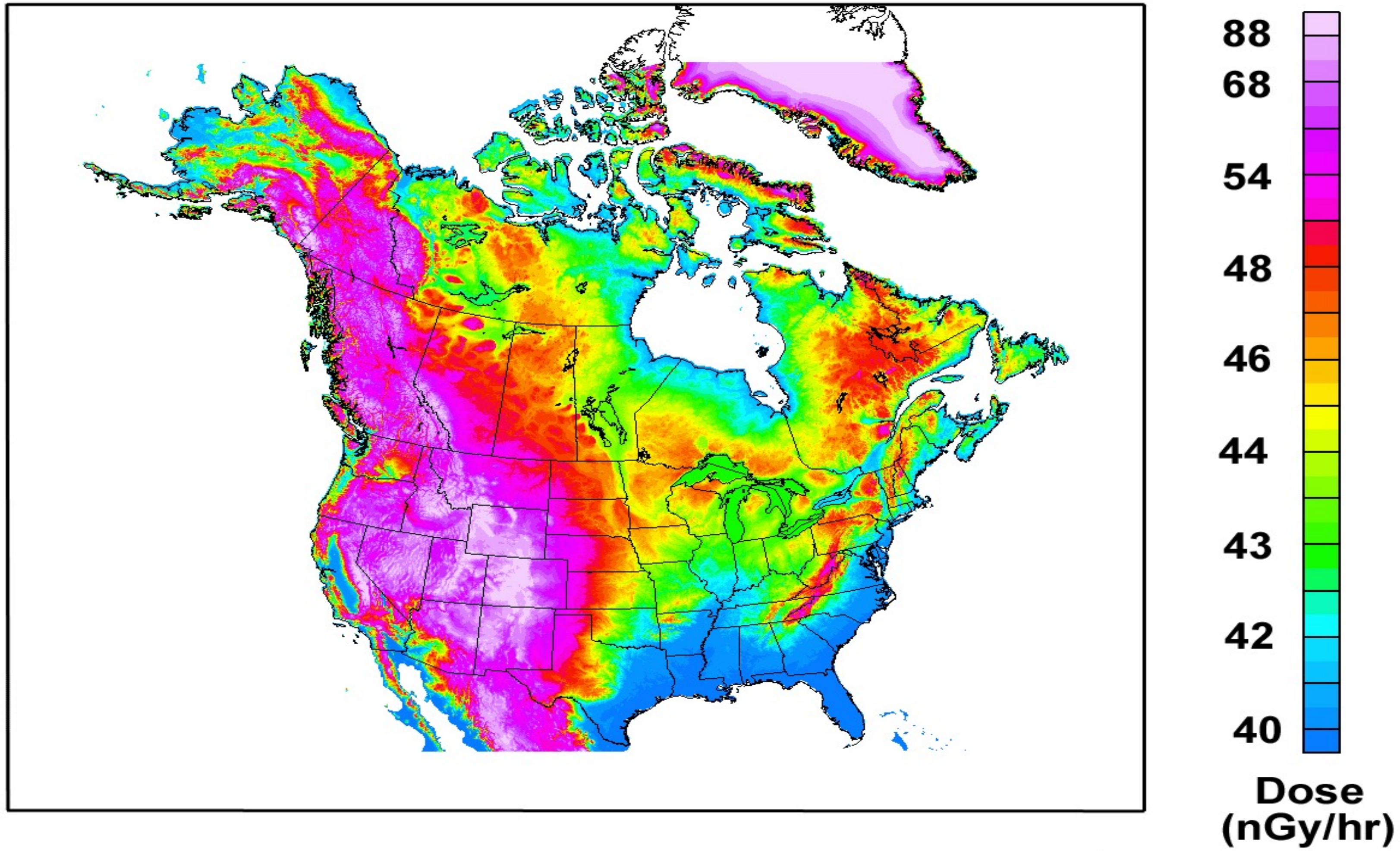


Cosmic

Dose to Astronauts:

- Moon (10 days): 5 mSv
- Mars (2–3 years): >1,000 mSv

Cosmic



Terrestrial

Grand Central Station:
1.2 mSv/yr

US Capital Building:
1 mSv/yr

Internal

^{40}K = 15 Bq

0.1 μSv

^{3}H = 1–7 Bq/L

=

^{40}K = 5,000 Bq

^{14}C = 3,000 Bq

^{238}U = 1.1 Bq

^{3}H = 23 Bq

^{210}Po = 37 Bq

^{226}Ra = 1.1 Bq

20 μSv

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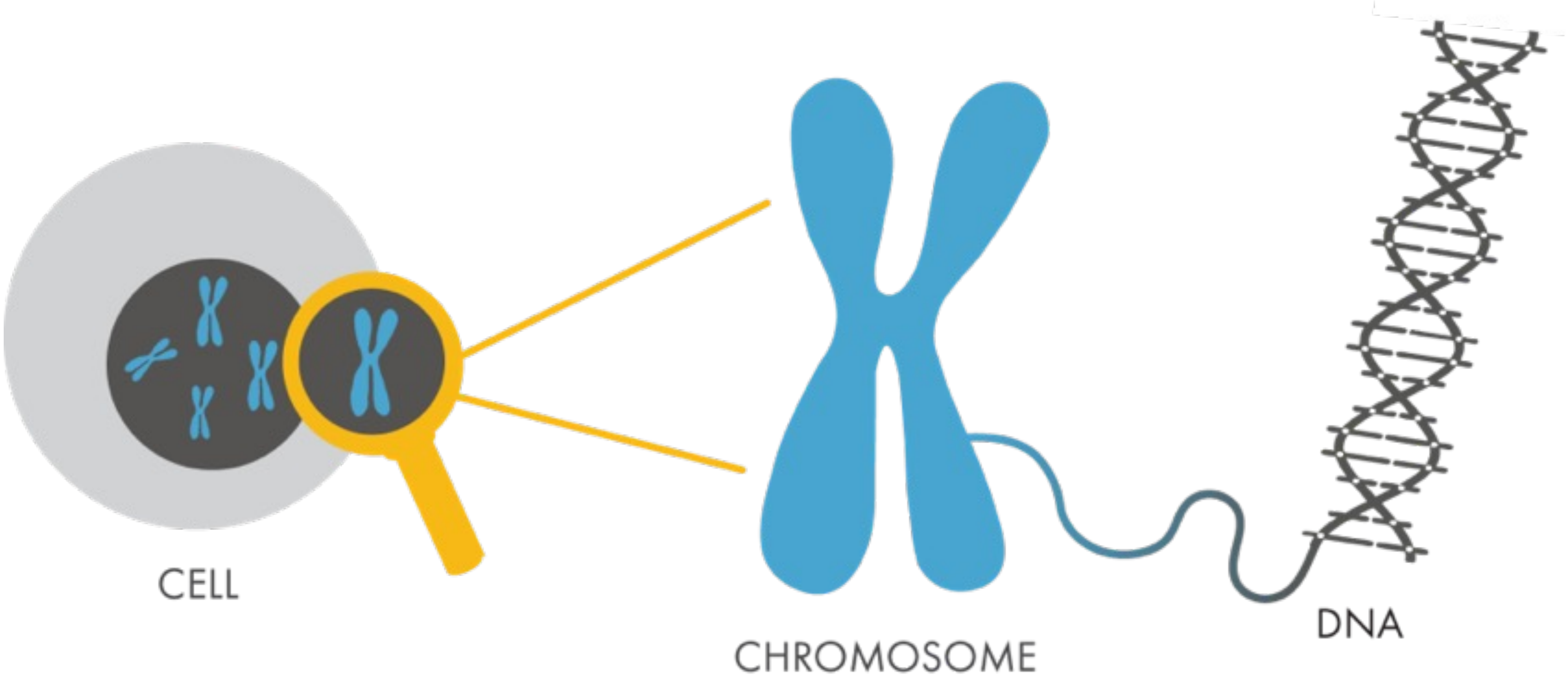
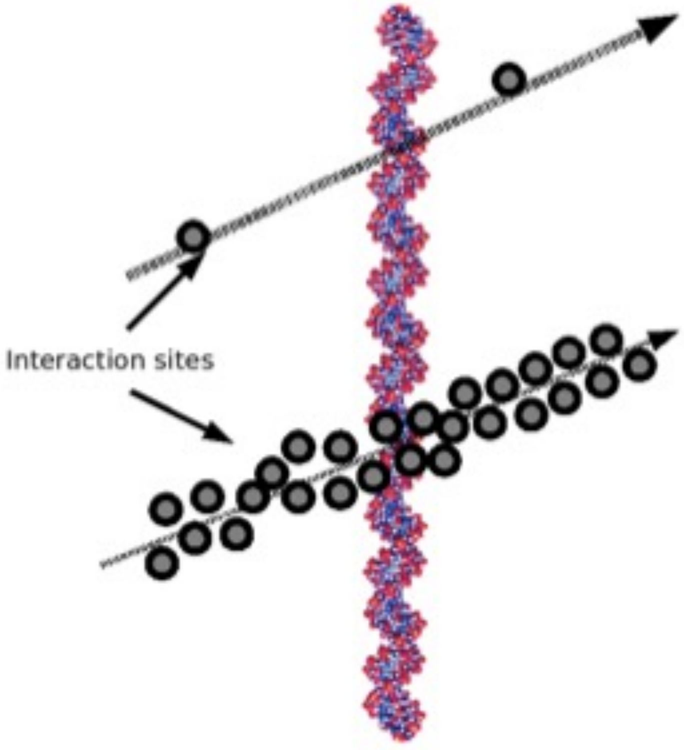
Radiobiology

DNA is the critical target



Linear energy transfer

Radiation tracks

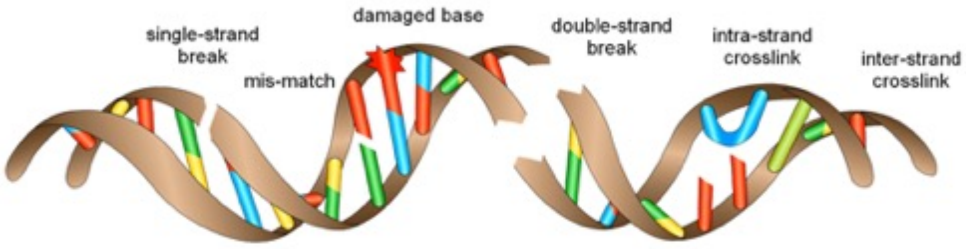


DNA segment

Radiation	LET (keV/µm)
^{60}Co (1.2 MeV)	0.3
250 kVp X-rays	2
10 MeV protons	4.7
150 MeV protons	0.5
14 MeV neutrons	12
2.5 MeV alpha	166

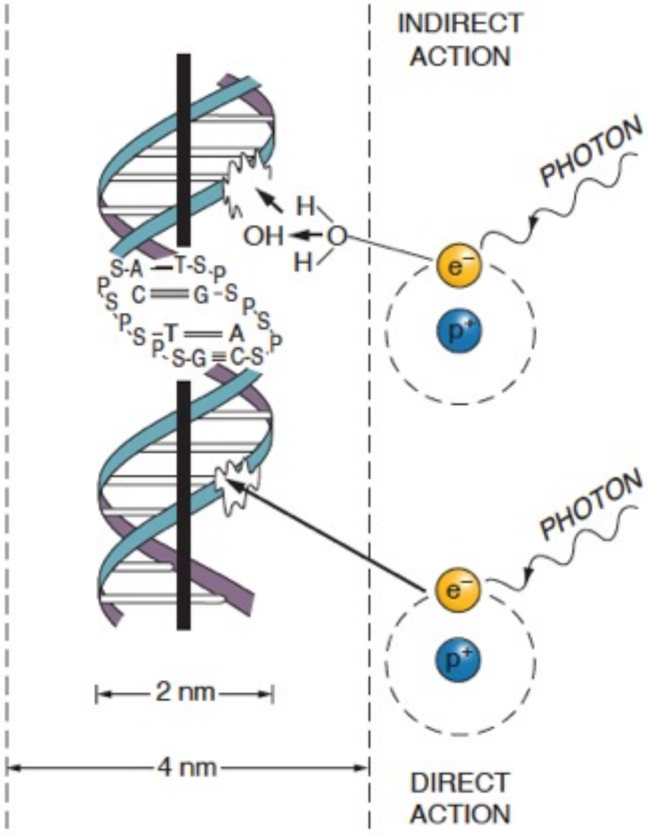
DNA damage

Type of lesion	Number (per Gy)
Base damage	1000–2000
Sugar damage	800–1600
Crosslink	30–150
Single strand break	500–1000
Double strand break	40



Direct vs indirect effect

Direct Effect	Indirect Effect
Radiation	Radiation
↓	↓
	Free radicals/ROS
	↓
DNA damage	DNA damage



Radiochemistry

$$H_2O \rightarrow H_2O\cdot^{+} + e^{-}$$

$$H_2O \rightarrow H_2O^{*}$$

$$e^{-} + H_2O \rightarrow e_{aq}^{-}$$

$$e^{-} + H^{+} \rightarrow H\cdot$$

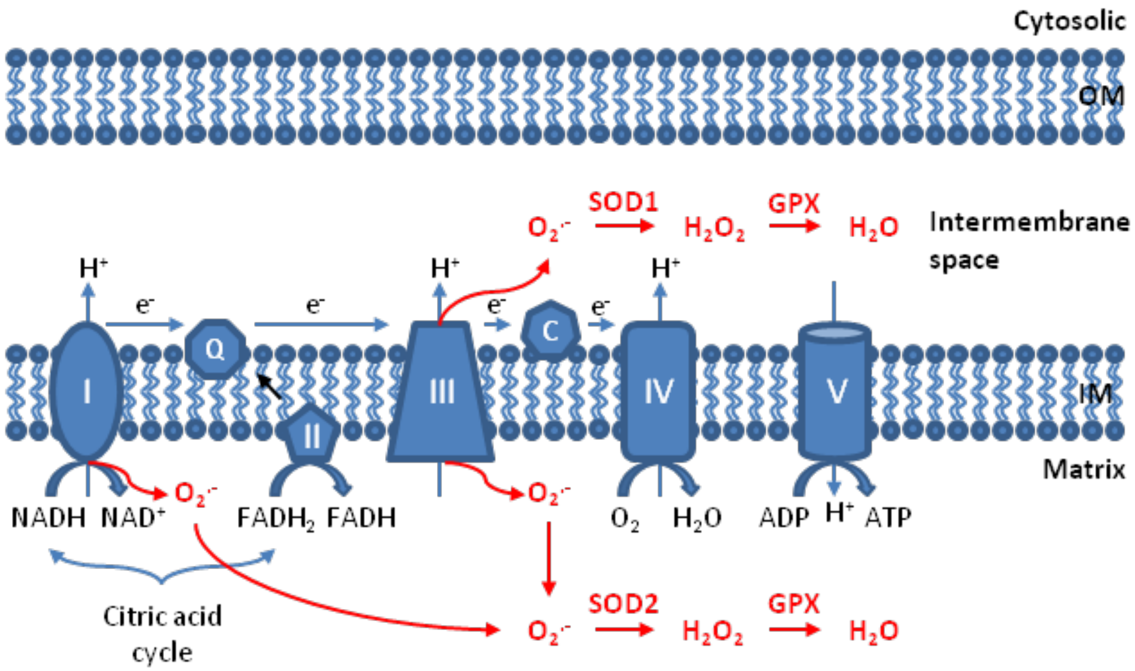
$$H_2O\cdot^{+} \rightarrow H^{+} + OH\cdot$$

$$H_2O^{*} \rightarrow OH\cdot + H\cdot$$

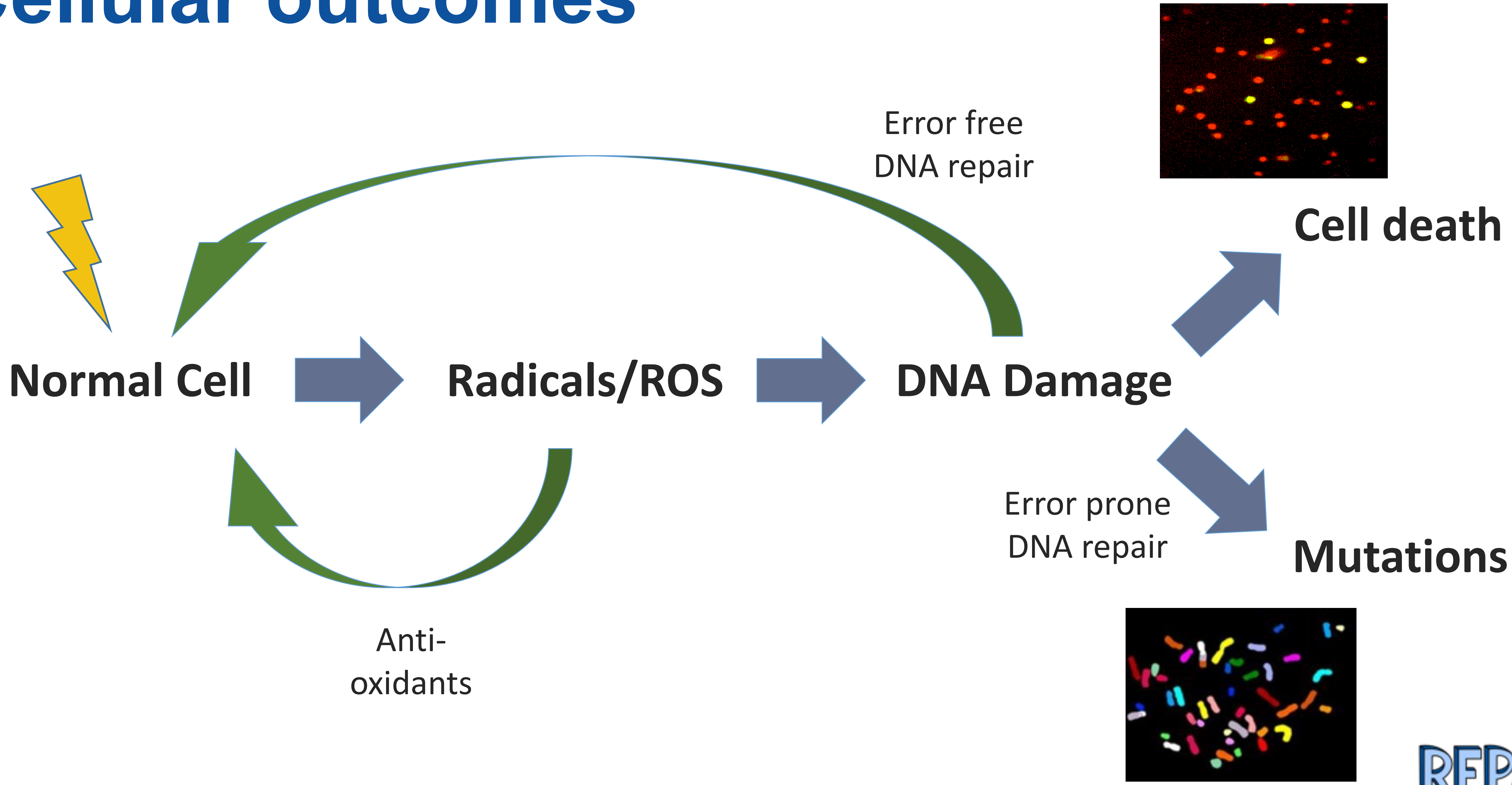
Natural ROS

Free radicals are produced naturally during cellular respiration

- 5,000 to 10,000 DNA interactions per hour



Cellular outcomes



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Model systems

Humans:

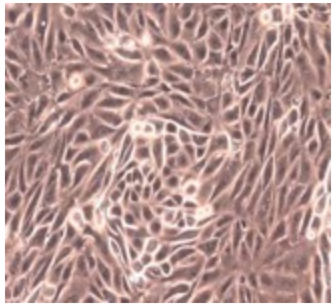
- Atomic bomb survivors
- Nuclear accidents
- Occupational exposures

Animals:

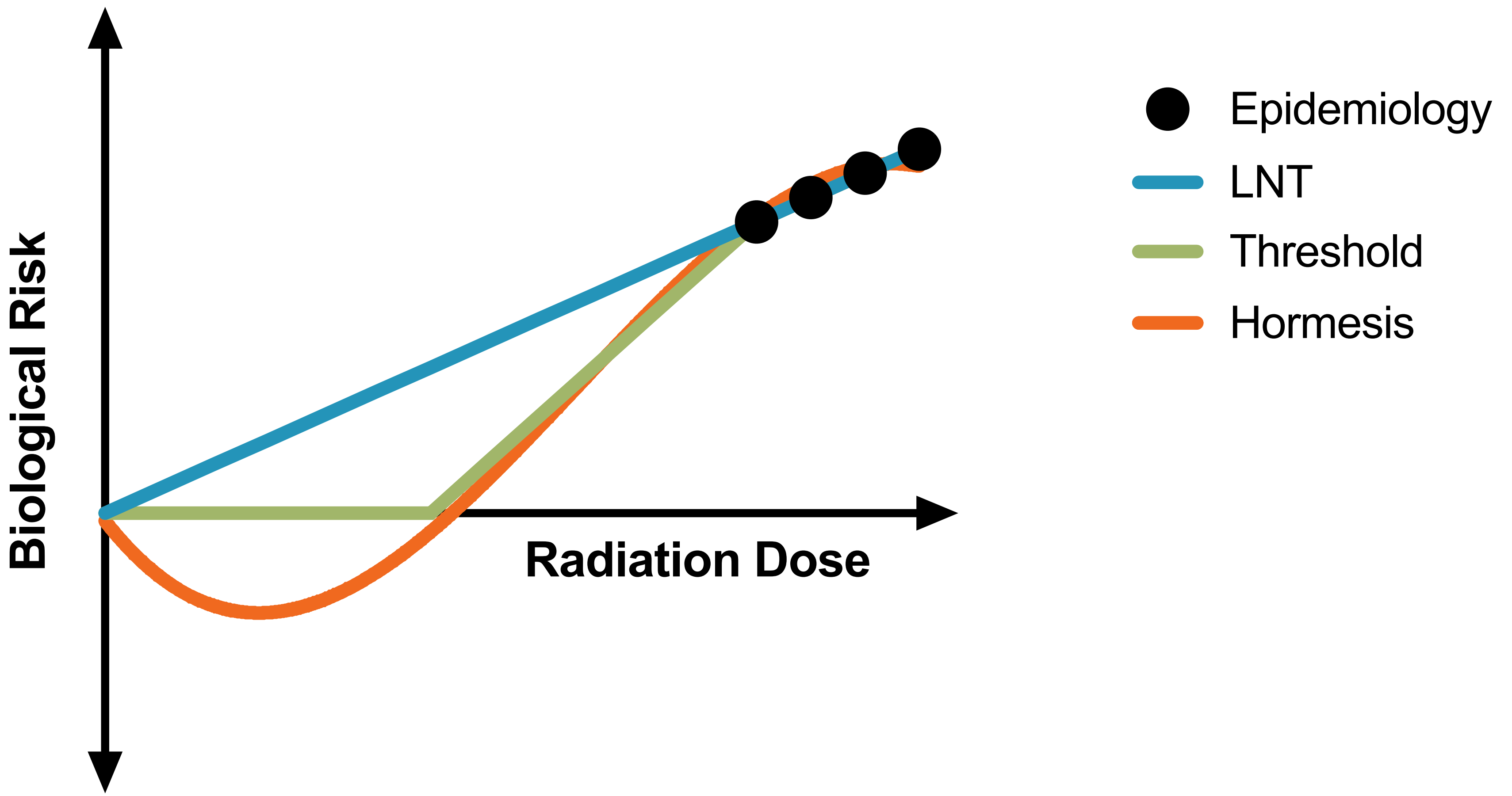
- Mice
- Rats

Cell culture:

- Primary cells
- Cell lines

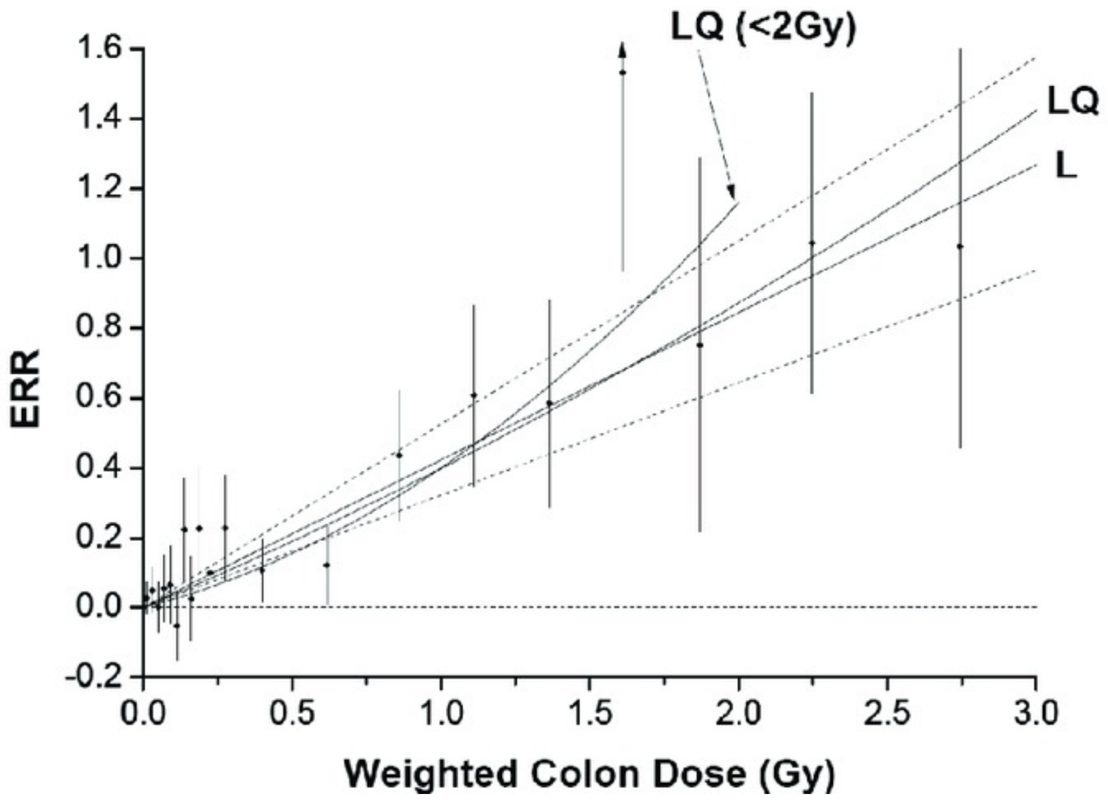


Models of risk

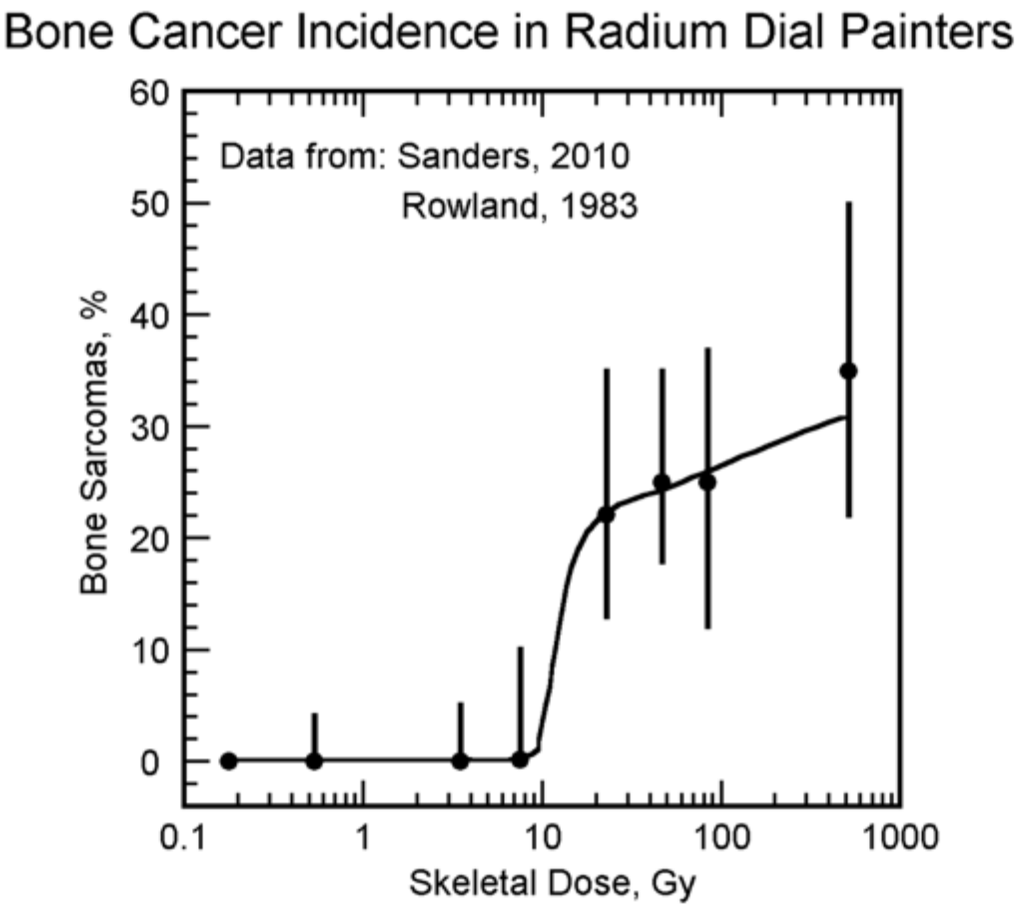


Linear no-threshold model

Solid cancer risk



Threshold model



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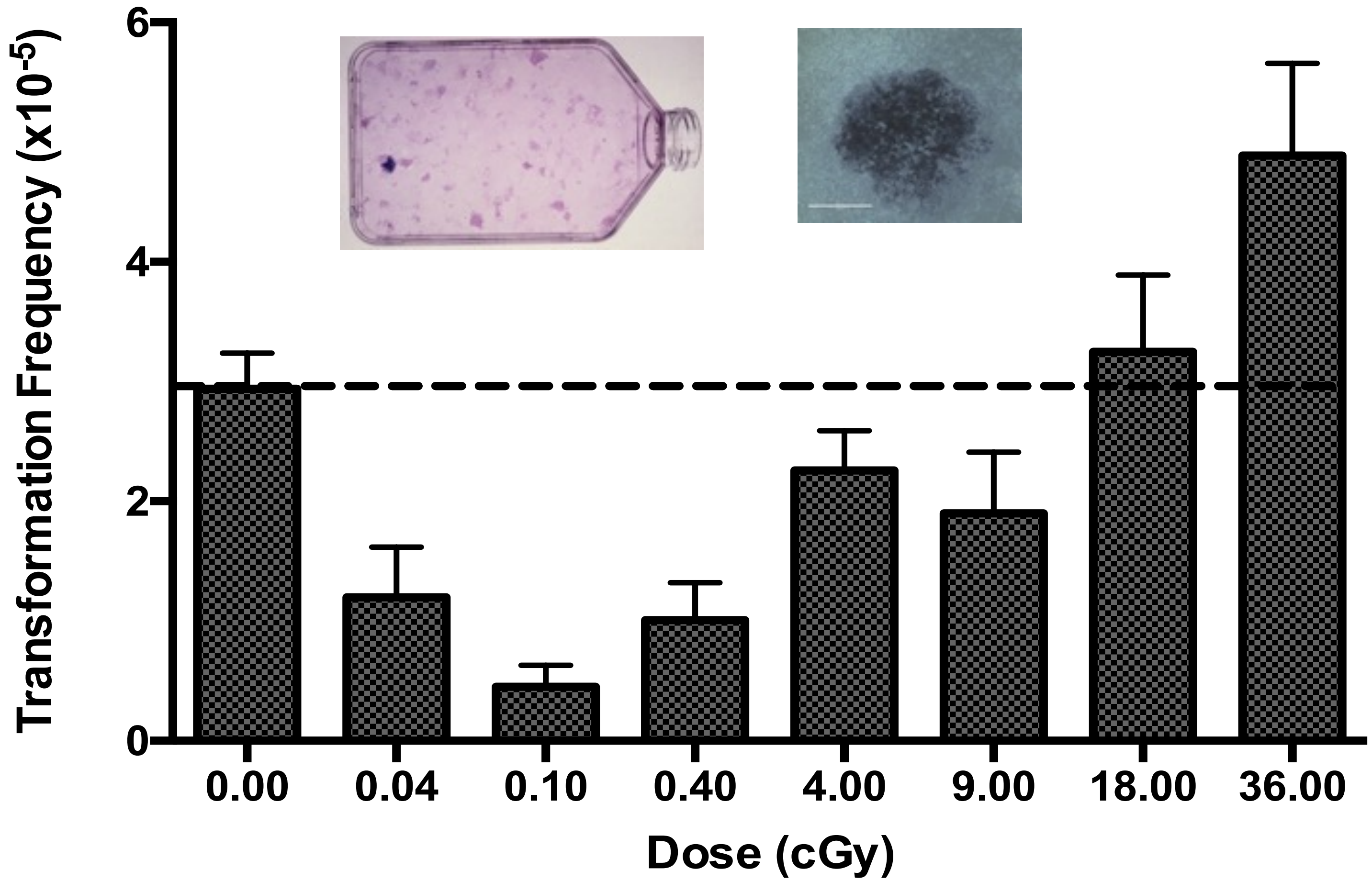
Hormetic model



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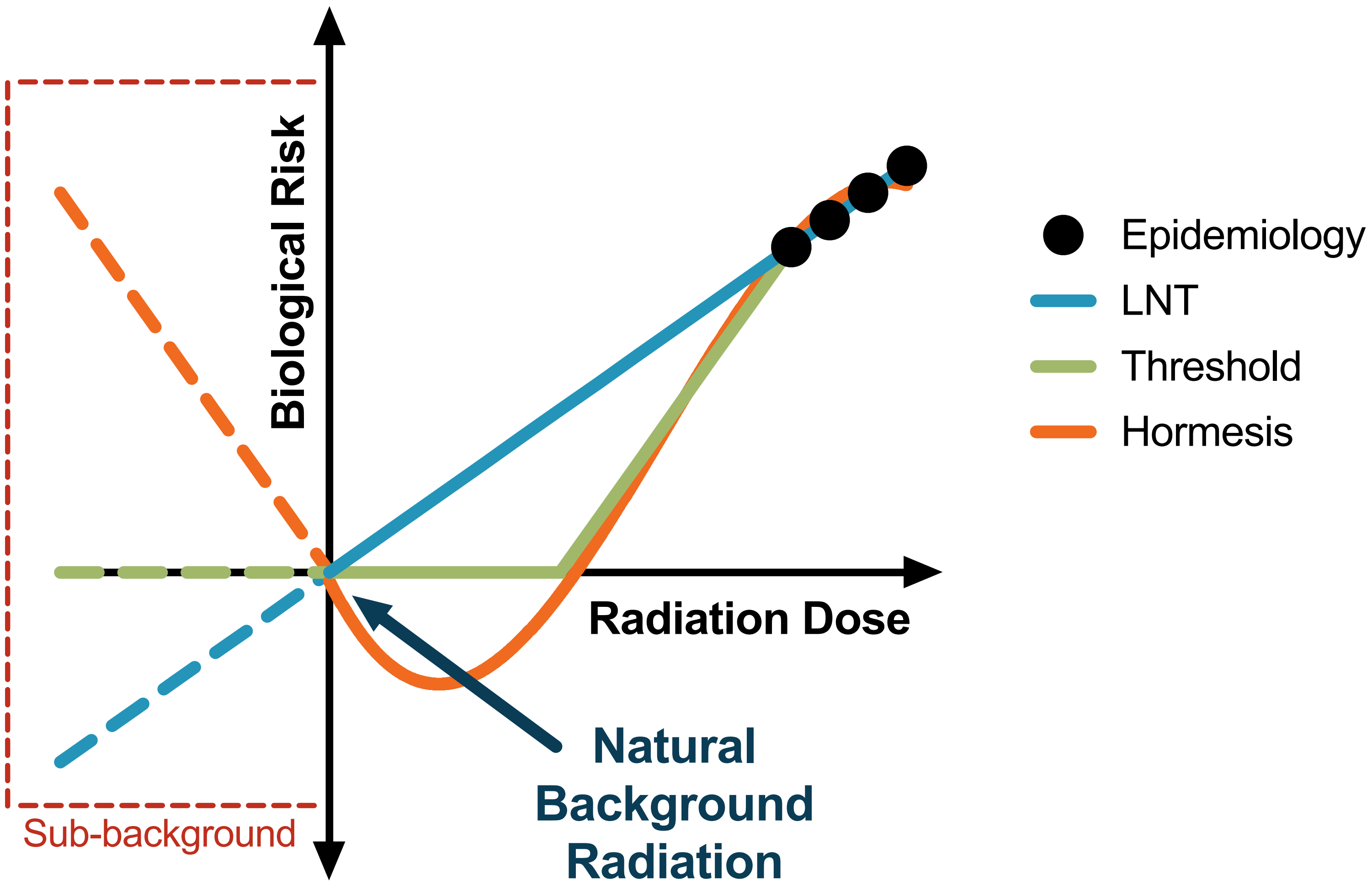
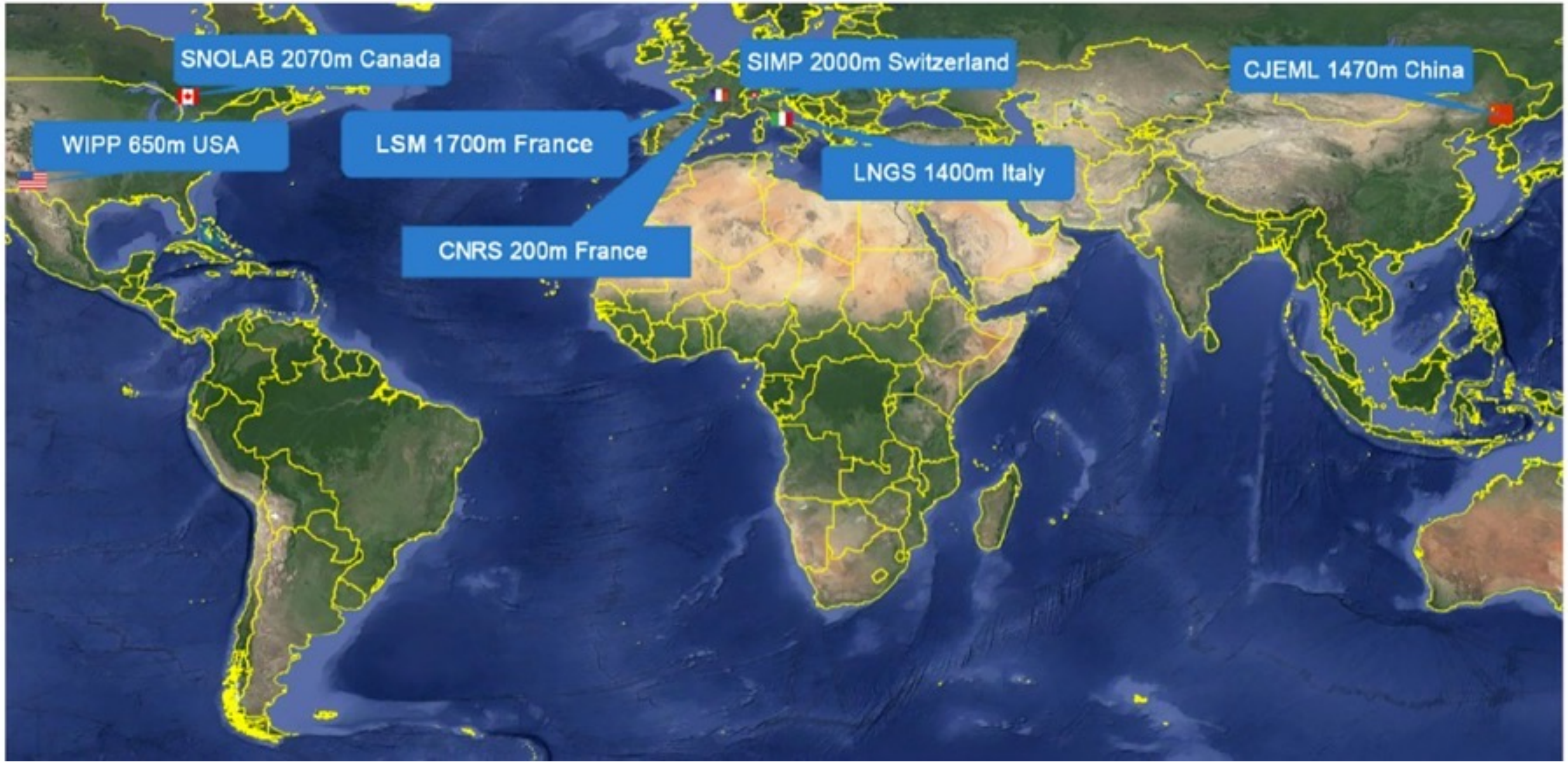
Models of risk



Why underground labs?

- Rock overburden – cosmic ray shielding
- Air filtration – reduction in radon levels
- Clean room facilities – reduce biological contamination
- Infrastructure – incubators, microscopes, etc.

Underground biology labs



Sub-NBR effects

1. Removal of natural background radiation impairs growth. Growth rates are restored once radiation is artificially reintroduced:
   - ❑ Paramecium (Planel *et al* 1976)
   - ❑ Blue-green algae (Conter *et al* 1983)
   - ❑ *Deinococcus radiodurans* (Smith *et al* 2011)
   - ❑ Yeast (Gajendiran and Jeevanram 2002)
   - ❑ Mammalian cell lines (Taizawa *et al* 1992, Kawanishi *et al* 2012, Satta *et al* 2002)

Sub-NBR effects

2. Removal of natural background radiation increases genomic damage and reduces repair capacity:

- ❑ Survival fraction (Gajendiran and Jeevanram 2002)
- ❑ Background/induced mutation rates (Satta *et al* 2002)
- ❑ Micronuclei formation (Carbone *et al* 2010)
- ❑ ROS scavenging (Carbone *et al* 2010)

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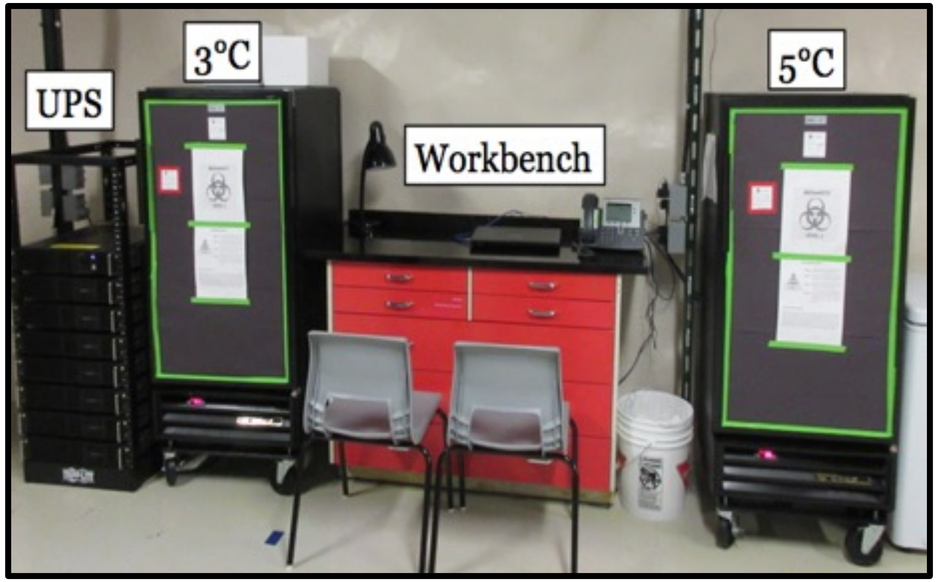
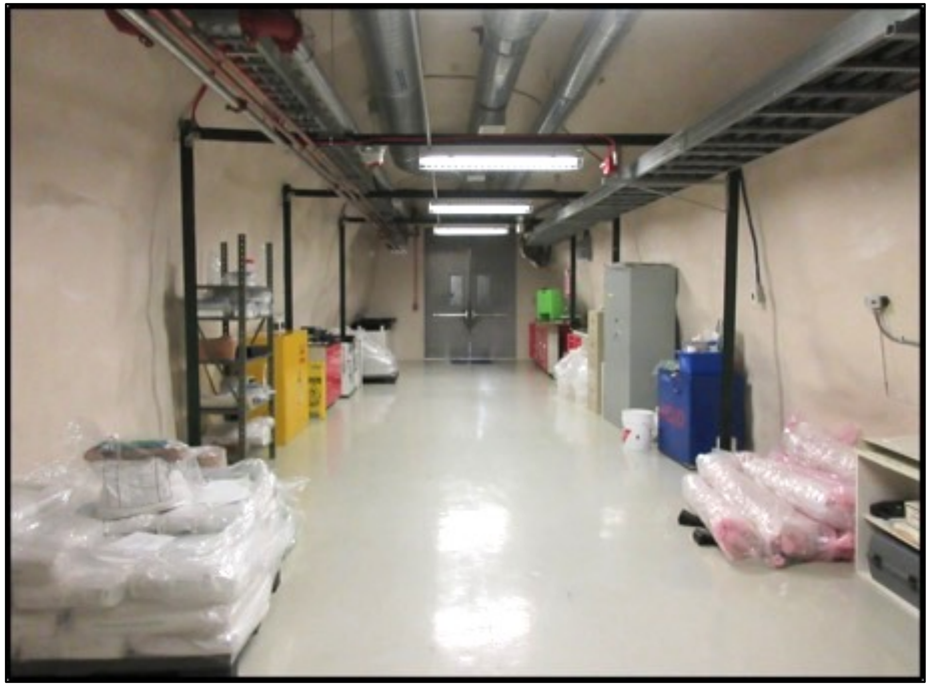
SNOLAB Life Sciences Laboratory

2015 – 2017





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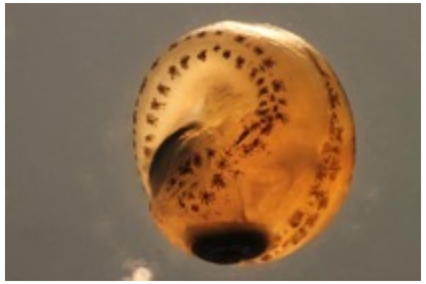
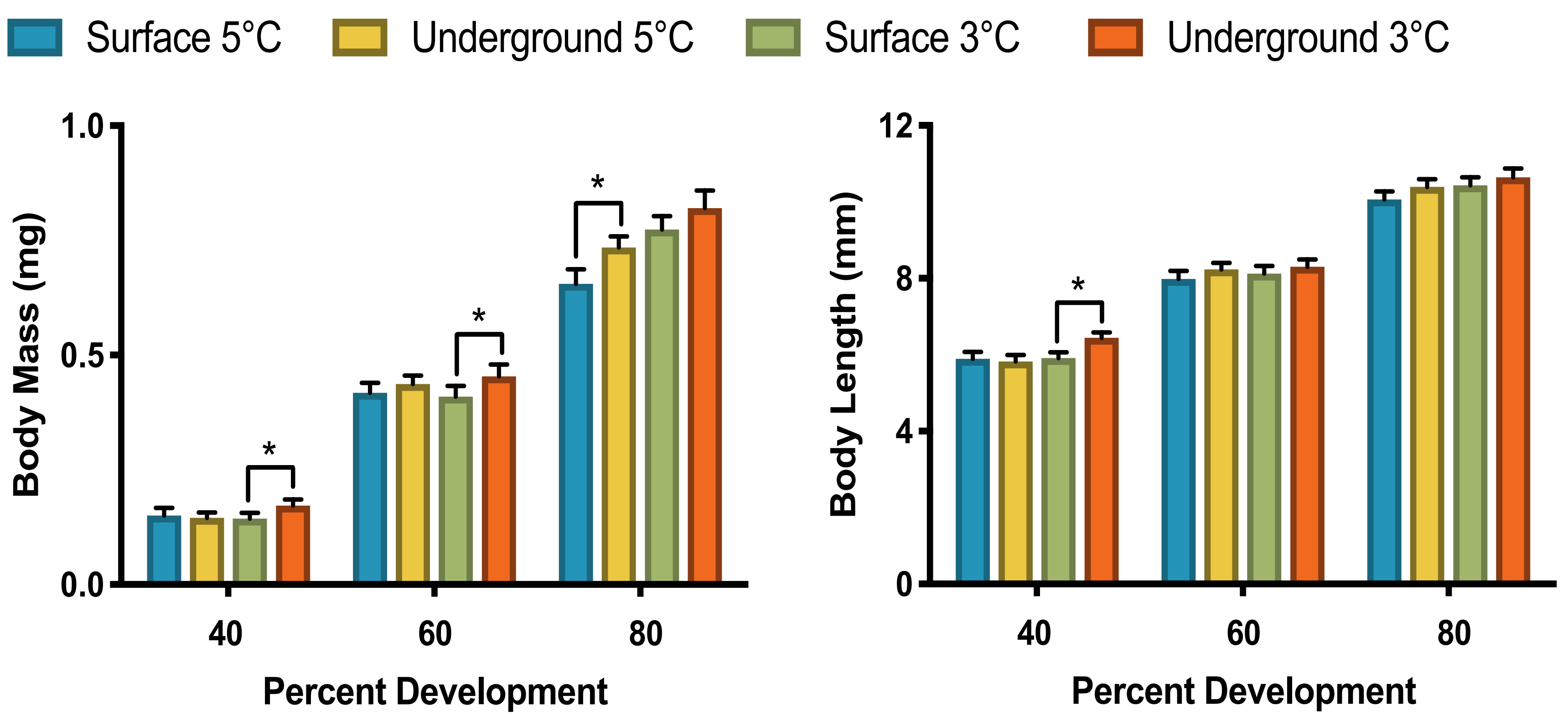
Pilot project: lake whitefish

	Temperature (°C ± SD)	Dishes	Embryos	Sampling timepoint (dpf*)		
				40%	60%	80%
Surface 5°C	4.7 ± 0.2	39	1,950	38	58	79
Underground 5°C	4.6 ± 0.3	43	2,150	38	58	79
Surface 3°C	3.3 ± 0.4	38	1,900	50	73	101
Underground 3°C	3.4 ± 0.2	42	2,100	50	73	101



Pilot project: lake whitefish

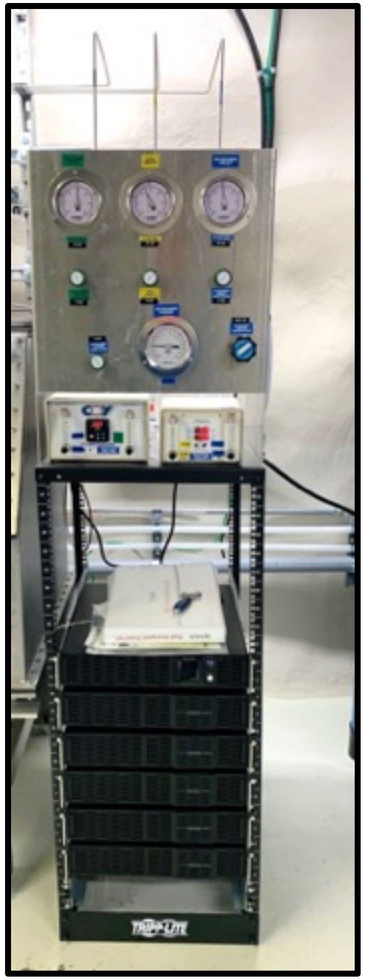


Pirkkanen et al. 2020 *Front Earth Sci*

SNOLAB Life Sciences Laboratory

Current

Additional NBR control

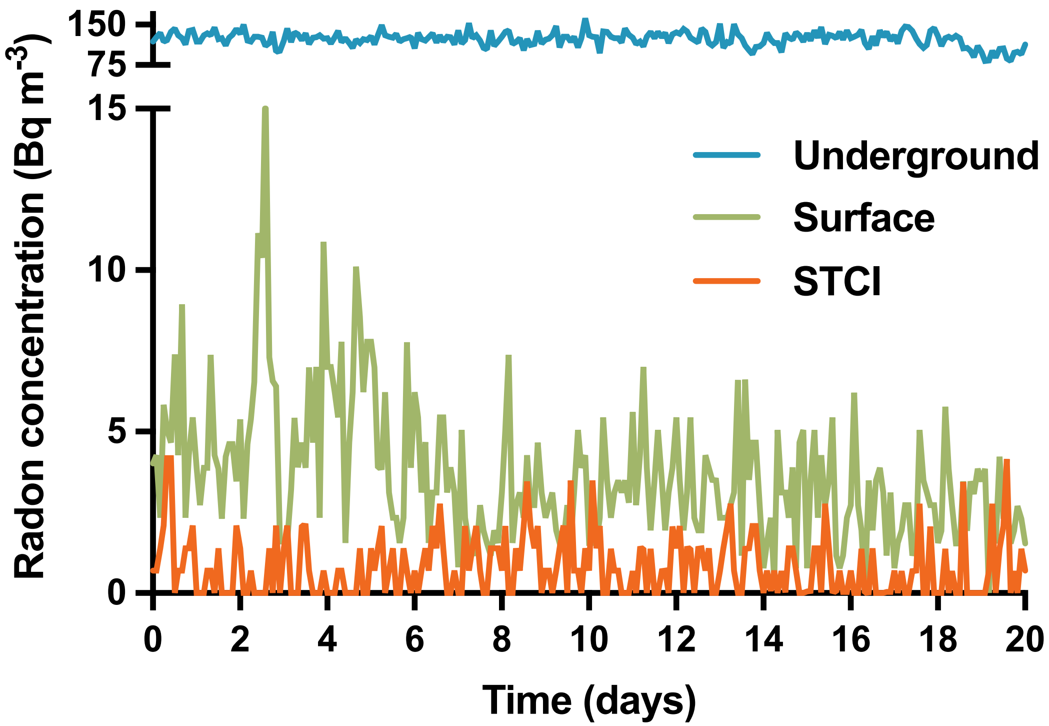


Pirkkanen et al. 2021 *J Environ Radioact*

Experimental environments

1. **Underground control:** standard tissue culture incubator in SNOLAB
2. **Surface control:** standard tissue culture incubator at NOSM
3. **Sub-background:** underground specialized tissue culture incubator (STCI)

Radon



Underground = 123 ± 16 Bq/m^3 (3.3 ± 0.4 pCi/L)

Surface = 3.7 ± 2.1 Bq/m^3 (0.10 ± 0.05 pCi/L)

STCI = 0.79 ± 0.93 Bq/m^3 (0.02 ± 0.02 pCi/L)

Gas cylinders (CO_2, N_2, O_2) feeding the STCI are aged underground for a minimum of one month

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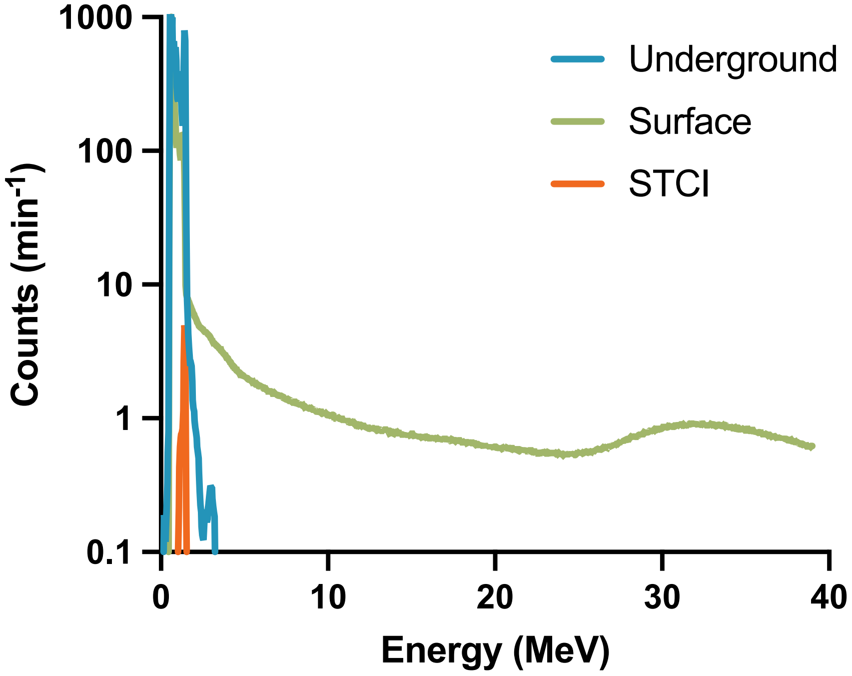
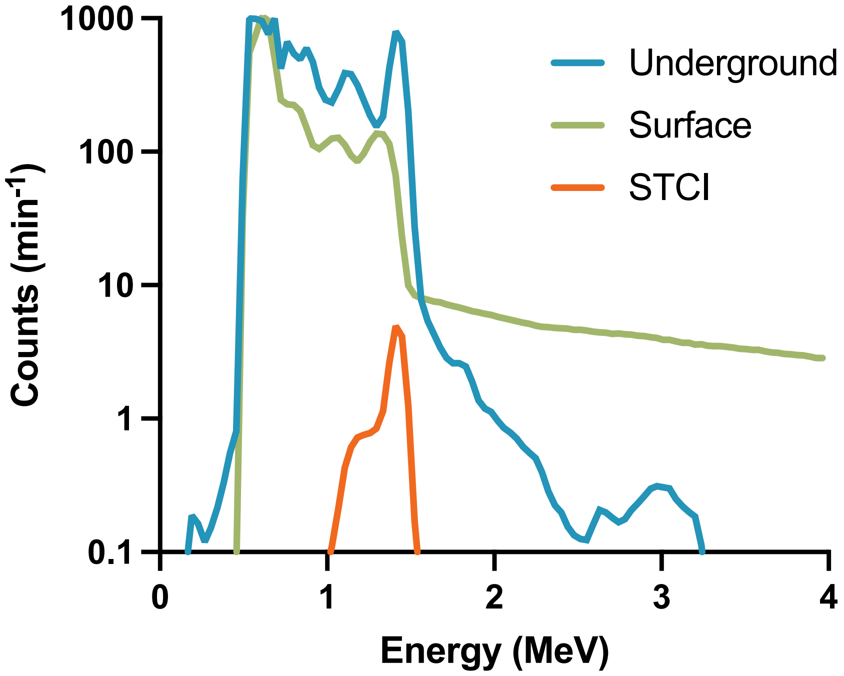
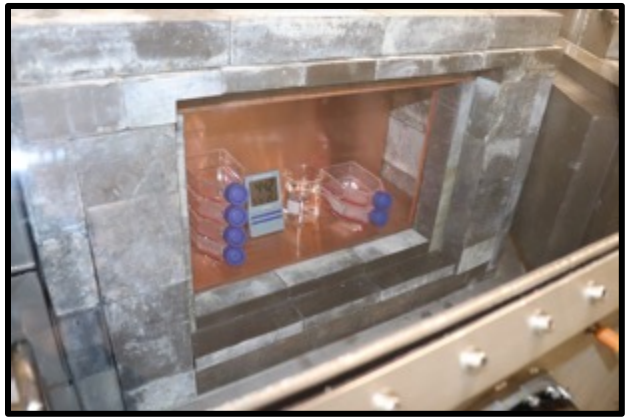
Gamma



Counts (min-1)
1000
100
10
1
0.1
0
10
20
30
40
Energy (MeV)
Underground
Surface
STCI



Counts (min-1)
1000
100
10
1
0.1
0
1
2
3
4
Energy (MeV)
Underground
Surface
STCI



Internal

40-Potassium

8.0 ± 0.6 Bq/L
(216 ± 16 pCi/L)

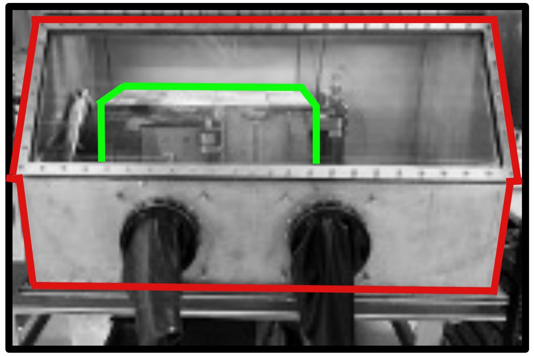
14-Carbon

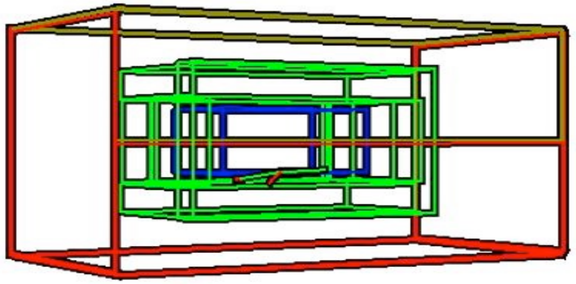
0.612 ± 0.004 Bq/L
(16.5 ± 0.1 pCi/L)

Absorbed dose rates

Dose rates in each experimental environment were calculated using GEANT4 for:

- ❑ Gamma
- ❑ Neutron
- ❑ Muon





Dose rates in each experimental environment were calculated using activity concentrations for:

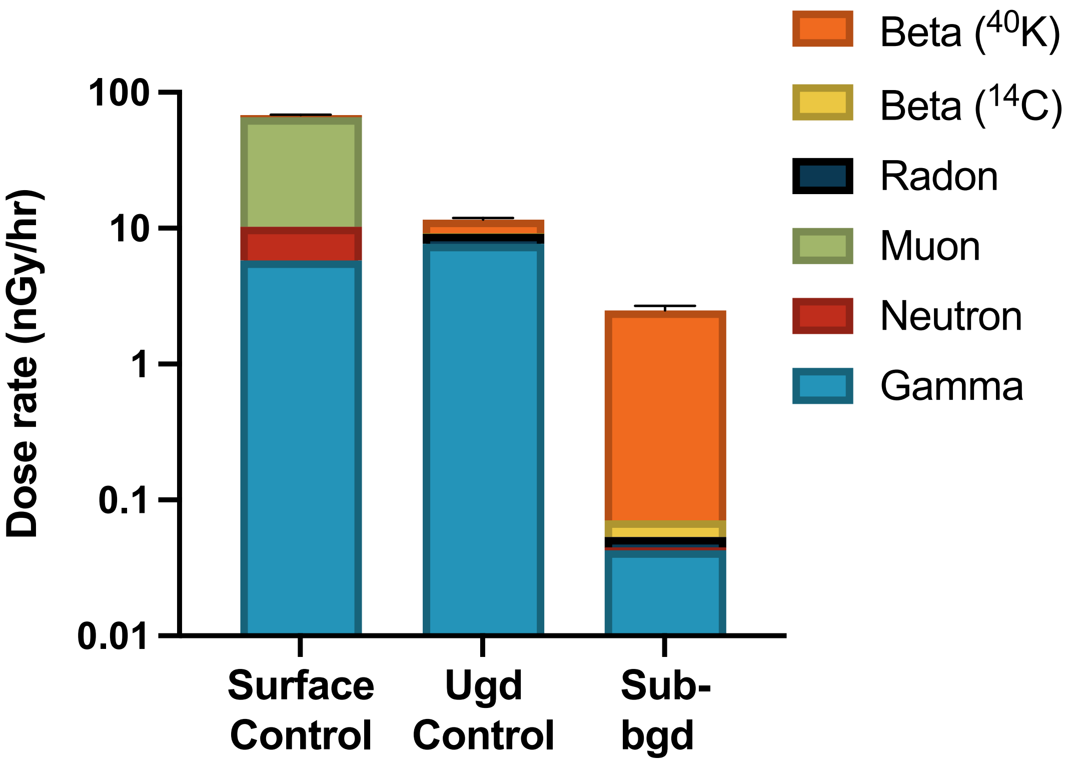
- ❑ Radon
- ❑ ^{40}K
- ❑ ^{14}C

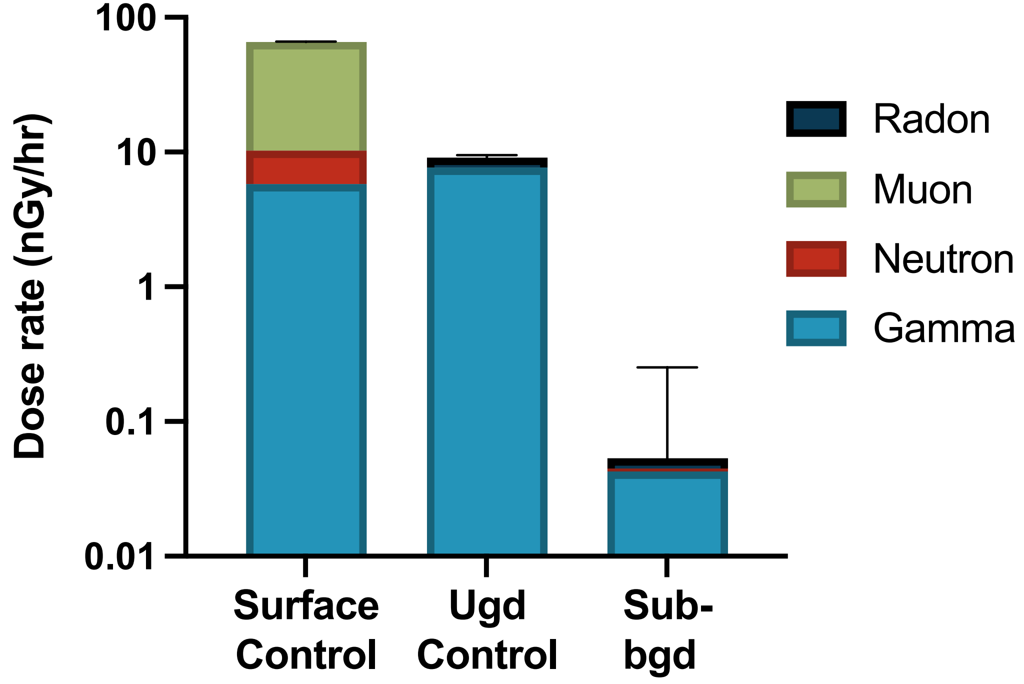
Absorbed dose rates

Particle type	Surface control (nGy hr^{-1})	Underground control (nGy hr^{-1})	Sub-background (nGy hr^{-1})
Gamma	5.78 ± 0.03	7.67 ± 0.01	0.0427 ± 0.0013
Neutron	4.52 ± 0.04	0.0045 ± 0.0002	0.00169 ± 0.00002
Muon	55.27 ± 0.40	Negligible	Negligible
^{222}Rn	0.044 ± 0.014	1.45 ± 0.17	0.009 ± 0.011
^{40}K	2.41 ± 0.19	2.41 ± 0.19	2.41 ± 0.19
^{14}C	0.0175 ± 0.0001	0.0175 ± 0.0001	0.0175 ± 0.0001
Total	**68.04 ± 0.67**	**11.55 ± 0.37**	**2.48 ± 0.20**

Kennedy et al. 2021 *Rad Prot Dosim*

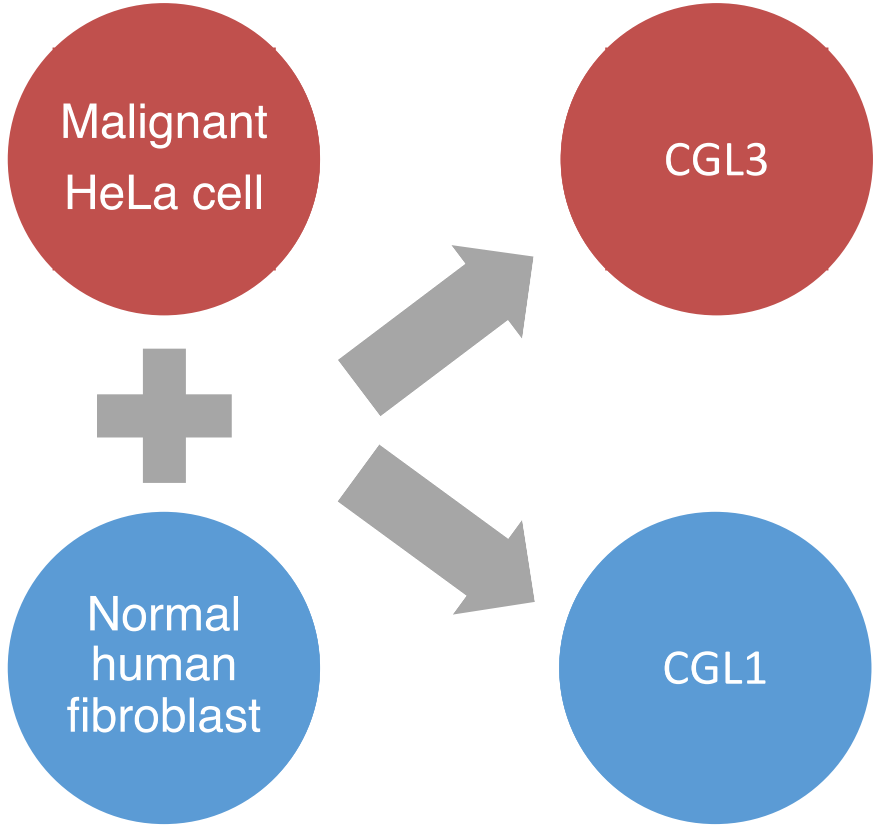
Absorbed dose rates

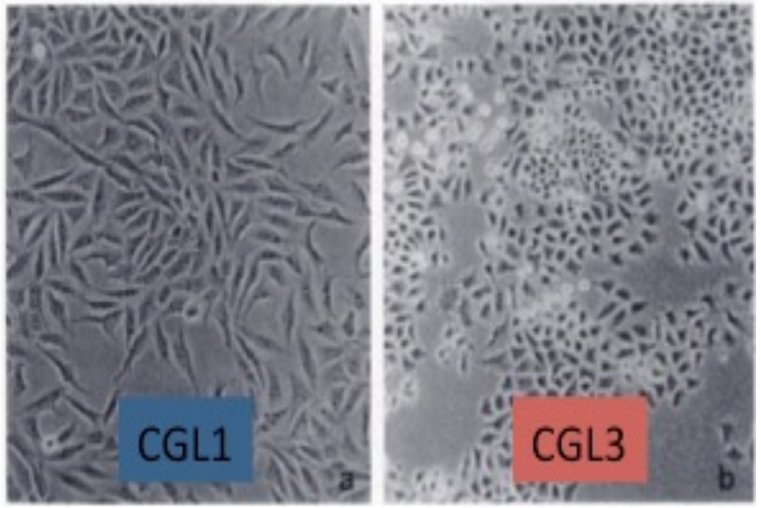




Kennedy et al. 2021 *Rad Prot Dosim*

Human cell culture





Tumorigenic cell

Non-tumorigenic cell

Sub-NBR experiments

- 4 weeks
- 8 weeks
- 12 weeks
- 16 weeks

Sub-NBR adapted cells

1. **Baseline response**
2. **Radiation challenge**

- Growth
- Survival
- Genomic damage
- Oxidative stress
- Carcinogenesis

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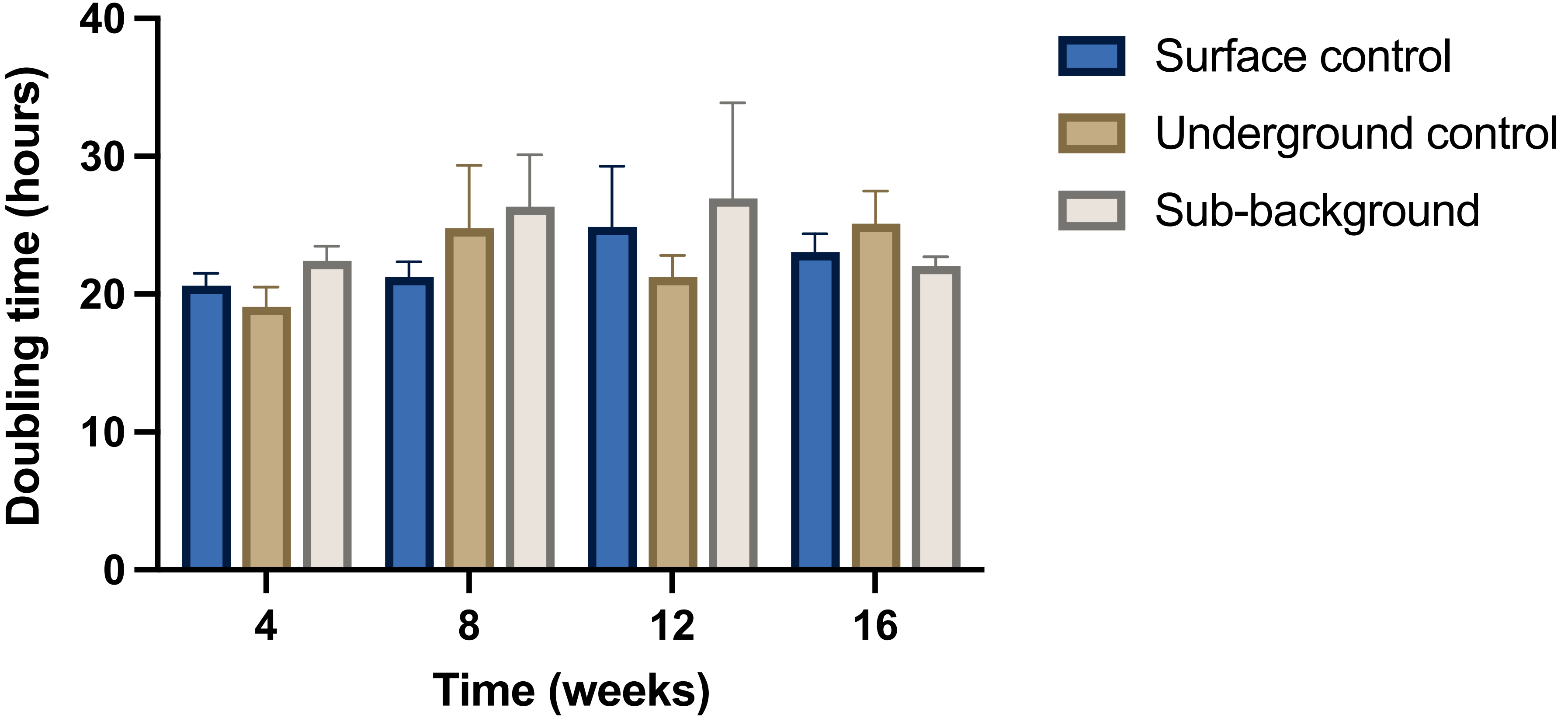
Growth rate



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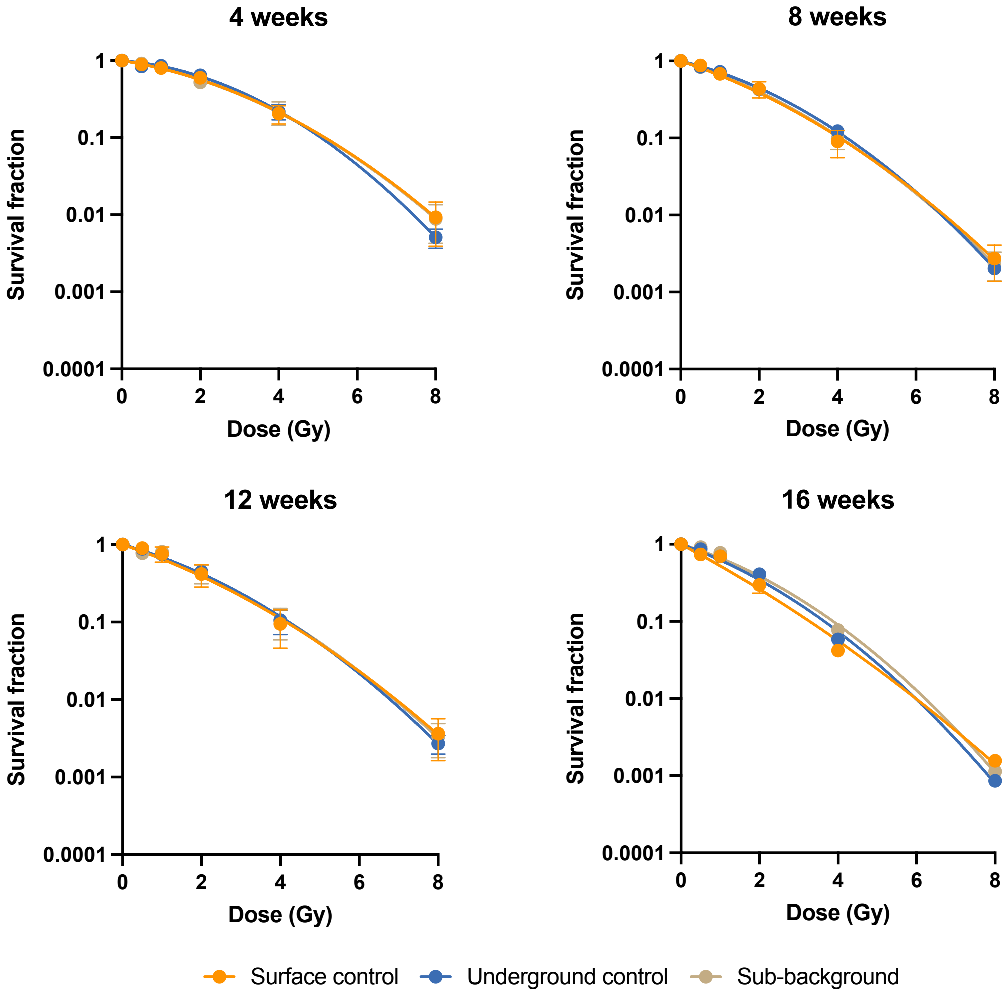
Radioresistance



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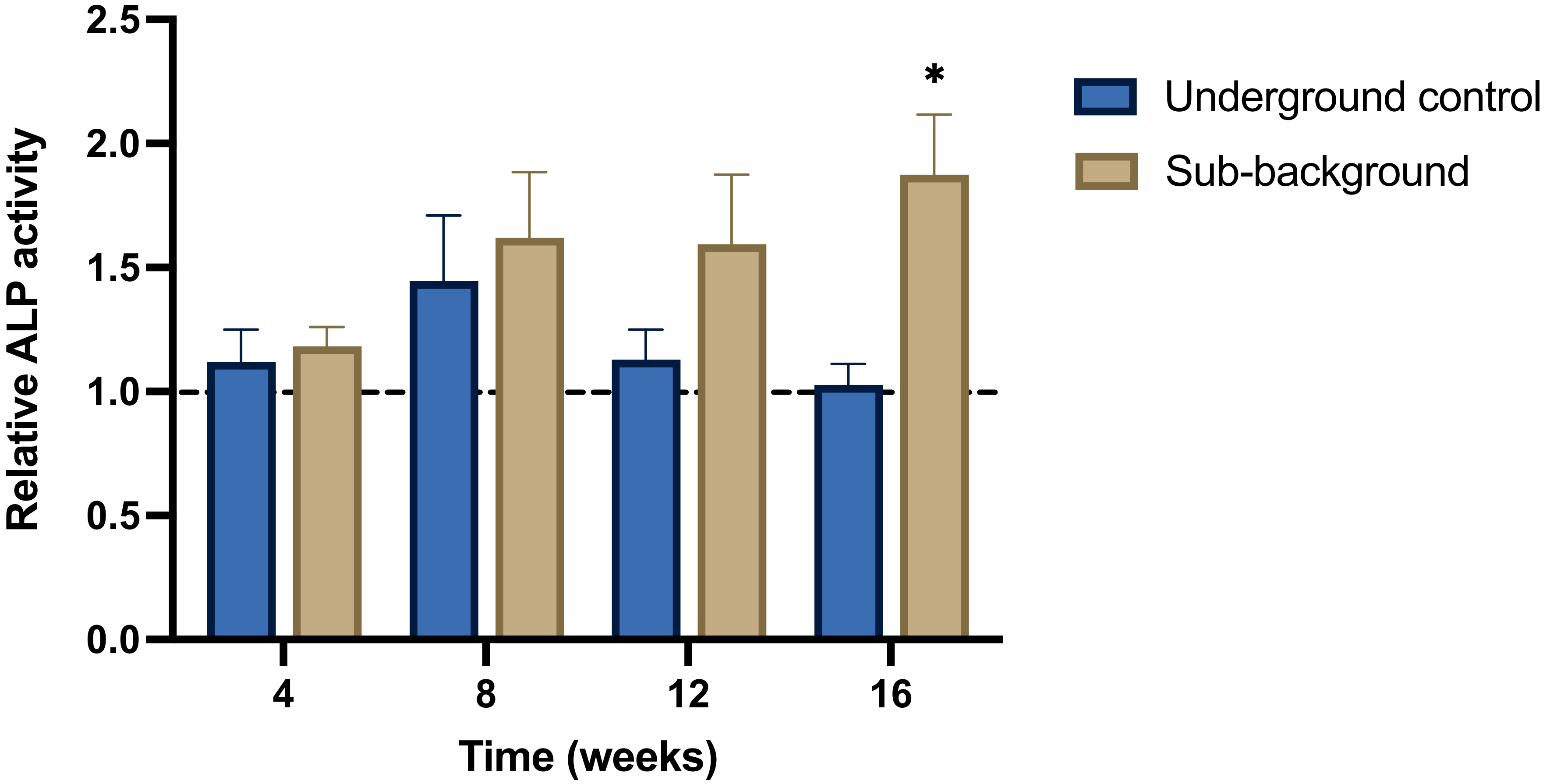
Carcinogenesis



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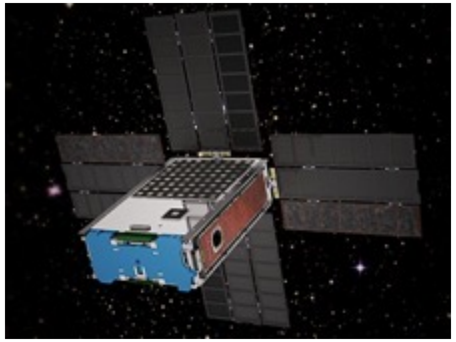
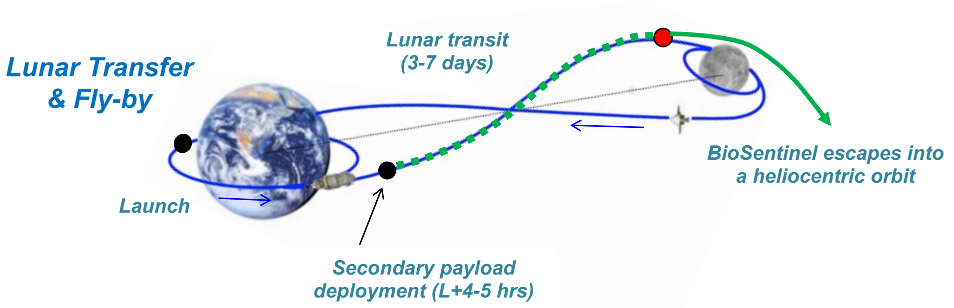
Yeast

- Can survival in a state of anhydrobiosis
  - No food
  - No water
  - No oxygen
- ○ Genomic damage still accumulates while desiccated
- ○ Measure biological effects upon rehydration





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Sub-NBR experiments

4 weeks

48 weeks

Baseline radiation response when rehydrated

- Growth
- Survival
- Metabolism

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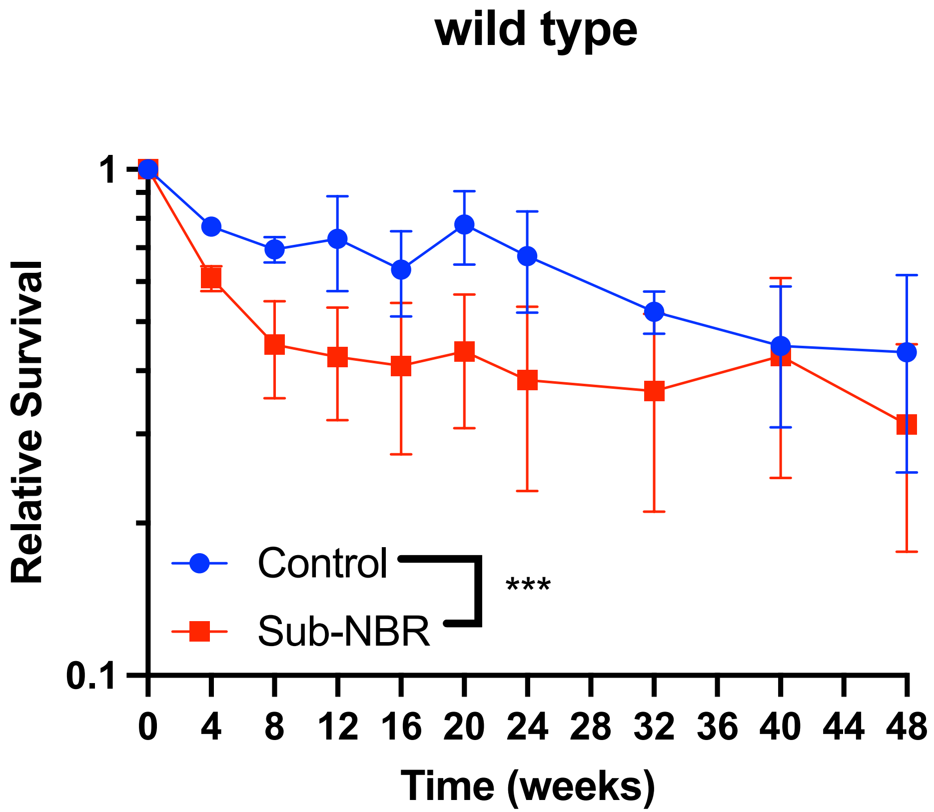
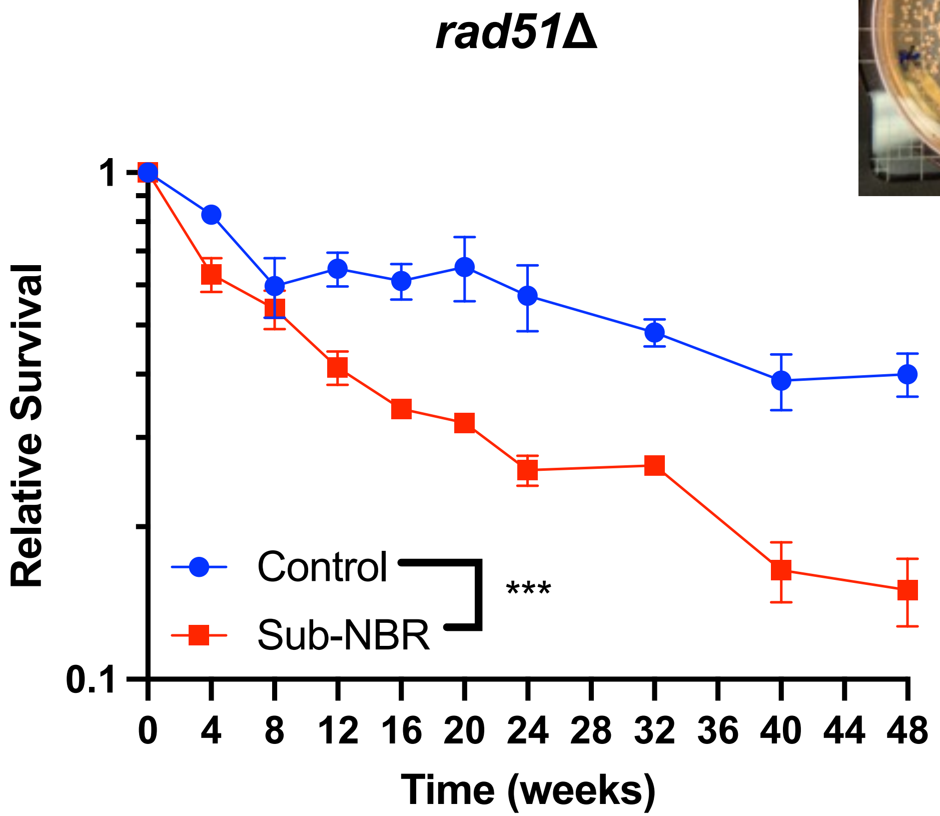
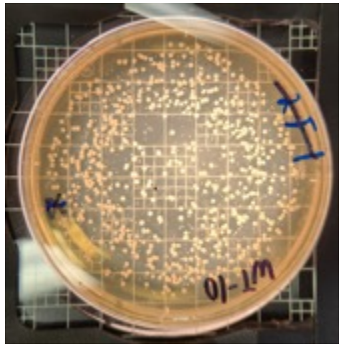
Survival







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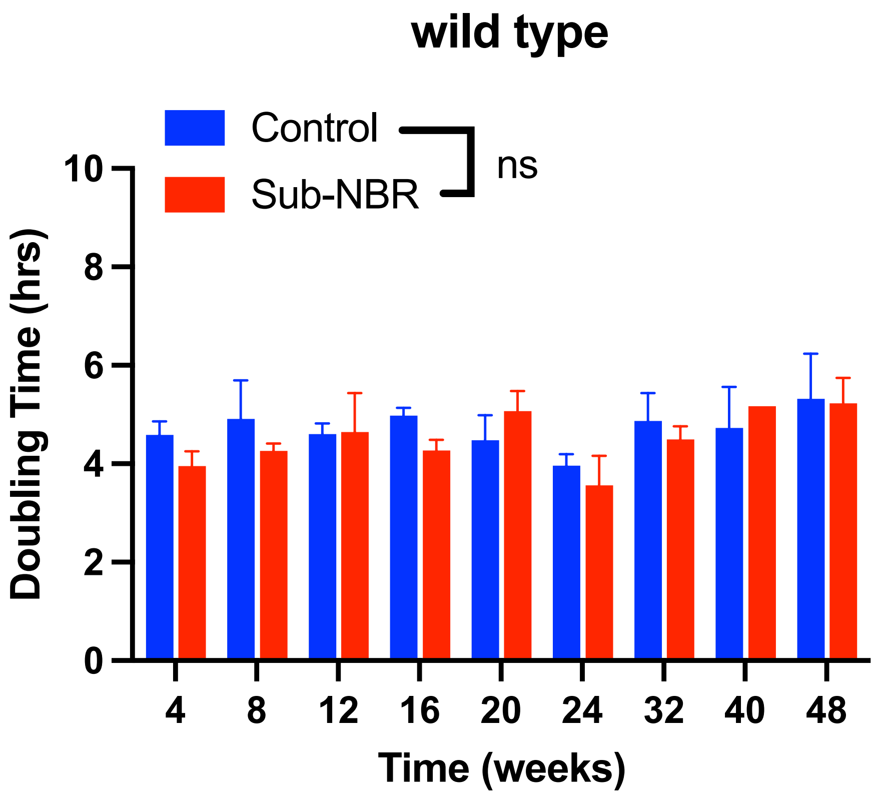
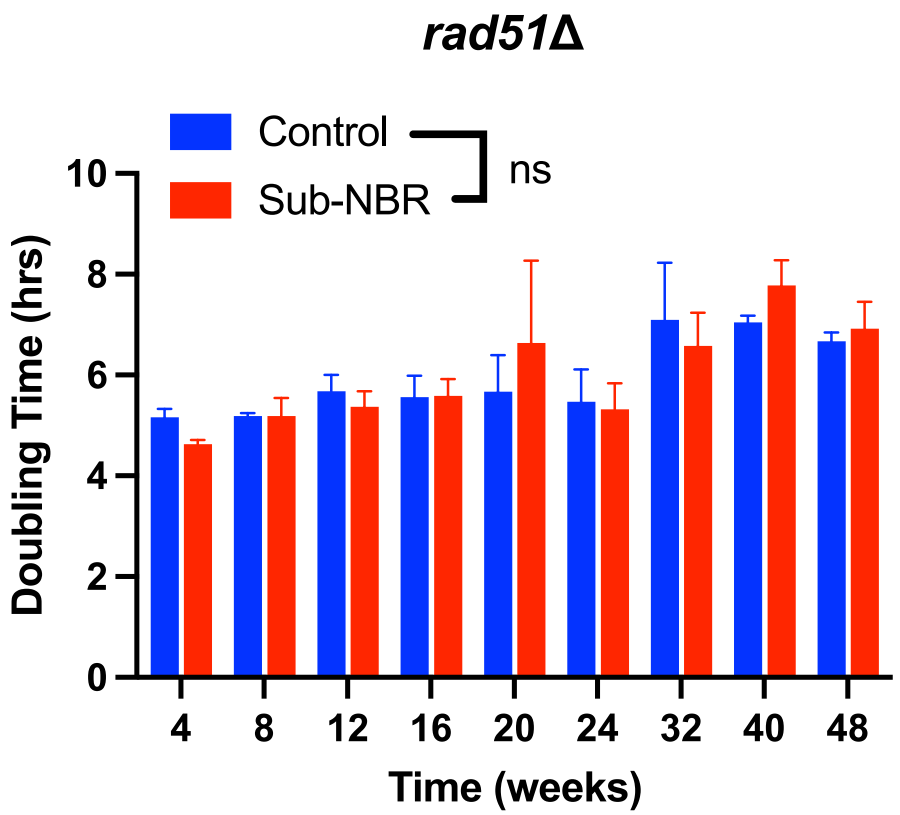
Growth





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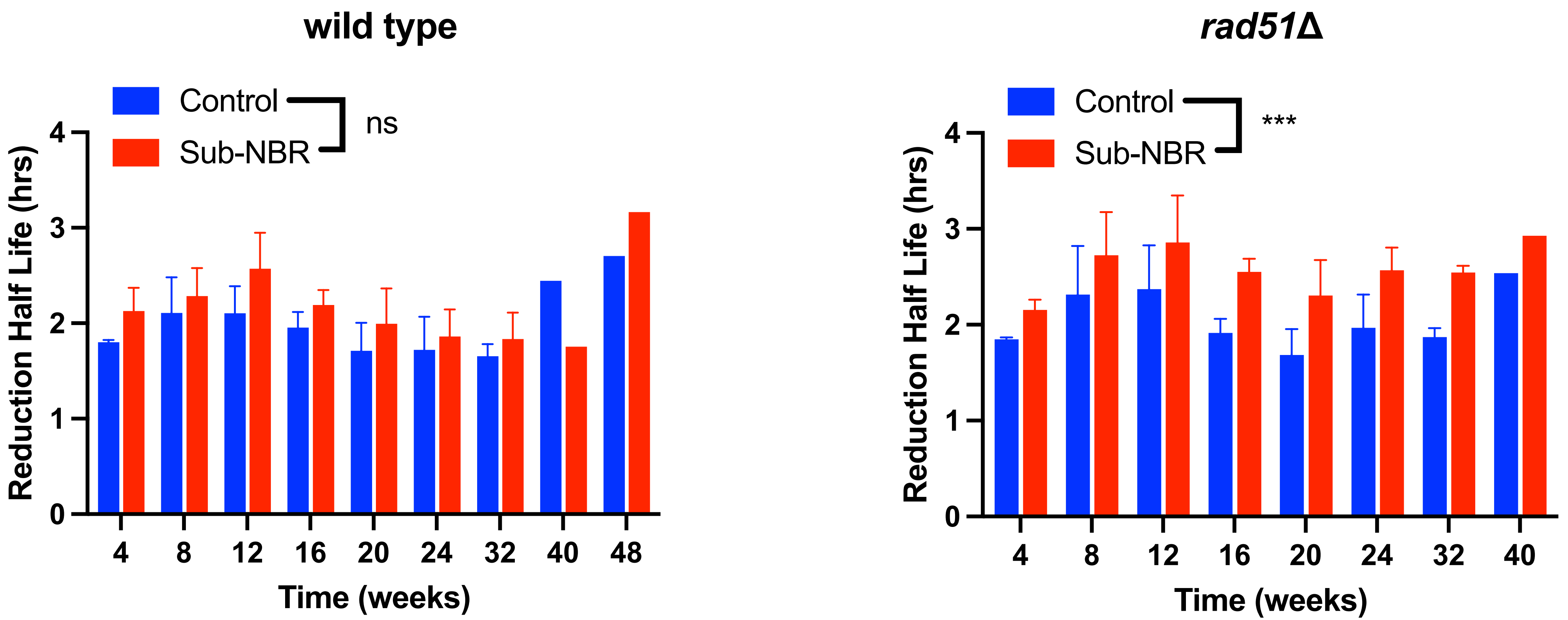
Metabolism



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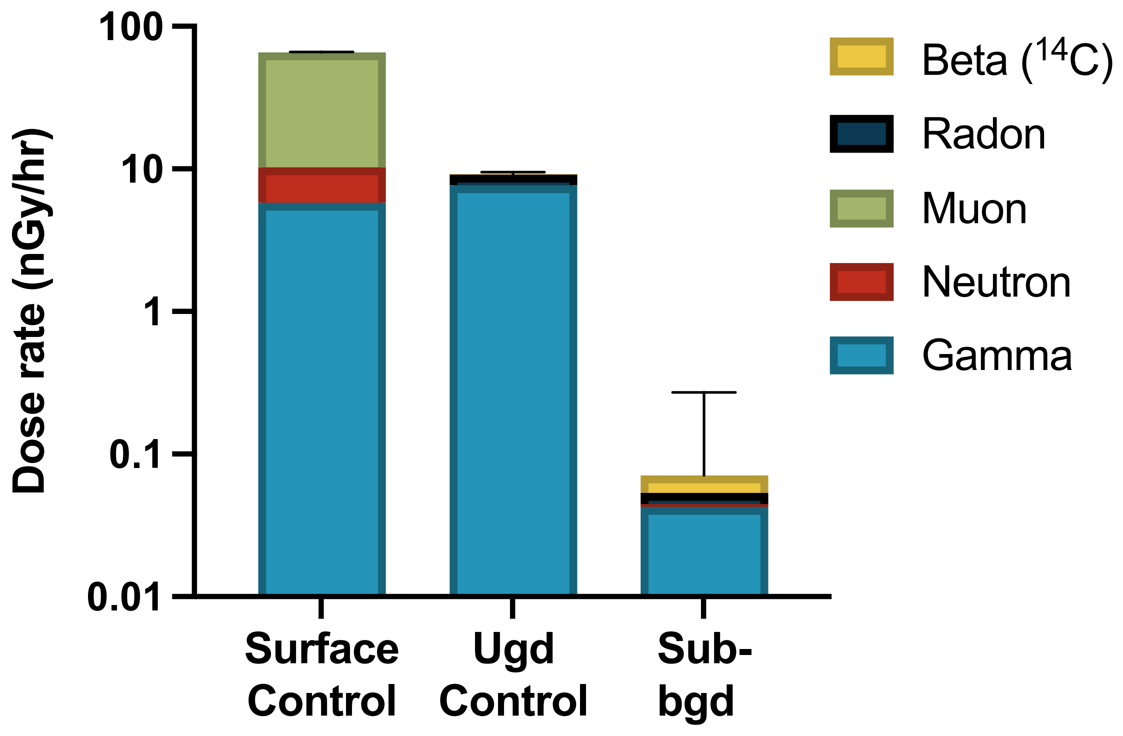
Next steps

- Endogenous dose reduction
- Molecular mechanisms
  - Transcriptomics
  - Proteomics
- Model systems
  - C elegans
  - Organoids



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Mary Ellen Cybulski
Jayden Peterson
Sana Malik
Dylan Reitze
Luc Couture
Lennyn Pineda
Alyssa Labelle
Forest Mahoney

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