LSC

DULIA-bio III, York

Life in low background radiation

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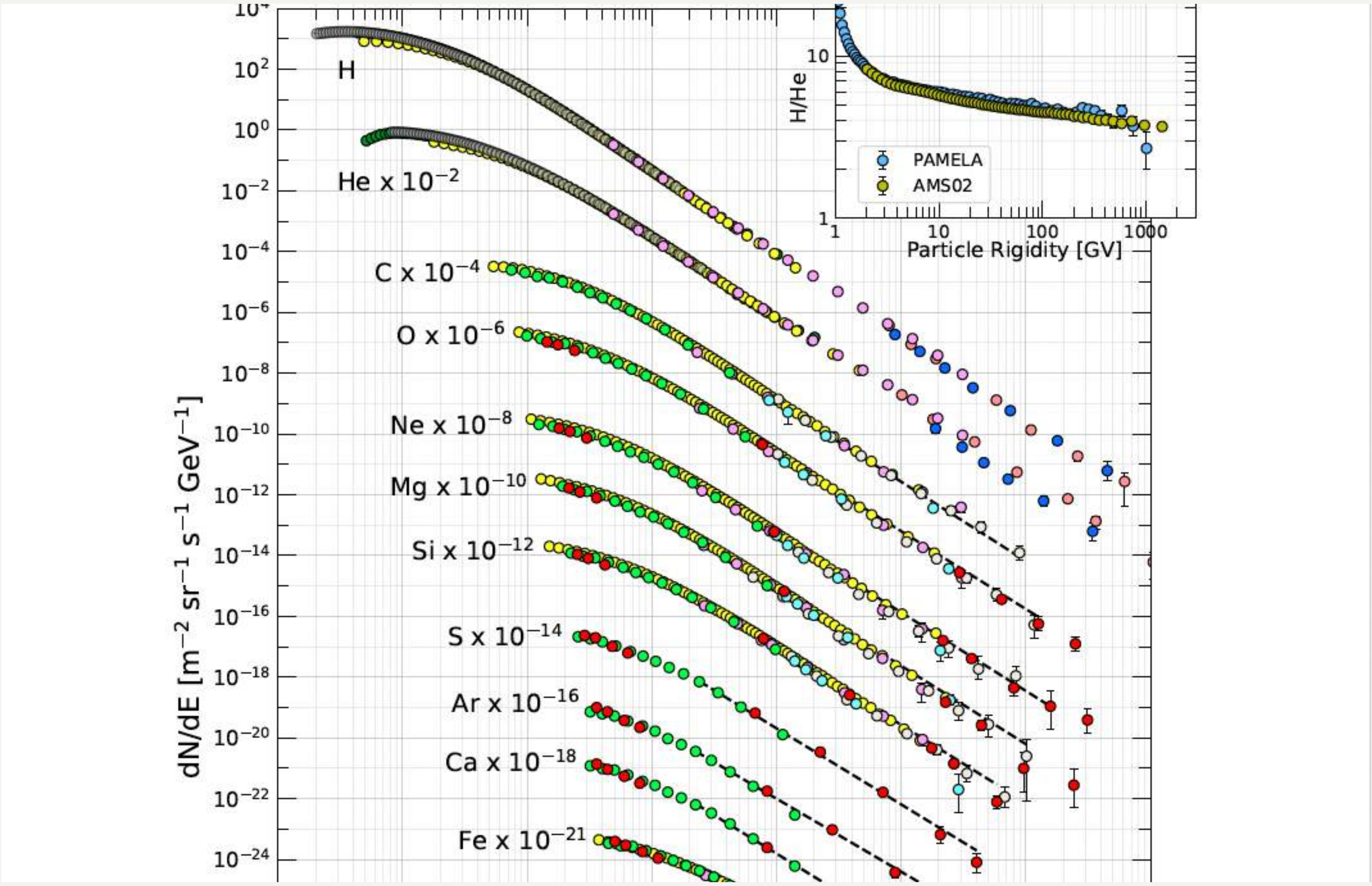
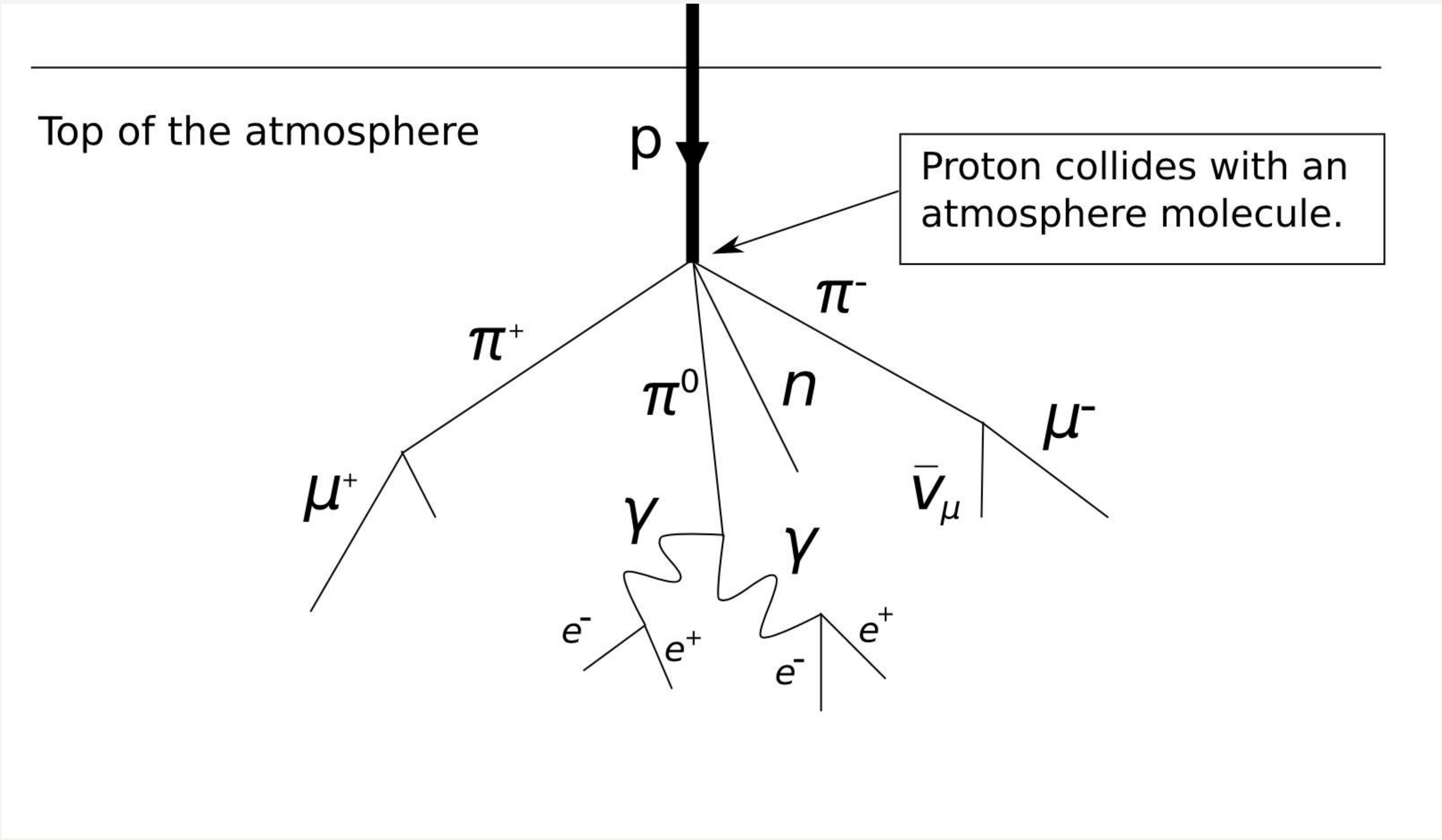
Cosmic rays (Hess, 1912) are mainly protons (90%) and He (9%), mostly galactic sourced by supernova, with a low energy solar contribution and a higher energy extragalactic component. Cosmic rays collide with the Earth's atmosphere producing an air shower of secondary radiation. Secondaries: Muons (107.66 MeV, 2.2 μs) are the most numerous charged particles at sea level, discovered in CRs (Anderson-Neddermeyer, 1936) [who ordered that?, time dilation, …].



1GeV 1TeV 1PeV



Muons show smaller deceleration radiation, far more penetrating than electrons.

$$\langle -dE/dx \rangle = a(E) + b(E)E$$

Produced at about 15 km high
Loose about 2 GeV down to surface

Vertical muons 60/m^2/s/sr.
Angular distribution (cos^{2}z).
Varies with altitude, latitude, time, …
Flux@surface: 170 /m^2/s (1/cm^2/min)
Flux@DUL <10^{-3} /m^2/s

Mean energy at surface is 4 GeV.
Energy loss in medium: >2 MeV/cm

TABLE V-9. Muons in Soft Tissue (ICRP)

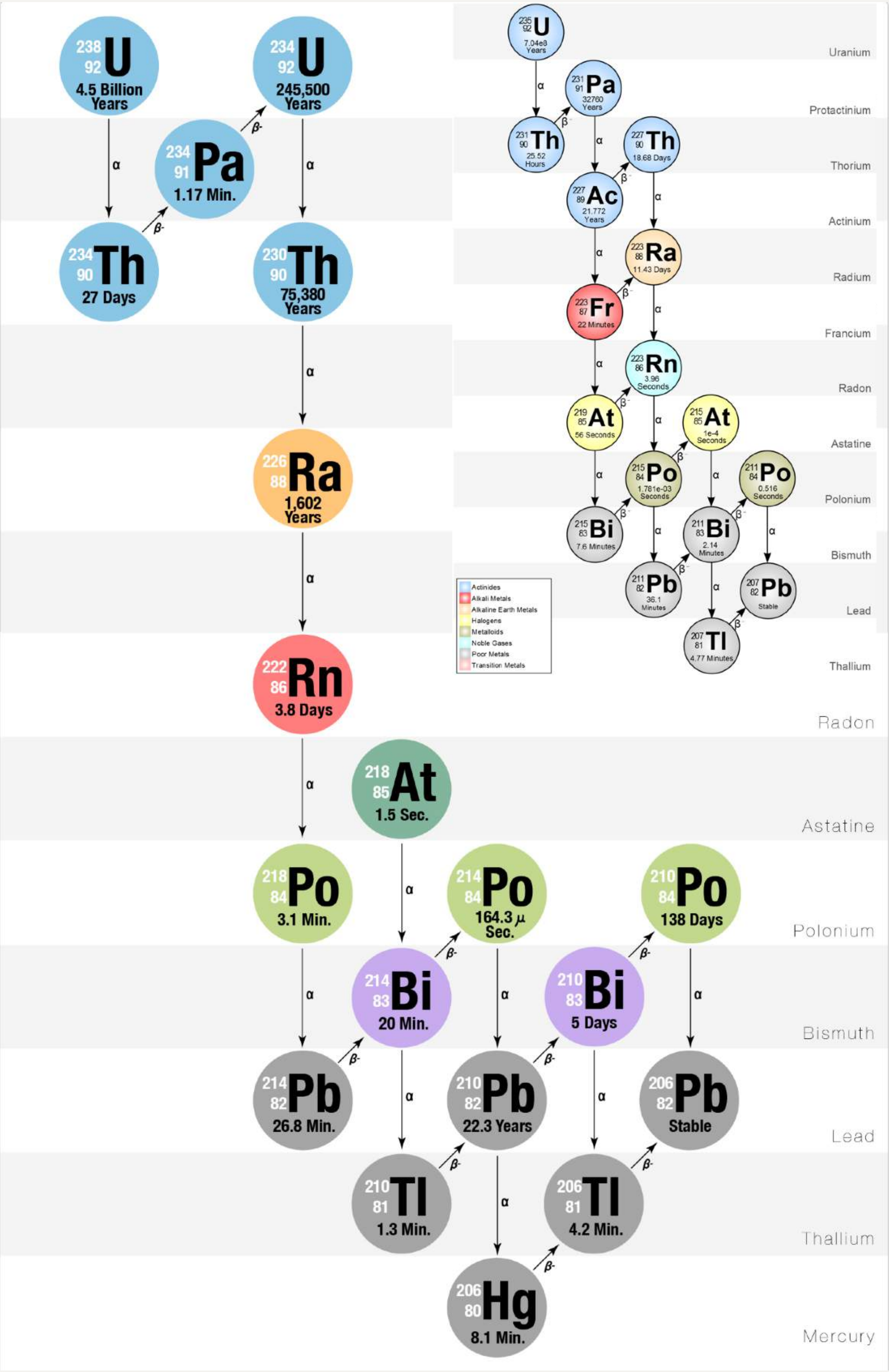
See page 209 for Explanation of Tables

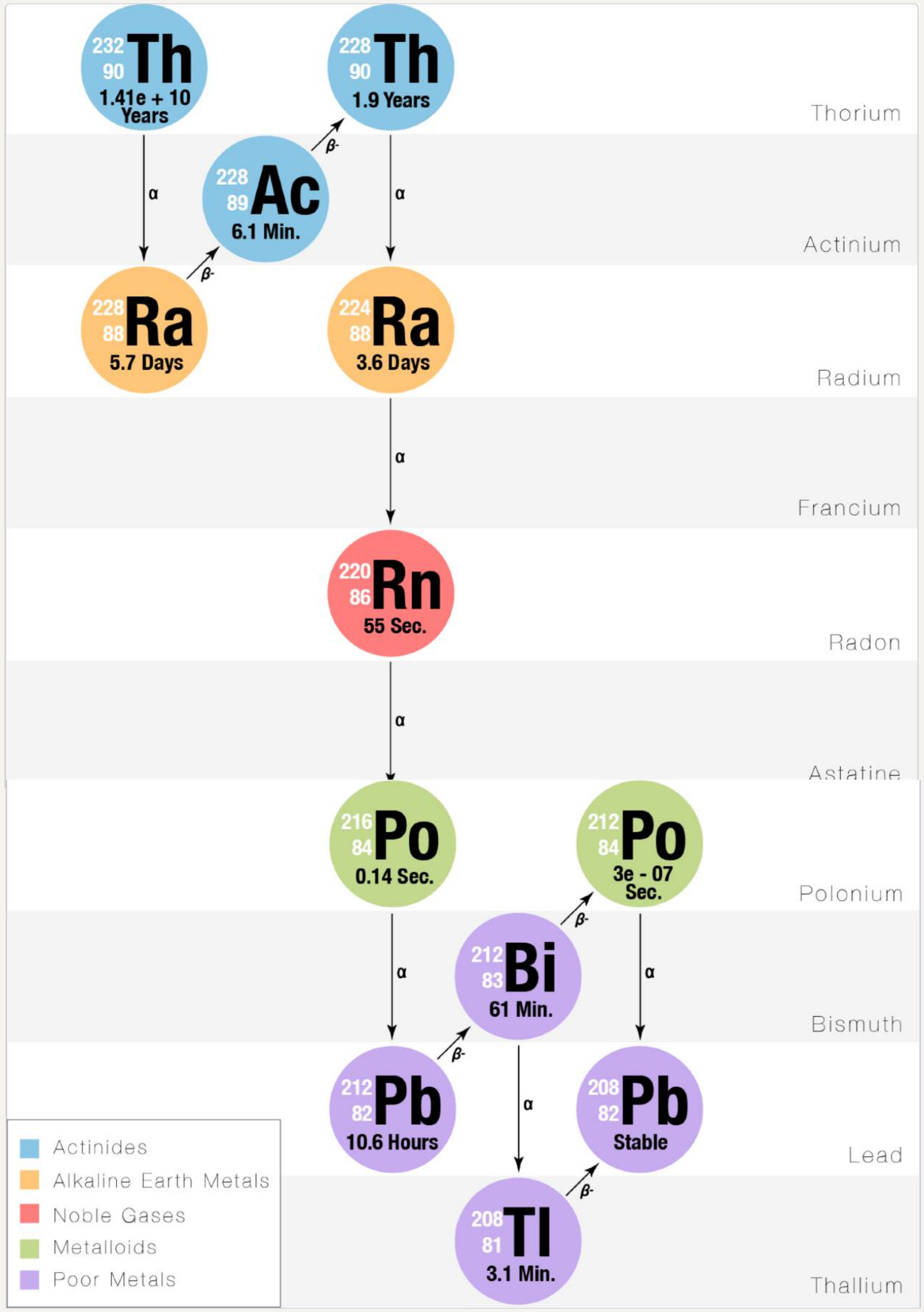
Muon stopping power by Groom et al, doi:10.1006/adnd.2001.0861

$\langle Z/A \rangle$	ρ [g/cm^3]	I [eV]	a	$k = m_s$	x_0	x_1	$\overline{C}$	δ_0
0.55121	1.000	72.3	0.08926	3.5110	0.2211	2.7799	3.4354	0.00

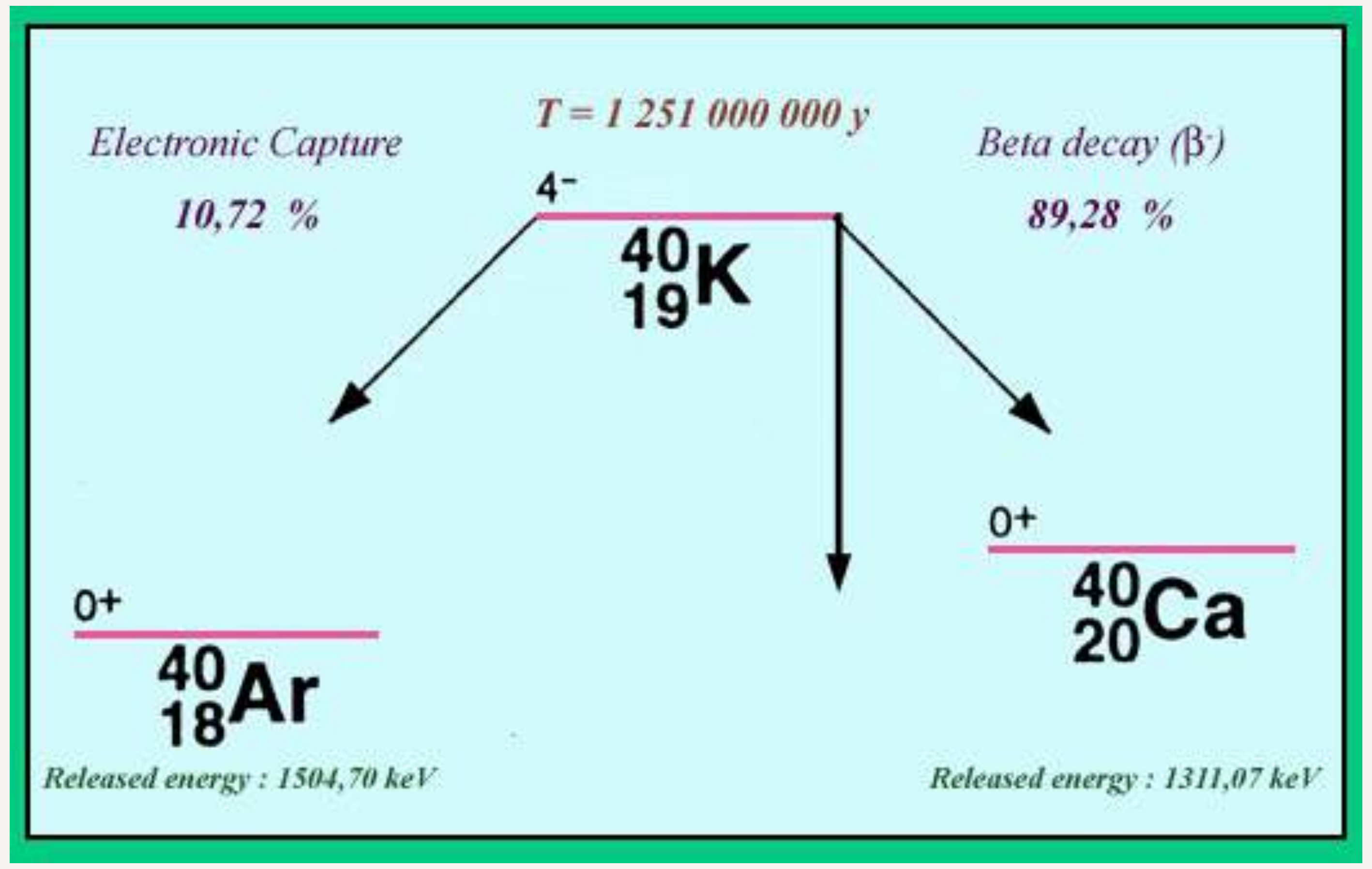
T	p [MeV/c]	Ionization [MeV cm^2/g]	Brems	Pair prod	Photonucl	Total	CSDA range [g/cm^2]
10.0 MeV	4.704×10^1	7.947				7.947	7.043×10^{-1}
14.0 MeV	5.616×10^1	6.198				6.198	1.280×10^0
20.0 MeV	6.802×10^1	4.839				4.839	2.389×10^0
30.0 MeV	8.509×10^1	3.754				3.754	4.768×10^0
40.0 MeV	1.003×10^2	3.205				3.205	7.670×10^0
80.0 MeV	1.527×10^2	2.406				2.406	2.254×10^1
100. MeV	1.764×10^2	2.262				2.262	3.113×10^1
140. MeV	2.218×10^2	2.106				2.107	4.954×10^1
200. MeV	2.868×10^2	2.017				2.017	7.877×10^1
300. MeV	3.917×10^2	1.982			0.000	1.983	1.289×10^2
318. MeV	4.105×10^2	1.982			0.000	1.982	*Minimum ionization*
400. MeV	4.945×10^2	1.988			0.000	1.989	1.793×10^2
800. MeV	8.995×10^2	2.063	0.000		0.000	2.063	3.769×10^2
1.00 GeV	1.101×10^3	2.097	0.000		0.000	2.098	4.730×10^2
1.40 GeV	1.502×10^3	2.152	0.000		0.001	2.153	6.611×10^2
2.00 GeV	2.103×10^3	2.213	0.001	0.000	0.001	2.215	9.356×10^2
3.00 GeV	3.104×10^3	2.283	0.001	0.001	0.001	2.286	1.379×10^3
4.00 GeV	4.104×10^3	2.332	0.001	0.001	0.002	2.336	1.812×10^3

Radioactivity: Ionization by ^{238}U (99.3%), ^{232}Th (99.98%) and ^{40}K (0.0012%) decay products (MeV energies)





^{40}K in body: 3.7-5.2 mmol/kg



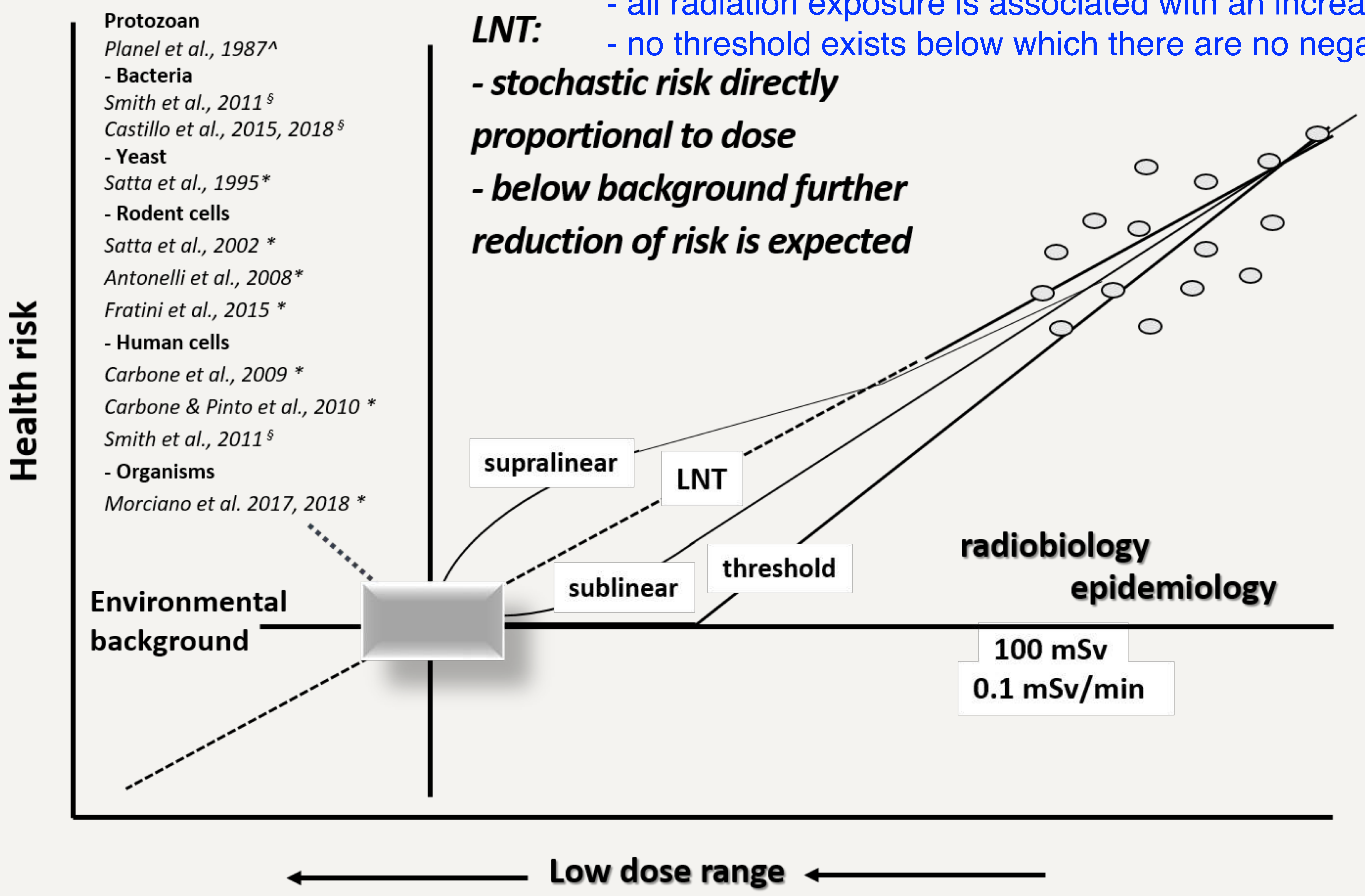
Alpha (beta) [gamma] travel less than 0.01 (1) [10] cm in tissue: external and internal radioactivity

After radiation passed by the medium, its sudden democratic **ionization impacts on the redox regulation of cell-cycle progression**. Slowly, ionization will be shifted from firstly ionized molecules to the ones with the smallest ionization potentials. The cellular redox environment is a balance between the **production of reactive oxygen species** (ROS), reactive nitrogen species (RNS), and their removal by antioxidant enzymes and small-molecular-weight antioxidants. Oxygen is the terminal electron acceptor during energy production. It accepts an additional electron to create superoxide, a more reactive form of oxygen. ROS, oxygen-containing molecules that are highly reactive in redox reactions, are primarily produced intracellularly by two metabolic sources: the mitochondrial electron-transport chain and oxygen-metabolizing enzymatic reactions. It is well established that **cellular ROS levels could function as toxins or as messengers regulating** numerous cellular processes, including proliferation.

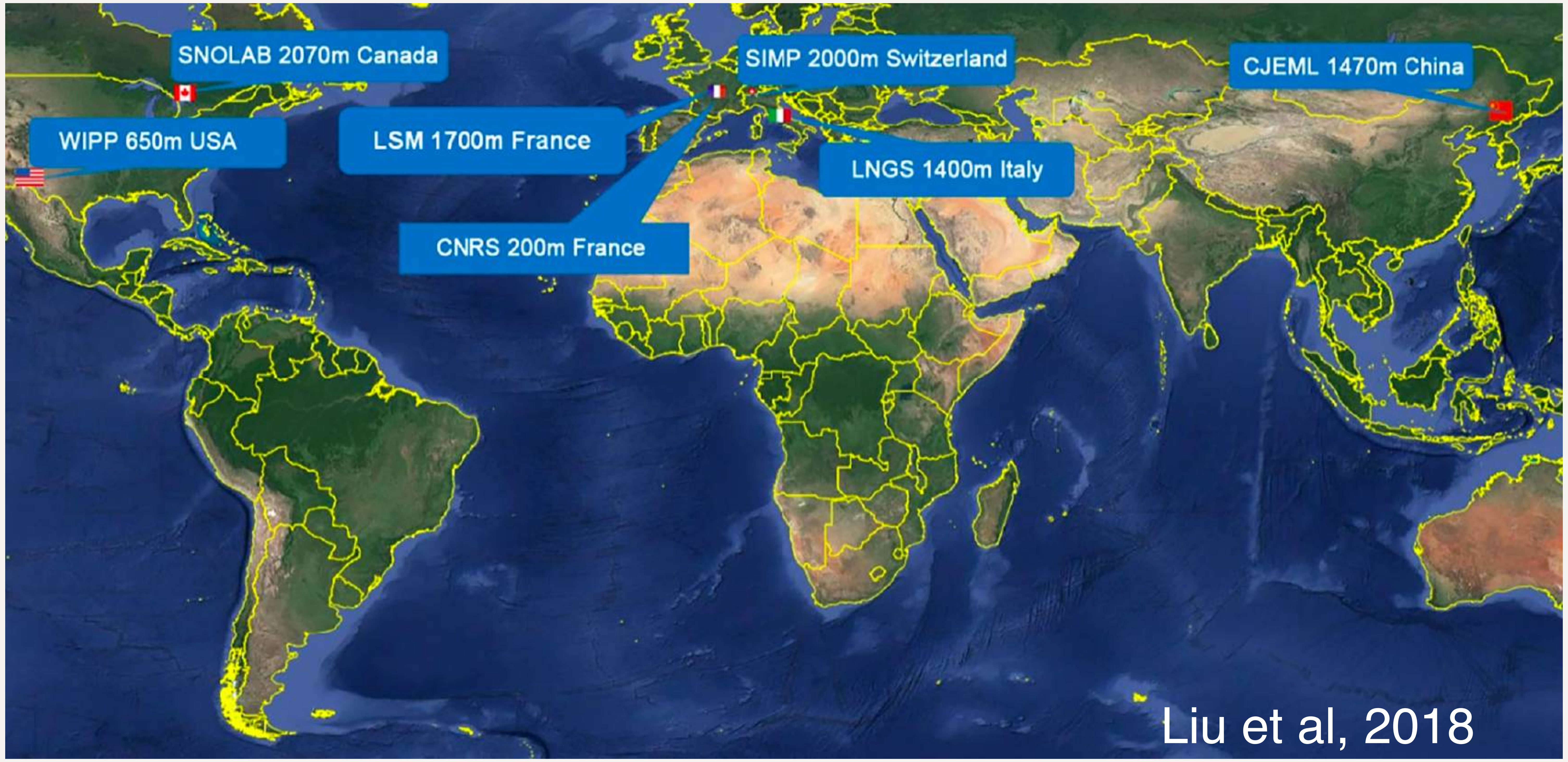
The ubiquity of background radiation as an abiotic component of earth’s surface environment may have led to the incorporation of the biophysical and biochemical effects of background radiation levels into fundamental cellular processes during the evolution of organisms living on or near surface environments.

NA 1: The variety of radiation sources may lead to different biological responses.
NA 2: Additional factors in DUL may have potential biological effects.

- all radiation exposure is associated with an increased biological risk
- no threshold exists below which there are no negative effects



Pioneering work by: Eugster (1964), Planel (1987), Satta (1995), Smith (2011), Lampe (2016), Thome (2017), Xie (2017). Until 2019, most of the experiments had been performed at LNGS/WIPP.



1. **Growth of cells** cultured in DUL: **Alteration in growth kinetics** in several organisms including bacteria (Smith et al. 2011, Castillo et. al 2018), unicellular eukaryotes (Satta et al. 1995), mammalian cell lines (Satta et al. 2002, Liu et al. 2020), and small multicellular organisms (Morciano et al. 2019, Pirkkanen et al. 2020, Van Voorhies et al 2020). Multicellular organisms exhibited positive growth phenotypes: increased life span in Drosophila (Morciano et al. 2018), increased egg laying in C. elegans (Van Voorhies et al 2020), and increased body weight and length in lake whitefish embryos (Pirkkanen et al. 2020). In the case of Drosophila, a decrease in female and male fertility was observed which could be indicative of **defective DNA repair**.

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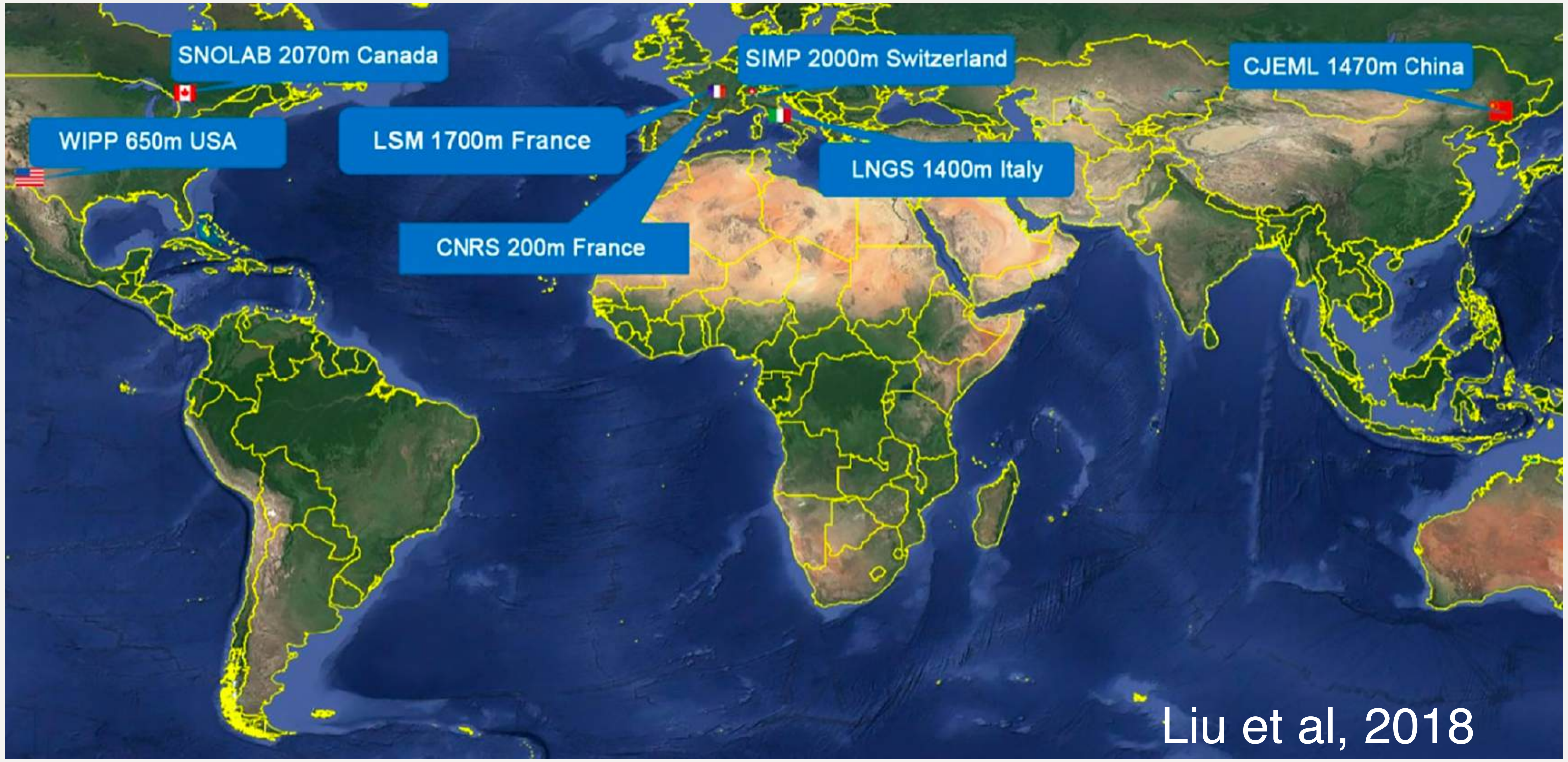
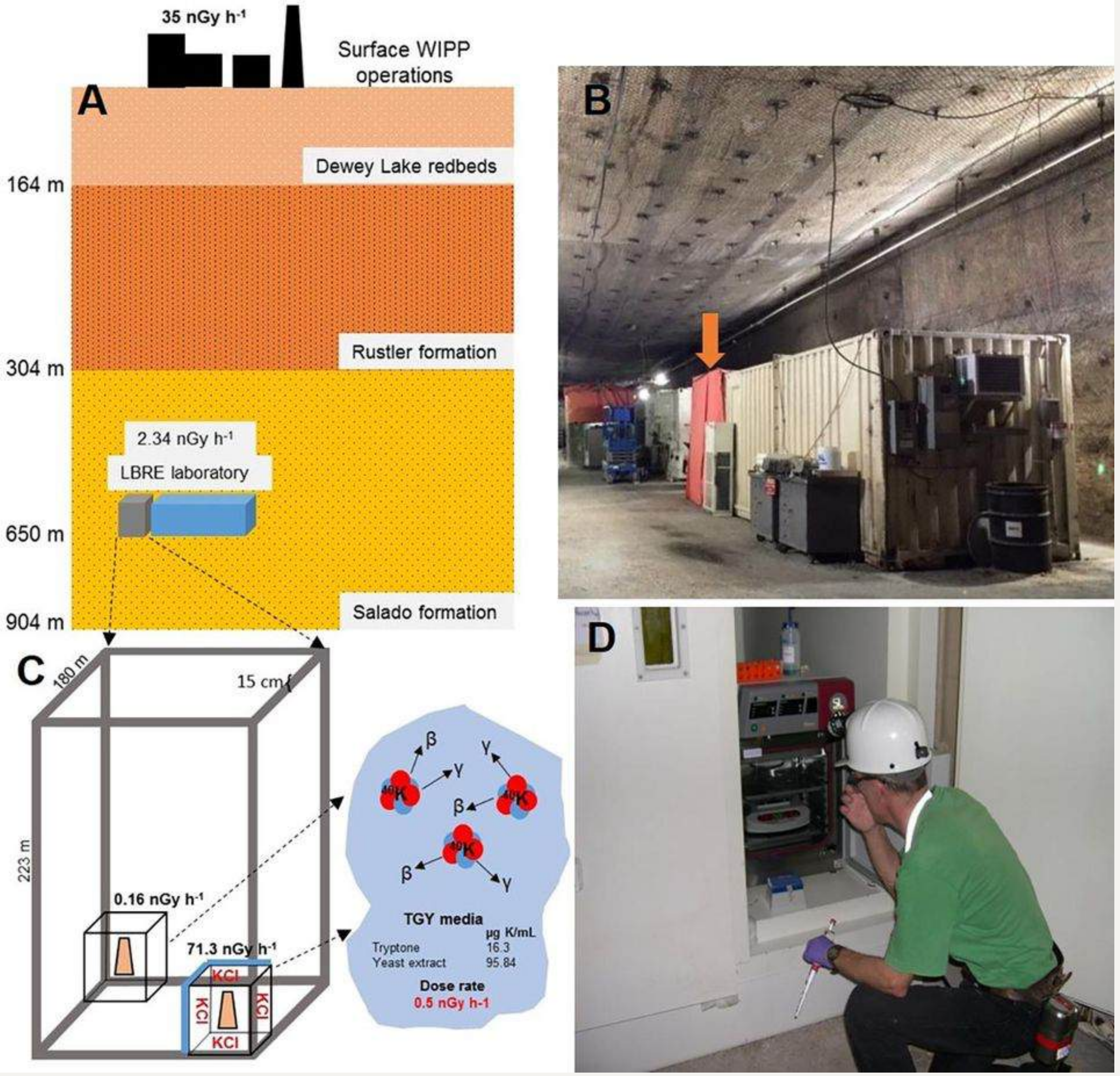


2. **Metabolism of cells** cultured in DUL: Cells were more sensitive to acute exposures to radiation at the level of DNA damage (**lower repair**) and oxidative metabolism compared to cells cultured in the standard background environment [unicellular eukaryotes (Satta et al. 1995) and mammalian cell lines (Antonelli et al. 2000, Satta et al. 2002, Fratini et al, 2015)]. Data suggest that environmental radiation contributes to the defense mechanisms in living organisms. Evidence of stress response in bacteria (Castillo et al. 2015, 2017, 2018) with **up-regulation** of membrane transporters **and down-regulation** of ribosomal proteins and tRNA genes. A l**arger number of studies** is **required** to understand the underlying pathways.

Biology in DUL: WIPP vs LNGS

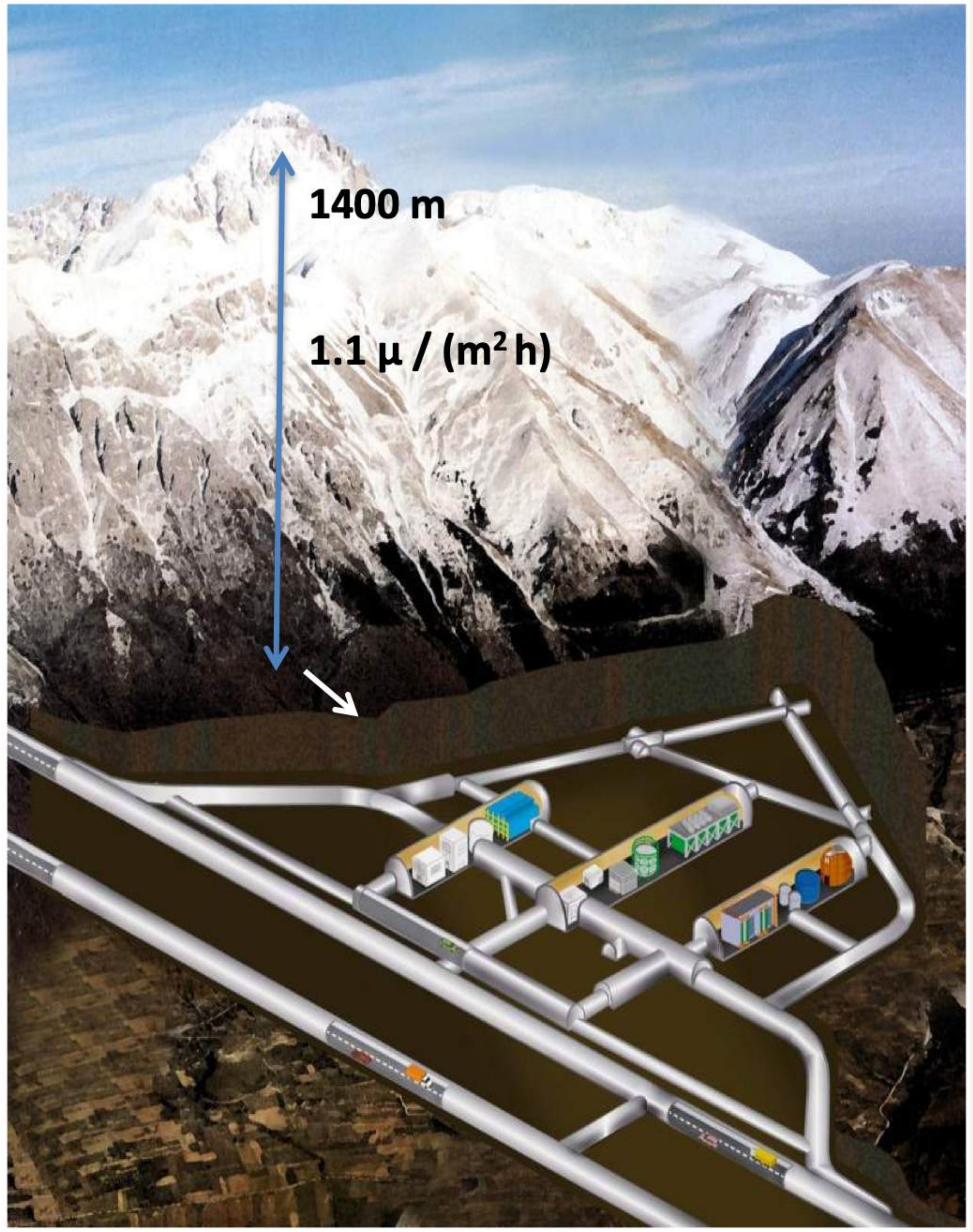
Until 2019, most of the experiments had been performed by Rome@LNGS and NMSU@WIPP



- 42.46° N 13.57° E
- Surface: 17 800 m^2
- Volume: 180 000 m^3
- Ventilation: 1 vol / 3.5 hours
- Rn in air: 20-80 Bq m^{-3}
- Muon flux: 3.0 10^{-4} $m^{-2}s^{-1}$
- Neutron flux:

  2.92 10^{-6} $cm^{-2}s^{-1}$ (0-1 keV)

  0.86 10^{-6} $cm^{-2}s^{-1}$ (> 1 keV)



Different cosmic muons and natural radioactivity environment among WIPP and LNGS biology labs.

Dulia-bio III

The REPAIR project: investigating the effects of sub-natural background radiation exposure within SNOLAB - (in-persoı
Chris Thome

Adaptive and evolutionary responses of microalgae to ultra-low radioactivity at the Modane Underground Laboratory - (in-person)
Vincent Breton

Effects of microgravity and below-background radiation in the pathogenesis of Orsay virus infection of Caenorhabditis elegans - (remote)
Santiago Elena

Investigating the effect of low background radiation in the origin of animals - (remote) *Patricia Suárez Ara*
Council Chamber, The Guildhall, York 16:00 - 16:30

DISCOVER22 radiobiology project at Gran Sasso National Laboratory - (remote) *Patrizia Morciano*
Council Chamber, The Guildhall, York 16:30 - 17:00

Microdosimetry of low dose radiation fields in the framework of the DISCOVER22 project - (remote) *Anna Bianchi*
Council Chamber, The Guildhall, York 17:00 - 17:30

The Effect of Natural Background Radiation on Stem Cell Biology - (in-person) *Umberto Galderisi*
Council Chamber, The Guildhall, York 09:00 - 09:30

Stem cells long term preservation - (remote) *Guillaume Warot*
Council Chamber, The Guildhall, York 09:30 - 10:00

Does ionizing radiation affect HIV release from human macrophages? - (remote) *David Nkwe*
Council Chamber, The Guildhall, York 10:00 - 10:30

Activity has increased since last Dulia-bio, with new experimental results obtained at LNGS, LSC, LSM and SNOLab, some will be discussed later in this meeting.

BUL, Callio, SURF, and future DUL (CJPL, PAUL) plan to host experiments testing life in cosmic silence.

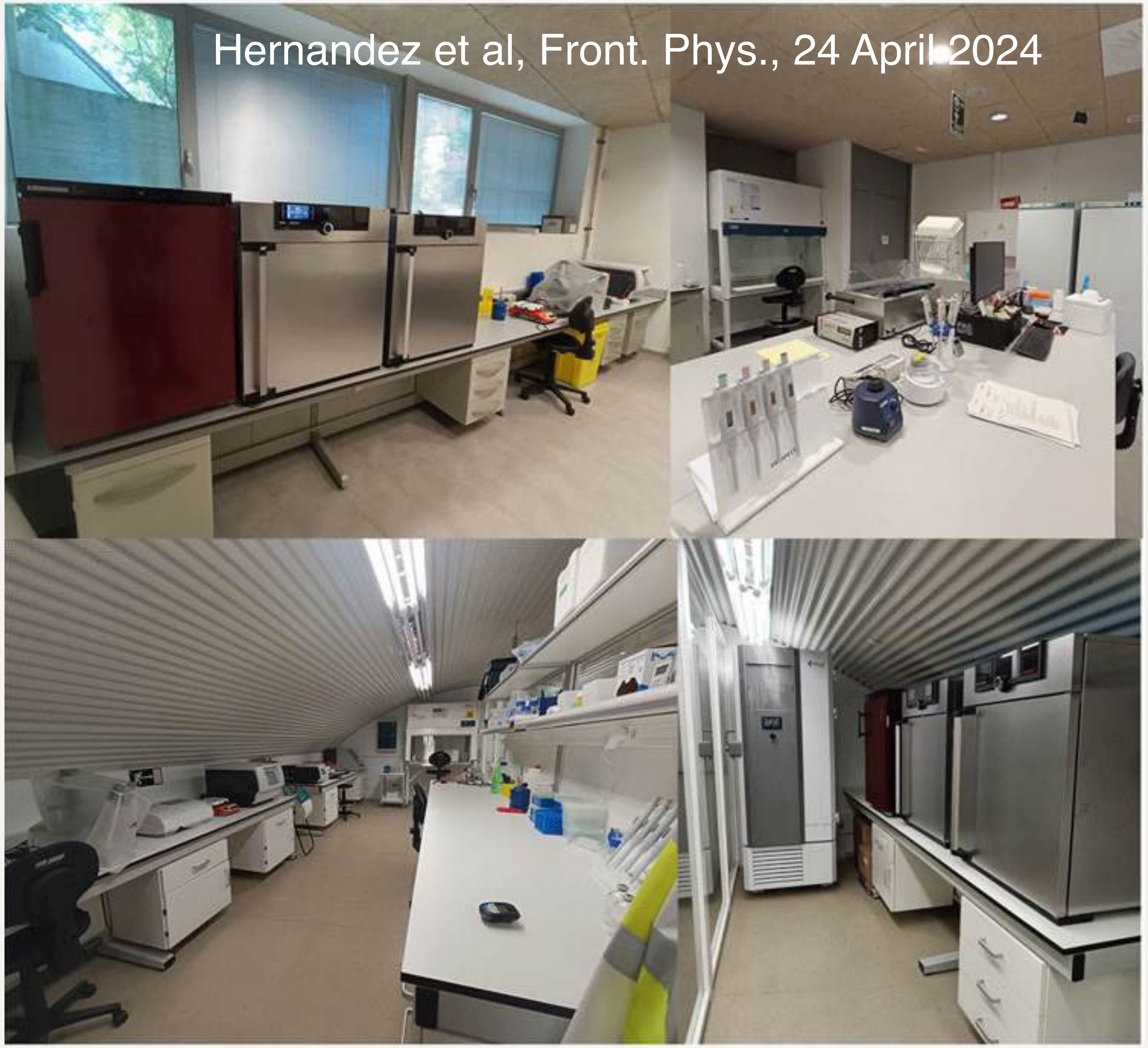
Muons and radiation ionize our cells. How does the lack of ionization modify celular processes? Replicated biolabs on surface and underground. Team: Rebecca Hernández, Laura Cid, Enrique Roig, Amal Rahmeh, CPG. Two calls for proposals (Jan-Apr & Jul-Oct) evaluated by LSC SC (May and November). After approval, lab time and service/collaboration mode is assigned.

First experiment @LSC - Gollum (2014)
Biology Platform design started in 2019.
Replicated labs running since 2022.

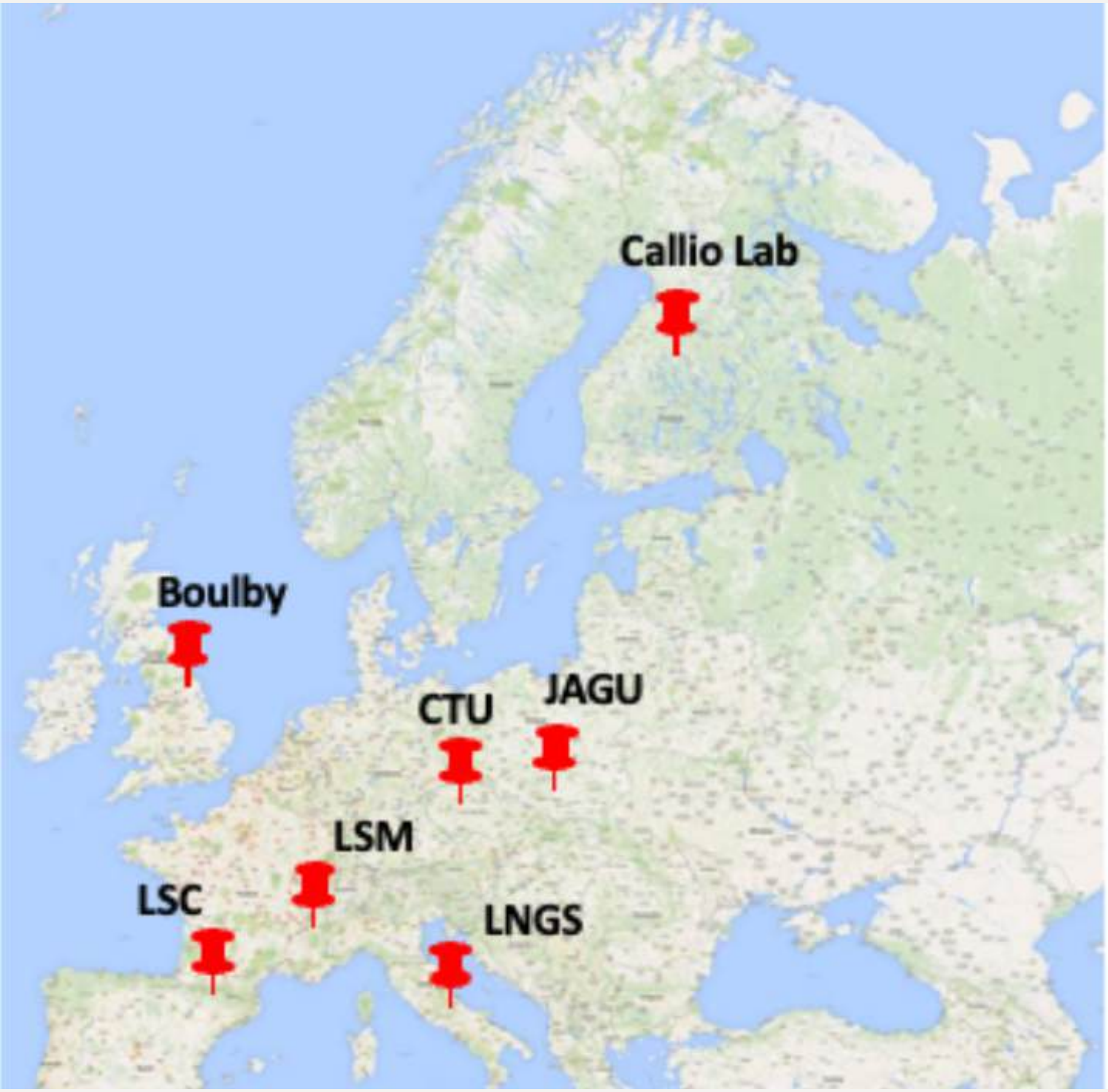
2022
- **Bacteria in heavy water** (Sobrino et al)
- **Interaction between host and pathogens** (C. elegans, Elena et al)
- **Genetic radiation tolerance**

2023
- **Luria-Delbrück 2.0** (E. coli, Buceta et al)
- **Yeast chronological aging and mutation rate** (S. cerevisae, Otero et al)
- **Multicellular structure formation** (C. owczarzaki/S. arctica, Ruiz et al).
- **Ticking of epigenetic and senescence aging clocks** (Menendez et al, human cells)
- **Unravelling mechanisms on living systems** (enzymatic reactions, Stepanova et al)

2024
- **Fishnauts** (zebrafish/sea bass embryos, Ribas)


Hernandez et al, Front. Phys., 24 April 2024

HORIZON-INFRA-2024-DEV - DEEPEN-STUDI, DevElopment of a EuroPEan Network for Science and Technology in deep UnDerground Infrastructures.



Motivation: Share current practices in background model characterization. Coordinate the strategy to validate reproducibility and variability of DUL biology experiments and long term evolution of life in cosmic silence .

Tasks :
- Characterize the radioactivity background model in biology experiments (improve experiments if needed)
- Selection and study of a common model organism sampled in different bio-platforms (verify experimental results and characterize variability)
- Selection of model organisms and monitor them over a long period of time in cosmic silence (determine long term effects).

Pioneering work has already shown an increase of ROS, a reduction of DNA repair and down- and up-regulated mechanisms in cosmic silence, with impact in the celular growth rate and in the life expectancy and fertility of organisms. A larger number of studies is required to understand the underlying pathways.

The **heterogeneity** among Deep Underground Laboratories **offers a great opportunity** to study life in low background radiation: ongoing studies are focusing on the adaptive response, immune system, modulation of ageing, long-term preservation, multicellularity, … in cosmic silence.

We are just at the beginning:

1. Promote access to a wider community: burst of ideas with new proposals and applications, …
Join the discussion: **Reproducibility and networking**

2. Lots of work ahead for DUL: background models, reproducibility, long term experiments, …

3. Be ready for surprises! Join the discussion: **Future strategies**

Laboratorio Subterráneo Canfranc

Exploring Life in Cosmic Silence