INFN-DISCOVER22 at LNGS: gaining insight into the role of environmental radiation in modulating immune response in living organisms

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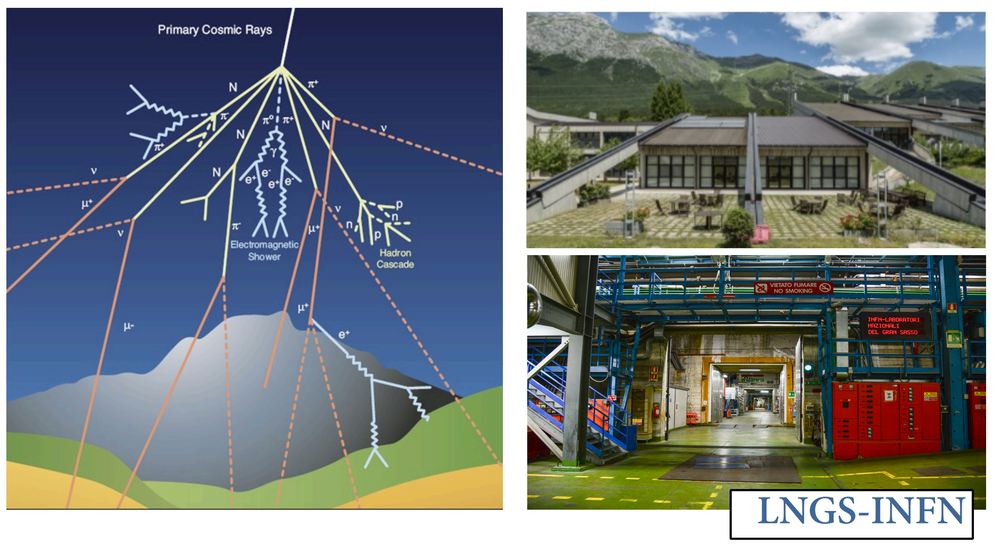
- Deep underground laboratories represent ideal facilities for **below-background radiation** studies

  → *what happens to living organisms when* **natural background radiation (NBR)** *is reduced?*

  → *what has been (and is) the role of* **NBR** *in shaping life over millions of years of evolution?*

- **INFN LNGS, Italy,** is one of the largest infrastructure offering the opportunity for **underground radiobiology** measurements



- Biological responses in underground laboratories (**low-radiation environment, LRE**) compared to above-ground (**reference radiation environment**, **RRE**) overall suggest that **NBR** is an **essential stimulus** to efficiently activate the **stress response** capability in many living organisms
- The interaction between **low dose radiation** and the **immune system** is a hot topic, with complex and contradictory results

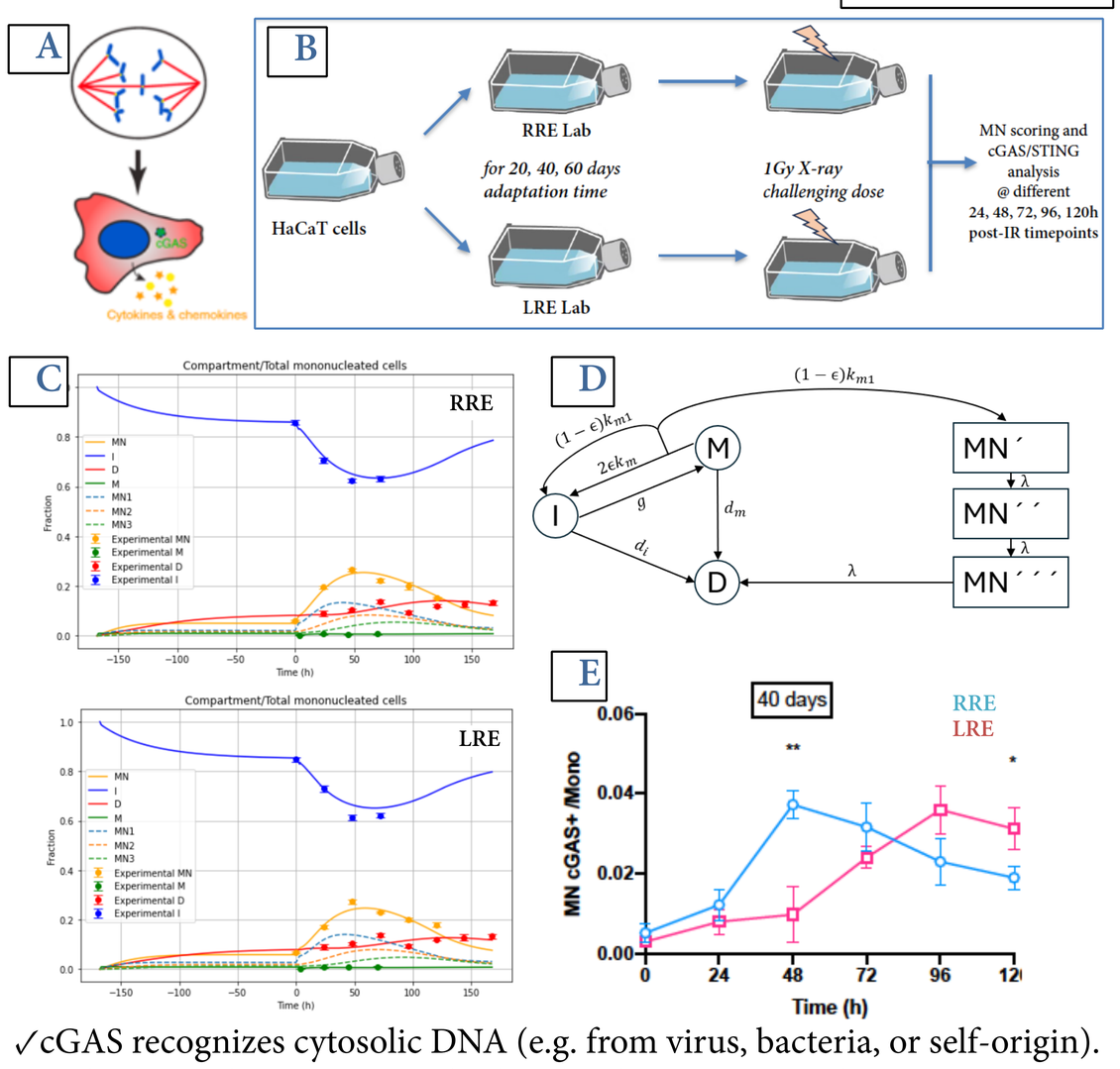
  → *what is the impact of the* ***LRE*** *in the underground lab in the modulation of the* ***immunological responses*** *?*

DISCOVER22 (Exp. + Modelling/Data Analysis)

WP1/Task1 (Roma3+PV) Innate immune response
Activation of the cGAS/STING pathway following radiation-induced DNA damage (micronuclei) in human keratinocytes (HaCaT)

WP1/Task2 (Roma1+PV): Immune cell differentiation
Ability of human immature immune cells (HL60) to differentiate into macrophages and neutrophils and to maintain their biological functions

WP1/Task1

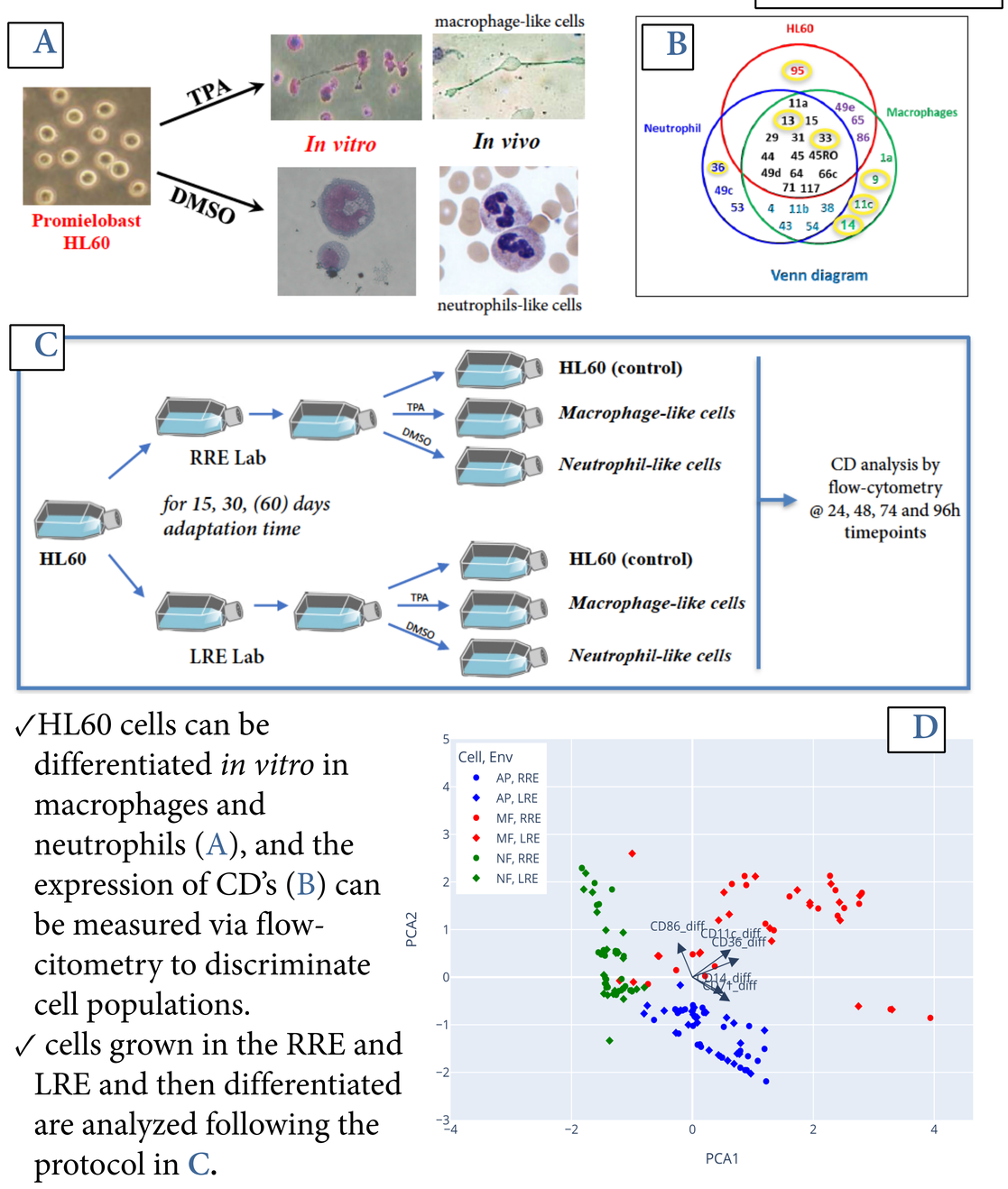


✓cGAS recognizes cytosolic DNA (e.g. from virus, bacteria, or self-origin). Radiation induces micronuclei (MN), whose rupture release DNA in the cytosol and activate cGAS (A).

✓ cells grown in the RRE or LRE and then irradiated with 1Gy (experimental protocol in B) show the same progression in the cell cycle, death rate and rate of MN induction. Data (C) are reproduced by a compartmental model with ordinary differential equations (scheme in D) with parameters perturbed by the challenging 1Gy dose.

✓ the time dynamics of cGAS signalling is different between RRE and LRE (E) and c-GAS activation seems slower for cells grown in LRE! Inclusion of c-GAS activation in the model is in progress.

WP1/Task2



✓HL60 cells can be differentiated *in vitro* in macrophages and neutrophils (A), and the expression of CD's (B) can be measured via flow-citometry to discriminate cell populations.

✓ cells grown in the RRE and LRE and then differentiated are analyzed following the protocol in C.

✓ PCA was applied on CD expression data (D), effectively separating cell types but not distinguishing between environmental conditions, suggesting the differentiation stimulus overcomes differences due to the LRE and RRE radiation environments.

DISCOVER22 overview in *Morciano et al., Front. Phys. (2023)* | doi.org/10.3389/fphy.2023.1263338
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