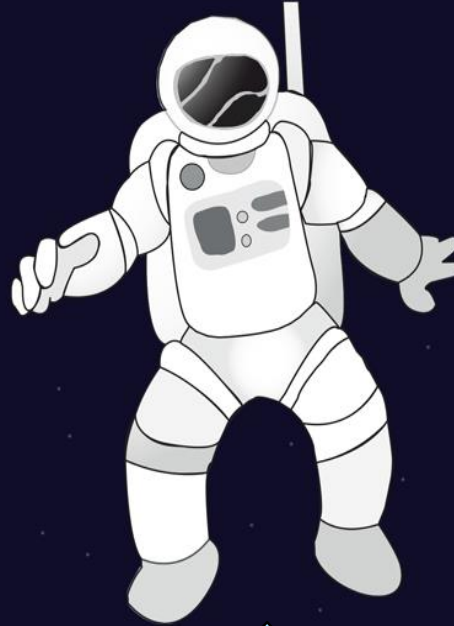


sck cen
Belgian Nuclear Research Centre

Dr. Bjorn Baselet

Biomedical countermeasures to increase radiation resistance of astronauts

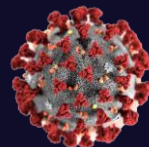
Ionizing radiation



Altered gravity



Psychological stress



COVID-19

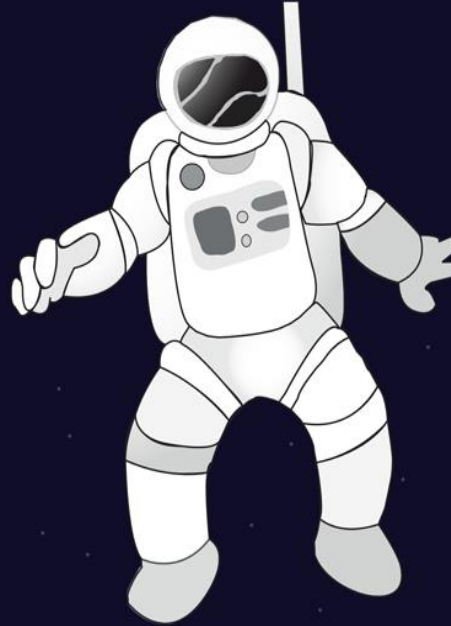


Visual impairment

Degenerative tissue effects

Cancer

Cardiovascular disease



Muscle atrophy

Cataract

Central nervous system injury

Acute radiation syndrome

Motion sickness

Osteoporosis

Immune dysfunction

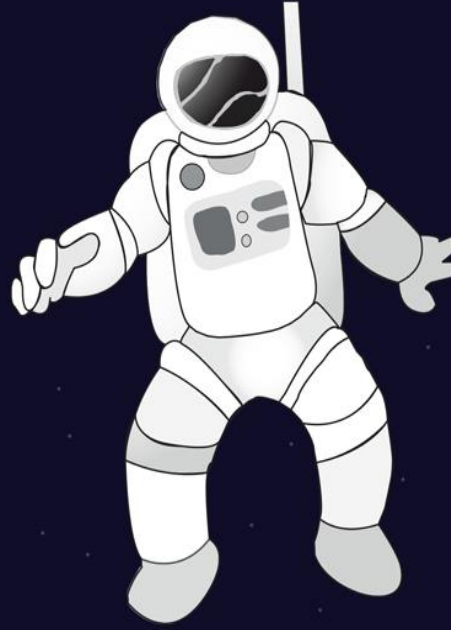
Fluid distribution

Visual impairment

Degenerative tissue effects

Cancer

Cardiovascular disease



Muscle atrophy

Cataract

Central nervous system injury

Acute radiation syndrome

Motion sickness

Osteoporosis

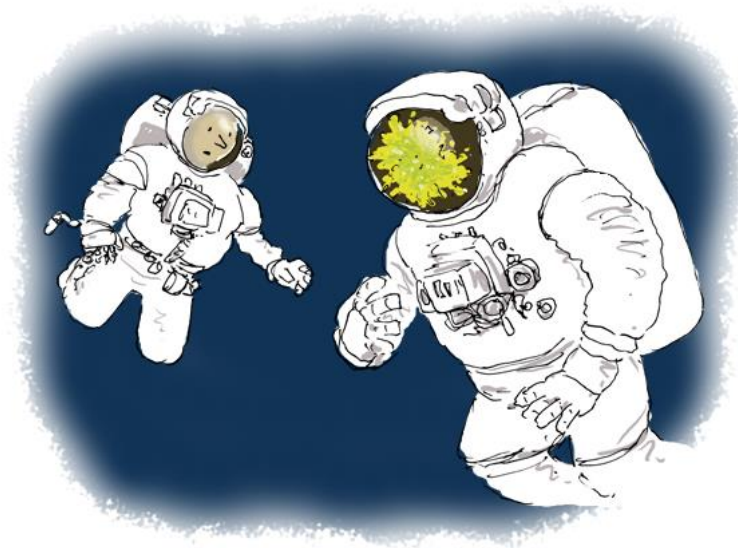
Immune dysfunction

Fluid distribution



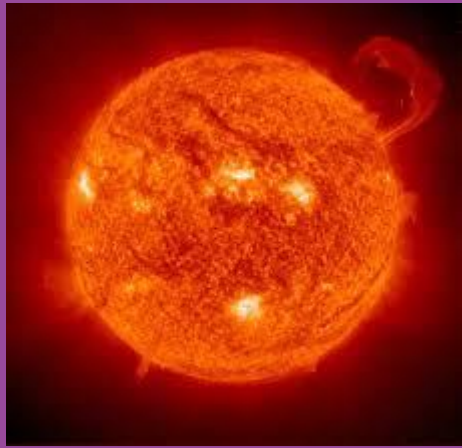
Open research questions in space human biology

How do **space stressors** cause adverse health effects in humans?



➡ How can we **prevent** this from happening with countermeasures?

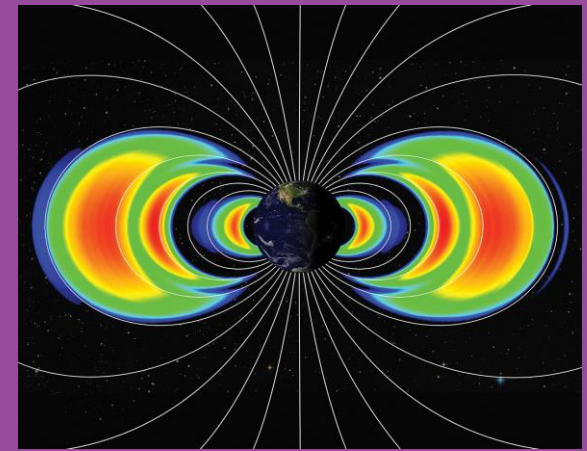
Space radiation environment



Solar particle events



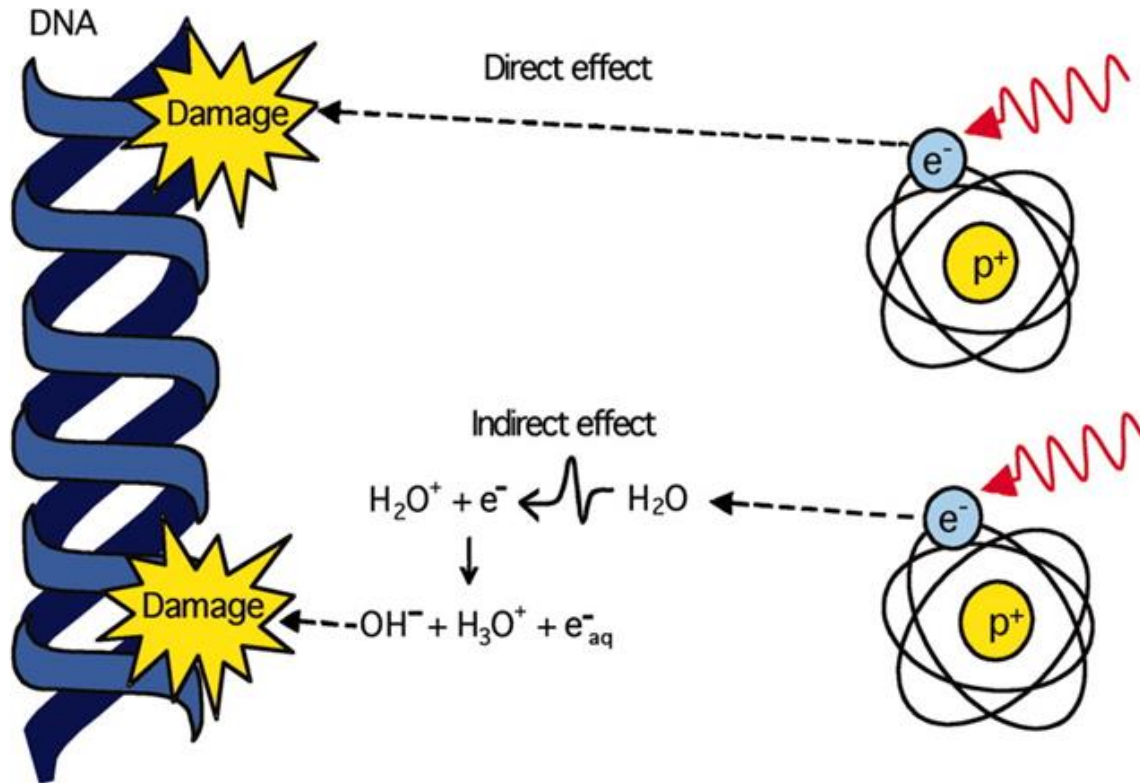
Galactic cosmic rays



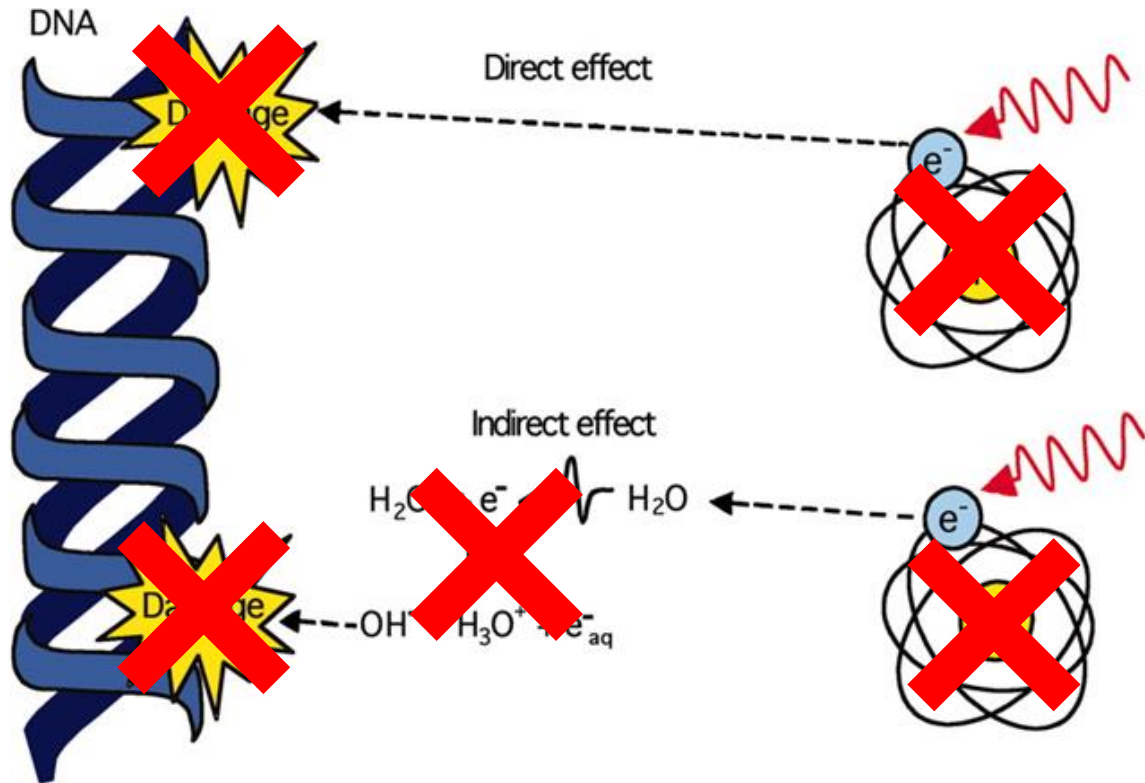
Van Allen Belts

MORE DAMAGING

Radiobiology basics: DNA damage paradigm



Levels of radiation protection



1. Stop Radiation

2. Stop ROS

3. Repair damage

Level 1: Stopping radiation

Stopping radiation

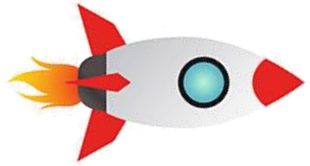
- No known effective biological mechanism to stop or shield from ionizing radiation
- Solutions:
 - Operational countermeasures
 - Limit time in space
 - Shortening overall mission duration
 - Reducing extravehicular activity time or spacewalks
 - Plan space missions during times of reduced solar storm activity
 - Engineering countermeasures
 - Structures or tools to shield astronauts from radiation e.g. Zvezda



Level 2 and 3: Stopping ROS Repairing damage

Stopping ROS and repairing damage

- Can be done at the level of an **individual**!
- **Biology** comes into play

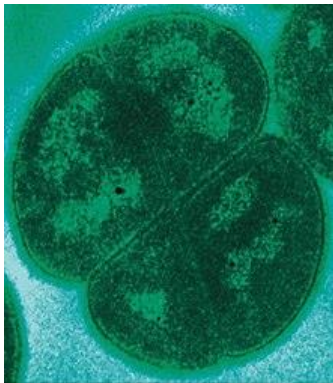


Radiation resistance mechanisms



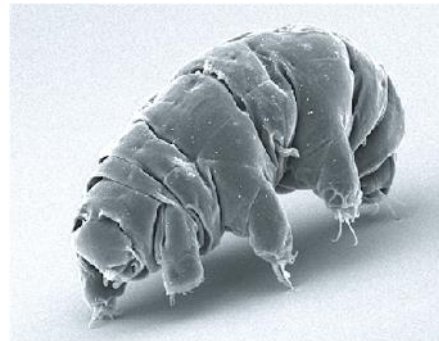
What is radiation resistance?

- Capacity of an organism to **protect** against, **repair** and **remove damage** caused by ionizing radiation
- Varies greatly between different organisms & individuals (LD50/30)



Deinococcus radiodurans

7 000 Gy



Tardigrades

5 000 Gy



Humans

4 – 5 Gy

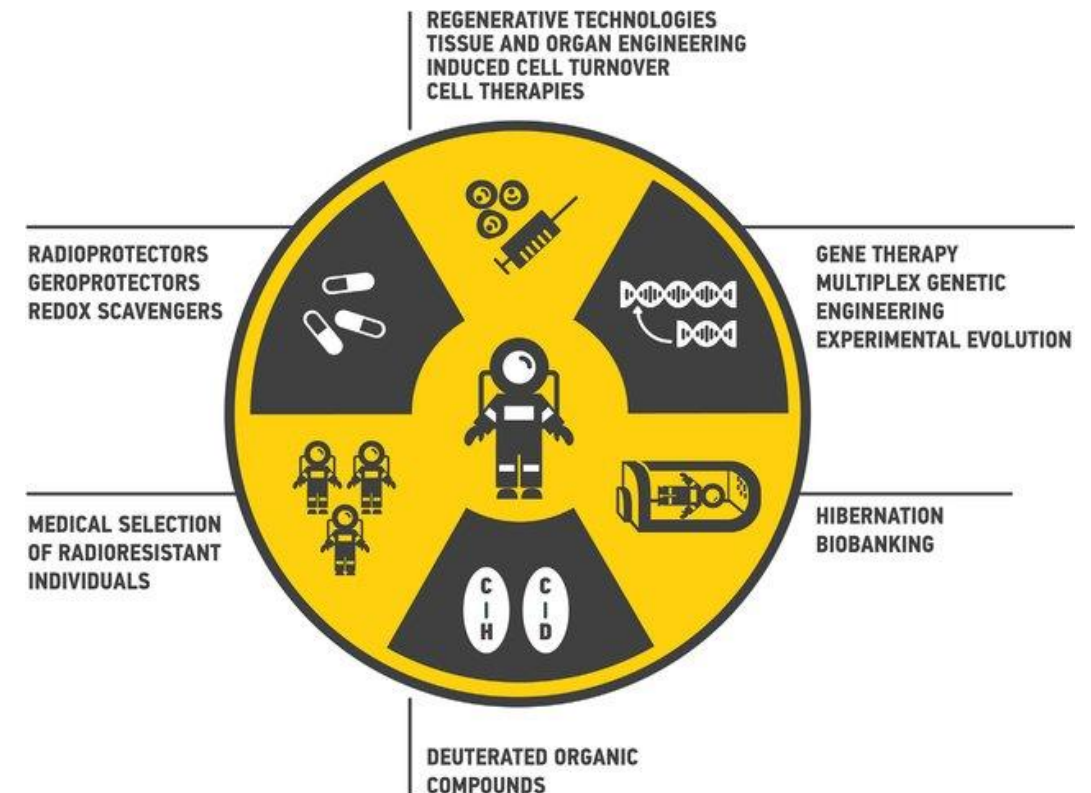
Roadmap towards enhancing human radiation resistance

www.impactjournals.com/oncotarget/

Oncotarget, Advance Publications 2018

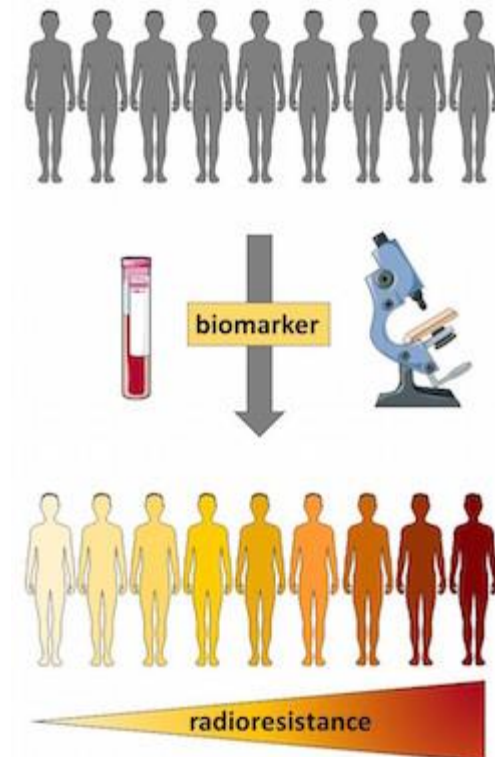
Vive la radiorésistance!: converging research in radiobiology and biogerontology to enhance human radioresistance for deep space exploration and colonization

Franco Cortese^{1,2}, Dmitry Klovov^{3,4}, Andreyan Osipov^{5,6,7}, Jakub Stefaniak^{1,8}, Alexey Moskalev^{7,9,10}, Jane Schastnaya⁵, Charles Cantor¹¹, Alexander Aliper^{5,12}, Polina Mamoshina^{5,13}, Igor Ushakov⁶, Alex Sapetsky⁶, Quentin Vanhaelen⁵, Irina Alchinova^{14,15}, Mikhail Karganov¹⁴, Olga Kovalchuk^{16,17}, Ruth Wilkins¹⁸, Andrey Shtemberg¹⁹, Marjan Moreels²⁰, Sarah Baatout^{20,21}, Evgeny Izumchenko^{5,22}, João Pedro de Magalhães^{1,23}, Artem V. Artemov⁵, Sylvain V. Costes²⁴, Afshin Beheshti^{25,26}, Xiao Wen Mao²⁷, Michael J. Pecaut²⁷, Dmitry Kaminskiy^{1,28}, Ivan V. Ozerov^{5,6}, Morten Scheibye-Knudsen²⁹ and Alex Zhavoronkov^{1,5}



1 | Selection of radioresistant crews

- Individual response to ionizing radiation
- Assessment by use of biomarkers and assays
- Include test to determine astronaut individual radiosensitivity?



2 | Pharmaceutical interventions

- **Radioprotectors**

- Protect DNA from radiation interaction
- E.g. Amifostine



- **Geroprotectors**

- Stop aging = stop radiation effects?
- E.g. metformin, curcumin



- **Redox scavengers**

- Remove oxidants from the cells
- E.g. ascorbic acid, melatonin



3 | Hibernation: sleeping your way out

- Hibernation = torpor = dormancy
 - Low-energy state linked to sleep
 - Considerable slowdown of all the vital processes in the body→ Synthetic Torpor
- Slows down body temperature and metabolism, and induces tissue hypoxia
- No food and water intake = <<< €€€



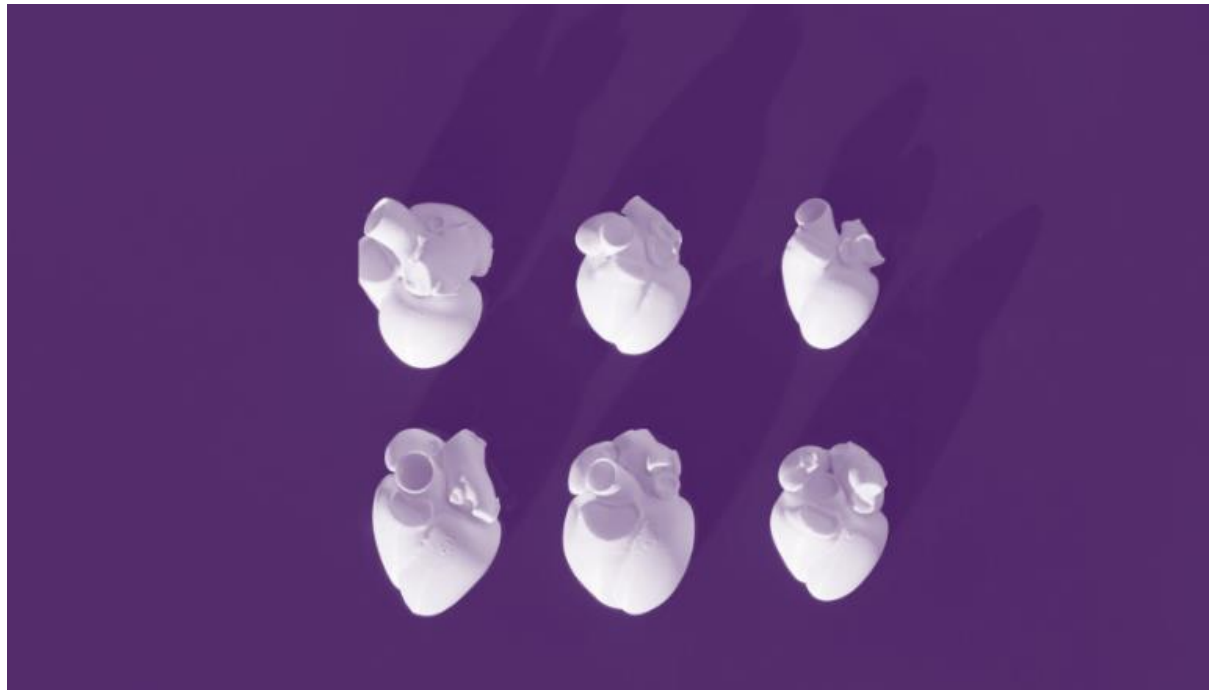
3 | Biobanking: having spare parts

- Biorepository that stores biological samples for future use
- Preservation of viability, completely stop all biological reactions
- Storage temperature?
- Liquid nitrogen -196°C
 - Cost?
 - Explosion risk?
- Cryoprotectants?



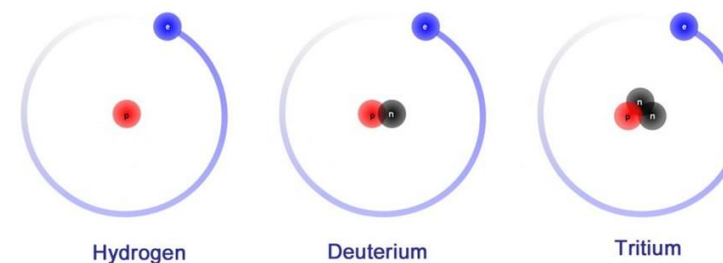
4 | Tissue engineering and regenerative medicine

- Facilitate the elimination and substitution of endogenous cells damaged by cosmic irradiation
- Replace old organs and make fresh ones!



5 | Deuterated organic compounds

- Deuterium: stable hydrogen isotope
 - Organic compounds contain carbon-hydrogen (C-H) bonds
 - C-²H is stronger than C-¹H
 - More energy required to break bond
 - Less DNA damage if DNA was deuterated
 - Heavy water (D₂O) as radioprotective strategy?
 - Issues:
 - Organisms are not energetically adapted to break down organic compounds containing deuterium
 - Rate of metabolic reactions may be slower: deterioration normal metabolism
 - Extremely costly
- ➔ Requires good titration and safety levels!



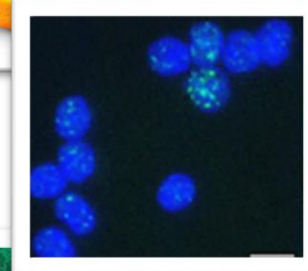
6 | Gene therapy

- (Over)expression of endogenous and exogenous genes

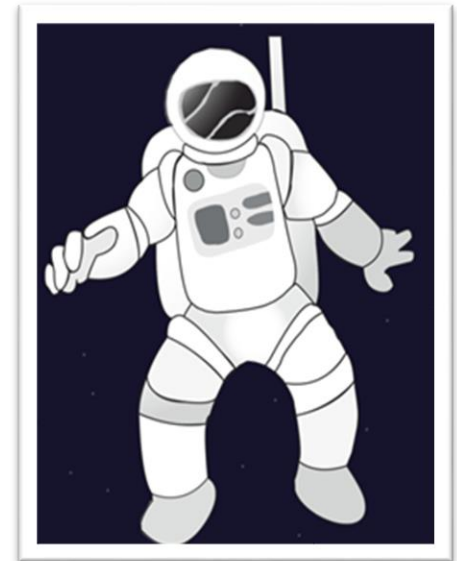
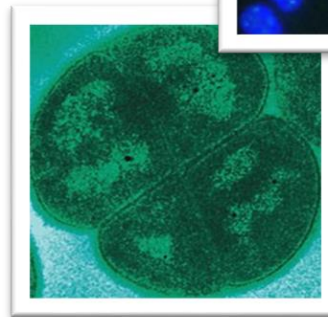
1. Antioxidants



2. DNA repair genes



3. Radioprotective transgenes



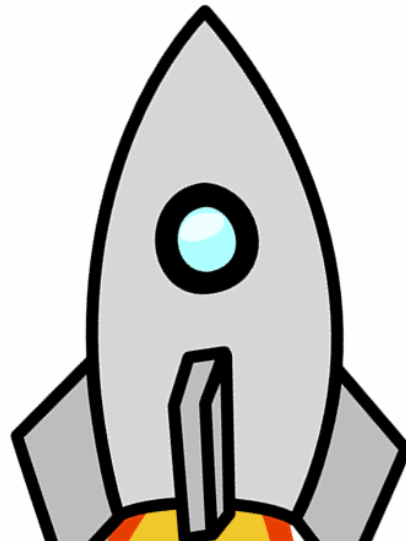
Food for thought

- Currently there is **minimal research** being done for radioresistance against space radiation
- All the approaches could significantly **empower our ability to protect** space mission crew members against cosmic radiation, but has also a **value on earth** e.g. in cancer treatment
- Although speculative, these strategies should be considered as a **foundation for future** research directions



The end

Thank you for your attention



Copyright © SCK CEN

PLEASE NOTE!

This presentation contains data, information and formats for dedicated use only and may not be communicated, copied, reproduced, distributed or cited without the explicit written permission of SCK CEN.

If this explicit written permission has been obtained, please reference the author, followed by 'by courtesy of SCK CEN'.

Any infringement to this rule is illegal and entitles to claim damages from the infringer, without prejudice to any other right in case of granting a patent or registration in the field of intellectual property.

SCK CEN

Studiecentrum voor Kernenergie
Centre d'Etude de l'Energie Nucléaire
Belgian Nuclear Research Centre

Stichting van Openbaar Nut
Fondation d'Utilité Publique
Foundation of Public Utility

Registered Office: Avenue Herrmann-Debrouxlaan 40 – BE-1160 BRUSSELS
Operational Office: Boeretang 200 – BE-2400 MOL