

CELL LINES WITH INCREASED RADIOTOLERANCE THROUGH HETEROLOGOUS EXPRESSION OF A BDELLOID ROTIFER DNA LIGASE

KEYWORDS

- Engineered cell lines
- Radiation tolerance
- Space research
- Cancer research

Biological material

Cell lines HEK-AvLigE-A/B described in Nicolas *et al.* Nat Commun **14**, 7638 (2023) - [DOI](#).

Co-owners: UNAMUR, UCLOUVAIN, ULB

Inventors

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THE RESEARCH TOOL IN A NUTSHELL

Cell lines with improved radiotolerance as research tools applicable in a broad range of fields spanning from space research to cancer therapy.

STATE OF THE ART

Some organisms known as the extremophiles are tolerant to extremely harsh environment. Besides bacteria such as *Deinococcus radiodurans*, some animals also exhibit a high DNA damage tolerance when experiencing desiccation or exposure to high doses of ionizing radiations. Among those, bdelloid rotifers present striking tolerance to ionizing radiation. The *Adineta vaga* species can for instance survive doses up to 5 kGy of X-ray (Front. Microbiol, 11: 1792). At such high radiation doses, bdelloid rotifers experience considerable DNA damages including double-strand breaks. Those organisms however manage to recover DNA integrity after irradiation through an active DNA repair process.



Adineta vaga
size: 100-200 µm

THE RESEARCH TOOL

The researchers identified an atypical and horizontally acquired DNA ligase of *Adineta vaga* (*A. vaga*) with a structural core similar to prokaryotic DNA ligase E (AvLigE) that strongly contributes to the DNA ligation activity of *A. vaga* upon DNA damage induction and is thereby key to the radiotolerance of this species. Heterologous expression of AvLigE within human cell lines significantly improved their stress response, in particular their survival upon exposure to ionizing radiation. It could as well be demonstrated that AvLigE expression increased DNA ligation activity of the corresponding CRISPR/Cas9 modified stable cell lines.

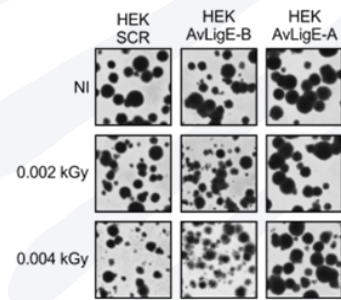
CONTACT

KEY ADVANTAGES OF THE TECHNOLOGY

- Human cell lines with improved radio-resistance readily available
- Heterologous expression of the DNA ligase:
 - > improves the cell line tolerance to exogenous stress;
 - > provides efficient molecular repair system for cell genome integrity maintenance.

FIELDS OF APPLICATIONS

- Biological research tool for space research characterized by higher radiation exposure in space than on the surface of earth.
- Research tool in the field of cancer cell therapy, in particular T Cells engineering to improve their radio-tolerance.



Colonies formed by the cell lines HEK 293T derivative expressing AvLigE variants (AvLigE-B or AvLigE-A gene) and the control cell line (HEK SCR) in different conditions of irradiation (NI : non-irradiated control conditions)

THE TEAM



After a post-doctoral stay at Harvard University and a position of associate professor at UNamur, Prof **Karine Van Doninck** founded the research unit of Molecular Biology and Evolution at ULB in 2020 to pursue fundamental research at the interface of molecular and evolutionary biology. Central to her research are micro-organisms called bdelloid rotifers which exhibit unique adaptation mechanisms to survive the most hostile environments (freezing, desiccation, ionizing radiation and outer space). She and her research team study the underlying mechanisms of their evolution, while also disentangling the processes behind their adaptations to extreme environments through interdisciplinary approaches. She was awarded with a European Research Council (ERC) Consolidator grant in 2017 and a European Space Agency project, both related to her research on rotifers. Two experiments have already been launched by SpaceX to the International Space Station, with a third planned in 2024.



Bdelloid rotifers in space: The Rob-1 Experiment enabled to study *Adineta vaga* in space on board of the ISS using the Kubik ESA incubator

RELEVANT PUBLICATIONS

> [Horizontal acquisition of a DNA ligase improves DNA damage tolerance in eukaryotes](#), *Nature Communications*, **14**, 7638 (2023) - DOI: [10.1038/s41467-023-43075-8](https://doi.org/10.1038/s41467-023-43075-8)

RESEARCH TOOL AVAILABILITY

Cell lines may be sourced directly from non-exclusive authorized distributors

- > CancerTools.org (EU, GB) – Cat. #: [162126](#), [162125](#), [162124](#)
- > Applied Biological Materials -ABMGood (US, CA)