Improving human DNA repair using the tiny tardigrade

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The tardigrade is a microscopic animal that resists several extreme environmental conditions, including high-intensity ionizing radiation. A study shows that this resistance is made possible by an enzymatic DNA repair system of extraordinary efficiency that could be used as inspiration for the treatment of human diseases.

During the evolution of life on Earth, all species must have acquired characteristics that maximize their probability of surviving and passing their genes to their offspring.

Illustration of a tardigrade, a tiny animal capable of surviving in very hostile environments such as the vacuum of space. It also tolerates extreme temperatures and the absence of water and food, among other things. FOTOLIA ILLUSTRATION

From a scientific point of view, there is enormous interest in studying these adaptation mechanisms, not only to improve our knowledge of the world around us, but also to identify certain molecular processes that could be applied to the treatment of diseases that affect humanity.

INVINCIBLE BEAR CUBS !

The tardigrade is a good example of an animal that, while evolutionarily very distant from humans, possesses several intriguing characteristics with therapeutic potential.

Nicknamed "water bear", the tardigrade is a tiny animal (between 0.1 and 1.5 mm long) which has incredible resistance to several extreme environmental conditions, fatal for all living organisms, whether extreme temperatures (-270°C to +150°C), the absence of atmospheric pressure or on the contrary overwhelming pressures, the absence of water and food or even high intensity ionizing radiation (X-rays or UV).

This last case is particularly interesting: it has been shown that tardigrades can survive radiation of 5,000-6,000 Gray (Gy), i.e. 1,000 times more than the lethal dose for a human.

LARGE-SCALE REPAIR

A recent study provides a better understanding of the biochemical mechanisms responsible for this adaptation to radiation (1). In this study, the researchers first observed that the exposure of a species of tardigrade (*Hypsibius exemplaris*) to high doses of gamma radiation (4,360 Gy) induced considerable short-term damage in their DNA, but that the animal recovered quickly, with complete repair of these molecular breaks in the following 24 hours.

Further analysis showed that this recovery was correlated with an increase in the expression of several genes, in particular those of enzymes involved in DNA repair.

In certain cases, the increase in expression of these genes is of an extraordinary magnitude, never before observed in this type of study. The levels of certain genes increased more than 300 times following irradiation, reaching levels as high as those involved in maintaining basic biological functions of the animal, which is exceptional.

HIGH PERFORMANCE REPAIRERS

An important question is whether these genes involved in the tardigrade's DNA repair and resistance to radiation can perform a similar protective function if introduced into the cells of another organism.

Initial results obtained by the researchers suggest yes. Using the bacterium Escherichia coli as a model, they observed that the insertion of these genes significantly increased the survival of the bacteria to a massive dose of gamma rays, suggesting that they are sufficient to confer resistance to irradiation, whatever the origin of the DNA.

These super-efficient DNA repair enzymes could be used for the treatment of certain human pathologies involving irreversible DNA damage, for example certain rare genetic diseases that cause premature aging, or for the repair of mutated DNA, following excessively prolonged solar exposure.

These repair enzymes could also be used to minimize the side effects of radiotherapy on healthy tissues surrounding tumors during oncology treatment.

Another example which demonstrates that the simplest forms of life are essential to the survival of the most complex.

(1) Clark-Hachtel CM et al. The tardigrade *Hypsibius exemplaris* dramatically upregulates DNA repair pathway genes in response to ionizing radiation. Curr. Biol.; 2024; S0960-9822(24)00316-6.

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