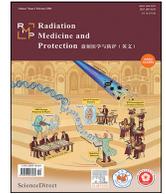




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Review

An orchestra of survival: Molecular mechanisms of radiation resistance across extremophiles

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ABSTRACT

An orchestra of molecular mechanisms endows radiation-resistant extremophiles with extraordinary survival capabilities under extreme ionizing radiation. This review systematically explores the arsenal of key molecular strategies underpinning extreme radioresistance, including efficient DNA damage response and repair pathways, robust reactive oxygen species (ROS) scavenging systems, specialized protective proteins (e.g., Dsup, Ppr1), and coordinated regulatory networks. This review extensively examines species-specific adaptations in a diverse range of radioresistant organisms, such as *Deinococcus radiodurans*, archaea, lichens, bdelloid rotifers, *Drosophila melanogaster*, cockroaches, *Caenorhabditis elegans*, and tardigrades. Despite the conservation of core mechanisms such as DNA repair machinery, significant interspecies variations exist in antioxidant defense systems and cellular structure remodeling strategies. Based on the available data, this review further conducts an analysis of convergent vs. divergent evolution and quantitative efficiency metrics across species. Finally, translational applications of these mechanisms in radiobiology, medicine and space science are discussed, with future research directions highlighted that aim to exploit these natural radioprotective systems for technological and therapeutic innovations.

1. Resilient radiation-resistant extremophiles

Extremophiles comprise a diverse group of organisms capable of thriving under extreme environmental conditions often lethal to most other forms of life, including intense temperatures, high salinity, and extreme radiation. They are most commonly microorganisms like bacteria and archaea, but some are more complex, such as certain types of worms, insects, and even the famous tardigrades (water bears). Specifically, microorganisms that can withstand extreme doses of ionizing radiation (IR) are originally termed radioresistant or radiation-resistant extremophiles.¹ Although prolonged or intense exposure to γ -rays, X-rays, and ultraviolet radiation generates mutagenic and cytotoxic DNA lesions that can lead to cell death, certain microorganisms may endure and flourish under such conditions. Their survival is attributed to a suite of defensive strategies based on primary and secondary metabolites, such as extremolytes and extremozymes that repair, shield, and stabilize cellular components. These organisms have attracted

significant scientific interest due to their potential for scientists to gain insights into the basic rules of radiation biology and the incredible adaptability of life. Research into the survival mechanisms of extremophiles is advancing efforts to address critical challenges in human health, with the understanding of these adaptive strategies holding promise for developing innovative solutions to a range of medical issues.²

The effort to explore how organisms respond to radiation dates back to the early 20th century, with the discovery of radioactive elements and the understanding of radiation effects. In 1956, American scientists isolated a red Gram-positive coccus *Deinococcus radiodurans* from γ -irradiated meat cans, and found that it could survive at doses of 5000 Gy, roughly a thousand times the human lethal dose. Instantly, the bacterium was established as the archetype of radiotolerance.³ Two decades later in the 1970s, a study demonstrated that 80 %–90 % of fungal spores retained the ability to germinate after exposure to 3 kGy γ -rays, two orders of magnitude beyond the LD_{90} of most vegetative

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