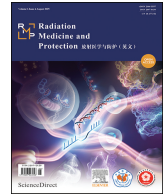




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Review

Advances in research on the molecular mechanisms of miRNAs in radiation responses

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ABSTRACT

MicroRNAs (miRNAs), a class of non-coding RNA molecules, play key roles in post-transcriptional regulation of gene expression in various biological processes such as cell differentiation, stress responses, and disease progression. Recent studies have highlighted the mechanisms underlying the dynamic regulation of miRNAs in modulating cellular responses to radiation, along with their potential for clinical applications. Radiation exposure alters the expression of miRNAs, depending on radiation dose, radiation type, and cell specificity. In contrast, miRNAs affect cellular radiosensitivity and the repair of radiation-induced damage by regulating DNA repair, oxidative stress responses, cell cycle progression, and apoptosis pathways. In the context of radiotherapy, specific miRNAs can enhance tumor radiosensitivity or mediate radioresistance by targeting specific genes, serving as new targets for optimizing the efficacy of radiotherapy. In addition, miRNAs, combined with metabolomics and long non-coding RNA (lncRNA) analyses, hold multidimensional potential as biomarkers of radiation injury. However, it is necessary to address challenges posed by the multi-target nature, tissue specificity, and clinical translation bottlenecks of miRNAs using technologies such as single-cell sequencing and gene editing. This paper reviews the molecular mechanisms of miRNAs involved in radiation responses and aims to provide a theoretical basis and propose research directions to enhance the understanding of miRNAs in radiation biology and to promote their clinical applications.

1. Introduction

miRNAs are 19–23 nucleotide non-coding RNAs that regulate gene expression by binding to target mRNAs, affecting cell differentiation, tissue development, and other processes.¹ In 1993, Ambros and Lee² discovered two small RNA molecules encoded by the nematode *lin-4* gene, which were validated by Ruvkun's team, revealing the mechanism by which small RNAs regulate the expression of target genes through base pairing. The comparative features of the other non-coding RNAs relative to miRNAs are listed in Table 1. In this review, we summarize the regulatory mechanisms and clinical potential of miRNAs in response to radiation, providing a reference for future research.

2. miRNAs involved in radiation responses

Ionizing radiation (IR), a significant environmental factor, exerts profound effects on living organisms, including both targeted effects on DNA and non-targeted effects mediated through intercellular signaling. IR directly induces DNA damage in targeted cells, leading to cell death. This principle is employed in radiotherapy to eliminate tumor cells. However, IR triggers non-targeted effects, such as the bystander effect, which influence the overall therapeutic outcome and produce side effects on surrounding healthy tissues and, thus, cannot be ignored.

2.1. Radiation-induced targeted and non-targeted effects

Radiation target theory argues that IR hits specific molecules or

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