5 - 54 MitoQ-mediated Autophagy: A Novel Strategy for Precise Radiation Protection*

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There were significant differences in energy metabolism between normal and tumor cells (normal cells depend on mitochondrial respiration for energy supply, while tumor cells rely on aerobic glycolysis)[1,2]. Based on this difference, this study aims to provide a new therapeutic strategy for precise radiation protection of normal cells through utilizing selective autophagy induced by MitoQ-constructed pseudo-mitochondrial membrane potential (PMMP) by targeting mitochondrial respiration.

Normal cells HA were identified as mitochondrial respiration energy phenotype, while tumor cells A172 were identified as aerobic glycolysis energy phenotype. MitoQ was selectively enriched in mitochondria in HA cells, and induced higher PMMP in normal cells than tumor cells. PMMP disrupted energy metabolism in HA cells, thereby selectively inducing autophagy through the AMPK/mTOR pathway. Thus, MitoQ-constructed PMMP effectively protected the survival of HA cells but didn't affect the proliferation inhibition of A172 cells under radiation. MitoQ also protected normal tissue against X-rays but didn't influence the tumor-killing efficacy of radiation in mice bearing orthotopic glioma.

MitoQ-constructed PMMP could successfully protect the normal cells from radiation-induced damage without affecting the tumor-killing efficacy of radiation by utilizing selective autophagy (Fig. 1). Thus, MitoQ-constructed PMMP provides a new therapeutic strategy for specific radiation protection.

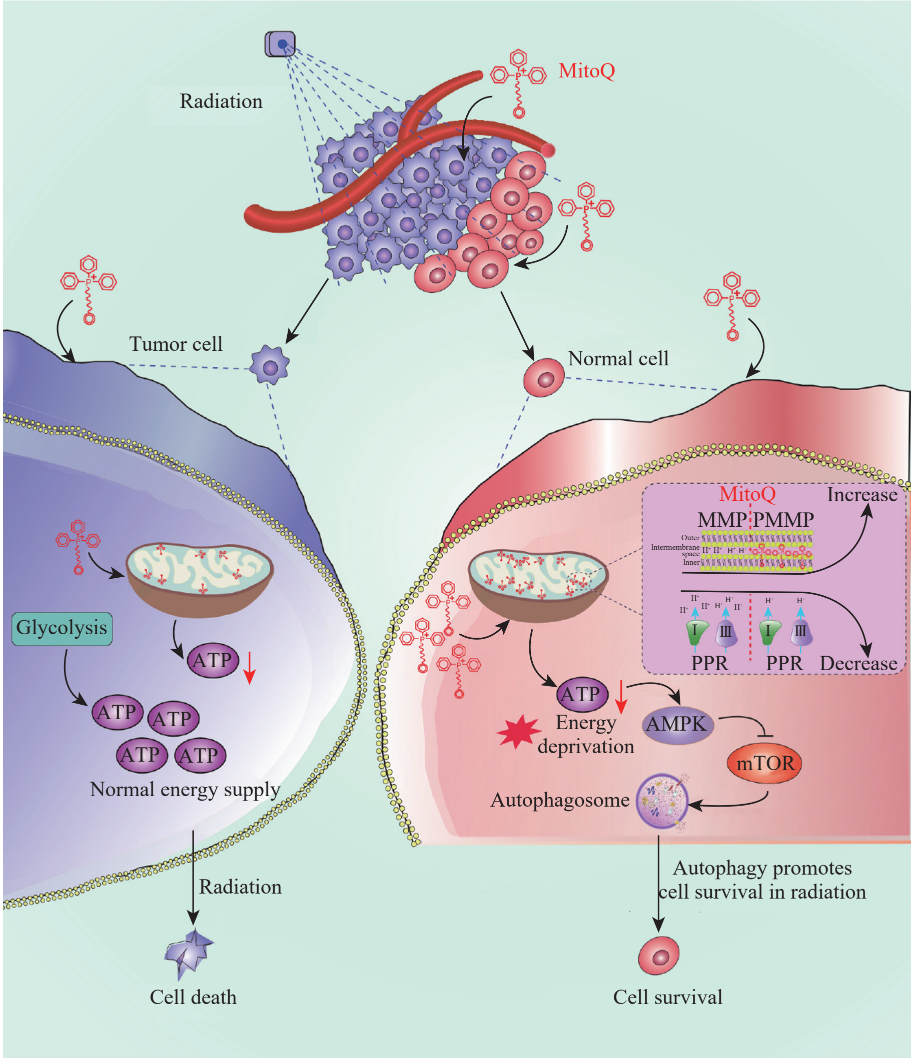

Fig. 1 (color online) Schematic diagram of MitoQ inducing selective autophagy to exert precise radiation protection.

References

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5 - 55 Identifification of Therapeutic Targets and Prognostic Biomarkers Among Frizzled Family Genes in Glioma

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The biological functions of the frizzled gene family (FZDs), as the key node of wingless-type MMTV integration site family (Wnt) and mammalian target of rapamycin signaling pathways, have not been fully elucidated in glioma[1,2]. This study aims to identify novel therapeutic targets and prognostic biomarkers for gliomas, which may help us understand the role of FZDs. RNA-sequence data were downloaded from The Cancer Genome Atlas (TCGA) and Genotype-Tissue Expression (GTEx) projects. Survival analyses, Cox regression analyses, nomograms, calibration curves, receiver operating characteristic (ROC) curves, gene function enrichment analyses, and immune cell infifiltration analyses were conducted using R statistical language High expressions of FZDs were positively associated with the activation of mTOR signaling. FZD1/2/3/4/5/7/8 was significantly highly expressed in tumor tissues, and the high expression of FZD1/2/5/6/7/8 was significantly positively associated with poorer prognosis. FZD2 and FZD6 positively served as independent predictors of poor prognosis. Gene function analysis showed that FZDs were associated with mTOR signaling, immune response, cytokine-cytokine receptor interaction, extracellular matrix organization, apoptosis, and p53 signaling pathway. Our finding strongly indicated a crucial role of FZDs in glioma. FZD1/2/5/6/7/8 could be an unfavorable prognostic factor in glioma and FZD2 and FZD6 may be novel independent predictors of poor prognosis in glioma.

References

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