3 - 57 Protective Effect of Diallyl Disulfide on Carbon Ion Irradiation-induced Cell Death in Mouse Testis via p73 Signaling Pathway, But Not p53*

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Diallyl Disulfide (DADS) is the main organosulfur component of garlic and it is known for multiple pharmacological actions. Currently, DADS has been well documented to ameliorate the testis injuries caused by X-ray irradiation[1−4]. However, the effect of DADS against heavy-ion-induced testis damage, particularly cell apoptosis, is still largely unknown. In this regard, based on ground experiments at accelerators, this study has been undertaken to estimate the protective mechanisms of DADS against carbon ion-induced cell apoptosis at the level of signal transduction pathway in mouse testis.

Here, we investigated the role for DADS in inhibiting apoptosis in testis of mice exposed to irradiation and studied the mechanism of action. Young Kun-Ming mice were divided into six groups: control group, irradiation group, irradiation group plus solution and three DADS plus irradiation-treated groups. An acute study was carried out to determine morphological damage, apoptotic cells, mRNA and protein levels of p53, Tap73 and ΔNp73 as well as proteins expression involved in mitochondria dependent apoptosis in mouse testis 24 h after irradiation with a single dose of 4 Gy. In irradiated mice, a serious morphological damage and significant rise in apoptosis (TUNEL positive) was accompanied by activated expression of p53 and TAp73, and down regulation of ΔNp73 as well as alterations of protein levels of the mitochondrial pathways (Bax, Bcl-2, cytochrome c, caspase-3)(Fig. 1). Different concentration of DADS was applied prior to carbon ion irradiation. However, DADS supplementation was better able to reduce radiation-induced morphological damage and resulted in a significant ($P < 0.05$) protection in radiation-induced apoptosis. Interestingly, DADS supplementation could activate ΔNp73, and down regulate Tap73 expression, but could not reduce p53 expression, implying its inhibition of apoptosis via p73 signally pathway. Additionally, DADS decreased the Bax/Bcl-2 ratio, cytochrome c release and caspase-3 expression in mouse testis exposed to carbon ion irradiation, indicating its reduction of apoptosis via the mitochondrial pathway.

Our data, for the first time, indicate that DADS deduces apoptosis in testis of mice exposed to carbon ion irradiation via activation of TAp73/ΔNp73 –mediated apoptotic protein levels of the mitochondrial pathways, but not p53.

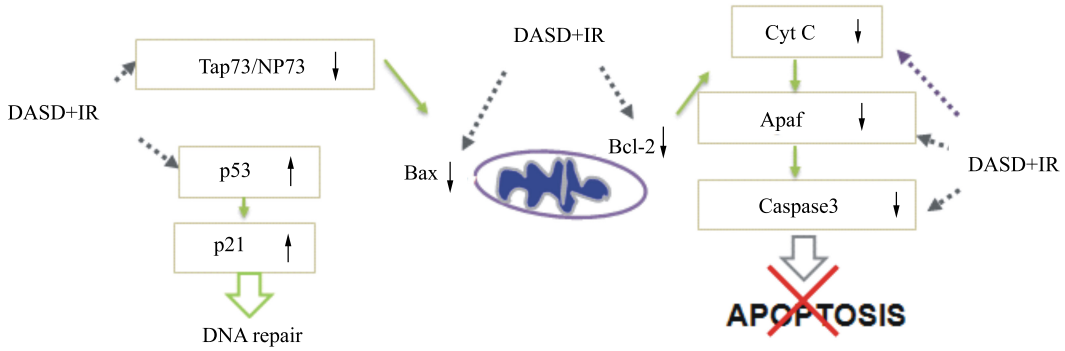

Fig. 1 (color online) Potential targets of DADS and carbon ion irradiation on apoptosis-inducing mitochondrial pathway in mouse testis.

References

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