

Molecular delineation of gamma-ray-induced NF-kappaB activation and pro-inflammatory genes in SMP30 knockout mice.

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Abstract

Exposure to gamma radiation causes a wide variety of biological damages and alterations, including oxidative stress. Among the key cellular components that are exquisitely sensitive to oxidative stress is the transcription factor nuclear factor (NF)-kappaB, which plays a central role in the activation of various pro-inflammatory genes. Recently, senescence marker protein 30 (SMP30), which has been used as an aging marker, was shown to have an antioxidant property. In the current study, using SMP30 knockout (SMP30^{-/-}) mice that are vitamin C-deficient, we explored the effect of radiation on the activation of NF-kappaB and several key pro-inflammatory genes. Six groups of mice were studied. Group 1 mice were not irradiated and were supplemented with vitamin C (2.5 mg/kg/day). Group 2 mice were irradiated and were not supplemented with vitamin C. Group 3, 4 and 5 mice were irradiated with 1, 3 and 5 Gy of gamma radiation (⁶⁰Co), respectively, without vitamin C supplementation. The wild-type mice (SMP30^{+/+}) in group 6 were not irradiated or supplemented. At 24 h after irradiation, mice were killed humanely and the kidneys were removed analysis. The results showed that gamma radiation induced oxidative stress with corresponding NF-kappaB activation; this activated NF-kappaB led to the up-regulation of several major pro-inflammatory mediators such as COX-2, iNOS, VCAM1, ICAM1 and E-selectin in irradiated groups with no vitamin C supplementation. Our data provide molecular insights into mechanisms through which gamma radiation enhances oxidative stress-induced inflammation by showing the activation of NF-kappaB signaling pathway in vitamin C-deficient SMP30^{-/-} mice. In addition, our present study produced evidence that gamma radiation exerts its deleterious action by activating the inflammatory process that are known to be a major risk factor for many chronic diseases. Furthermore, our data revealed vitamin C may play an important protective role in attenuating the adverse gamma-radiation-induced adverse effects by suppressing adverse oxidative effects and pro-inflammatory mediators.

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