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# Effects of celastrol against gamma irradiation-induced damage by modulating inflammatory mediators

**Hong Wang and Gautam Sethi**
National University of Singapore, Singapore

The present study was aimed to explore the possible radioprotective effects of celastrol and relevant molecular mechanisms in an *in vitro* cell and an *in vivo* mouse model exposed to gamma radiation. Human keratinocyte HaCaT and BJ skin fibroblast cells were exposed to gamma radiation of 20Gy, followed by treatment with celastrol for 24h. Cell viability, reactive oxygen species (ROS), nitric oxide (NO), and glutathione (GSH) production, lipid peroxidation, DNA damage, inflammatory cytokine levels, and NF-κB pathway activation were examined. The survival rate, levels of interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) in blood, and p65 and phospho-p65 expression were also evaluated in mice after exposure to gamma radiation and celastrol treatment. The gamma irradiation of HaCaT cells induced decreased cell viability, but treatment with celastrol significantly blocked this cytotoxicty. Gamma irradiation also increased free radical production, e.g. ROS and NO, decreased the level of GSH, and enhanced oxidative DNA damage and lipid peroxidation in cells, which were effectively reversed by celastrol treatment. Moreover, inflammatory responses induced by gamma irradiation, as demonstrated by increased levels of IL-6, TNF-α, and IL-1β, were also blocked by celastrol. The increased activity of NF-κB DNA binding following gamma radiation was significantly attenuated after celastrol treatment. In the irradiated mice, treatment with celastrol significantly improved overall survival rate, reduced the excessive inflammatory responses, and decreased NF-κB activity. As an NF-κB pathway blocker and antioxidant, celastrol may represent a promising pharmacological agent with protective effects against gamma irradiation-induced injury.

## Biography

Dr Wang Hong has her expertise in evaluating the effects of natural products on radiation protection. She has investigated the function of celastrol, ursolic acid, Des-Aspartate-Angiotensin I, et al. in animal models and *in vitro* against gamma radiation induced damage.

snrwh@nus.edu.sg

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