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Inhibition of NF-kappa B, a key inflammatory protein, reduced radiation toxicity in zebrafish

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Directly inhibiting the activity of a key protein mediator of inflammation reduced radiation toxicity in zebrafish embryos, and may ultimately be of help to patients receiving radiation therapy, according to researchers from the Kimmel Cancer Center at Jefferson.

Reporting in *Molecular Cancer Therapeutics*, the researchers found that inhibitors of NF-kappa B not only protected against radiation toxicity when given before exposure to treatment, but also lessened the radiation toxicity when given one to two hours post-exposure.

In the study, both NF-kappa B inhibitors and proteasome inhibitors were examined for their potential to alleviate the negative effects of radiation. However, the proteasome inhibitors tested, which included the FDA-approved bortezomib (Velcade), did not show the same effect. In fact, they actually exacerbated the harmful radiation effects.

"Although proteasome inhibitors demonstrate activity against NF-kappa B, they also target many other pathways," said Ulrich Rodeck, M.D., Ph.D., professor of Dermatology and Cutaneous Biology at Jefferson Medical College of Thomas Jefferson University. "We suspect that these agents may radiosensitize due to inhibition of these other targets."

This study was led by Dr. Rodeck and Adam Dicker, M.D., Ph.D., professor and interim chairman of the department Radiation Oncology at

Jefferson.

"We started with the premise that NF-kappa B activity might be helpful in protecting cells against the harmful effects of radiation," Dr. Rodeck said. "We actually found quite the opposite - inhibiting the activity is an advantage that increased the survival in zebrafish and protected the individual organs from harmful effects of radiation."

According to Dr. Rodeck, the key is to downmodulate the NF-kappa B activity, rather than ablating it completely, as excessive NF-kappa B activation is potentially detrimental even in the absence of radiation therapy.

Drs. Rodeck and Dicker will be moving this research forward so that it may ultimately help individuals exposed to "dirty bombs," or cancer patients receiving radiation therapy. Their research team pioneered using zebrafish embryos as a vertebrate model system to investigate the effects of radiation therapy.

Source: Thomas Jefferson University (news : web)