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Lightning rod for head and neck cancer

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They say lightning never strikes the same place twice—unless, of course, that place is a lightning rod. An enzyme called UROD acts like a lightning rod for cancer cells, drawing radiation and chemotherapy toward specific spots in diseased tissue, a new study in mice and humans reports in *Science*.

The findings suggest that UROD—identified for the first time in this paper as a key player in human cancer--could help decrease treatment side effects for people with head and neck cancer, the eighth most common cancer worldwide. Despite many advances over the last few decades, the toxic side effects associated with current therapies have made for disappointing outcomes in many patients. Head and neck tumors are often found near critical organs, so destroying the diseased tissue is often a delicate challenge that could lead to life-threatening conditions.

Here, Emma Ito and colleagues show that targeting UROD can selectively enhance the effects of radiation and chemotherapy in head and neck tumors, while minimizing toxicity to normal tissues. By focusing therapy toward specific parts of tissue, lower doses of radiation and chemotherapeutic drugs could potentially be administered to patients without compromising treatment efficacy. Uroporphyrinogen decarboxylase or UROD is an enzyme involved in the production of a molecule called heme, which is vital for all of the body's organs (though it is most abundant in the blood, bone marrow, and liver).

Heme is an essential component of iron-containing proteins called

hemoproteins, including hemoglobin, the protein that carries oxygen in the blood.The authors discovered by high-throughput RNA interference screening that UROD is a potent tumor-selective sensitizer for both radiation and chemotherapy. In mice, blocking expression of the UROD gene increased cancer cell death. Analyses of head and neck cancer tissue samples revealed that UROD levels were significantly higher in tumors than in normal tissues.

Moreover, the researchers determined that improved clinical outcome was linked to lower UROD levels in patients, suggesting that UROD could potentially be used to predict patients' response to radiation. The authors hope that UROD inhibitors could one day be used in conjunction with radiation and chemotherapy to minimize side effects.

More information: "Uroporphyrinogen Decarboxylase Is a Radiosensitizing Target for Head and Neck Cancer," by E. Ito et al., *Science*, January 2011.

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