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Key Enzyme That Affects Radiation Response Identified

Cancer researchers at Princess Margaret Hospital (PMH) have discovered that targeting an enzyme called uroporphyrinogen decarboxylase (UROD) can sensitize diseased tissue to radiation and chemotherapy, which could mean fewer side effects for individuals with head and neck cancer.

The findings, published online in Science Translational Medicine, are significant because they suggest that targeting UROD -- identified for the first time as a key player in human cancers -- can selectively boost the effects of radiotherapy and chemotherapy in head and neck tumors, while minimizing toxicity to normal tissues.

"Our analysis of patient biopsies revealed that UROD levels were significantly higher in tumor tissues versus normal tissues. Cancer patients with lower UROD levels prior to radiation treatment had improved clinical outcome, suggesting that UROD could potentially be used to predict patients' response to radiation therapy," says principal investigator, Dr. Fei-Fei Liu, Professor of Radiation Oncology at the University of Toronto and PMH, and Senior Scientist at the Ontario Cancer Institute and The Campbell Family Cancer Research Institute.

Lead author Dr. Emma Ito adds: "This means that lower doses of radiation and chemotherapeutic drugs could potentially be administered to patients without affecting treatment efficacy."

"Despite the advances over the last few decades, the toxic side effects associated with current therapies for head and neck cancer have caused disappointing outcomes in many

patients," says Dr. Ito. Head and neck tumors are often found near critical structures, so destroying the diseased tissue is often a delicate challenge that can lead to life-threatening conditions.

"UROD is an enzyme involved in the production of a molecule called heme, which is vital to all body organs. Targeting UROD creates an opportunity to exploit the heme synthesis pathway, which disrupts the equilibrium of iron and free radical levels in cells which in turn kills cancer cells," says Dr. Liu.

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Source: E. Ito, S. Yue, E. H. Moriyama, A. B. Hui, I. Kim, W. Shi, N. M. Alajez, N. Bhogal, G. Li, A. Datti, A. D. Schimmer, B. C. Wilson, P. P. Liu, D. Durocher, B. G. Neel, B. O'Sullivan, B. Cummings, R. Bristow, J. Wrana, F.-f. Liu. Uroporphyrinogen Decarboxylase Is a Radiosensitizing Target for Head and Neck Cancer. Science Translational Medicine, 2011; 3 (67): 67ra7 DOI: 10.1126/scitranslmed.3001922