HIF gene mutation found in tumor cells offers new clues about cancer metabolism

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For the first time, a mutation in HIF2?, a specific group of genes known as transcription factors that is involved in red blood cell production and cell metabolism, has been identified in cancer tumor cells.

Researchers from Huntsman Cancer Institute (HCI) at the University of Utah and the National Institutes of Health found the mutation in tumor cells of two patients with the rare cancers paraganglioma/pheochromocytoma and somatostatinoma. The mutation was previously identified in connection with a non-cancerous hereditary condition, but never before in spontaneously arising cancers. The research results appear in the September 6, 2012 issue of the New England Journal of Medicine.

Transcription factors are proteins that bind to specific sequences of DNA to regulate cell functions. Hypoxia-inducible factors (HIFs) are transcription factors that control a wide range of functions connected to the way cells respond to oxygen, including metabolism (the way energy is produced) and the creation of red blood cells. Increased amounts of HIF in cancer cells was found to be responsible for the unique way they generate energy, referred to as the Warburg effect, named for Otto Warburg, a German physiologist who received the 1931 Nobel Prize in Physiology for this research.

"These HIF pathway mutations were first discovered while studying people with a condition called polycythemia that makes the body overproduce red blood cells," said one of the senior authors, Josef Prchal, M.D., professor in the Division of Hematology and Hematologic Malignancies at the University of Utah School of Medicine, an HCI investigator, and an expert on polycythemic disorders who has previously discovered other mutations in other HIF pathway genes.

The findings raise some important questions for future research. "The patients in which we found these mutations have a rare combination of diseases, paraganglioma/pheochromocytoma and polycythemia, yet they shared similar mutations," said Prchal. "Learning whether HIF pathway mutations are present in other cancers could increase understanding of the mechanisms of cancer cell metabolism and offer a possible new target for cancer treatment development."

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