Gene Gives a Boost to Tumor Suppression

August 18 2006

Angiogenesis, or the growth of new blood vessels, is an important naturally occurring process in the body. As with normal tissues, tumors rely on angiogenesis to supply them with the oxygen and nutrients they need for growth.

This understanding has led researchers to explore antiangiogenic therapies for the suppression of tumor growth. Among the most potent known inhibitors of tumor angiogenesis are C-terminal fragments of collagen, one of the most abundant proteins in the body. However, it was unknown how production of antiangiogenic fragments from full-length collagen was controlled.

Now, researchers at the University of Massachusetts Medical School have demonstrated a connection between p53, a commonly known tumor suppressor, and the production of antiangiogenic collagen fragments.

Dubbed the “guardian of the genome,” p53 is the body’s primary tumor suppressing protein. Involved in regulating the response of cells to stress, p53 has the ability stop cells from dividing when they are damaged and, in some cases, to encourage such cells to destroy themselves via programmed cell death, or apoptosis. In the continuing efforts to understand how p53 influences cell death, scientists have found that the presence of p53 in tumors also influences angiogenesis.

In their paper, “p53-Mediated Inhibition of Angiogenesis through Upregulation of a Collagen Prolyl Hydroxylase,” published in the August 18 issue of Science, UMMS scientists, led by Howard Hughes Medical

Institute Investigator Michael R. Green, MD, PhD, the Lambi and Sarah Adams Chair in Genetic Research and professor of molecular medicine and biochemistry & molecular pharmacology, sought to define the mechanisms by which p53 influences the regulation of angiogenesis. In doing so, Dr. Green and colleagues identified a gene—alpha II collagen prolyl hydroxylase [?(II)PH]—that is not only stimulated by p53 but is also necessary for the p53-mediated production of antiangiogenic collagen fragments. Remarkably, when ?IIPH was delivered to mice, tumor growth could be dramatically inhibited. These findings reveal both a genetic and biochemical linkage between the p53 tumor suppressor pathway and the production of antiangiogenic collagen fragments, as well as new strategies for combating cancer.

Source: University of Massachusetts Medical School, Worcester