Understanding the KLF6 Gene May Help Treat Metastatic Cancer

Goutham Narla, MD, PhD, Assistant Professor of Medicine and of Genetics and Genomic Sciences, was just a medical student at Mount Sinai when he discovered the KLF6 gene while working in the laboratory of Scott L. Friedman, MD, Professor of Medicine and Chief of the Division of Liver Diseases.

Today, as a faculty member, he continues to make new discoveries about the role of KLF6 that have laid the groundwork for improving the diagnosis and treatment of malignancies like liver, prostate, and lung cancer. His research was featured last month in the Howard Hughes Medical Institute Bulletin.

“I fell in love with the project as a student,” says Dr. Narla, who also received the Howard Hughes Medical Institute Physician-Scientist Early Career Award for his research last year. “We became the first group to identify KLF6 as a tumor suppressor. It is the brake that slows things down—it tells the cells to stop growing.”

The breakthrough was published in Science in 2001, but the clinician in Dr. Narla wanted to do more. He wanted to figure out how this discovery could be used to treat metastatic cancer, which has a very poor prognosis.

Two years ago, Dr. Narla started his own lab with the support of Paul Klotman, MD, Professor and Chairman of the Department of Medicine, and Robert Desnick, MD, Professor and Chairman of the Department of Genetics and Genomic Sciences. They joined forces with John Martignetti, MD, Associate Professor of Genetics and Genomic Sciences, Pediatrics, and Oncological Sciences, and had yet another breakthrough. His team identified a splice variant of the KLF6 gene, known as KLF6-SV1, which causes the cancerous cells to grow out of control.

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They turn on the accelerator and turn off the brake. This balance between the brake and the accelerator determines what happens in terms of cell growth and ultimately decides how aggressive a tumor will become.”

Now that they have discovered KLF6-SV1, the next step is to find a way to turn the accelerator off and stop tumor growth.

Drawing on new research, Dr. Narla and his colleagues have found that a small RNA molecule can inhibit the accelerator and decrease tumor size in mice. These results were published in The Journal of Clinical Investigation. Dr. Narla hopes to move to a Phase 1 trial in patients soon, but some of his discoveries can already be translated from bench to bedside.

“One of the things we have to decide in patients with cancer is how aggressively we want to treat them,” says Dr. Narla. “If we know their tumor is aggressive, we should treat them with chemotherapy and follow them more closely. If it isn’t, we would spare them the side effects of these drugs, which can cause serious side effects or contribute to the patient’s death. KLF6-SV1 helps tell us that.”