Tapping the body's own defenses, researchers look to cutting-edge gene therapy for bladder cancer

January 10 2012

Bladder cancer, most frequently caused by smoking and exposure to carcinogens in the workplace, is one of the top 10 most common forms of cancer in men and women in the U.S. More than 70 percent of bladder cancers are diagnosed in stage T1 or less and have not invaded the muscle layer. At these early stages, standard treatment is surgery (transurethral resection) and the burning away of tumors with high energy electricity (fulguration). Many patients also may receive subsequent intravesical chemotherapy because there is often a high-risk for cancer recurrence.

The prognosis for recurrent cancer is poor, which drives clinician-scientists like William Larchian, MD, Urologic Oncologist, University Hospitals Urology Institute at University Hospitals Case Medical Center, and Associate Professor of Surgery, Case Western Reserve University School of Medicine, and his colleagues to develop an immunotherapy for bladder cancer that will stimulate the body's own natural defense mechanisms to cure the disease and prevent recurrence.

"What is interesting is that our bodies are capable of identifying, responding to and killing tumor cells naturally," explained Dr. Larchian. "We are developing a vaccination system to enhance this response and drive an effective immune response against existing and future bladder tumor cells in patients diagnosed with bladder cancer."

IL-2, a cytokine-signaling molecule, stimulates the T-cell immune response to cancer cells in the bladder. Dr. Larchian and his colleagues have developed a system that reliably introduces multiple copies of IL-2 DNA into bladder cancer cells.

"This method allows for more gene copies to enter the cells," he said, "and we are able to see higher rates of transfection compared to retroviral methods."

The enhanced IL-2 protein expression has been shown to successfully stimulate T-cell response and eliminate bladder tumors in a mouse model, particularly when followed by transfection with B7.1 gene. The addition of the B7.1 gene, which encodes an immune co-stimulatory molecule, enhanced T-cell production logarithmically and produced a 70 percent cure rate. Rechallenge with new cancer cells was also prevented. Clinical translation of this research has been submitted for Institutional Review Board approval at UH Case Medical Center.

Other research by Dr. Larchian and his colleagues aims to leverage this work to develop a gene-therapy system that can be utilized to deliver other key defense genes.

"Our future pursuits," he said, "will include using this system with very specific biological response modifiers, including anti-angiogenesis factors, and with the tumor suppressor gene, MCP3." Dr. Larchian also is developing a targeted drug delivery system using nanoparticles for bladder cancer treatment.

Provided by University Hospitals Case Medical Center