Pancreatic Cancer Treatment with Lentiviral shRNA (Small Hairpin RNA) Suppresses Cyclin D1 Expression for Tumor Reduction, Anti-Angiogenesis

Technology #j-530

This pancreatic cancer treatment inhibits the expression of the protein cyclin D1 in pancreatic cancer cells. Using a lentivirus-based small hairpin RNA (shRNA) system targeted to cyclin D1, researchers were able to significantly reduce the protein’s levels in pancreatic cancer cells. By injecting a single dose of the lentiviral shRNA directly into pancreatic tumors, researchers were able to slow the growth of pre-existing tumors from two distinct pancreatic cancer cell lines.

The attenuated tumor growth also correlated with a decrease in cell proliferation and levels of the signal protein, vascular endothelial growth factor (VEGF). VEGF encourages angiogenesis, or the growth of new blood vessels and arteries which feed the tumor and allow it to grow.

The most common type of pancreatic cancer, pancreatic ductal adenocarcinoma, is the fourth leading cause of cancer death in the United States. Pancreatic cancer is incredibly difficult to treat successfully because of a number of factors. The cancer is characterized by multiple mutations in the Kras gene, which, in its healthy form, instructs the body to make a protein responsible for regulating cell division. These mutations cause rapid and unregulated cell division, causing the cancer to grow very quickly. This cancer also inactivates several tumor-suppressing genes and shows abnormal upregulation of multiple growth factors blood vessel creation and their related receptors. Pancreatic cancer is also very resistant to chemotherapy. As a result of all these factors, long-term survival of pancreatic cancer is typically limited to patients who have had surgery in the very early stage of the disease.

In vitro tests have shown that this lentivirus-delivered shRNA targeted to the cyclin D1 protein suppresses the growth, invasiveness, tumorigenicity, and pro-angiogenic potential of human pancreatic cancer cells. Intra-tumoral injections of viruses targeting cyclin D1 have the potential to be an effective treatment for the most common form of pancreatic cancer.

Applications

- Treatment of pancreatic ductal adenocarcinoma, the fourth leading cause of cancer death in the United States
- Reduced tumor growth
- Reduced angiogenesis
- Attenuated signal protein expression, preventing the cancer from spreading
Advantages

- Improved survival for later stage pancreatic cancer patients
- Pre-surgical treatment to improve the elimination of the cancer
- Acts on existing tumors to stop their growth and prevent spread of the cancer

Inventors

Dr. Murray Korc, Chair of the Department of Medicine, Adjunct Professor of Medicine, Pharmacology & Toxicology, The Dartmouth Institute

Dr. Korc received his medical degree from Albany Medical College in 1974. He completed training in endocrinology, diabetes, and metabolism at University of California, San Francisco. After teaching and doing cancer research at the University of Arizona and University of California, Irvine, Dr. Korc joined the faculty of Dartmouth School in 2003 as Professor and Chair of Medicine and Professor of Pharmacology and Toxicology. Most of the work in Dr. Korc's laboratory explores aberrant signaling pathways in cancer cells. Studies include signaling by the epidermal growth factor (EGF) receptor, fibroblast growth factor (FGF) receptors, transforming growth factor beta (TGF-b) receptors and vascular endothelial cell growth factor (VEGF) receptors.