Targets Cancerous Cells and Uses Tissue-Specific Promoters to Promote Gene Expression

This gene therapy utilizes rAAV vectors to target metastatic medullary thyroid carcinoma cells, providing a treatment for the highly aggressive form of thyroid cancer. With available treatments, medullary thyroid carcinoma is incurable once metastasized; for example, tyrosine kinase inhibitors provide only palliative, not curative, treatment. While metastatic medullary thyroid carcinoma is a rare form of thyroid cancer, accounting for less than 12 percent of all thyroid cancers, its aggressive nature results in a high mortality rate of 72 percent for stage IV patients. Medullary thyroid carcinoma is treatable if diagnosed early, but is difficult to detect as the condition is rare and relatively symptomless. As a result, medullary thyroid carcinoma often metastasizes.

Researchers at the University of Florida have developed an rAAV vector gene therapy that treats metastatic medullary thyroid carcinoma by targeting the cancerous cells. This gene therapy utilizes unique targeting strategies and tissue-specific promoters. Additionally, this gene therapy can utilize calcitonin promoter/enhancer regions to further provide gene expression in metastatic medullary thyroid carcinoma cells.

Application

Gene therapy that treats metastatic medullary thyroid carcinoma through rAAV vector targeting

Advantages

- Treats targeted cells after medullary thyroid carcinoma cells metastasizes, providing a method of treatment after the aggressive cancer spreads
- Incorporates engineered calcitonin promoter/enhancer regions into the rAAV vectors, further providing specific gene expression in targeted metastatic medullary thyroid carcinoma cells

Technology

Most cases of medullary thyroid carcinoma result in the disease metastasizing; further, current treatments, including the use of tyrosine kinase inhibitors, stop medullary thyroid carcinoma’s progression but do not cure the disease. This gene therapy for metastatic medullary thyroid carcinoma cells uses specific rAAV vectors, targeting strategies, and tissue-specific promoters to treat medullary thyroid carcinoma. In particular, it utilizes particular mutations of rAAV2 vectors, modified to include capsid surface amino acids, to enhance transduction efficiency in targeted cells. The gene therapy combines these mutated rAAV vectors with tissue-specific promoters to target and treat metastatic
medullary thyroid carcinoma cells. It incorporates engineered calcitonin promoter/enhancer regions into the mutated rAAV vectors, resulting in specific gene expression in the targeted metastatic medullary thyroid carcinoma cells.

**Inventors**

**Jacqueline Hobbs M.D., Ph.D.**, is a faculty member in the Department of Psychiatry at the University of Florida. She earned her master's degree and Ph.D. from Indiana University School of Medicine, and completed psychiatry training at Mount Sinai School of Medicine, Indiana University School of Medicine, and the University of Florida. Dr. Hobbs received funding from the Stanley Medical Research Institute, as a resident, to study viral etiologies of schizophrenia.

**Scott Rivkees, M.D.**, is a professor and chairman of pediatrics in the College of Medicine’s Child Health Research Institute at the University of Florida. He earned his M.D. at the University of Medicine and Dentistry of New Jersey, and received postdoctoral training at Massachusetts General Hospital and Harvard Medical School. Dr. Rivkees is a member of the American Thyroid Association Public Health Committee, and is the Chair of the Lawson Wilkins Pediatric Endocrine Society Public Policy Committee.

**Arun Srivastava, Ph.D.**, is a George H. Kitzman professor of genetics and division chief in the Department of Pediatrics at the University of Florida. He serves on an NIH Study section and the editorial boards of many top journals in his field. Dr. Srivastava researches the use of parvoviruses for gene therapy applications and is developing gene therapy for several genetic diseases and malignant disorders.

**Laura Adamson-Small, Ph.D.**, earned her Ph.D. in Microbiology and Immunology from the University of Florida and earned the UF Medical Guild Research Incentive Award in 2010.