# Gene Therapy By The Letters

Researchers at Applied Genetic Technologies Corporation (AGTC), based in UF's Sid Martin Biotechnology Development Incubator, are exploring the use of adeno-associated virus, or AAV, as a vehicle to deliver beneficial genes to critically ill patients.

UF researchers Kenneth Berns and Nicholas Muzyczka pioneered the use of AAV as a vector that could be modified to carry corrective genes into the body. Berns is director of the UF Genetics Institute, and Muzyczka is chairman of the board of AGTC and an eminent scholar in the Department of Molecular Genetics and Microbiology.

AGTC's first product using AAV will treat Alpha-1 Antitrypsin Deficiency, a disease that results in people as young as 25 developing emphysema. Alpha-1 is caused by mutations in a single gene that lead to a reduced level of a protein that normally protects the lungs. Patients feel the current treatment for this disease, a protein product taken by injection, is inadequate.

"Protein replacement patients require weekly IV injections, which are very expensive and painful," says Dr. Terry Flotte, an associate professor of pediatrics, molecular genetics and microbiology in UF's College of Medicine who is conducting clinical trials on the therapy. "Plus, there's been a limited supply of the protein."

The company is also developing products to treat Leber's Congenital Amaurosis, a form of congenital blindness; Pompe's Disease, which causes muscle weakness and death due to heart failure; and Age-Related Macular Degeneration, a form of progressive vision loss in people over 45.

"AAV has all the properties required to treat a chronic disease or a genetic disease, in that it has good efficiency for entering cells, good stability once it gets a gene into the cell, and the gene that gets 'turned on' tends to stay activated as long as the cell is around," says Flotte. "It also has a tremendous safety advantage over other viral gene-transfer vectors."

Unlike some other vectors, AAV has not been linked to any side effects. In fact, an estimated 80 percent of humans live with the virus in their system, with no apparent illness.

**Related web site:**
www.agtcfl.com

*Research scientist David Knop looks over a subculture medium at the laboratory of Applied Genetic Technologies Corp. in Alachua. AGTC is using the adeno-associated virus, or AAV, gene therapy vector developed at UF to pursue genetic cures for emphysema and other diseases.*

*The Gainesville Sun/Rob C. Witzel*