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Nonviral Vectors for the Treatment of Disease

Progress in the use of extruded DOTAP:Cholesterol liposome mediated delivery of nucleic acids in various disease models will be presented. These liposomes condense nucleic acids on the interior of invaginated structures. PCNA (proliferating cell nuclear antigen) targeted ribozymes were developed to inhibit vascular smooth muscle cell proliferation contributing to restenosis. DOTAP:Chol-ribozyme complexes were tested in a porcine stenosis model using a drug delivery catheter in the artery followed by stent placement. Treated arteries showed a significant reduction in percent stenosis compared to saline treated controls. In adult mouse eyes, tissue expression following subretinal injections of E1-deleted adenoviral and DOTAP:Cholesterol encapsulated vectors encoding β -gal showed differences in barrier penetration of these two vector systems. Following adenoviral transduction, gene expression was detected only in retinal pigment epithelial cells adjacent to the delivery site, while injections using liposomes produced expression in the choroid indicating penetration by the complexes of the posterior blood retinal barrier. C3H mice injected intravenously with DOTAP:Chol- β -gal complexes showed high levels of β -gal throughout the lungs at 48 hours post-injection. Intratumoral injections of DOTAP:Chol-p53 DNA liposome complexes were effective for the treatment of human p53 null H1299 subcutaneous tumor xenografts in nude mice. The p53 expression was distributed throughout the tumor which correlated with apoptotic cell death in the tumor cells and suppression of tumor growth. No p53 expression or apoptotic cell death were detected in tumors injected with naked p53 DNA or in untreated control mice. Extruded DOTAP- β -gal complexes transfected 50% of H1299 lung cancer cells in culture. Extruded DOTAP-DNA:liposome complexes transfected H1299 cells and 293 cells more efficiently than FuGENE 6. Other studies suggest that DOTAP:Chol-nucleic acid complexes may be effective for the treatment of HIV-1 related disease.

1973	B.S., City College of the City University, New York, NY
1982	M.S., Genetics and Cell Biology, University of Connecticut, Storrs, CT
1988	Ph.D., Molecular Biology and Biochemistry, Wesleyan University, Middletown, CT
1989-1991	Biotechnology Fellow, Laboratory of Pathology, National Cancer Institute, NIH, Bethesda, MD
1991-1994	Senior Staff Fellow, Molecular Hematology Branch, NHLBI, NIH, Bethesda, MD
1994-1995	Senior Scientist, Megabios Corp., Burlingame, CA
1995-1998	Scientist, NCI-FCRDC, ABL-Basic Research Program, Frederick, MD
1998-present	Assistant Professor, Department of Molecular and Cellular Biology, Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX
Honors	
1972	Awarded Scholarship for Women's Scholars, City College of New York
1973	Graduated Magna Cum Laude, City College of New York
1981-1982	Connecticut State Graduate Student Scholarship, University of Connecticut
1990	National Cancer Institute Officer's Recognition EEO Award, NCI, NIH