Leaf Huang, Ph.D.

Professor
University of Pittsburgh
School of Medicine
Department of Pharmacology
W1351 Biomedical Science Tower
Pittsburgh, PA 15261
United States

1968	B.S. Physics, National Taiwan University, Taipei, Taiwan
1974	Ph.D. Biophysics, Michigan State University, East Lansing, MI
1974-1976	Postdoctorate, Biochemistry/Biophysics, Institution of WA, Baltimore, MD
1976-1991	Assistant Professor, Associate Professor, and Professor, Department of Biochemistry, University of Tennessee, Knoxville, TN
1991-1999	Professor, Department of Pharmacology, University of Pittsburgh, School of Medicine, Pittsburgh, PA
1999-present	The Joseph Koslow Professor of Pharmaceutical Sciences, and Director, Center for Pharmacogenetics, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA

Honors

1981-1986	Research Career Development Award, NIH
1991-1997	Editor-in-Chief, *Journal of Liposome Research*
1997	Fellow, American Association of Pharmaceutcal Scientists
1998-1999	Chairman, Nonviral Gene Therapy Committee, American Society for Gene Therapy
1999-present	Associate Editor, *Gene Therapy*; Associate Editor, *Molecular Therapy*

LPD Nanoparticles for Gene Delivery

We have contributed to the development of the first generation cationic liposome. One such formulation, DC-chol/DOPE liposome, was the first to be tested in human clinical trials in 1992. Like many other similar cationic lipid formulations, DC-chol/DOPE liposome does not condense DNA strongly and tends to aggregate with DNA at high concentrations. Although the formulation is effective for local and regional administration, systemic administration with this type of liposome has proven to be difficult. Further improvement by adding a DNA condensation reagent, such as protamine, has resulted in small (<100 nm) and highly condensed nanoparticles which we named LPD formulation. LPD has a unique structure as revealed by cryo EM. It contains a condensed core, which is surrounded by two lipidic membranes, similar to an enveloped virus. Intravenous administration of LPD causes systemic gene expression, primarily in the lung and spleen. Interestingly, metastatic tumor cells in the lung are also transfected. Using several anticancer genes, including RB and p53, we have demonstrated anticancer activities of the LPD formulation. However, the activity is further augmented by the immune-stimulating CpG motifs in the plasmid DNA, which causes rapid induction of TNF-alpha, gamma-IFN, and other pro-inflammatory cytokines. Such an immune response has significantly contributed to the final anticancer activity by inducing a specific CTL response in the host. Several preclinical gene therapy studies will be discussed.