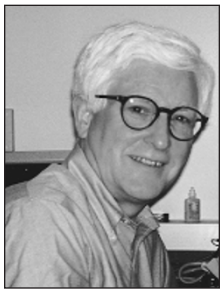
Donald M. McDonald, M.D., Ph.D.



Professor
University of California, San Francisco
Cardiovascular Research Institute and
Department of Anatomy
Box 0452, Room S-1363A
San Francisco, CA 94143-0130
United States

Dr. McDonald is a Professor of Anatomy and Investigator of the Cardiovascular Research Institute at the University of California, San Francisco. He received his M.D. and Ph.D. degrees from UCSF. Dr. McDonald's research focuses on endothelial cell biology in health and disease with an emphasis on angiogenesis and cellular mechanisms of vascular permeability regulation. His interest in cationic liposomes currently emphasizes their uptake by endothelial cells and use as vehicles for delivering diagnostic and therapeutic agents to sites of angiogenesis.

Uptake of Cationic Liposomes by Normal and Angiogenic Endothelial Cells In Vivo

This presentation will examine the uptake of cationic liposomes by endothelial cells. Cationic liposomes, when complexed with plasmid DNA for gene delivery and injected into the bloodstream, do not cross the vascular endothelium in most organs and, therefore, do not have access to cells outside the vasculature. Instead, they are taken up by monocyte/macrophages accessible from the circulation, and they bind to and are internalized by endothelial cells. Although endothelial cells in many organs show little or no uptake of cationic liposomes, those in the lung have avid uptake. In addition, cationic liposomes are avidly taken up by blood vessels of tumors and other sites of angiogenesis.

In addressing the uptake of cationic liposomes by endothelial cells, this presentation will focus on (1) the organ distribution after intraarterial or intravenous injection; (2) the attachment and entry of complexes into endothelial cells; (3) the relation between uptake and transfection as evidenced by reporter transgene expression; and (4) the avid uptake at sites of angiogenesis in tumors and chronic inflammation. These findings have important implications regarding the intravascular delivery of cationic liposome-DNA complexes for gene therapy. For most cationic liposome-DNA formulations, access is limited mainly to endothelial cells, intravascular leukocytes, and macrophages. However, the avid uptake by endothelial cells at sites of angiogenesis raises the possibility of preferential delivery of diagnostic or therapeutic agents to blood vessels in cancer and chronic inflammatory disease.