Abstract Submitted
for the TSF13 Meeting of
The American Physical Society

Proposed Mechanisms of cellular uptake of LDL-DNA complexes[1]

JUAN GUEVARA, TROY MCWHORTER, NATALIA GUEVARA, University of Texas at Brownsville — Low-density lipoproteins, LDL, have been shown to be natural vehicles for transport and delivery of exogenous genetic materials to the cell nucleus. The process involves binding of LDL and nucleic acids, binding of the complex to a receptor, endocytosis, release of complex, and translocation to nucleus. Understanding of LDL function in gene delivery may provide insights into mechanisms of infectious diseases and cancer metastasis. However, it has not been studied extensively, and needs phenomenological description, as well as structural basis. The main focus of this study is to determine the fate of LDL-DNA complexes after cell entry. Using fluorescence microscopy, we confirm three possible outcomes of LDL-DNA endocytosis: an endosome/lysosome fusion, co-transit of LDL and DNA to the nucleus, and dissociation of LDL-DNA complex followed by DNA translocation to the nucleus (perhaps mediated by another DNA carrier). We propose that each step in the delivery process is mediated by Lysine- and Arginine-rich motifs located within nucleic acid-binding domains, receptor ligand motifs, and nuclear localization signal sequences of apo B100 and apo E, characteristic proteins of LDL. Similar motifs are abundant in proteins of Dengue viruses 1-4. Comparison of primary and tertiary structures of these unrelated families of proteins suggests that the mechanisms for LDL-mediated cell entry of DNA are similar to the process utilized by viruses in intracellular delivery of their genetic material.

[1]Supported by NIH grant 5SC3GM099637-03.

Natalia Guevara
University of Texas at Brownsville

Date submitted: 13 Sep 2013 Electronic form version 1.4