Abstract Submitted
for the NEF13 Meeting of
The American Physical Society

Family of pH-Low-Insertion-Peptides (pHLIPs) DHAMMIKA WEERAKKODY, MAK THAKUR, OLEG ANDREEV, YANA RESHETNYAK, University of Rhode Island, BIOLOGICAL AND MEDICAL PHYSICS, URI TEAM — pHLIP (pH (Low) Insertion Peptide) is a novel delivery system for targeting of acidic diseased tissue such as solid tumors, sites of inflammation, arthritis and others pathological states. The molecular mechanism of pHLIP action is based on a pH-dependent insertion and folding of pHLIP in membrane. We performed sequence variation and investigated 16 pHLIP variants with main goals of understanding the main principles of peptide-lipid interactions and tune delivery capability of pHLIP. The biophysical studies including thermodynamics and kinetics of the peptides interaction with a lipid bilayer of liposomes and cellular membranes were carried out. We found that peptides association to membrane at neutral and low pH could be modulated by 3-4 times. The apparent pK of transition from surface bound to membrane-inserted state could be tuned from 6.5 to 4.5. The rate of peptide's insertion across a bilayer could be enhanced 100 times compared to parent pHLIP. As a result, blood clearance and tumor targeting were modulated in a significant degree. The work is supported by NIH grants CA133890 to OAA and YRK.

Dhammika Weerakkody
University of Rhode Island

Date submitted: 13 Sep 2013 Electronic form version 1.4