Abstract Submitted
for the MAR12 Meeting of
The American Physical Society

Targeting tumor acidity YANA K. RESHETNYAK, Physics, University of Rhode Island, DONALD M. ENGELMAN, Mol. Biophys & Biochem., Yale, OLEG A. ANDREEV, University of Rhode Island, URI TEAM, YALE TEAM — One of the main features of solid tumors is extracellular acidity, which correlates with tumor aggressiveness and metastatic potential. We introduced novel approach in targeting of acidic tumors, and translocation of cell-impermeable cargo molecules across cellular membrane. Our approach is based on main principle of insertion and folding of a polypeptide in lipid bilayer of membrane. We have identified family of pH Low Insertion Peptides (pHLIPs), which are capable spontaneous insertion and folding in membrane at mild acidic conditions. The affinity of peptides of pHLIP family to membrane at low pH is several times higher than at neutral pH. The process of peptides folding occurs within milliseconds. The energy released in a result of folding (about 2 kcal/mol) could be used to move polar cargo across a membrane, which is a novel concept in drug delivery. pHLIP peptides could be considered as a pH-sensitive single peptide molecular transporters and conjugated with imaging probes for fluorescence, MR, PET and SPECT imaging, they represent a novel in vivo marker of acidity. The work is supported by NIH grants CA133890 and GM073857 to OAA, DME, YRK.

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Date submitted: 08 Nov 2011 Electronic form version 1.4