

Abstract Submitted  
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**Energy of membrane-associated folding of pHLIP peptide could be used for selective delivery of molecules across membrane of cancer cells and targeting tumors in vivo**<sup>1</sup> ALEXANDER KARABADZHAK, DHAMMIKA WEERAKKODY, MAK THAKUR, MICHAEL ANDERSON, DAYANJALI WIJESINGHE, LAN YAO, JENNIFER DANIELS, SIDA ZHENG, OLEG ANDREEV, YANA RESHETNYAK, University of Rhode Island — We study spontaneous insertion and folding across a lipid bilayer of moderately polar membrane peptide pHLIP - pH Low Insertion Peptide. pHLIP has three major states: soluble in water, bound to the surface and inserted across the bilayer as an alpha-helix. We employ variety of biophysical techniques to reveal steady-state and kinetics thermodynamic parameters for transitions between states. Membrane-associate folding is accompanied with the release of energy, which could be used to translocate cell-impermeable cargo molecules across membrane only at slightly acidic environment, which is a characteristic for various pathological states. We show that pHLIP peptide can translocate cell-impermeable cargo molecules through the membrane in cytoplasm in a pH-dependent manner. Among translocated molecules are fluorescent dyes, toxins and gene regulation agents. In vivo fluorescence imaging was used to demonstrate ability of pHLIP to target acidic tumors with high accuracy.

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