

Abstract Submitted  
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**Membrane Fusion Mediated by pH-Low-Insertion-Peptide (pHLIP)**<sup>1</sup> JENNIFER DANIELS, University of Rhode Island, LAN YAO, Binghamton University, DONALD ENGELMAN, Yale University, OLEG ANDREEV, YANA RESHETNYAK, University of Rhode Island — Liposomes are traditionally used as drug delivery carriers. The major mechanism of liposome entry into cell is endocytotic. First, the endocytotic pathway of cellular entry is non-specific: the delivery of therapeutics occurs to cells in both diseased and healthy tissues. Second, liposomes are usually trapped in endosome/lysosome, which prevents delivery of therapeutics to cytoplasm. We proposed to use pHLIP (pH-Low-Insertion-Peptide) to promote selective delivery of the liposome content to cytoplasm of cancer cells. We showed that liposomes coated with PEG polymer and pHLIP peptide enhance membrane fusion in acidic environments. pHLIP promotes fusion between lipid bilayer of liposome and plasma membrane or membrane of endosome/lysosome, which results in intracellular delivery of payload. Liposomes composed of 5 % pHLIP and 5 % PEG were ideal for the delivery. Since cancer and other pathological states produce an acid extracellular environment, this allows the liposome to target diseased tissue while avoiding healthy tissue (with neutral pH in extracellular space). The work is supported by NIH grants CA133890 to OAA, DME, YRK.

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