



Novel approach for the targeting of acidic tissue: pHLIP – pH (Low) Insertion Peptide

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We found a way to target acidic tissue *in vivo*. Our technology is based on the discovery of a pH (Low) Insertion Peptide (pHLIP™). pHLIP™ is a 35 residues water-soluble membrane peptide that inserts and folds across lipid bilayer in cells or liposomes in response to low pH. Membrane-associated folding of pHLIP™ occurs within seconds and is accompanied by a release of energy (about 2 kcal/mol) that can be used to target acidic tissue *in vivo* and move cell-impermeable cargo-molecules across cellular membranes. pHLIP possesses dual delivery capabilities: it can inject and release cargo molecules into the cytoplasm and/or it can tether cargo molecules to the cell surface. In the first scenario, a cargo molecule is attached to the pHLIP C-terminus via a cleavable S-S bond while in the second it is conjugated to the N-terminus via a non-cleavable bond. Among molecules tethered for the surface of cancer cells *in vivo* are fluorescent dyes, PET and SPECT imaging agents. Fluorescent pHLIP™ can target primary tumors with high accuracy, mark tumor borders and stain millimeter-sized tumor spots and metastatic lesions. The extent of tumor labeling directly correlates with tumor aggressiveness. Among cell-impermeable molecules translocated across a cell membrane are cyclic peptides, toxin – phalloidin and PNAs. Our technology opens the new opportunity to target cancer tumors with high selectivity and decreased side effects.

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Biography

Yana K. Reshetnyak is an Associate Professor at the University of Rhode Island and one of the main inventors of pHLIP-technology together with Profs Andreev and Engelman. She has MS in Molecular Physics from the Saint-Petersburg State University, and Ph.D. in Biophysics in Pushchino, Russian Academy of Science, followed by postdoctoral work in the Cancer Center in Texas, and in Yale. In 2003 a National Science Foundation Award took her to the University of Rhode Island. She is a Laureate of the G. Weber International Competition in Biological Fluorescence. He has published more than 40 papers in reputed journals.