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Targeting of breast tumors by fluorescent pHLIP®s RAMONA ADOCHITE, Physics Department, University of Rhode Island, Kingston, RI, RENATO GUERRIERI, Physics Department, University of Rhode Island, Kingston, RI and Department of Biology, Davidson College, Davidson, NC, ANNA MOSHNIKOVA, OLEG ANDREEV, YANA RESHETNYAK, Physics Department, University of Rhode Island, Kingston, RI — One of the main similarities of all cancer cells, especially metastatic ones, is low pH (pH<6.5) at the surface of their plasma membrane. Low pH triggers protonation of Asp/Glu residues in the moderately-hydrophobic membrane peptides, pHLIP®s (pH (low) insertion peptide), which leads to the increase of peptides hydrophobicity, followed by partition and folding of the peptides into bilayer to adopt stable transmembrane orientation. Thus, membrane-associated pH-dependent folding of pHLIPs allows targeting acidic cancer cells in tumors. Three pHLIP variants (WT, Var3 and Var7), which show difference in interaction with lipid bilayer of membrane, were conjugated with Alexa546 and IR680 fluorescent dyes and injected into mice bearing tumors. NIR fluorescent imaging was performed to monitor tumor targeting and distribution of fluorescent pHLIPs in mice. We demonstrated much better targeting of small (acidic) 4T1 breast tumors compare to big (less acidic) tumors; showed targeting of spontaneously developed breast tumors in the transgeneic mice model; and investigated co-localization of fluorescent pHLIPs and fluorescent 2deoxy-glucose in transgenic mice. The obtained data clearly demonstrate pHLIP's ability to target breast tumors in different breast cancer models including transgenic. The ability of pHLIPs to distinguish acidic and less acidic tumors may provide a new approach for assessing of cancer invasiveness.

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