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Formulation and delivery of lipophilic drugs to cancer cells by pHLIP® coated liposomes

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Extracellular acidity is not only a universal biomarker for carcinoma and several other pathological conditions, but also a significant factor for pathological cell functioning and proliferation. Here, we report how we can exploit this biomarker to design novel, pH-sensitive nanomedicine for therapeutics & diagnostics using pHLIP® technology. We formulated pHLIP® coated small, unilamillar vesicles with high stability and prolong shelf life to deliver hydrophobic agents to disease sites in more effective and safer way. For regular cell functioning, the right balance of ions in intracellular and extracellular spaces is vital. Any alterations done to this vital balance of ions could induce the cell death in both healthy and diseased cells. Apart from the extracellular acidity, the reverse pH gradient (intracellular pHi is higher than extracellular pHe) is another signature for cancerous cells. Here we report a stout mechanism to deliver nano-pores to cancer cells to disrupt the monovalent cation balance and induce apoptosis using pHLIP® coated liposomes. In this work, a gramicidin A is used to form monovalent cation conductive nano-pores. Another example is a delivery of lipophilic antineoplastic chemotherapeutic drug, paclitaxel (PTX), by pHLIP® coated liposomes. New formulation of PTX in pHLIP® coated liposomes shows high efficiency of PTX encapsulation and high stability. We show that PTX could be delivered to various forms of malignant cancers by pHLIP® coated liposomes. In both applications, pH dependent fusion of the liposomes is facilitated by the pH (Low) Insertion Peptide (pHLIP® peptide) attached to the liposomes.

Biography

Mohan C Pereira is a final year Doctoral candidate at University of Rhode Island. He earned his BS from University of Colombo with Physics major and Pure and Applied Mathematics minors. In 2014, he received S Letcher scholarship for his academic and research achievements. His research interests include nanotechnology for medicine, targeted drug delivery and tumor targeting, pHLIP technology, hyperthermia for treatment, fluorescent imaging, radiation physics and physics and mathematics education.

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