

Title	Development of iRGD conjugated semifluorinated nanoassemblies for targeted drug delivery to solid tumors
Keywords (up to 5)	iRGD, semifluorinated polymer, active targeting
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Abstract	The use of small molecule anti-cancer drugs leads to an inevitable side effects on patients due to nonselective properties of the drugs. Development of delivery carriers has been extensively studied to overcome the nonselective properties and also to prolong the blood circulation time of small molecules. We have developed a novel semifluorinated polymer, containing a tri-perfluoro-tert-butyl (PFtB _{TRI}) group as a fluorophilic segment that can be used as carriers in drug delivery systems. ¹ Our previous studies have demonstrated that the use of a fluorocarbon moiety in triphilic copolymers provides enhanced stability to the corresponding self-assembled nanoparticles, thus allowing longer <i>in vivo</i> circulation times. However, the limited accumulation of nanoparticles at the tumor site, through passive targeting (EPR effect), is still a major hurdle for achieving high therapeutic efficiency. We utilized the internalizing RGD (iRGD) peptide, an active targeting ligand, to improve tumor targeting and tissue penetration. The iRGD initially binds to αv integrins and subsequently undergoes proteolytic cleavage exposing a sequence recognized by the neuropilin-1 receptor. This second receptor induces transcytosis with consequent tissue penetration of the nanoparticles to which the iRGD ligand is conjugated. ² The iRGD was successfully conjugated to our semifluorinated triblock copolymer. The self-assembled micelles prepared from iRGD functionalized semifluorinated polymer maintained a small size (~ 15 nm) similar to that of the non-functionalized micelles. Our results demonstrate high encapsulation efficiency, high stability of the micelles, and negligible cytotoxicity of the synthesized semifluorinated polymer. Compared to non-functionalized micelles, iRGD conjugated micelles provided higher accumulation and cytotoxic effects. Studies will be presented on the efficacy of this delivery system on various cell lines.
References	1. Decato, S.; Bemis, T.; Madsen, E.; Mecozi, S., Synthesis and characterization of perfluoro-tert-butyl semifluorinated amphiphilic polymers and their potential application in hydrophobic drug delivery. <i>Polymer chemistry</i> 2014 , <i>5</i> (22), 6461-6471. 2. Sugahara, K. N.; Teesalu, T.; Karmali, P. P.; Kotamraju, V. R.; Agemy, L.; Girard, O. M.; Hanahan, D.; Mattrey, R. F.; Ruoslahti, E., Tissue-penetrating delivery of compounds and nanoparticles into tumors. <i>Cancer cell</i> 2009 , <i>16</i> (6), 510-520.