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Synthesis and evaluation of the targeted binding of RGD-containing PEGylated-PEI/DNA polyplex micelles as radiotracers for a tumor-targeting imaging probe

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Receptor-mediated gene transfer is believed to be of enormous significance in the clinical translation as promising gene delivery technique. Plasmid DNA (pEGFP) and polycations produce polyplexes, which can be proficient probes for molecular imaging when accompanied with gamma emitter. Hence we have demonstrated the physico-biological characterization of a radiotracer for tumor imaging in a HeLa tumor-bearing mouse model. Polyplex micelles were formed with pEGFP and Arg-Gly-Asp (RGD) peptide-modified poly(ethylene glycol)-grafted polyethylenimine (E[c(RGDyK)]$_2$-PEG-g-PEI) and labeled with ^{99m}Tc for *in vivo* study. The sizes and zeta potentials of the PEG-g-PEI/DNA polyplexes were 90-135 nm and 40-50 mV, respectively. The biophysical characterization of pEGFP in polyplexes was evaluated via various methods, including determination of the condensation efficiency of the polymers and the biodistribution, in vitro stability, in vivo application, and kinetics of the radiolabeled polyplexes. The polyplex of PEG-g-PEI/DNA fabricated with a PEG/PEI ratio of 10:1 and N/P=1, i.e., PP10/D, exhibited the lowest cytotoxicity and the highest transfection efficiency. The cyclic-RGD peptide-modified polyplex PEG-g-PEI/DNA (RPP10/D) had significantly higher binding affinity and transfection efficiency than the non-targeting PP10/D did. Through *in vivo* SPECT/CT images, it was determined that RPP10/D-^{99m}Tc presented higher uptake in the tumor than PP10/D-^{99m}Tc at all of the post-injection times studied. We found that the two tracers of radioactive complexes mainly accumulated in the liver, spleen and kidneys at 24 h after intravenous injection in female BALB/c nude mice bearing subcutaneous HeLa tumors. The accumulation of the site-specifically labeled RPP10/D-^{99m}Tc was lower in liver, kidney and spleen compared with non-targeting PP10/D-^{99m}Tc.

Biography

Professor Ging-Ho Hsiue received his B.S. in Chemistry from Nippon University, Japan, in 1963 and his M.Sc. in Polymer Chemistry from Tokyo University, Japan, in 1967. After completion of his Ph.D. in 1972 from Tohoku University, Japan, did a professor assignment at National Tsing Hua University, Hsinchu, Taiwan, ROC from 1973-2009 in the Department of Chemical Enginerring. Then GH Hsiue promoted as a director of the Bioengineering Center (2000), director of the Biomedical Center (2007 - 2009), Dean (2000-2002) and Vice President (2000 -2001) in National Tsing Hua University. Also he won University Distinguished professor awards. After his retairedment from National Tsing Hua University, Ging-Ho Hsiue started to work as emarite professor in Chung Yuan Christian University, Chungli, Taiwan, ROC. His current research interests include polymer synthesis and physical property, shape-based self-assembly, biomedical materials, controlled drug delivery and optical polymeric materials.