Tumor microenvironment-responsive activation of nano delivery systems

Nanostructures such as nanosheets and nanoballs have been studied for delivery of chemical anticancer drugs and oligonucleotides. Graphene-based nanosheets were studied for tumor microenvironment-responsive anticancer drug delivery. The biofunctionalization of graphene-based nanosheets with melittin peptide derivatives of phospholipids selectively activated the release of melittin in tumor microenvironment. The activation of pore-forming melittin in tumor tissues increased delivery of anticancer drug-loaded GNS to tumor cells. Moreover, the overexpression of matrix metalloproteinase (MMP) in tumor microenvironment was used for responsive delivery systems. We designed graphene oxide (GO) nanotheranostics loaded with MMP-activatable image probe derivative and therapeutic peptide. As an MMP-activatable therapeutic model molecule, pore-forming buforin IIb chimeric peptide with GO-anchoring peptide at the end was designed. GO loaded with imaging probe derivative and buforin chimeric peptide did not show fluorescence due to the quenching of the probe by GO. However, in the presence of MMP-2, the surface-modified GO selectively recovered fluorescence by liberating PEG-Cy5.5 conjugate moiety to environment and killing of tumor cells. Moreover, the surface-modified GO did not exert pore-forming activity in the absence of MMP. The MMP-sensitive de-shielding of PEG resulted in the exposure and sequential activation of therapeutic peptide on GO. In SCC7 tumor-bearing xenograft, the surface-modified GO showed the activated recovery of fluorescence at tumor tissues, and greater antitumor effect than other comparison groups. These studies provide the potential of tumor microenvironment-responsive delivery and imaging systems for next generation nanomedicine products.

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Biography
Yu-Kyoung Oh has completed her Bachelor’s and Master’s degrees from Seoul National University and PhD degree from State University of New York at Buffalo in 1994. She obtained Post-doctoral training at Harvard Medical School (1994-1996). Her research interests focus on delivery of chemical drugs and nucleic acid-based drugs using versatile nanobiomaterials. She has published more than 180 papers in reputed journals and has been serving as an Associate Editor for Journal of Controlled Release, and Asian Journal of Pharmaceutical Sciences, and as an Editorial Board Member of Advanced Drug Delivery Review, and Acta Pharmaceutica Sinica B.

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