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Cover Story

Critical role of molecular imaging for substantially improved anticancer therapy

Nanoparticulate drug delivery systems have been used extensively for the development of effective cancer therapy. Despite extensive research efforts, however, there are only a few nanoparticulate formulations that are in clinical use, e.g., Myocet™, Doxil®, and Abraxane® approved by FDA and European Medicines Agency [1]. One of the difficulties in developing effective nanoparticulate formulations has been the lack of clear understanding on the biodistribution of the nanoparticles after intravenous injection. It is well known that nanoparticles injected into the blood will go to the tumor site by the enhanced permeation and retention (EPR) effect. Most of the studies utilizing nanoparticle formulations, however, have not examined the targeting efficiency of the nanoparticles, and thus, precise biodistribution and subsequent therapeutic results in cancer therapy are not known.

In an article by Professor Sang Yoon Kim and his group in this issue used real-time molecular imaging to identify the tumor targeting properties of different nanoparticles [2]. Glycol chitosan (GC) was hydrophobically modified with N-acetyl histidine (NAcHis) to three different extents, 3.3%, 6.8%, and 7.8%, to form NAcHis-GC-1, 2, and 3, respectively. NAcHis-GC self-assembled into nanoparticles for loading of doxorubicin (DOX). NAcHis and doxorubicin were labeled with ^{131}I for non-invasive evaluation of biodistribution in tumor bearing mice. Both NAcHis-GC2 and NAcHis-GC3 formed nanoparticles with a mean diameter of 250–265 nm. On the other hand, NAcHis-GC1, having low degree of NAcHis modification, was water-soluble due to insufficient hydrophobicity. However, NAcHis-GC1 was able to form polymer micelles with a mean diameter of 220–292 nm with encapsulation of DOX (DOX-NAcHis-GC1), presumably due to the increased hydrophobicity by the loaded drug. NAcHis-GC2 and 3 formed more dense nanoparticles with reduced hydrodynamic volume. This result indicates that hydrophobic drug facilitated the formation of self-assembled nanoparticles and induced dense hydrophobic core.

Professor Kim and his group made a very interesting observation when they compared tumor targeting properties of bare nanoparticles. The apparent NAcHis-GC concentration in tumor tissues was much higher in mice administered with NAcHis-GC3 than in those receiving NAcHis-GC1 after 3 days. This is understandable, since NAcHis-GC1 did not form micelles and stayed in liquid form at pH 7.4, it resulted in low tumor specific accumulation possibly due to the absence of the EPR effect. However, NAcHis-GC3 nanoparticles circulated in the blood stream and clearly delineated the tumor against surrounding tissues, thereby showing the highest tumor targeting efficiency. The interesting observation here is that DOX-NAcHis-GC1 showed a higher tumor targeting efficiency than DOX-NAcHis-GC3 in mice. The biodistribution of drug-loaded nanoparticles (DOX-NAcHis-GC) is opposite of what one can expect from that of bare nanoparticles (NAcHis-GC).

The study by Professor Kim and his group clearly demonstrated using the scintigraphic imaging method that bare nanoparticles and drug-loaded nanoparticles have markedly different biodistribution profiles, and thus, different abilities to deliver a drug to the tumor tissues. It is common that the formulation scientists do not consider using polymers that do not form micelles in the absence of a drug. But it seems that those are the ones we should make for drug loading. The exact mechanisms of the increased tumor targeting efficiency and biodistribution of GC with low extent of hydrophobic modification need to be understood, but the observation provides a new way of preparing polymeric micelles for tumor targeting.

References

[1] L. Zhang, F.X. Gu, J.M. Chan, A.Z. Wang, R.S. Langer, O.C. Farokhzad, Nanoparticles in medicine: therapeutic applications and developments, Clin. Pharmacol. Ther. 83 (2008) 761–769.

[2] B.S. Lee, K.S. Park, S.J. Park, G.C. Kim, H.J. Kim, S.J. Lee, H.S. Kil, S.J. Oh, D.Y. Chi, K.M. Kim, I.C. Kwon, S.Y. Kim, Tumor targeting efficiency of bare nanoparticles does not mean the efficacy of loaded anticancer drugs: importance of radionuclide imaging for optimization of highly selective tumor targeting polymeric nanoparticles with or without drug, J. Control. Release. 147 (2010) 253-260.

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