Journal of Controlled Release 155 (2011) 343

Contents lists available at SciVerse ScienceDirect

Journal of Controlled Release

journal homepage: www.elsevier.com/locate/jconrel

Cover Story

Shockwave-ruptured nanopayload carriers (SHERPAs) for ultrasound-triggered drug release

Effective drug delivery to the target sites requires a few important properties, such as long circulation time, extravasation, and localized drug release. The properties that convey long circulation times to drug delivery vehicles are not often the properties that allow efficient passage through cell membranes. A multi-layer approach can help address this challenge where the outer layers of the vehicle convey long circulation properties and the inner payloads have efficient cellular penetration. This requires the triggered removal of that outer layer once the vehicle reaches the desired location. In the case of cancer therapy, a major challenge is to find a reliable and predictable trigger that is tumor specific. The low biochemical contrast between tumor and healthy tissue causes either low activation efficiency of vehicles that pass through the tumor, or uncontrolled activation in non-tumor tissue. For a vehicle to be triggered with true tumor specificity there must be a substantial and predictable difference between the tumor and the healthy tissue. A high contrast triggering option is to artificially highlight the tumor using low intensity ultrasound.

Ultrasound has been used effectively for improving drug deposition at specific sites of the body. Ultrasound can be focused efficiently into deep tissue and deposit usable amounts of energy into small focal volumes. This energy can be used to rupture microbubbles, generating heat as well as mechanical force in a noninvasive way [1]. These triggered reactions occur only within the small focal region, and such focused ultrasound has been used for enhanced extravasation of drugs [2,3]. However, microbubbles by themselves can only carry a very limited amount of payload and are fragile structures. Thus, microbubbles are either coated with drug-loaded liposomes [4,5] or incorporated into the lipid bilayer of a liposome [6]. The microbubble will act as an ultrasound antenna and undergo size oscillations to mechanically release the encapsulated drug from these structures and enhance delivery. This can be done while keeping the ultrasound intensity below levels that would cause excessive tissue heating or damage.

A new spin on the use of microbubbles has been demonstrated in this issue by encapsulating them inside the aqueous space of drug loaded liposomes [7]. This new method of microbubble encapsulation creates a stable structure that fragments only in the ultrasound focal zone causing a burst release of contents. Since the outer membrane is destroyed the entire contents of the vehicle is released all at once with forceful jet-like patterns. A sequence of images showing this jet shooting out from the main debris cloud resulting from microbubble cavitation was captured by Dr. Ibsen and his coworkers for the first time (middle row of the cover figure). The nested design guarantees the colocalization of the microbubble with the liposome at all times ensuring each liposome will be activated. This triggerable vehicle simultaneously shields healthy tissue from the cell penetrating payload while shielding the payload from the immune system. This creates a platform that can be optimized for circulation time and can carry a wide array of highly efficient cell penetrating payloads. The approach described by Dr. Ibsen and his team presents a new dimension to targeted drug delivery.

References

[1] R. Deckers, C.T.W. Moonen, Ultrasound triggered, image guided, local drug delivery, J. Control. Release 148 (2010) 25–33.
[2] M.R. Böhmer, C.H.T. Chlon, B.I. Raju, C.T. Chin, T. Shevchenko, A.L. Klibanov, Focused ultrasound and microbubbles for enhanced extravasation, J. Control. Release 148 (2010) 18–24.
[3] C.-Y. Lin, T.-M. Liu, C.-Y. Chen, Y.-L. Huang, W.-K. Huang, C.-K. Sun, F.-H. Chang, W.-L. Lin, Quantitative and qualitative investigation into the impact of focused ultrasound with microbubbles on the triggered release of nanoparticles from vasculature in mouse tumors, J. Control. Release 146 (2010) 291–298.
[4] A.L. Klibanov, T.I. Shevchenko, B.I. Raju, R. Seip, C.T. Chin, Ultrasound-triggered release of materials entrapped in microbubble-liposome constructs: a tool for targeted drug delivery, J. Control. Release 148 (2010) 13–17.
[5] B. Geers, I. Lentacker, N.N. Sanders, J. Demeester, S. Meairs, S.C. De Smedt, Self-assembled liposome-loaded microbubbles: the missing link for safe and efficient ultrasound triggered drug-Delivery, J. Control. Release 152 (2011) 249–256.
[6] K.D. Buchanan, S.-L. Huang, H. Kim, D.D. McPherson, R.C. MacDonald, Encapsulation of NF-κB decoy oligonucleotides within echogenic liposomes and ultrasound-triggered release, J. Control. Release 141 (2010) 193–198.
[7] S. Ibsen, M. Benchimol, D. Simberg, C. Schutt, J. Steiner, S. Esener, A novel nested liposome drug delivery vehicle capable of ultrasound triggered release of its payload, J. Control. Release 155 (2011) 358–366.

Kinam Park
Purdue University, Departments of Biomedical Engineering and Pharmaceutics, West Lafayette, Indiana, USA
E-mail address: kpark@purdue.edu

0168-3659/$ – see front matter
doi:10.1016/j.jconrel.2011.09.073