Development of a Drug Encapsulated Micelle Loaded Photoresponsive Platform for the Treatment of Coronary Stenosis

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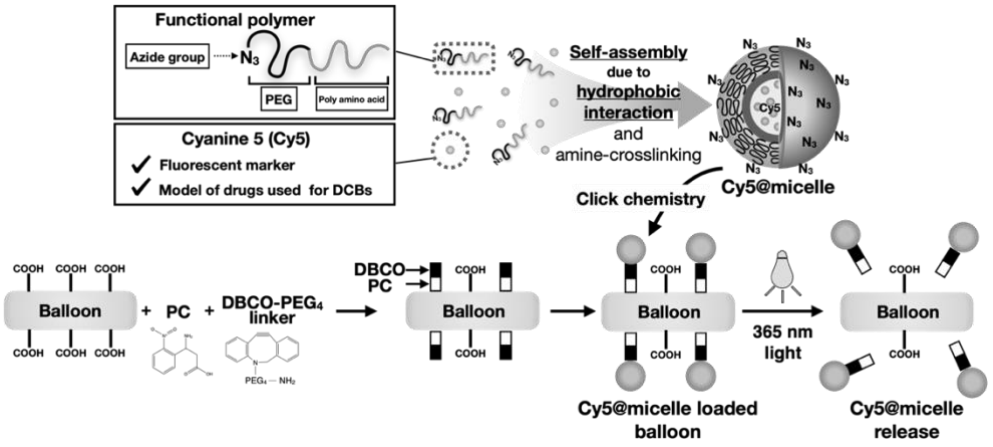
Drug coated balloon (DCB) has been attracting attention as a medical device for the treatment of coronary stenosis. However, with conventional DCBs, a large portion of the initially loaded drug were washed off from the balloon due to blood stream and another large portion remained on the balloon after delivery, which resulted in only about 1.4% of the initially loaded drug to reach the stenosis.[1] Past work has been conducted to enhance drug delivery efficiency by incorporating a photocleavable (PC) linker to covalently bond drugs onto balloon surface then initiate release through light irradiation.[2] However, because this platform required drug to be covalently conjugated onto the PC linker, drug denaturation could decrease its medicinal effect. To prevent this problem, we proposed to encapsulate drugs into micelles and load them onto balloons while preserving their photoresponsivity.

We fabricated a photocleavable linker, Azadibenzylcyclooctyne-PEG_4-3-amino-3-(2-nitrophenyl) propanoic acid (DBCO-PEG_4-ANP) and conjugated this onto the carboxyl group on the surface of medical balloons. Note here that ANP is a photocleavable group that cleaves in reaction to 365 nm light. We then fabricated azide (N_3) functionalized Cy5-micelle and conjugated this onto the linker. For initial evaluation, micelle load and photoresponsivity of the platform were validated via wettability measurement and fluorescent microscopy, respectively. The results of wettability and fluorescent microscopy showed that Cy5-micelles were successfully loaded onto the balloons at approximately 3.8×10^{-2} ug/mm^2 and also showed 80% release in event of light irradiation (365 nm, 360 mW/cm^2, 1 min.). Thus, we concluded that the proposed photocleavable platform has the potential to realize topical drug delivery with unprecedented efficiency.



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