# Smart materials for cardiovascular disease therapy

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Cardiovascular disease (CVD) remains the main cause of death worldwide. Novel therapeutics are urgently needed to deliver drugs to unstable atherosclerotic plaques as the underlying cause of CVD. More targeted approaches are also required to treat patients in an emergency (myocardial infarction and stroke) when therapeutics are ideally administered directly in the ambulance to prevent loss of vital tissue. However, the significant adverse effects of current drugs such as bleeding complications are major hurdles to overcome. Nanomedicine plays an increasingly important role in the development of smart and responsive therapies for CVD.

Unstable plaque rupture is responsible for more than two-thirds of fatal myocardial infarctions and the majority of strokes. Matrix metalloproteinase (MMP) 14, a membrane-type MMP, has been associated with plaque rupture and plays a pivotal role in activating collagen degradative activity of several other MMPs. To inhibit MMP 14, we have developed targeted 100 nm nanosponges by a metal catalyst polymerisation method and loaded them with the specific blocker Naphthofluorescein. The particles were functionalised with a collagen-binding peptide, an activatable cell-penetrating peptide to facilitate cell entry and a Cy3 dye for detection. Our novel construct has an immense translational potential for biologic drug development to stabilise the structural integrity of human plaques to prevent rupture-induced acute thrombosis.

In the event of a ruptured plaque, fast delivery of anticoagulants and/or thrombolytics using nanoparticles can restore blood flow and oxygen supply to affected tissues. We have exploited key biomechanical features specific to thrombosis such as increased blood shear stress and the presence of the pro-coagulant enzyme thrombin to achieve site-directed delivery of drugs. We demonstrated that shear-sensitive phosphatidylcholine based nanocapsules can deliver anti-thrombotic drugs and inhibit thrombus formation selectively under stenotic and high shear flow conditions while leaving thrombus formation under physiologic shear rates unaffected. Furthermore, we have developed state-of-the-art carriers that can deliver thrombolytic drugs such as plasminogen activators and that responds to the thrombus microenvironment to initiate thrombolysis. Our non-invasive and effective agent holds great promise for major progress towards a novel therapy for a large number of patients suffering from thrombotic diseases.

In conclusion, modern nanomedicine is increasingly been used in the CVD field to tackle some of the most pressing therapeutic challenges: the stabilisation of atherosclerotic plaques that are prone to rupture as well as delivery of potent clot busters in a more targeted way with reduced adverse effects. Future success in this area has the potential to benefit many patients with some of the most devastating CVD conditions.

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