Controlled intramyocardial release of engineered chemokines by biodegradable hydrogels as a treatment approach of myocardial infarction.

Myocardial infarction (MI) induces a complex inflammatory immune response, followed by the remodelling of the heart muscle and scar formation. The rapid regeneration of the blood vessel network system by the attraction of hematopoietic stem cells is beneficial for heart function. Despite the important role of chemokines in these processes, their use in clinical practice has so far been limited by their limited availability over a long time-span in vivo. Here, a method is presented to increase physiological availability of chemokines at the site of injury over a defined time-span and simultaneously control their release using biodegradable hydrogels. Two different biodegradable hydrogels were implemented, a fast degradable hydrogel (FDH) for delivering Met-CCL5 over 24 hrs and a slow degradable hydrogel (SDH) for a gradual release of protease-resistant CXCL12 (S4V) over 4 weeks. We demonstrate that the time-controlled release using Met-CCL5-FDH and CXCL12 (S4V)-SDH suppressed initial neutrophil infiltration, promoted neovascularization and reduced apoptosis in the infarcted myocardium. Thus, we were able to significantly
preserve the cardiac function after MI. This study demonstrates that time-controlled, biopolymer-mediated delivery of chemokines represents a novel and feasible strategy to support the endogenous reparatory mechanisms after MI and may compliment cell-based therapies.