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Positively Influencing Cardiac Wall Remodeling After Myocardial Infarction: Materials Designed to Apply the Brakes When Speeding Down a Deadly Road

Abstract: Myocardial infarction commonly triggers a remodeling response in the ventricular wall that functionally leads to end-stage ischemic cardiomyopathy (heart failure). The remodeling pathology, which is complex and occurs over weeks to months, is characterized at the chronic phase by a thinned, scar-rich wall in the region of the infarct and a dilated ventricle. The primary treatment options for patients that are in advanced stages of this organ failure are currently cardiac transplantation and mechanical circulatory support. Over the past two decades numerous strategies have been developed using biomaterial-based interventions early in the post-MI period to alter or slow the course of ventricular remodeling, and thus to alter the path towards deteriorating cardiac function. In our laboratory we have been pursuing two general intervention approaches that have centered on two distinct synthetic polymer-based strategies. In the first, the thermoresponsive behavior of N-isopropylacrylamide (NIPAAm)-based addition polymers is used to design injectable hydrogels that undergo a reversible sol-gel phase change between ambient and body temperature, allowing hydrogel injection in and around the infarct region for temporary mechanical support. In the second approach, polyurethane ureas incorporating labile soft-segments are solvent processed to form porous circular patches that are applied over the infarct to provide temporary mechanical support. In both cases the polymer design strategy can be tuned to meet hypothesized desired mechanical, biological and chemical properties. In pre-clinical models both of these interventions have shown an ability to alter the pathway of ventricular wall remodeling and to preserve cardiac function.