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Immunomodulation of Cardiac Macrophages by Phosphatidylserine-Presenting Liposomes Preserves Chamber Size after Myocardial Infarction in Rat

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A major challenge in modern cardiology is to optimize infarct healing and repair after myocardial infarction (MI). The common outcome after MI is scar formation and reduction in heart contractility, which are the final stages of an inflammatory event cascade. Primary players in this process are macrophages (MΦ) which constitutes classically-activated, pro-inflammatory MΦ (M1) and alternatively-activated, anti-inflammatory MΦ (M2). Here, we tested a novel hypothesis that manipulating MΦ on site, using phosphatidylserine (PS)-presenting liposomes to control excessive inflammation, would minimize MI-induced damages. This approach mimics natural body mechanism of clearing apoptotic cells by MΦ, while altering them into their anti-inflammatory phenotype.

Methods and Results

Rats (SD) underwent MI and 48h later were injected via the femoral vein with PS-presenting liposomes (10μmol/300μL; n=5) containing iron oxide (2mg/mL) or saline (n=3). Four days later, MRI and immunohistology revealed that MΦ, accumulated at the infarct, engulfed the PS-presenting liposomes. In functional experiments, rats were subjected to MI and 48h later were injection via the femoral vein with PS-presenting liposomes (10μmol/150μL; n=10), PS-lacking liposomes (10μmol/150μL; n=10) or saline (150μL; n=10). Echocardiography was performed 24h and 4 weeks after MI. Expansion index (0.59, 0.81 and 1.43; p=0.0037) and scar thickness (0.65, 0.59 and 0.33; p=0.007) as well as left ventricle end systolic (p=0.096) and diastolic (p=0.004) areas were significantly improved in PS-presenting liposomes-treated rats compared to PS-lacking liposomes or saline. Additionally, PS-presenting liposomes-treated rats showed greater vessel density compared to PS-lacking liposomes or saline (51, 35 and 31 #/mm2; p=0.037).

Conclusions

Our findings suggest that uptake of PS-presenting liposomes contribute to the healing process modification after MI. These favorable effects may be related to activation of reparative MΦ (M2).