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StemBell therapy stabilizes atherosclerotic plaques after myocardial infarction

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Background: After myocardial infarction (MI) atherosclerosis is accelerated leading to increased intraplaque inflammation and destabilization. This increases the risk for a second MI. Because of their immunomodulating properties, mesenchymal stem cells (MSC) are a promising therapeutic option for atherosclerosis. Previously, we demonstrated that complexing adipose tissue MSC to microbubbles (termed StemBells) in combination with ultrasound, increased their therapeutic potential after MI.

Purpose: In this study we aim to investigate the effect of StemBell therapy on atherosclerotic plaques in atherosclerotic mice after MI.

Methods: MI was induced in atherosclerotic Apolipoprotein E-deficient mice that were fed a high-fat Western diet for 10 weeks. Six days post-MI, the mice received either 5x10^5 StemBells or vehicle intravenously, followed by 1 minute of transthoracal ultrasound. The effects of StemBell treatment on the size and stability of aortic root atherosclerotic plaques and the infarcted heart were determined 28 days post-MI via (immuno)histological analyses. Moreover, monocyte subtypes and lipids in the blood were studied.

Results: StemBell treatment significantly increased cap thickness, decreased intra-plaque macrophage density and increased the percentage of intra-plaque anti-inflammatory macrophages. Plaque size and serum cholesterol and triglycerides were not affected. Furthermore, StemBell treatment significantly increased the percentage of anti-inflammatory macrophages within the infarcted myocardium, but did not affect cardiac function nor infarct size. Finally, the percentage of anti-inflammatory monocytes in the circulation was increased after StemBell therapy.

Conclusion: Systemic StemBell therapy led to decreased plaque inflammation and a more stable plaque morphology. These effects appeared to associate predominantly with local and systemic effects on macrophages/monocytes. Hence, StemBell therapy may be a therapeutic option to prevent atherosclerosis acceleration after MI.