Macrophage-derived osteopontin is fragmented by MMP-9 to hinder angiogenesis in the post-myocardial infarction left ventricle

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sound to assess aortic stiffness and PET/computed tomography (CT) with 18F-NaF to assess calcification severity. Thereafter, 8 animals were subsequently treated with local delivery of a mixture containing 500 μg zoledronate that was delivered on the cusps of the aortic valve, by a dedicated balloon catheter.

A placebo mixture was administered on the rest 8 animals (control group). At 28 days all animals underwent a follow-up cardiac imaging with PET-CT 18F-NaF. The progression of calcification was assessed by calculating the difference in SU Vmax, SU Vmean, TBRmax and TBR mean at baseline and at follow up both for AV and ascending aorta (AA).

Results: Baseline, all animals developed aortic valve stenosis with severe calcification. No differences regarding AVA were recorded between both groups. (21.37±1.76 vs 21.98±3.12, p=0.53). In all animals the local delivery of zole-
dronate and placebo mixtures was successful and uncomplicated. A total of 48 cusps were histologically examined. The cusps treated with zoledronate had significantly lower expression of calcium content compared to the cusps of the placebo group (16.40±0.90 vs 24.88±1.90% of the area, p<0.001), whereas the ascending aortas of both groups showed similar expression of calcium content (23.58±4.43 vs 23.12±5.05% of the area, p=0.78). Regarding PET/CT analysis, in the zoledronate group, TBRmax and TBRmax at the level of AA showed a significant increase of calcification during follow up (1.31±0.11 versus 1.63±1.84, p<0.001 and 1.42±0.11 versus 1.64±0.20, p<0.001). In the same group TBRmax and TBRmax at the level of AA showed a significant increase of calcification during follow up (1.31±0.11 versus 1.63±1.84, p<0.001 and 1.42±0.11 versus 1.64±0.20, p<0.001).

Purpose: The aim was to determine the biological function of the MMP-9 generated OPN fragment peptides upstream and downstream of the cleavage site.

Background/Introduction: Extracellular matrix (ECM) turnover is a key event during remodeling of the left ventricle (LV) following myocardial infarction (MI). Turnover includes ECM degradation of existing ECM to remove necrotic myocytes and synthesis to produce new ECM to form the intact scar. Matrix metalloproteinases (MMPs) are elevated post-MI, and MMP-9 has a strong link to post-MI heart failure. MMP-9 is expressed in the left ventricle during remodeling of the left ventricle (LV) following myocardial infarction (MI). MMP-9 regulates extracellular matrix turnover, cell migration and invasion, proliferation and angiogenesis. MMP-9 is also implicated in atherosclerosis, sepsis and cancer.

Results: Our results demonstrated that in vivo post-MI, MMP-9 increased coronary artery calcification (CACS) and total aortic calcification (TAC) in aortic valves. MMP-9 levels were elevated post-MI, and MMP-9 levels were positively correlated with CACS and TAC. MMP-9 levels were higher in the late H2 group compared to the early H2 group. MMP-9 levels were also higher in the late H2 group compared to the control group. MMP-9 levels were higher in the late H2 group compared to the early H2 group. MMP-9 levels were also higher in the late H2 group compared to the control group.