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Secretome of Apoptotic Peripheral Blood Cells (APOSEC) Attenuates Microvascular Obstruction in a Porcine Acute Myocardial Infarction Model: Role of Platelet Aggregation and Vasodilation

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Objective:
Our group has recently found that paracrine factors secreted from apoptotic peripheral blood mononuclear cells (APOSEC) attenuate the size of acute myocardial infarction (AMI). The aim of this study was to determine the influence of APOSEC on microvascular obstruction (MVO) in a porcine AMI model.

Methods and Results:
Treatment of AMI with cell culture supernatants derived from irradiated apoptotic peripheral blood mononuclear cells (APOSEC) resulted in a significantly improved microvascular perfusion (Myocardial blush grade: 1.3±0.3 vs. 2.5±0.3; p=0.033). Platelet activation markers (P-selectin, CD40L, PF-4, TSP-1) were reduced in plasma samples, suggesting an anti-aggregatory capacity of APOSEC. This finding was confirmed by *in vitro* tests showing significantly impaired aggregation of APOSEC treated platelets, paralleled by vasodilator-stimulated phosphoprotein-mediated inhibition. In addition, APOSEC evidenced a significant vasodilatory capacity of coronary arteries. HUVECs co-incubated with the compound upregulated iNOS expression. Treatment of isolated coronary arterial segments with APOSEC resulted in a dilation of the vessels in a dose dependent manner (APOSEC from $5*10^5$ cells: 23% dilation; $1*10^6$: 26%; $5*10^6$: 34%).

Conclusion:
Our data give first evidence that APOSEC reduces the extent of MVO during AMI. This explains the improved long-term outcome after APOSEC treatment in AMI as previously described.