COMPARISON OF VARIOUS NICHES FOR ENDOTHELIAL PROGENITOR CELL THERAPY ON ISCHAEMIC MYOCARDIAL REPAIR: COEXISTENCE OF HOST COLLATERALISATION AND AKT-MEDIATED ANGIOGENESIS PRODUCES A SUPERIOR MICROENVIRONMENT

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Objectives Comparative studies are lacking that show the effects of different micro environments on the activity of engrafted stem cells after myocardial infarction (MI). Here, we analysed the temporal and spatial variations of angiogenesis, collateralisation, and the expression of Akt-related signals after MI to test if the effects of endothelial progenitor cells (EPCs) were different.

Methods and Results After the induction of MI, pigs were selected that did not develop a collateral coronary circulation (CCC; R0) or developed a significant CCC (R2). Both sets were allocated randomly to four groups: PBS (intramyocardial [i.m.] injection of PBS); Tx (EPC transplantation); LY294002 (i.m. injection of an Akt inhibitor); and EPCs plus LY294002. Infarcted porcine hearts under different time-points and collateralised conditions exhibited a variety of vascular microenvironments. At 14 d post-MI, angiogenesis and the expression of Akt-mediated angiogenic cytokines predominated in R2 porcine hearts. When grafted into this microenvironment, EPCs induced the greatest effects in impeding the development of heart failure, preserving LV function and dimensions, and inhibiting infarct expansion. LY294002 significantly reduced these effects.

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Conclusions These findings suggest that the microenvironment that coexists with collateralisation and Akt-mediated angiogenesis appears to be more beneficial to cardiac repair induced by EFC therapy than other niches after MI.