Combined cord blood stem cells and gene therapy enhances angiogenesis and improves cardiac performance in mouse after acute myocardial infarction

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摘要

Abstract

BACKGROUND: Gene and stem cell therapies hold promise for the treatment of ischaemic cardiovascular disease. However, combined stem cell and angiogenic growth factor gene therapy for acute ischaemic myocardium has not been previously reported. This study hypothesized that combined stem cell and gene therapy would not only augment new vessels formation but also improve myocardial function in acute ischaemic myocardium. METHODS: Human angiopoietin-1 (Ang1) cDNA and VEGF(165) cDNA were ligated into AAV vector. The purified CD34(+) cells were obtained from human umbilical cord blood samples. Cord blood CD34(+) cells were transduced with AAV vector encoding either the human Ang1 (AAV-Ang1) or VEGF(165) (AAV-VEGF) cDNA alone, or both (AAV-Ang1 plus VEGF). Immediately after ligation of the left anterior descending coronary artery in male SCID mice, culture-expanded CD34(+) cells transduced with AAV-Ang1, AAV-VEGF or AAV-Ang1 plus VEGF were injected intramyocardially at the left anterior free wall. RESULTS: Western blot showed that Ang1 and VEGF protein expressions were enhanced in the CD34(+)cells transduced with AAV-Ang1 and AAV-VEGF, respectively. Infarct size significantly decreased and capillary density significantly increased after treatment with CD34(+)/AAV-Ang1 plus VEGF when compared with treatment by CD34(+) only. Combined therapy with CD34(+) and AAV-Ang1, CD34(+) and AAV-VEGF, CD34(+) and AAV-Ang1 plus VEGF, all showed significantly higher cardiac performance in

echocardiography than the therapy with CD34(+) alone 4 weeks after myocardial infarction. CONCLUSIONS: Combined therapy with human umbilical cord blood CD34(+) cells and both Ang1 and VEGF genes reduced infarct size, attenuated the progression of cardiac dysfunction and increased capillary density in acute myocardial infarction in mice.