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STABLE MYOCARDIAL-SPECIFIC LENTI-S100A1 GENE THERAPY RESULTS IN HEART FAILURE AFTER MYOCARDIAL INFARCTION RESCUE

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Objectives The incidence of heart failure after myocardial infarction is ever-growing, and it is urgent to develop improved treatments. An attractive approach is gene therapy; however, the clinical barrier has yet to be broken because of several issues, including the lack of an ideal vector supporting safe and long-term myocardial transgene expression.

Methods Here, we show that the use of a Lentiviral vector (Lenti-Here, we show that the use of a Lentiviral vector (Lenti-S100A1) containing a novel cardiac-selective enhancer/promoter element can direct stable cardiac expression of a therapeutic transgene, the calcium (Ca^{2+})-sensing S100A1, in a rat model of heart failure after myocardial infarction.

Results The heart failure-rescuing properties of myocardial S100A1 expression, the result of improved sarcoplasmic reticulum Ca^{2+} handling, included improved contractile function and left ventricular remodelling. Adding to the clinical relevance, long-term S100A1 therapy had unique and additive beneficial effects over β -adrenergic receptor blockade, a current pharmacological heart failure unique and additive beneficial effects over treatment.

Conclusions These findings demonstrate that stable increased expression of S100A1 in the failing heart can be used for long-term reversal of LV dysfunction and remodelling. Thus, long-term, cardiac-targeted Lenti-S100A1 gene therapy may be of potential clinical utility in human heart failure.