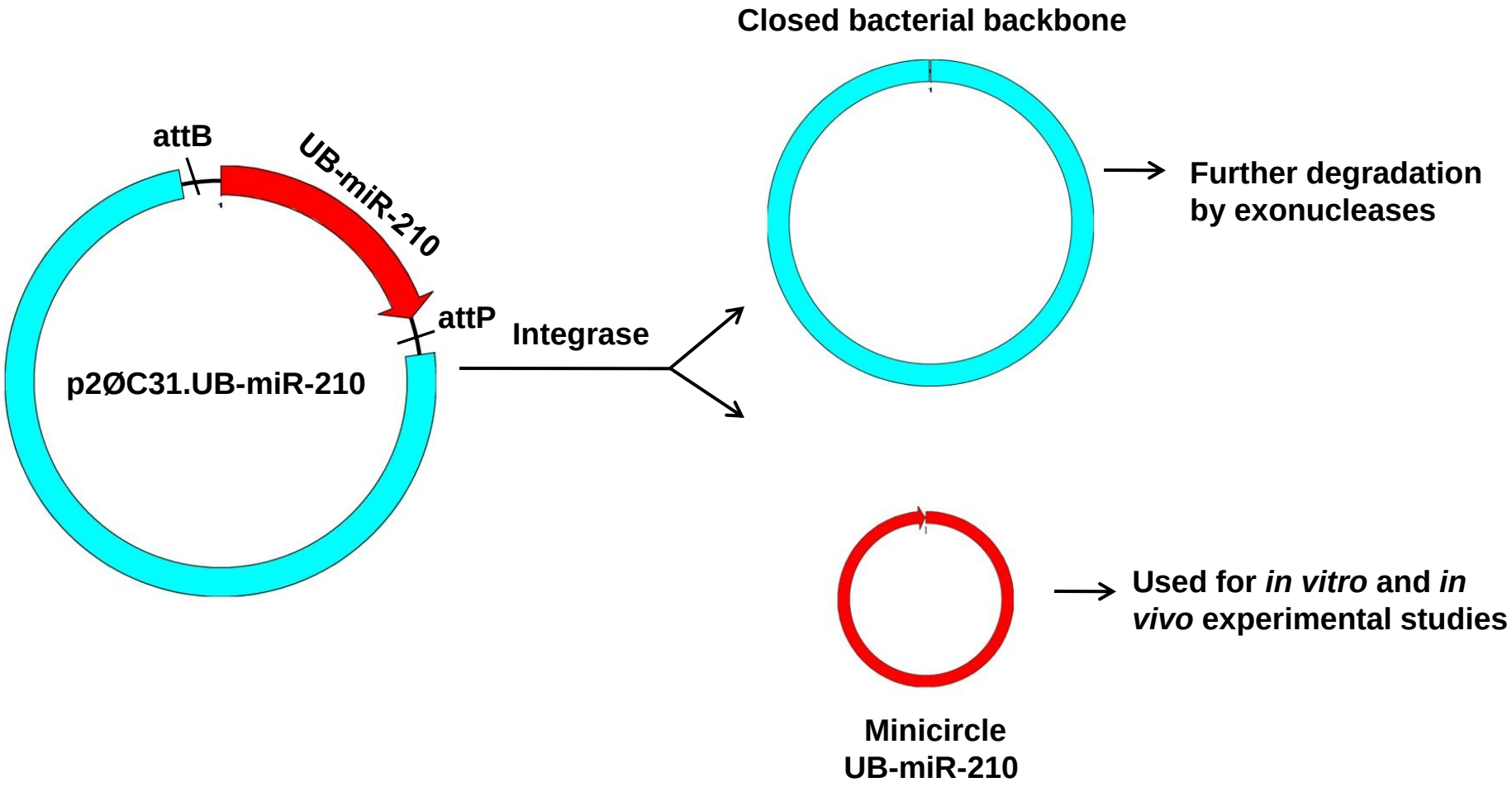
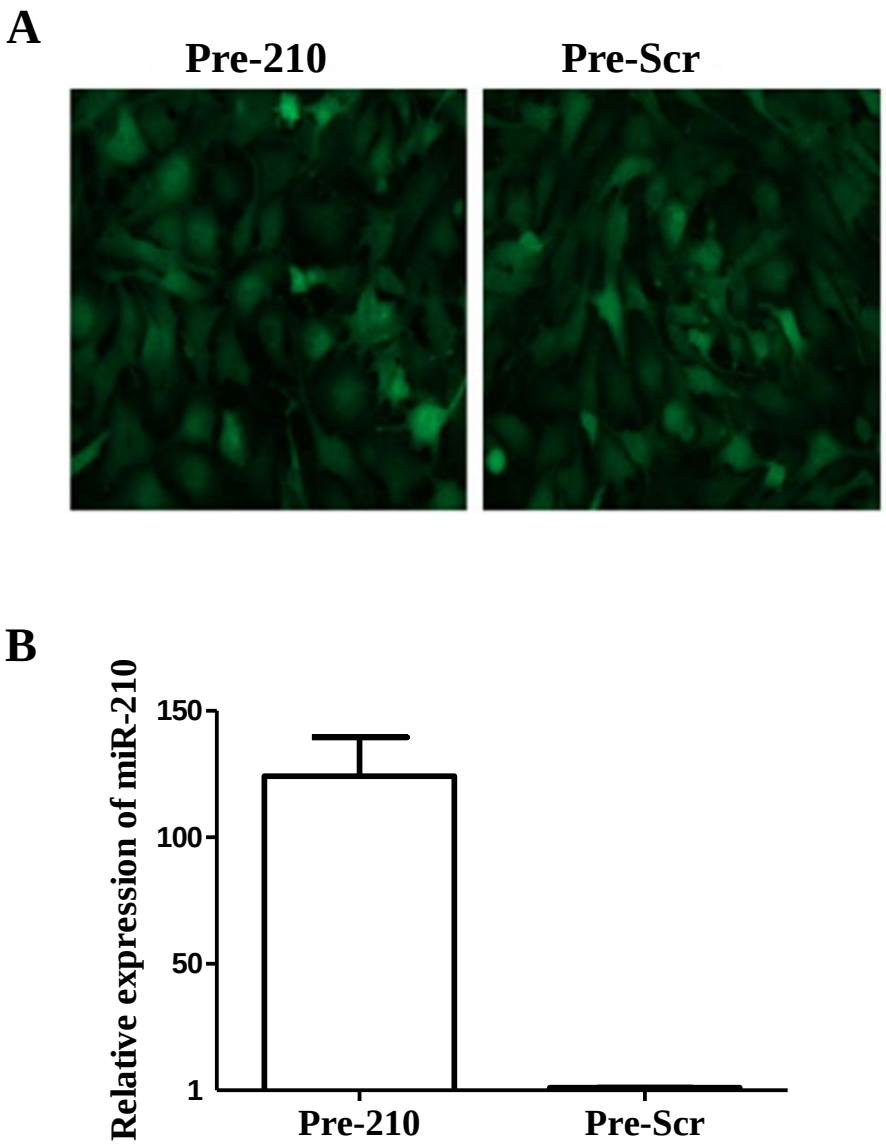
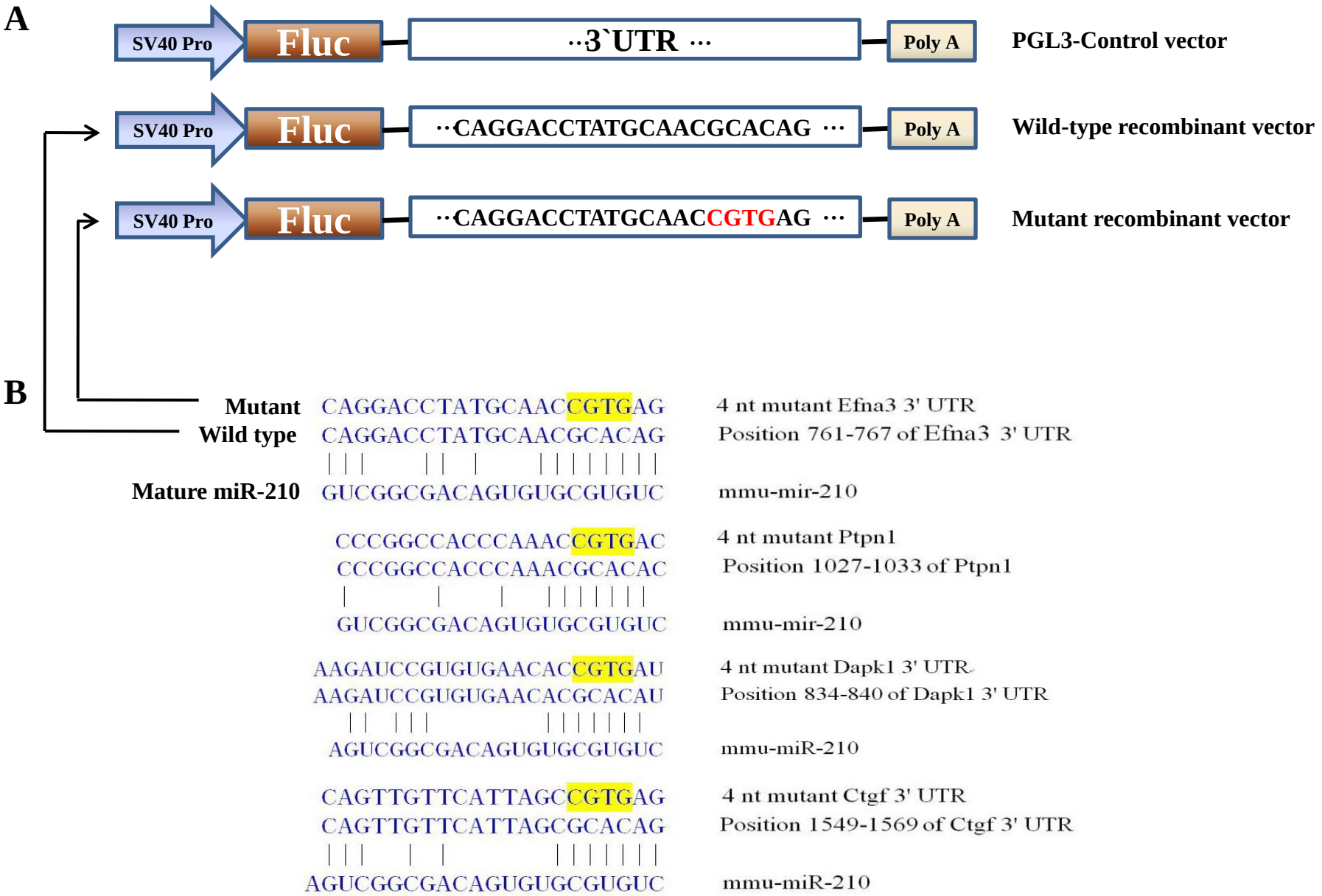
SUPPLEMENTAL MATERIAL



Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3

	W4			W8		
	MC-Scr	MC-210	Sham	MC-Scr	MC-210	Sham
LVESD, mm	3.05±0.09	2.78±0.09*	2.09±0.08†	3.11±0.13	2.82±0.07*	2.10±0.08†
LVEDD, mm	4.07±0.13	3.90±0.07	3.55±0.05†	4.11±0.08	3.82±0.05*	3.52±0.05†
FS (%)	25.1±1.9	28.7±2.4*	40.0±2.6†	24.2±2.7	27.8±1.9*	40.2±2.9†

Supplemental Table 1

	MC-Scr	MC-210	Sham
HR, beats/min	404±32	393±29	414±47
ESV, μl	51.9±2.8	45.3±4.2*	33.2±4.4†
EDV, μl	64.3±4.2	55.8±6.5*	44.1±3.2†
ESP, mmHg	54.3±6.2	65.6±3.1*	78.1±7.3†
EDP, mm Hg	55,7±2.8	45.3±5.2	33.3±4.4†
SV, ul	12.6±2.4	13.7±3.1	17.5±2.6†
CO, ml/min	33813±642	3962±535	5496±325.5†
dP/dtmax, mm Hg/μl	3073±213	3674±334*	4173±634†
dP/dtmin, mm Hg/μl	-2834±406	-3234±395	-3925±325†
SW, mm Hg/μl	379±107	433±163	638±273†
Tau-Glantz, ms	13.4±4.7	12.7±3.7	11.3±6.7
PAMP, mW/ml^2	9.3±3.3	13.5±2.9*	18.4±5.2†

Supplemental Table 2

Supplemental Figure 1: Schema of the production process for minicircles carrying miR-210 precursor driven by ubiquitin promoter (UB-miR-210). Minicircles are the product of site-specific recombination between the attB and attP sites driven by bacteriophage ΦC31 integrase. By adding 1%-L-arabinose to the bacterial culture media, the att sites of p2øC31.UB-miR-210 undergo intramolecular recombination. The end result is two circular DNAs: one is the minicircle (MC), which contains the therapeutic gene cassette and the right hybrid sequence (attR), and the other is the closed bacterial backbone, which contains the origin of replication, the antibiotic marker, and the left hybrid sequence (attL). The larger size closed bacterial backbone plasmid is then removed by bacterial exonucleases at 37 ℃.

Supplemental Figure 2: Expression of miR-210 in HL-1 cell. (A) HL-1 cells were transduced by lentivirus carrying miR-210 precursor or scramble sequence. >90% of the cells were GFP positive, indicating high transgene expression efficiency. (B) Quantitative RT-PCR showed miR-210 expression was 124±15 folds higher in miR-210 transduced cells compared to miR-scramble transduced cells.

Supplemental Figure 3: Schematic diagram for constructing miR-210 binding site into pGL3-control vector (Promega). (A) Take Efna3 as an example. The blank vector for luciferase assay is PGL3-Control vector from Promega. For the wild type vector construction, the target binding sequence was amplified by PCR and cloned downstream of firefly luciferase (Fluc) stop codon as 3`UTR of Fluc of PGL3-Control vector. This reconstructive vector plus normalizing vector pRL-TK (Promega) were transfected into NIH/3T3 cell for dual-luciferase assay. The mutant vector was reconstructed with 4 nucleotides mismatch using QuikChange® Lightning Site-Directed Mutagenesis Kit (Stratagene). (B) Complementarity between miR-210 and binding sites

of the four target genes. Mutant sequences for mutant vector construction were marked in yellow.

Supplemental Table 1: Quantitative analysis of left ventricular function among the 3 groups through echocardiogram. LVESD, LV End-diastolic dimension; LVESD, LV end-ystolic dimension; FS, fractional shortening. Values are means ± SE. *P<0.05 vs MC-Scr.

Supplemental Table 2: Invasive pressure-volume measurements of cardiac fuction. HR, heart rate; ESV, end-systolic volume; EDV, end-diastolic volume; ESP, end-systolic pressure; EDP, end-diastolic pressure; SV, stroke volume; CO, cardiac output; dP/dtmax, maximum first derivative of change in pressure rise with respect to time; dP/dtmin, maximum first derivative of change in pressure fall with respect to time; SW, stroke work; Tau-Glantz, time constant of fall in ventricular pressure by Glantz method; PAMP, preload-adjusted maximal power. Values are means ± SE. *P<0.05 vs MC-Scr.