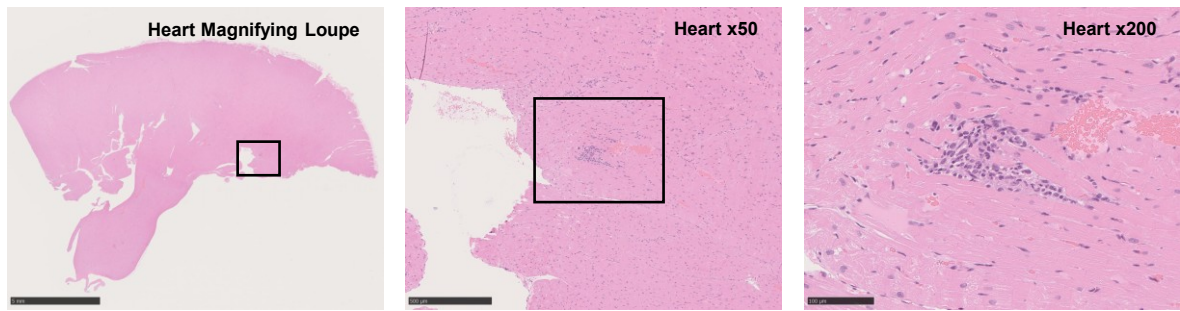


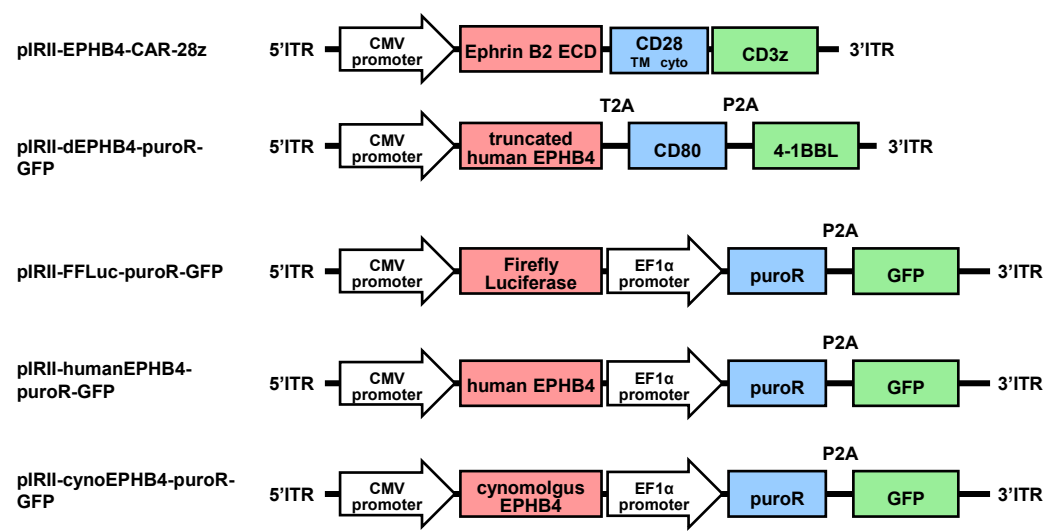
MACACA	MELRALLCWAASLAAALEETLLNNTKLETADLKWVTFPQVDGQWEELSGLDEEQHSVRTYEV	60
_HUMAN	MELRVLLCWAASLAAALEETLLNNTKLETADLKWVTFPQVDGQWEELSGLDEEQHSVRTYEV	
MACACA	CDVQRAPGQAHWLRGTGWVPRRGAVHVYATLRFTMLECLSLPRAGRCKETFTTVFYYESDA	120
_HUMAN	CDVQRAPGQAHWLRGTGWVPRRGAVHVYATLRFTMLECLSLPRAGRCKETFTTVFYYESDA	
MACACA	DTATALTPAWMENPYIKVDTVAAEHLTRKRPGAEATGKVNKTLRLGPLSKAGFYLAQD	180
_HUMAN	DTATALTPAWMENPYIKVDTVAAEHLTRKRPGAEATGKVNKTLRLGPLSKAGFYLAQD	
MACACA	QGACMALLSLHLFYKKAQLTVNLTRFPETVPRELVVPVAGSCVVDVAVPAPGSPSPSLYCR	240
_HUMAN	QGACMALLSLHLFYKKAQLTVNLTRFPETVPRELVVPVAGSCVVDVAVPAPGSPSPSLYCR	
MACACA	EDGQWAEQPVTCGSCAPGFEEAEGNTKCRACAQGTFFKPLSGEGSCQPCPANSHSNNIGSA	300
_HUMAN	EDGQWAEQPVTCGSCAPGFEEAEGNTKCRACAQGTFFKPLSGEGSCQPCPANSHSNTIGSA	
MACACA	VCQCRIGYFRARTDPRGAPCTTPPSAPRSVVSRLNGSSLHLEWSAPLESGGREDLTYALR	360
_HUMAN	VCQCRVGYFRARTDPRGAPCTTPPSAPRSVVSRLNGSSLHLEWSAPLESGGREDLTYALR	
MACACA	CRECRPGGSCAPCGDLTFDGPGRDLVEPWVVVRGLRPDFTYTFEVTALNGVSSLATGPV	420
_HUMAN	CRECRPGGSCAPCGDLTFDGPGRDLVEPWVVVRGLRPDFTYTFEVTALNGVSSLATGPV	
MACACA	PFEPVNVTTDREVPPAVSDIRVTRSSPSSLSLAWAVPRAPSGAVLDYEVKYHEKGAEGPS	480
_HUMAN	PFEPVNVTTDREVPPAVSDIRVTRSSPSSLSLAWAVPRAPSGAVLDYEVKYHEKGAEGPS	
MACACA	SVRFLKTSENRAELRGLKRGASYLVQVRARSEAGYGPFGQEHHSQTQLDENEGWREQLAL	540
_HUMAN	SVRFLKTSENRAELRGLKRGASYLVQVRARSEAGYGPFGQEHHSQTQLDESEGWREQLAL	
MACACA	IAGTAVVGVLVVLVIVVAVLCLRKQSNGREAEYSKHKGYLIGHGTVKYIDPFTYEDPN	600
_HUMAN	IAGTAVVGVLVVLVIVVAVLCLRKQSNGREAEYSKHKGYLIGHGTVKYIDPFTYEDPN	
MACACA	EAVREFAKEIDVSYVKIEEVI GAGEFGEVCRGRLKAPGKKECVAIKTLKGGYTERQRRE	660
_HUMAN	EAVREFAKEIDVSYVKIEEVI GAGEFGEVCRGRLKAPGKKECVAIKTLKGGYTERQRRE	
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_HUMAN	FLSEASIMGQFEHPNIIRLEGVVTNSMPVMILTEFMENGALDSFLRLNDGQFTVIQLVGM	
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_HUMAN	LRGIASGMRYLAEMSYVHRDLAARNILVNSNLVCKVSDFGLSRFLEENSSDPTYTSSLGG	
MACACA	KIPIRWTAPEAIAFRKFTSASDAWSYGIWMWEVMSFGERPYWDMSNQDVINAIEQDYRLP	840
_HUMAN	KIPIRWTAPEAIAFRKFTSASDAWSYGIWMWEVMSFGERPYWDMSNQDVINAIEQDYRLP	
MACACA	PPDCPTSLHQLMLDCWQKDRNARPRFPQVVSALDKMIRNPASLKI VARENGDLLRIGV	900
_HUMAN	PPDCPTSLHQLMLDCWQKDRNARPRFPQVVSALDKMIRNPASLKI VARENGDLLRIGV	
MACACA	TLAGHQKKILASVQHMKSQAKPGAPGGTGGFTPQY 935	
_HUMAN	TLAGHQKKILASVQHMKSQAKPGTPGGTGGFAPQY 935	

### Supplementary figure 1

Homology of the extracellular domain of human and cynomolgus EPHB4. Extracellular portion of EPHB4 amino acid sequence was highlighted in green (cynomolgus macaque; A0A2K5V953) and red (Homo Sapiens; P54760). Homology of the extracellular portion of human and cynomolgus EPHB4 was >99%.

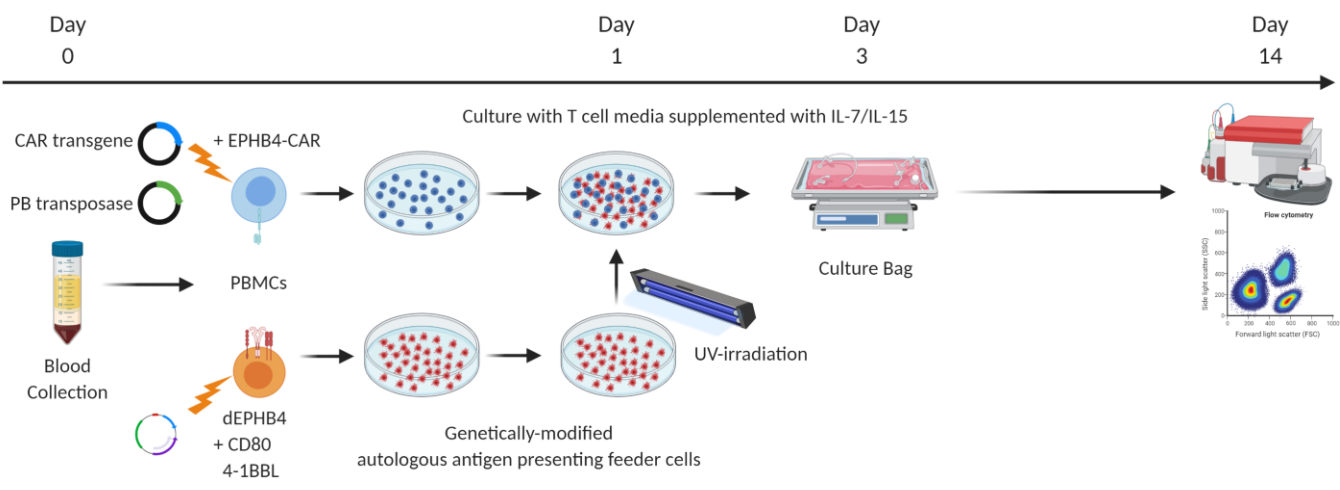
**No Tx group (Male)****Supplementary figure 2**

Histological image of heart in PBMC group. The infiltration of mononuclear cells was detected.



**Supplementary figure 3**

Transposon plasmids. ECD; Extra cellular domain, ITR; Inverted Tandem Repeat, puroR; puromycin resistant gene, GFP; Green fluorescent protein gene.



**Supplementary figure 4**

PB-EPHB4-CAR-T cell manufacturing scheme. Detailed manufacturing procedure was described in Materials and Methods.

## Hematology

Parameters (Unit)	n	Min	Max
HGB (g/dL)	525	10.8	15.9
HCT (%)	525	35.1	51.1
Retic ( $10^9/L$ )	525	11.9	115.4
WBC ( $10^3/\mu L$ )	524	3.48	22.08
Neut ( $10^3/\mu L$ )	518	0.47	11.27
Mono ( $10^3/\mu L$ )	522	0.14	1.11
Lymph ( $10^3/\mu L$ )	521	2.24	15.26
PLT ( $10^3/\mu L$ )	525	157	595

## Biochemistry

Parameters (Unit)	n	Min	Max
AST (U/L)	901	13	81
ALT (U/L)	902	8	122
LDH (U/L)	780	141	581
CK (U/L)	838	58	1316
CRP (mg/dL)	93	0.01	0.64
BIL (mg/dL)	905	0.03	0.31
TP (g/dL)	505	6.30	8.82
ALB (g/dL)	502	3.31	4.95
UN (mg/dL)	913	10.1	32.3
CRE (mg/dL)	911	0.47	1.01
Na (mEq/L)	913	143.4	166.9
K (mEq/L)	914	3.04	6.19

**Supplementary Table 1**

In-house data of blood examination. Two to four-years-old healthy cynomolgus macaques housed in Ina Research Inc. from 2016 to 2019 were subjected to a blood examination to obtain the reference values. The minimum and maximum values of each parameter were determined.

Name	clone	Product#	Company
Goat anti Ephrin B2	polyclonal	AF496	R&D SYSTEMS
PE anti-goat IgG Fc	polyclonal	F0107	R&D SYSTEMS
APC anti CD3	UCHT1	300412	Biologend
APC anti-CD8a	HIT8a	300912	Biologend
FITC anti-CD4	OKT4	317408	Biologend
FITC anti-CD45RA	HI100	304106	Biologend
APC anti-CCR7	G043H7	353214	Biologend
Recombinant human Ephrin B2-Fc chimera protein	-	7397-EB	R&D SYSTEMS
APC anti human IgG Fc	HP6017	409306	Biologend

**Supplementary Table 2**

List of antibodies used in this study.

(Forward Primer) 5'-GACTACATGAACATGACTCCCCG-3'

(Reverse Primer) 5'-GTCCAAAACATCGTACTCCTCTCT-3'

(probe) 5' FAM-ACCCGCAAGCATTACCAGCCCT-TAMRA 3'

**Supplementary Table 3**

Primer and Probe set for the detection of EPHB4-CAR transgene.