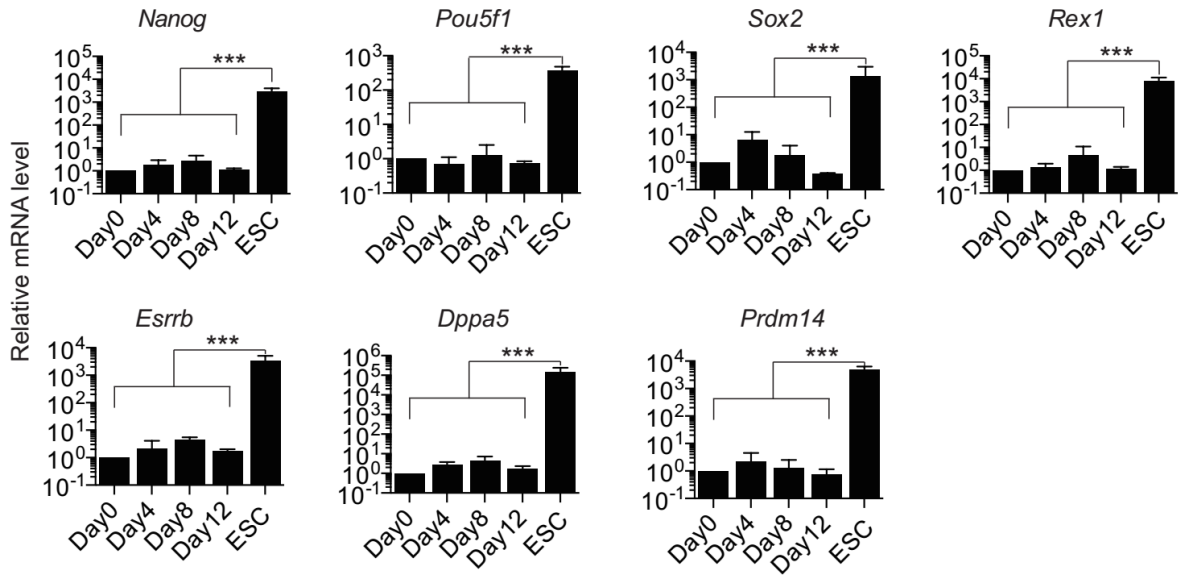
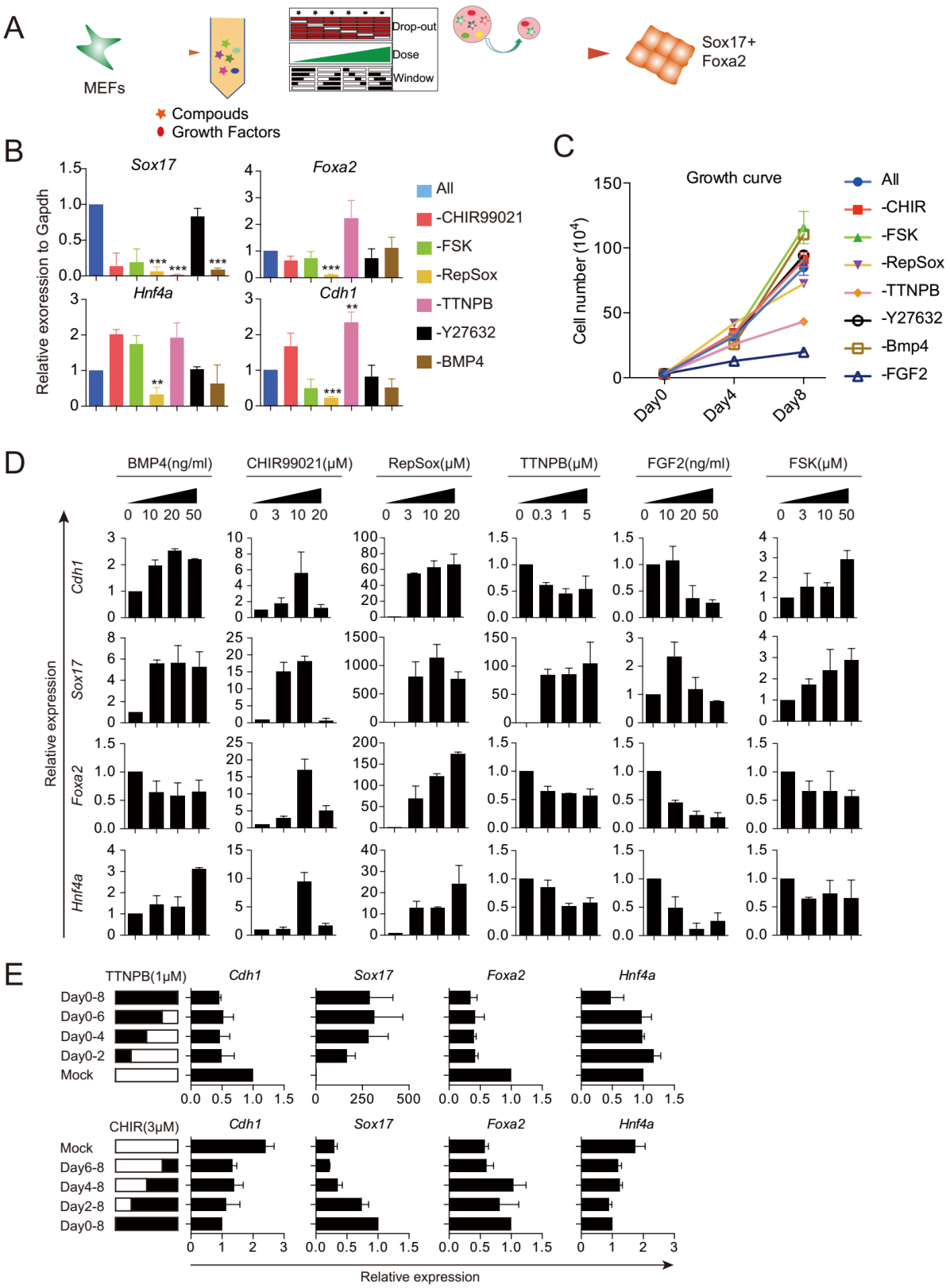
Supplementary Figures



Supplementary Figure 1. Related to Figure 1

Analysis of pluripotency-related genes during ciMET.

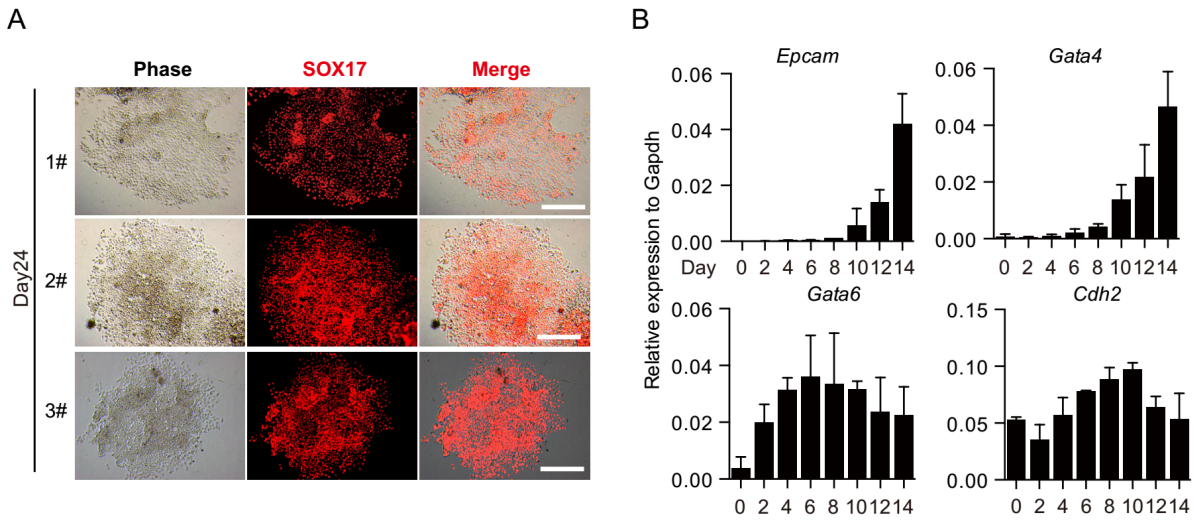
qRT-PCR analysis of pluripotent genes during ciMET. Data are means±s.d. n=3 independent experiments.***P<0.001.


A
MEFs
Compounds
Growth Factors
Drop-out
Dose
Window
Sox17+
Foxa2
B
Sox17
Foxa2
Hnf4a
Cdh1
Relative exoression to Gapdh
All
-CHIR99021
-FSK
-RepSox
-TTNPB
-Y27632
-BMP4
C
Growth curve
Cell number (10^4)
Day0
Day4
Day8
All
-CHIR
-FSK
-RepSox
-TTNPB
-Y27632
-Bmp4
-FGF2
D
BMP4(ng/ml)
CHIR99021(μM)
RepSox(μM)
TTNPB(μM)
FGF2(ng/ml)
FSK(μM)
0 10 20 50
0 3 10 20
0 3 10 20
0 0.3 1 5
0 10 20 50
0 3 10 50
Relative expression
Cdh1
Sox17
Foxa2
Hnf4a
E
TTNPB(1μM)
Day0-8
Day0-6
Day0-4
Day0-2
Mock
CHIR(3μM)
Mock
Day6-8
Day4-8
Day2-8
Day0-8
Cdh1
Sox17
Foxa2
Hnf4a
Relative expression

Supplementary Figure 2. Related to Figure 2

The optimization process of the ciEPC process.

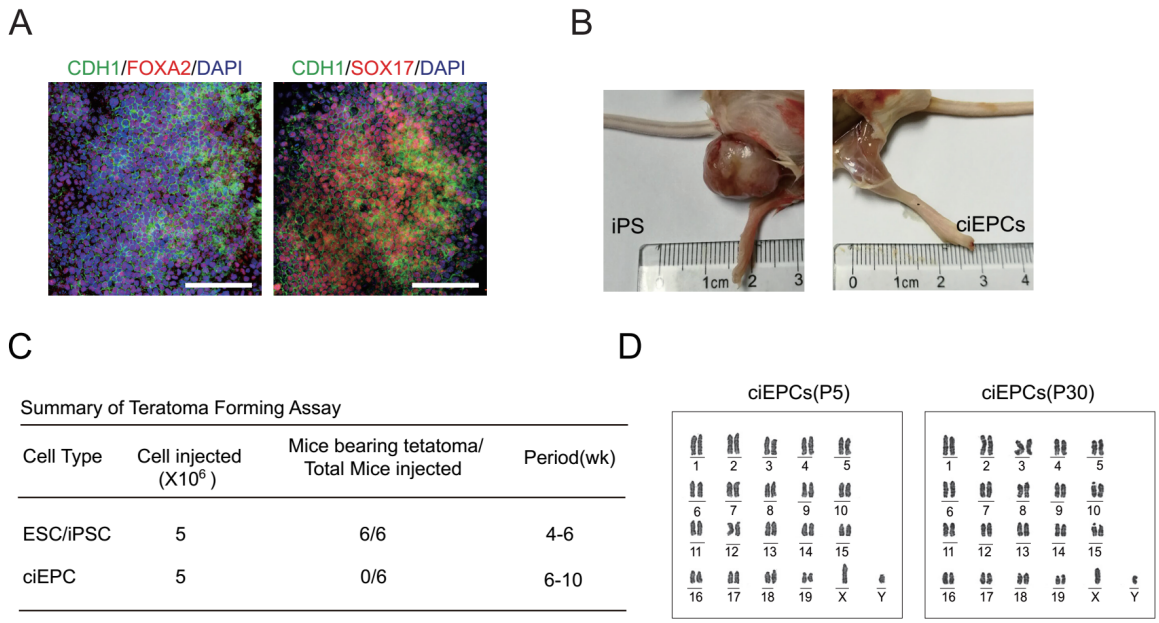
(A) Diagram showing the strategy for inducting endoderm progenitor cells from fibroblast by chemicals and growth factors. (B) MEFs were induced in 8 days with all the molecules or minus one as indicated and analyzed for the indicated genes by qRT-PCR. Data are means±s.d.; n=3 independent experiments. (C) The growth curve of cells cultured with all or one dropout as in (B). MEFs were seed at $3x10^4$ /well (12-well plate). Data are means±s.d. n=3 (triplicates) for each independent experiments. The experiments were repeated 3 times. (D) qRT-PCR analysis of endoderm and MET markers induced by BMP4, CHIR99021, RepSox, TTNPB, FGF2 and FSK at different doses as indicated. Data are means±s.d.; n=2 independent experiments. (E) qRT-PCR analysis of endoderm and MET markers induced by TTNPB or CHIR with indicated time windows. Data are means±s.d.; n=2 independent experiments.



Supplementary Figure 3: Related to Figure 2

The induction of ciEPCs

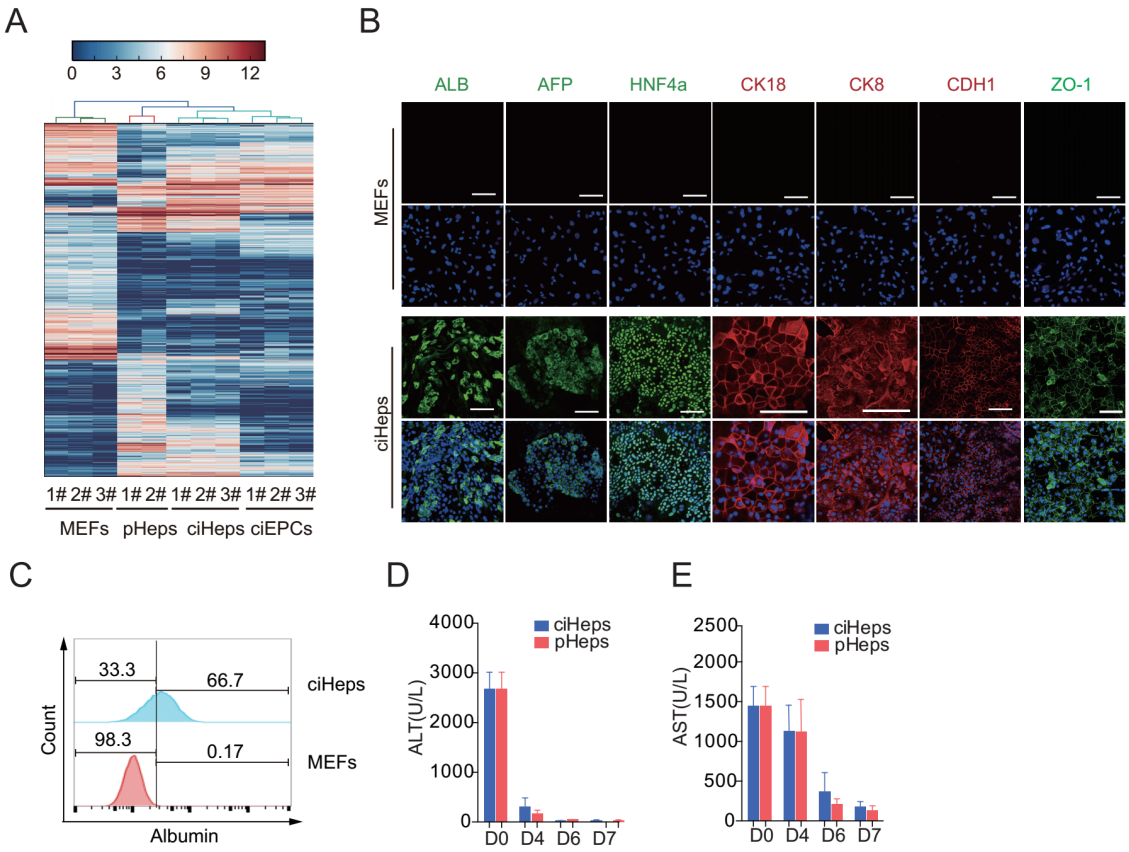
(A) Immuno-staining of SOX17 in the cells at Day 24 of the ciEPCs. Three typical Sox17^{+} cell clusters were showed. Scale bars, 250μm. (B) Time course analysis of Lineage and MET markers in ciEPCs protocol by qRT-PCR. Data are means±s.d.; n=3 independent experiments.



Supplementary Figure 4. Related to Figure 3

Characterization of ciEPCs

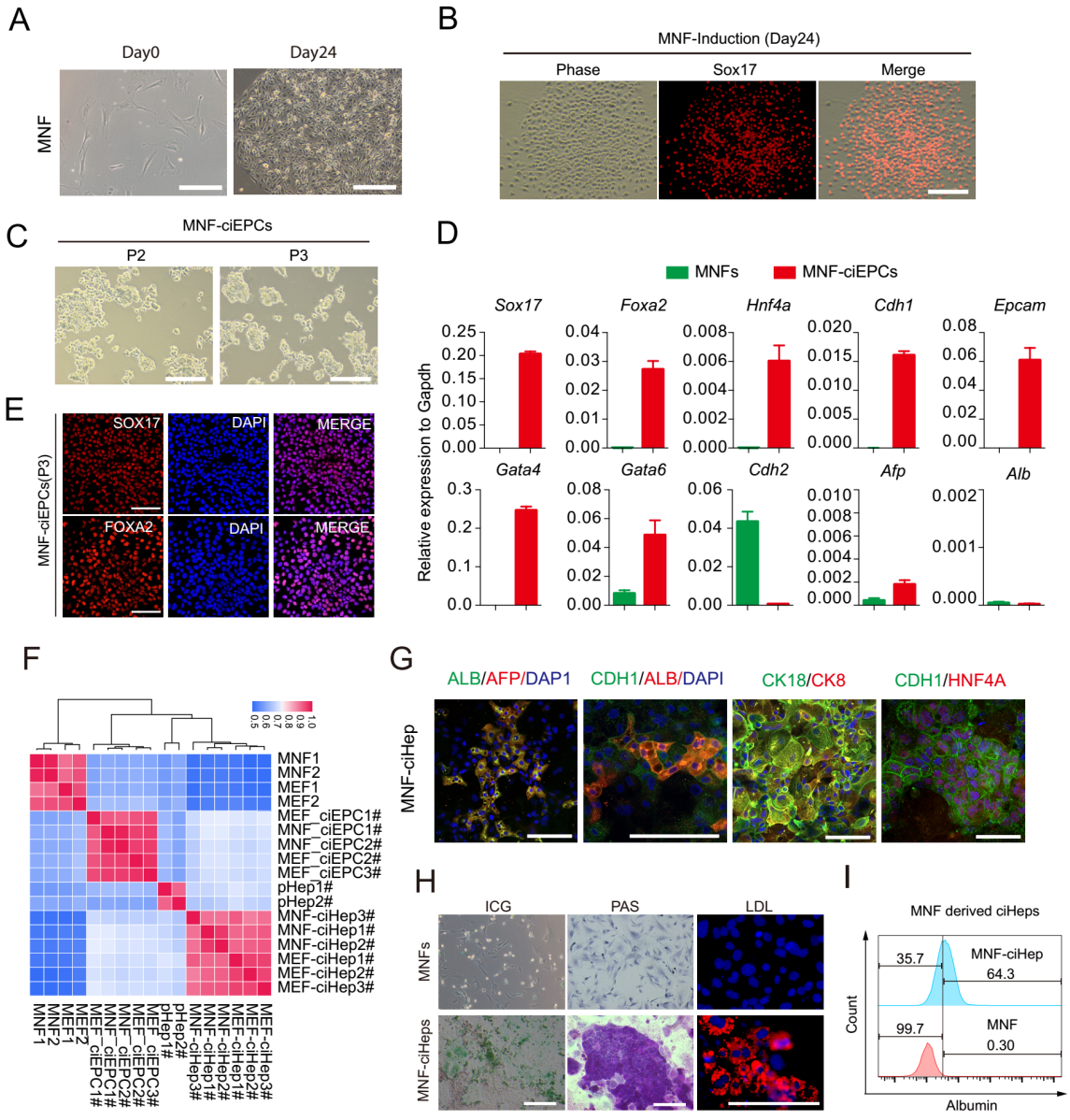
(A) Immuno-staining of CDH1/FOXA2, CDH1/SOX17 in ciEPCs. Scale bars, 100μm. **(B)** Images show teratoma formation in a mouse injected with iPSCs (left panel) and lack of tumor formation in a mouse injected with ciEPCs (right panel). **(C)** A summary of teratoma-forming ability of pluripotent stem cells (ESC/iPSC) and ciEPCs. **(D)** Normal karyotype of ciEPCs (Passage 5, left panel; Passage 30, right panel)



Supplementary Figure 5. Related to Figure 5

Characterization of ciHeps.

(**A**) Heat maps of RNA-seq data from MEFs, primary hepatocytes (pHeps), ciHeps, ciEPCs. **(B)**Immuno-straning of hepatocyte markers in MEFs and ciHeps. Scale bars, 100μm. **(C)** Flow cytometry analyses the expression of ALB in matured ciHeps and MEFs. **(D-E)** Serum levels of **ALT**(**D**) and **AST**（**E**）in Con-A-treated mice before (day 0) and after (day 4, day6 and day 7) transplantation of ciHeps and pHeps.

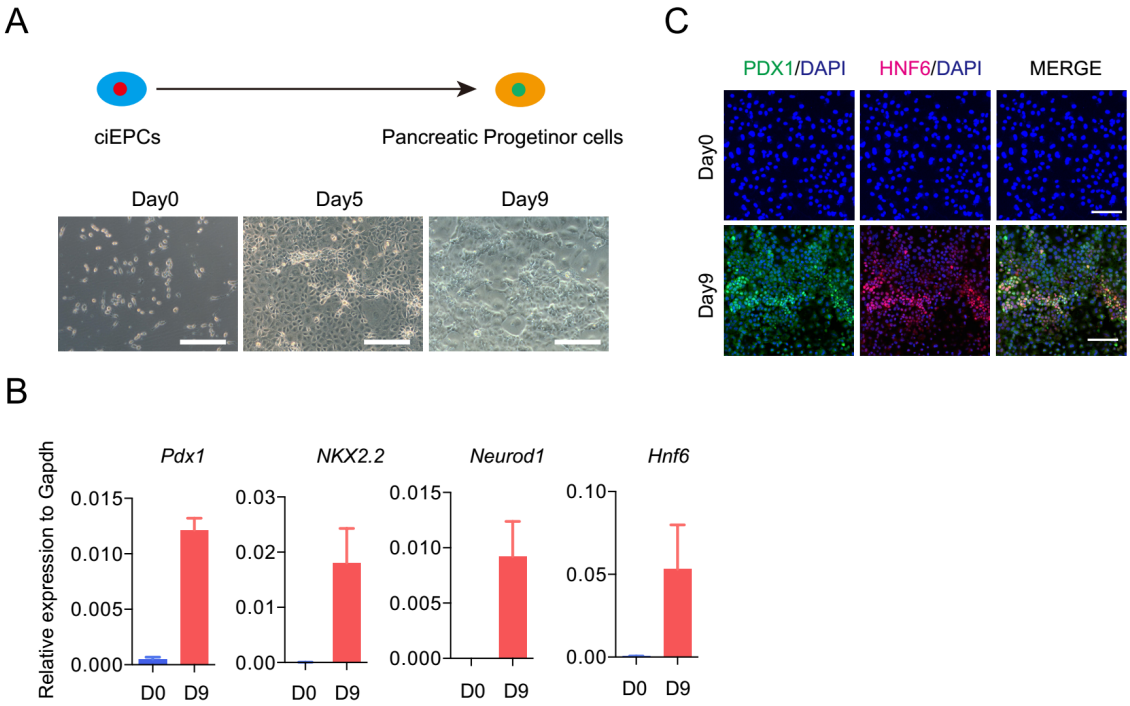


Supplementary Figure 6. Related to Figure 6

Chemical Reprogramming of MNF toward endoderm lineage.

(A) The representative images of MNF induced ciEPCs at different days. Scale bars, 250 μm. **(B)** Immuno-staining of SOX17 in MNF induced ciEPCs at Day24. Scale bars, 250μm. **(C)** Represented images of ciEPCs at different passages. Scale bars, 250μm. **(D)** qRT-PCR analysis of endoderm and MET markers in MNF, and MNF-ciEPCs. Data are means±s.d., n=3 independent experiments.**(E)** Immuno-staining of endoderm marker SOX17 and FOXA2 in MNF derived ciEPCs at passage 3. Scale bars, 100μm. **(F)** Heat maps for R2 correlation efficiency matrix of RNA-Seq data from MEFs, MNFs, MEF-ciEPCs, MNF-ciEPCs, MEF-ciHeps, MNF-ciHeps and pHeps. **(G)**

Immuno-staining of ALB, AFP, CDH1,CK18, CK8 and HNF4A in MNF derived ciHeps. Scale bars, 100μm. **(H)** Glycogen storage (PAS), DiI-ac-LDL and ICG uptake in MNFs and MNF derived ciHeps. Scale bars, 250μm. **(I)** Flow cytometry analyses the expression of ALB in MNFs and matured MNF-ciHeps.



Supplementary Figure 7

The induction of Pancreatic progenitor cells from ciEPCs

(A) The schedule and representative images for the conversion of ciEPCs to pancreatic progenitor cells. Scale bars, 250μm. **(B)** qRT-PCR analysis the expression of pancreatic markers during the pancreatic progenitor cells induction(Day0,Day9). Data are means±s.d., n=3 independent experiments. **(C)** Immuno-staining of pancreatic markers in ciEPCs (Day0) and induced pancreatic progenitor cells (Day9). Scale bars, 100μm.