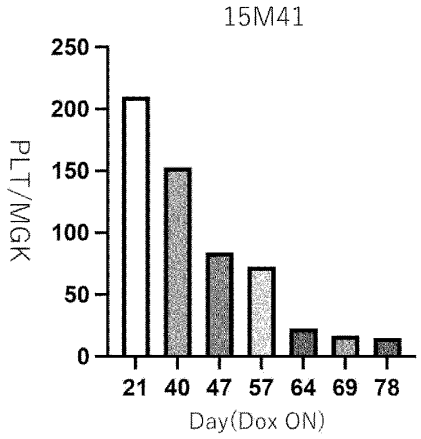
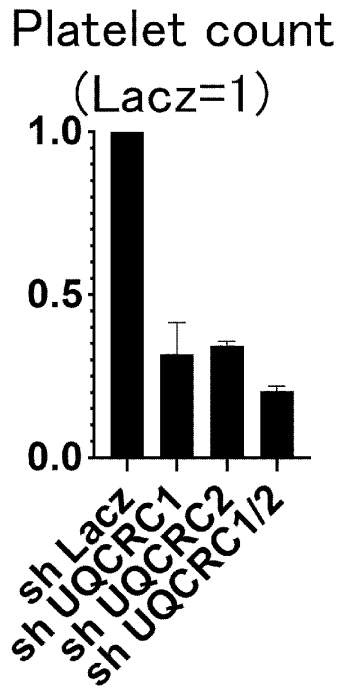
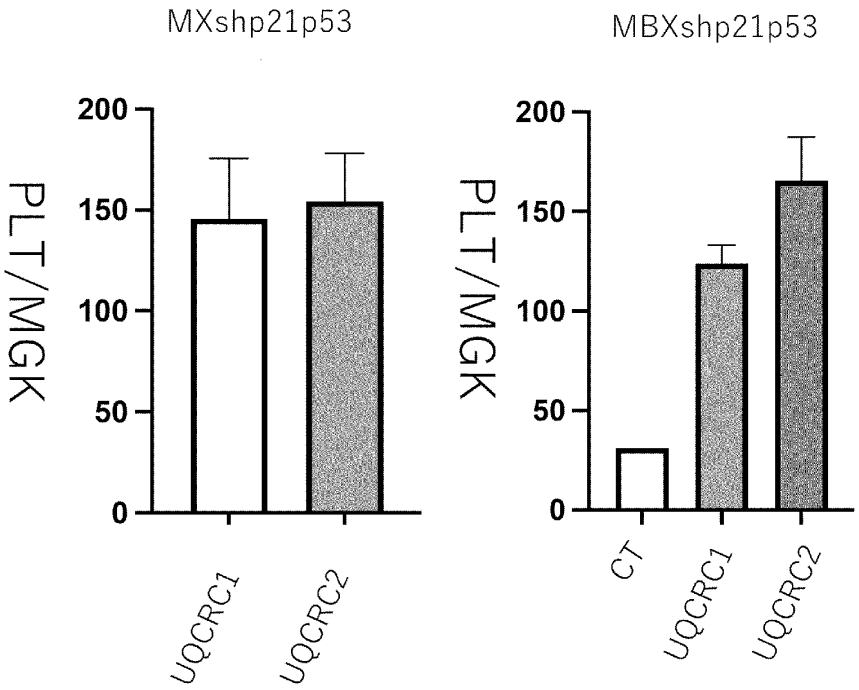
[図1]


15M41
250
200
150
100
50
0
PLT/MGK
21 40 47 57 64 69 78
Day(Dox ON)

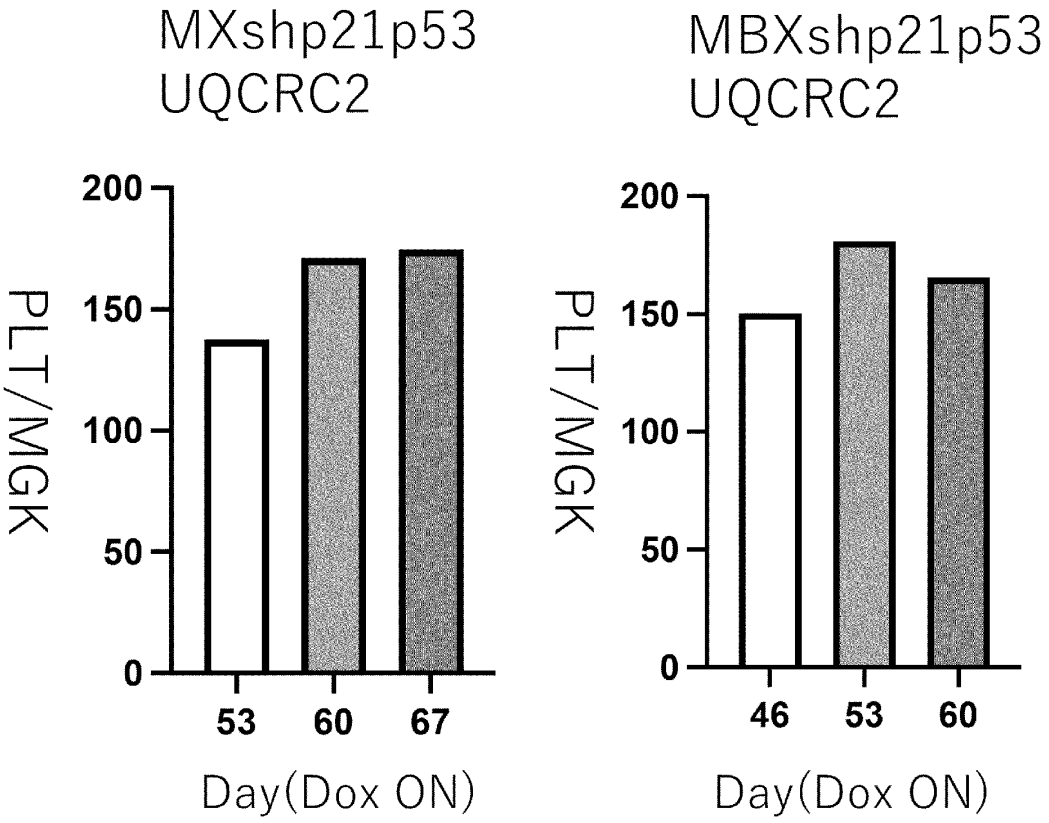
[図2]


Platelet count
(Lacz=1)
1.0
0.5
0.0
sh Lacz
sh UQCRC1
sh UQCRC2
sh UQCRC1/2

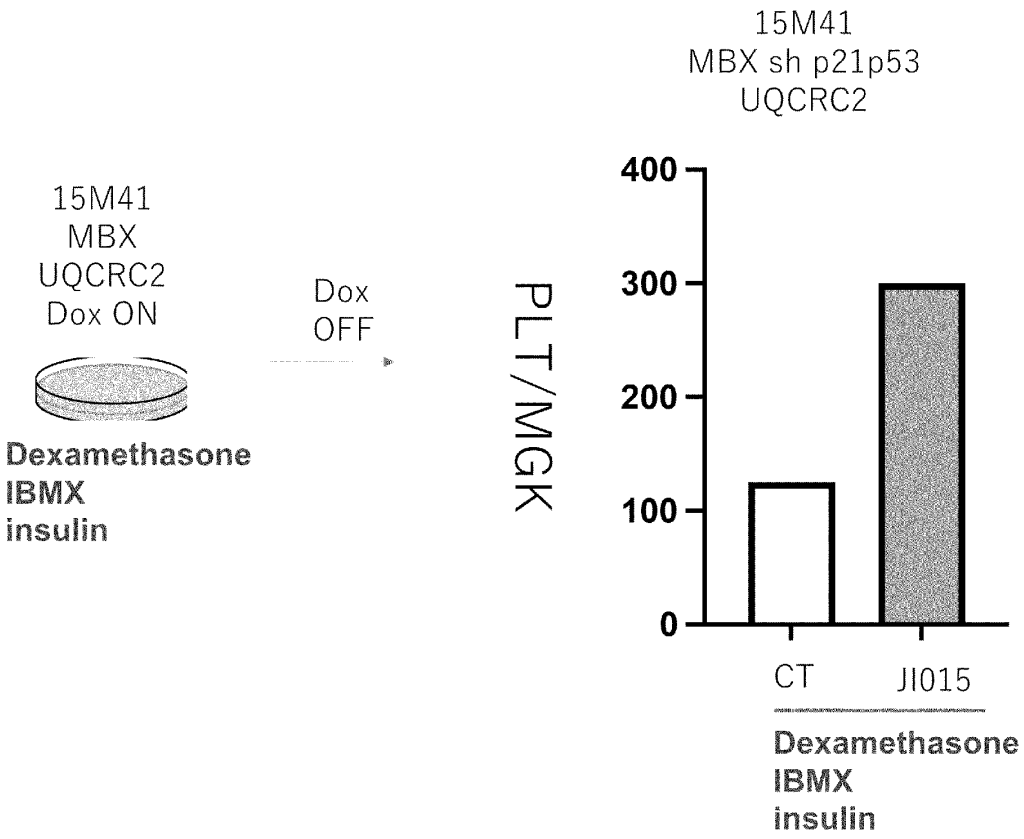
[図3]


MXshp21p53
MBXshp21p53
PLT/MGK
200
150
100
50
0
UQCRC1
UQCRC2
CT
UQCRC1
UQCRC2

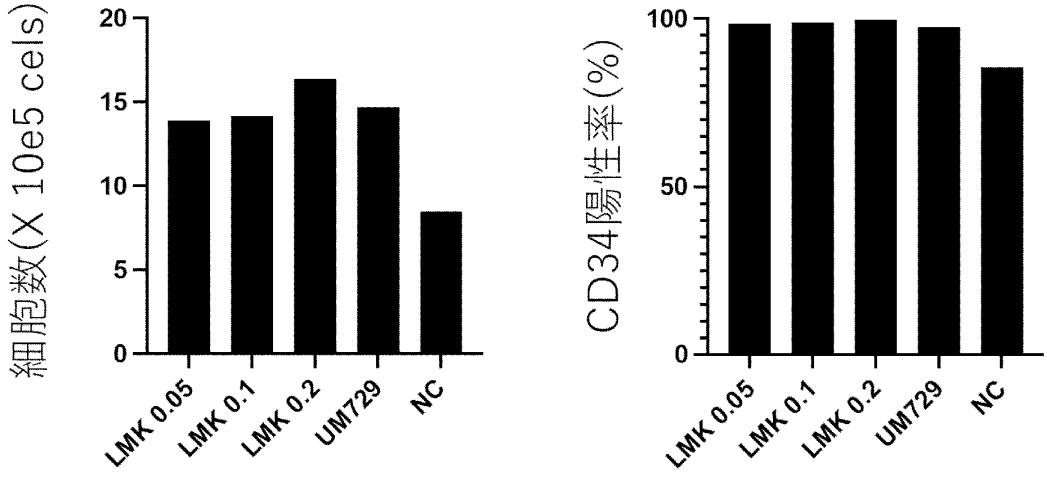
[図4]


MXshp21p53
UQCRC2
MBXshp21p53
UQCRC2
PLT/MGK
200
150
100
50
0
53
60
67
46
53
60
Day(Dox ON)
Day(Dox ON)

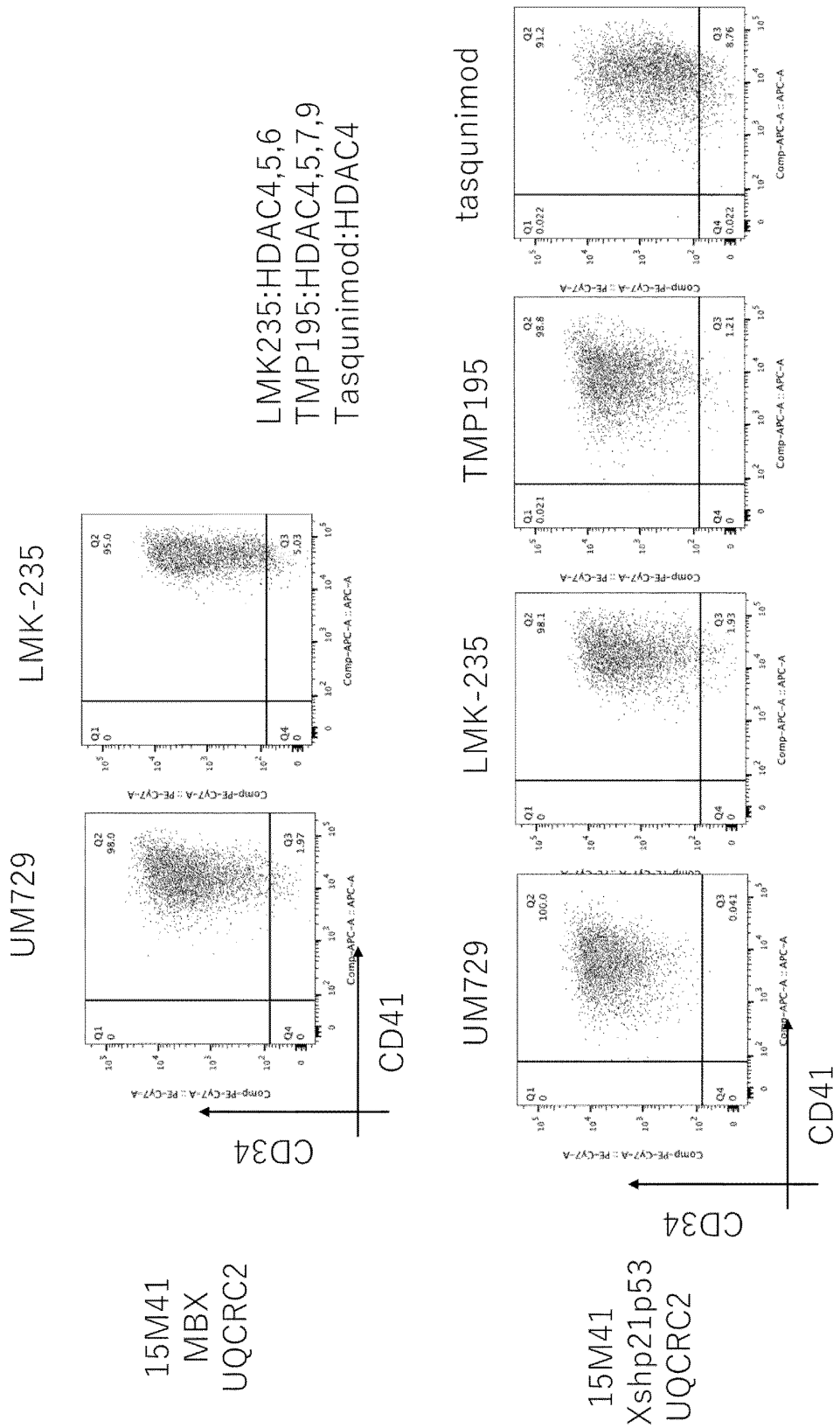
[図5]


15M41
MBX
UQCRC2
Dox ON
Dox
OFF
Dexamethasone
IBMX
insulin
15M41
MBX sh p21p53
UQCRC2
PLT/MGK
400
300
200
100
0
CT
JI015
Dexamethasone
IBMX
insulin

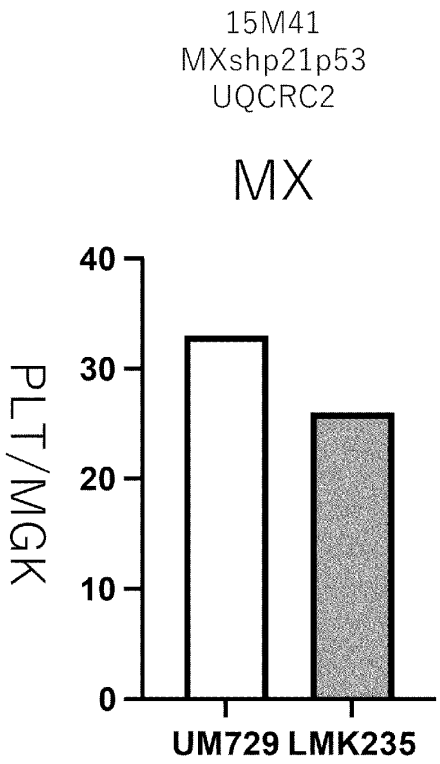
[図6]


細胞数(X 10e5 cels)
20
15
10
5
0
LMK 0.05
LMK 0.1
LMK 0.2
UM729
NC
CD34陽性率(%)
100
50
0
LMK 0.05
LMK 0.1
LMK 0.2
UM729
NC

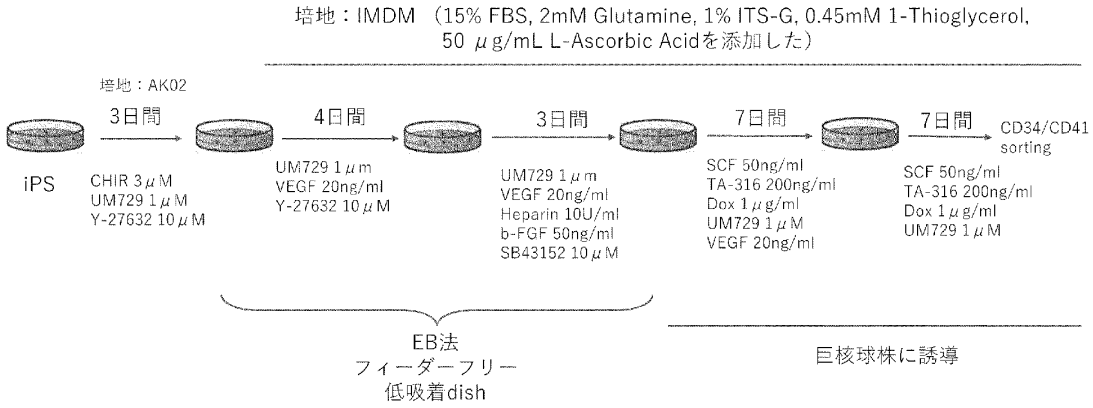
[図7]


15M41
MBX
UQCRC2
UM729
LMK-235
LMK235:HDAC4,5,6
TMP195:HDAC4,5,7,9
Tasqunimod:HDAC4
CD34
CD41
15M41
MXshp21p53
UQCRC2
UM729
LMK-235
TMP195
tasqunimod
CD34
CD41

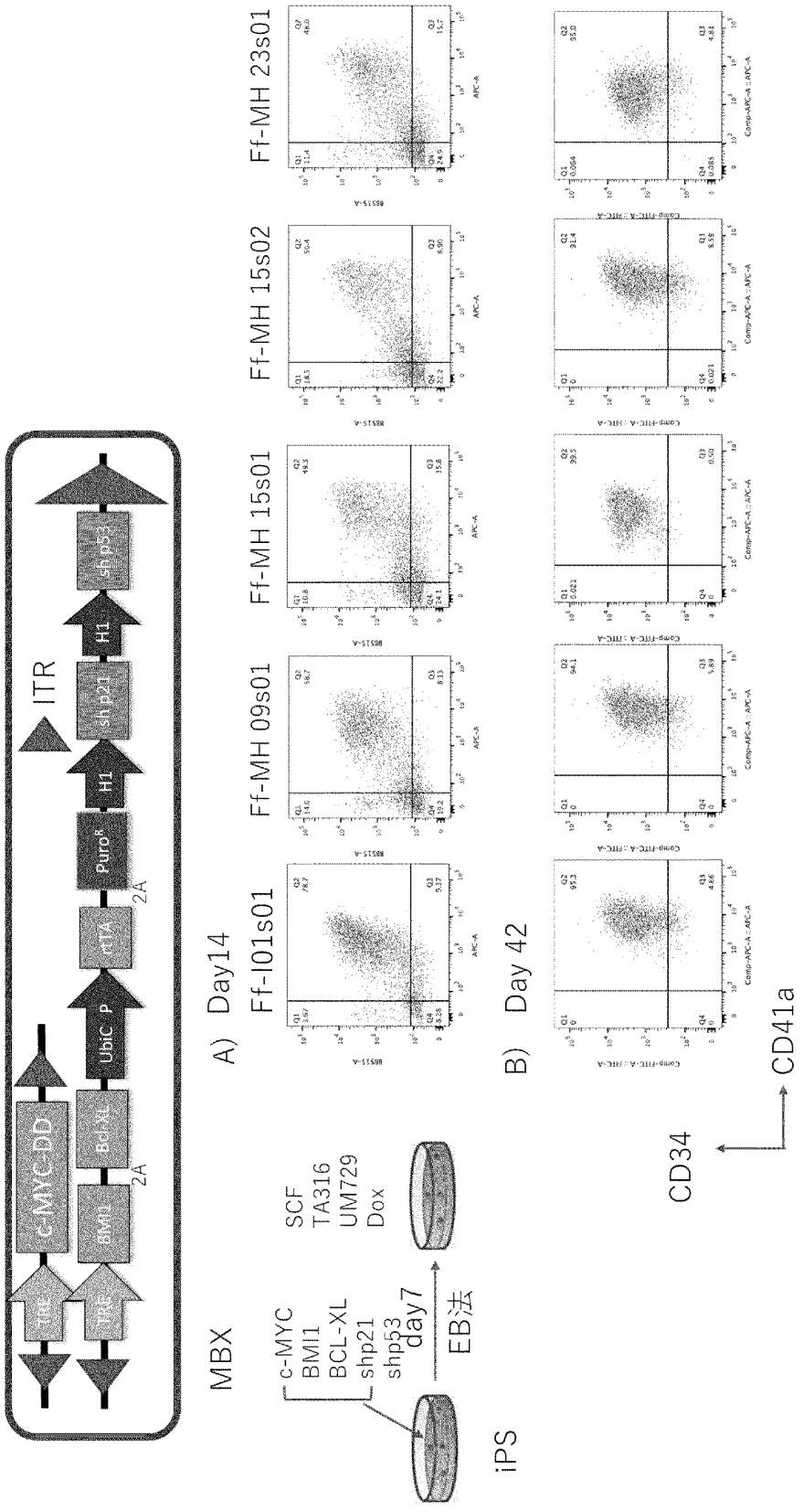
[図8]


15M41
MXshp21p53
UQCRC2
MX
PLT/MGK
40
30
20
10
0
UM729 LMK235

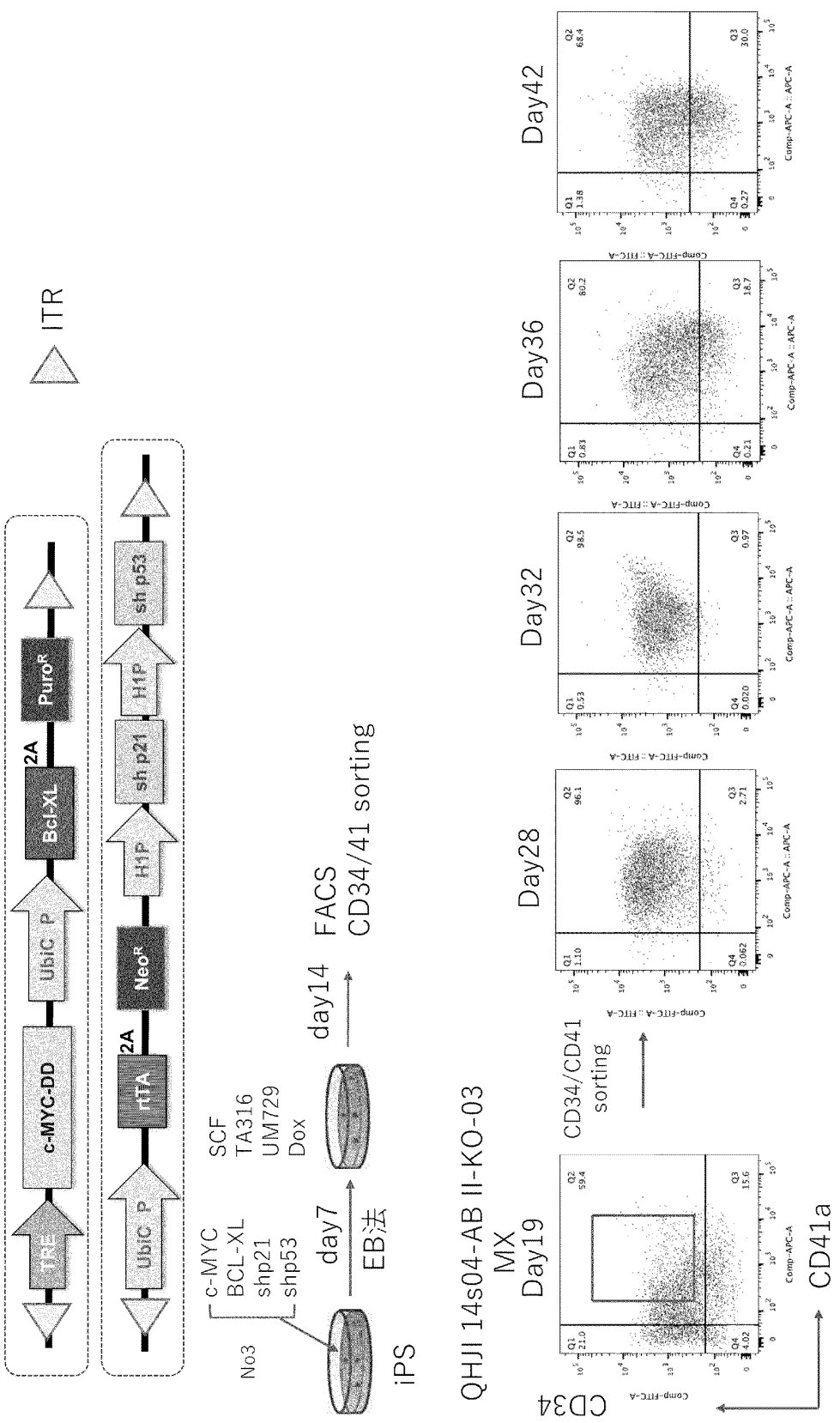
[図9]


培地：IMDM （15% FBS, 2mM Glutamine, 1% ITS-G, 0.45mM 1-Thioglycerol, 50 μg/mL L-Ascorbic Acidを添加した）
培地：AK02
3日間
4日間
3日間
7日間
7日間
CD34/CD41 sorting
iPS
CHIR 3μM
UM729 1μM
Y-27632 10μM
UM729 1μm
VEGF 20ng/ml
Y-27632 10μM
UM729 1μm
VEGF 20ng/ml
Heparin 10U/ml
b-FGF 50ng/ml
SB43152 10μM
SCF 50ng/ml
TA-316 200ng/ml
Dox 1μg/ml
UM729 1μM
VEGF 20ng/ml
SCF 50ng/ml
TA-316 200ng/ml
Dox 1μg/ml
UM729 1μM
EB法
フィーダーフリー
低吸着dish
巨核球株に誘導

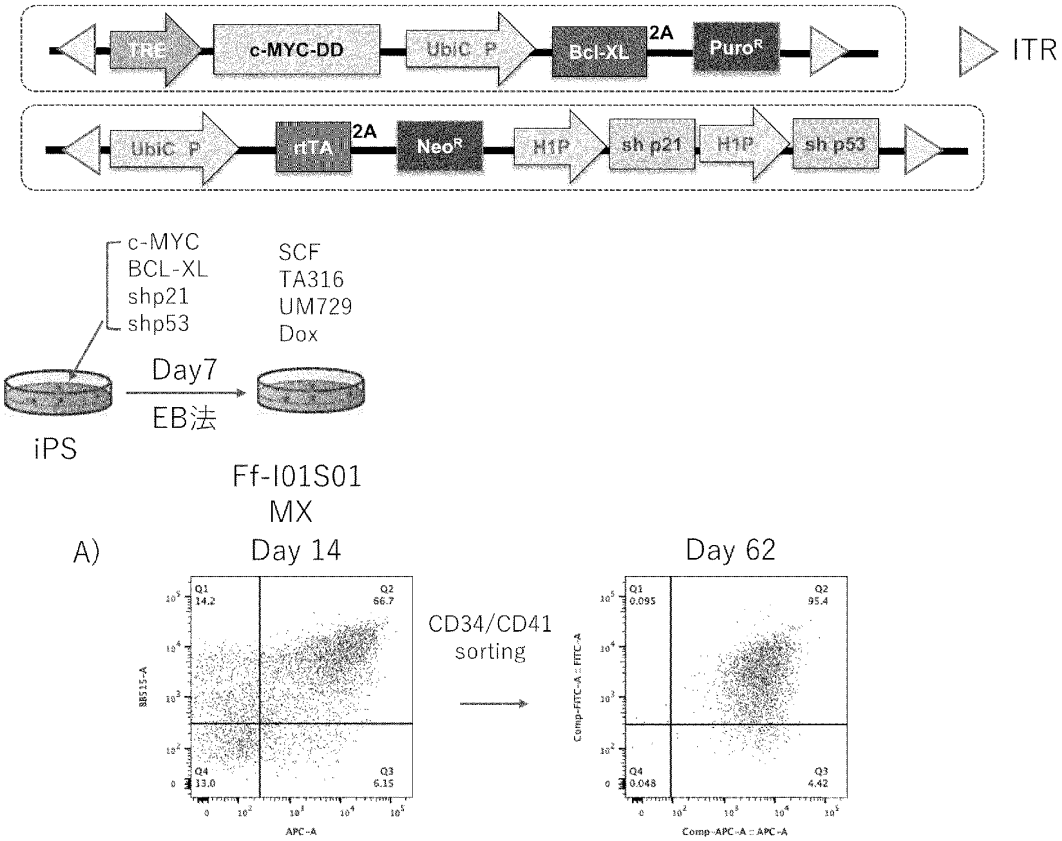
[図10]


MBX
ITR
c-MYC DD
2A
BMI1
Bcl-XL
2A
UbiC P
rtTA
Puro^R
H1
shp21
H1
shp53
iPS
c-MYC
BMI1
BCL-XL
shp21
shp53
day7
EB法
SCF
TA316
UM729
Dox
A) Day14
B) Day 42
Ff-I01s01
Ff-MH 09s01
Ff-MH 15s01
Ff-MH 15s02
Ff-MH 23s01
CD34
CD41a

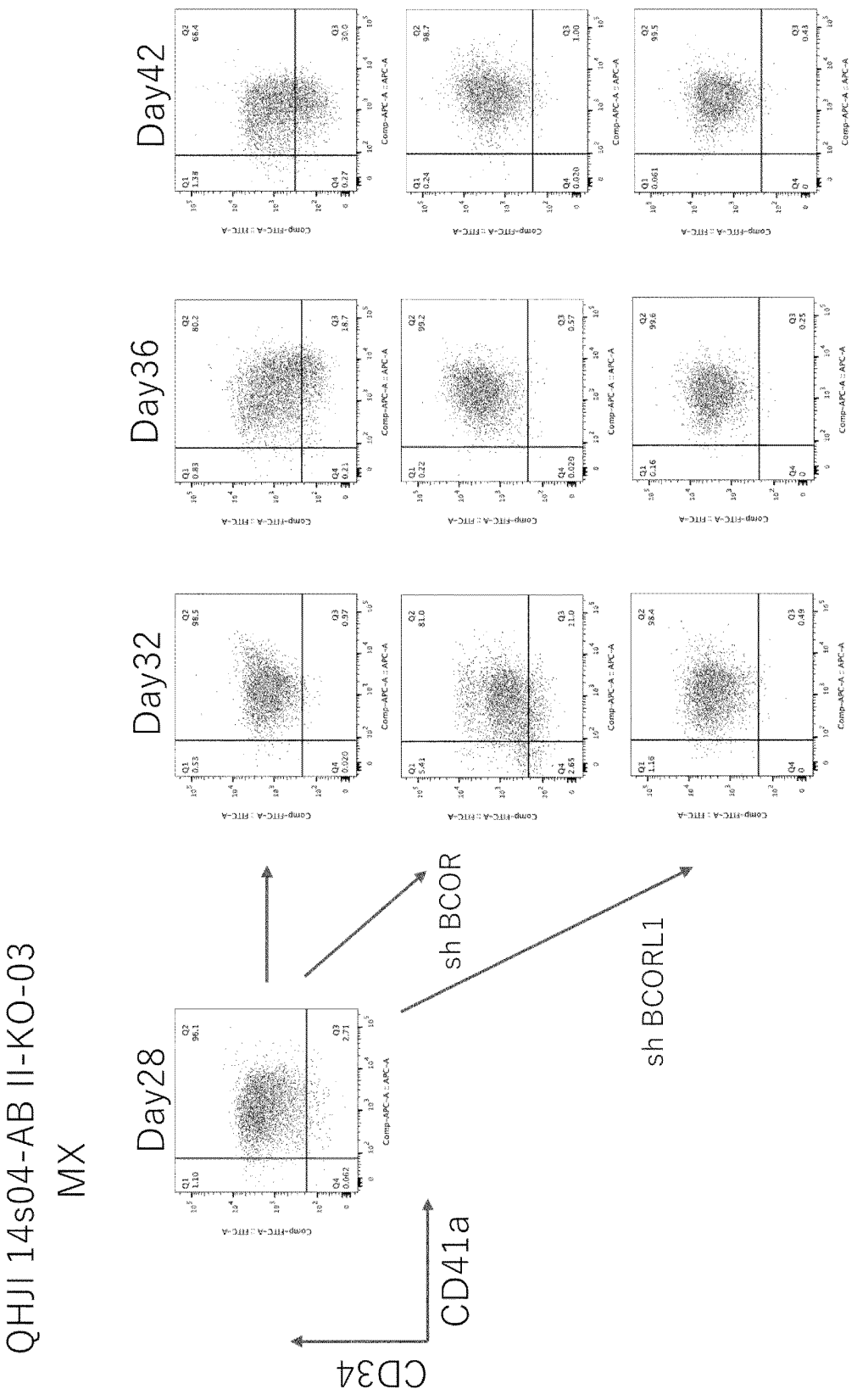
[図11]


ITR
TRE
c-MYC-DD
UbiC P
2A
Bcl-XL
PuroR
UbiC P
rtTA
2A
NeoR
H1P
sh p21
H1P
sh p53
No3
c-MYC
BCL-XL
shp21
shp53
iPS
day7
EB法
SCF
TA316
UM729
Dox
day14
FACS
CD34/41 sorting
QHJI 14s04-AB II-KO-03
MX
Day19
CD34
CD41a
CD34/CD41
sorting
Day28
Day32
Day36
Day42

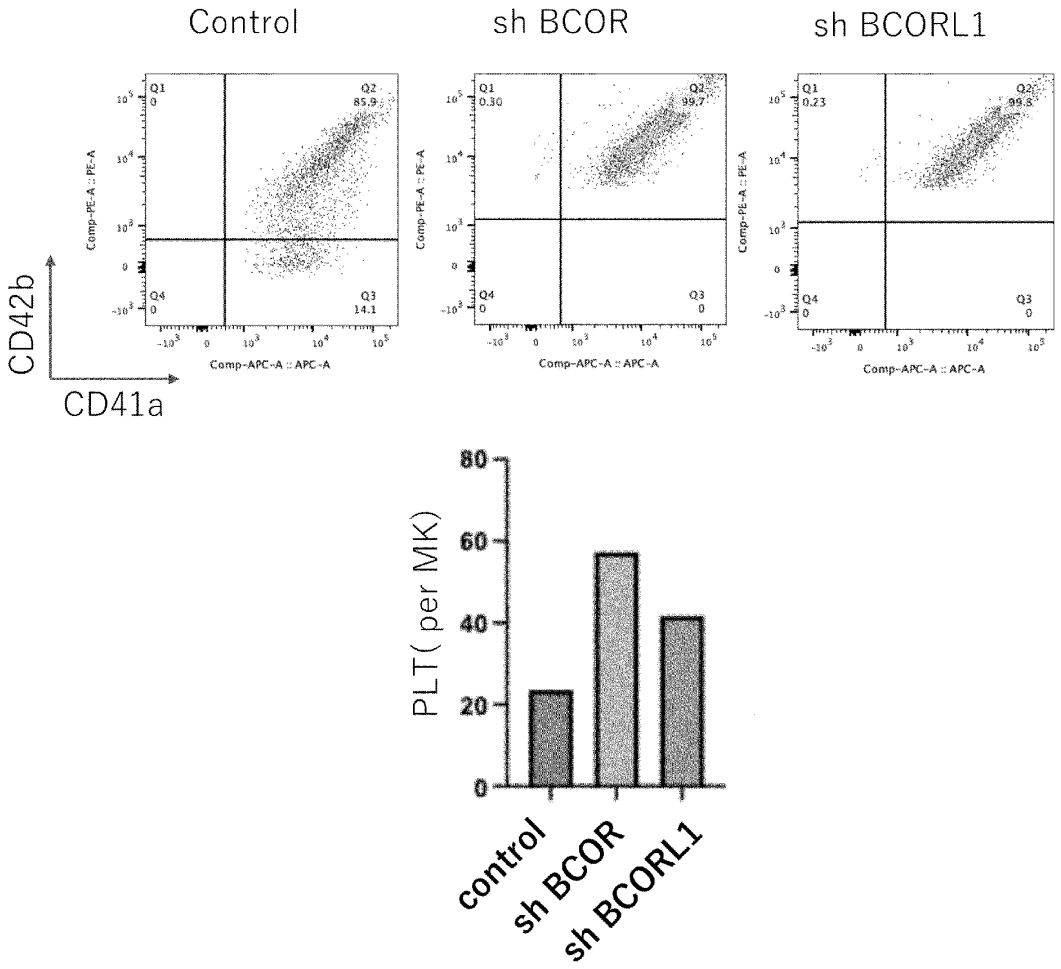
[図12]


TRE
c-MYC-DD
UbiC P
Bcl-XL
2A
Puro^R
ITR
UbiC P
rtTA
2A
Neo^R
H1P
sh p21
H1P
sh p53
c-MYC
BCL-XL
shp21
shp53
SCF
TA316
UM729
Dox
Day7
EB法
iPS
Ff-I01S01
MX
A)
Day 14
Day 62
CD34/CD41
sorting
Q1
14.2
Q2
66.7
Q4
13.0
Q3
6.15
BB515-A
APC-A
Q1
0.095
Q2
95.4
Q4
0.048
Q3
4.42
Comp-FITC-A :: FITC-A
Comp-APC-A :: APC-A

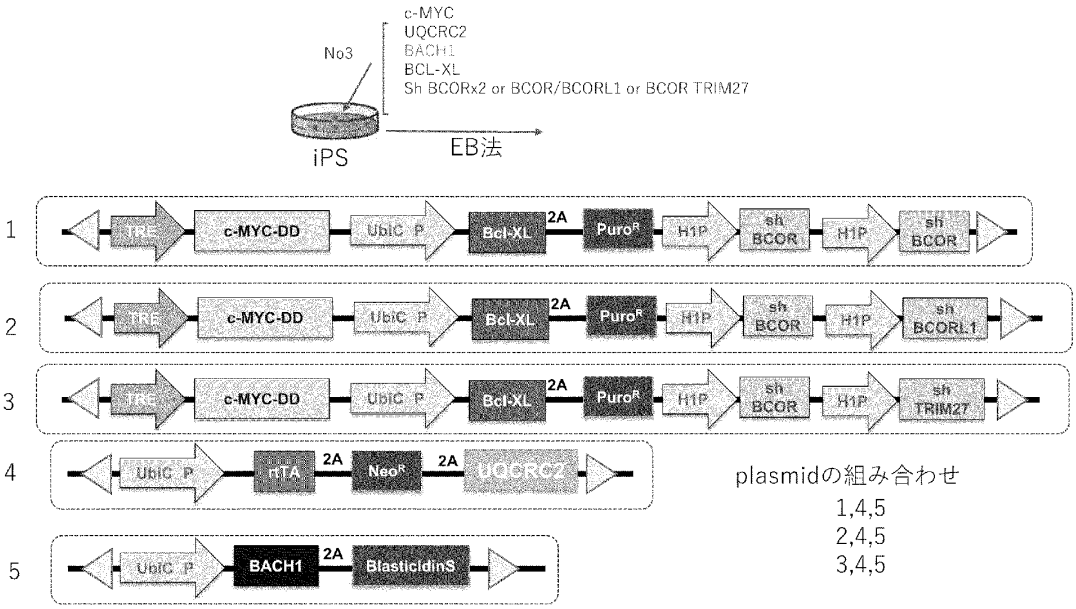
[図13]


QHJI 14s04-AB II-KO-03
MX
Day28
Day32
Day36
Day42
CD34
CD41a
sh BCOR
sh BCORL1

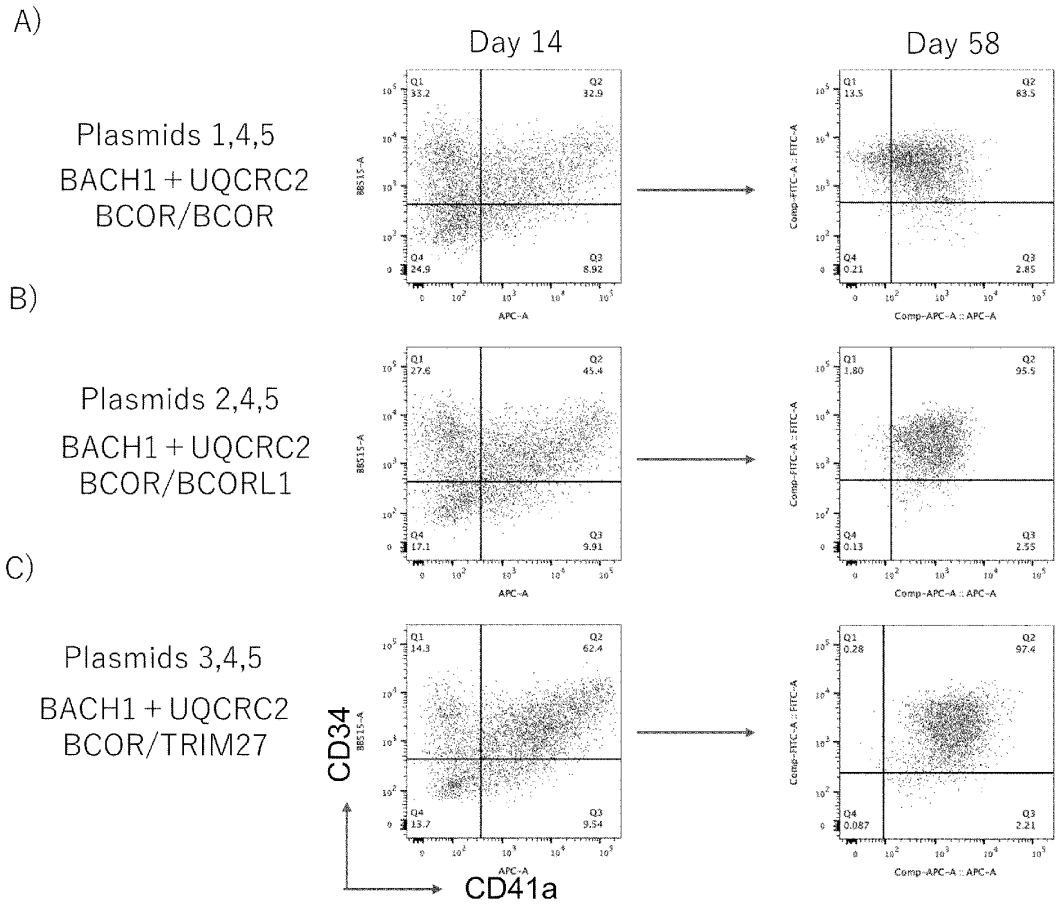
[図14]


Control
sh BCOR
sh BCORL1
CD42b
CD41a
Q1
Q2
Q3
Q4
85.9
14.1
99.7
0.30
99.8
0.23
Comp-PE-A :: PE-A
Comp-APC-A :: APC-A
PLT(per MK)
80
60
40
20
0
control
sh BCOR
sh BCORL1

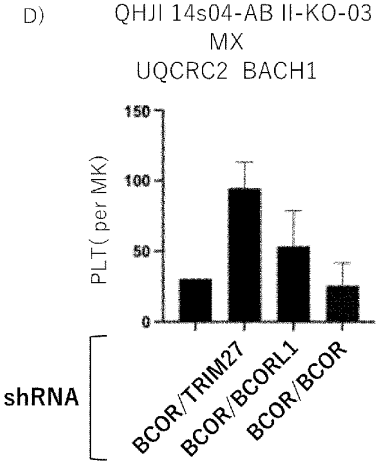
[図15]


c-MYC
UQCRC2
BACH1
BCL-XL
Sh BCORx2 or BCOR/BCORL1 or BCOR TRIM27
No3
iPS
EB法
1
2
3
4
5
TRE
c-MYC-DD
UbiC P
Bcl-XL
2A
PuroR
H1P
sh BCOR
sh BCORL1
sh TRIM27
rtTA
NeoR
UQCRC2
BACH1
BlasticidinS
plasmidの組み合わせ
1,4,5
2,4,5
3,4,5

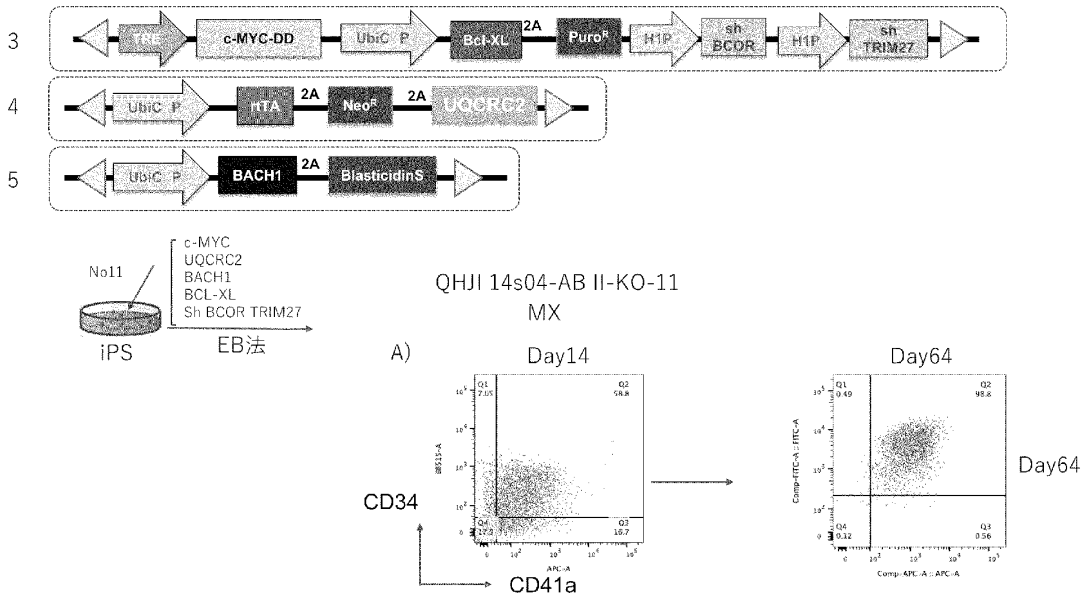
[図16-1]


A)
Plasmids 1,4,5
BACH1＋UQCRC2
BCOR/BCOR
B)
Plasmids 2,4,5
BACH1＋UQCRC2
BCOR/BCORL1
C)
Plasmids 3,4,5
BACH1＋UQCRC2
BCOR/TRIM27
Day 14
Day 58
CD34
CD41a
APC-A
Comp-APC-A :: APC-A
Comp-FITC-A :: FITC-A
Q1 33.2
Q2 32.9
Q4 24.9
Q3 8.92
Q1 13.5
Q2 83.5
Q4 0.21
Q3 2.85
Q1 27.6
Q2 45.4
Q4 17.1
Q3 9.91
Q1 1.80
Q2 95.5
Q4 0.13
Q3 2.55
Q1 14.3
Q2 62.4
Q4 13.7
Q3 9.54
Q1 0.28
Q2 97.4
Q4 0.087
Q3 2.21

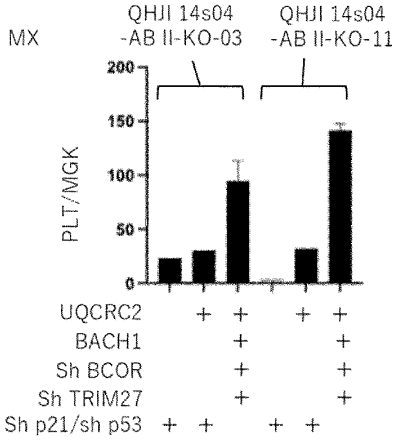
[図16-2]


D)
QHJI 14s04-AB II-KO-03
MX
UQCRC2 BACH1
PLT(per MK)
150
100
50
0
shRNA
BCOR/TRIM27
BCOR/BCORL1
BCOR/BCOR

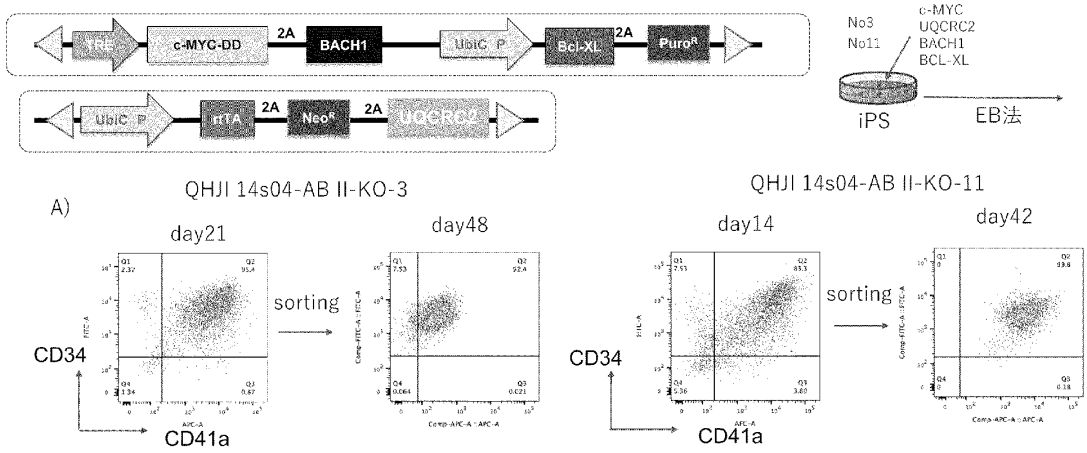
[図17-1]



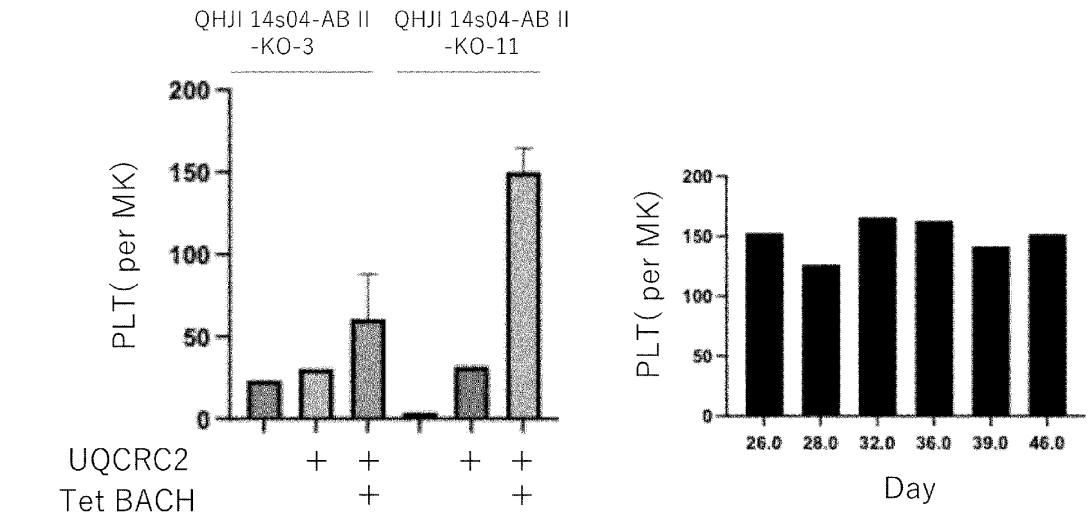
[図17-2]



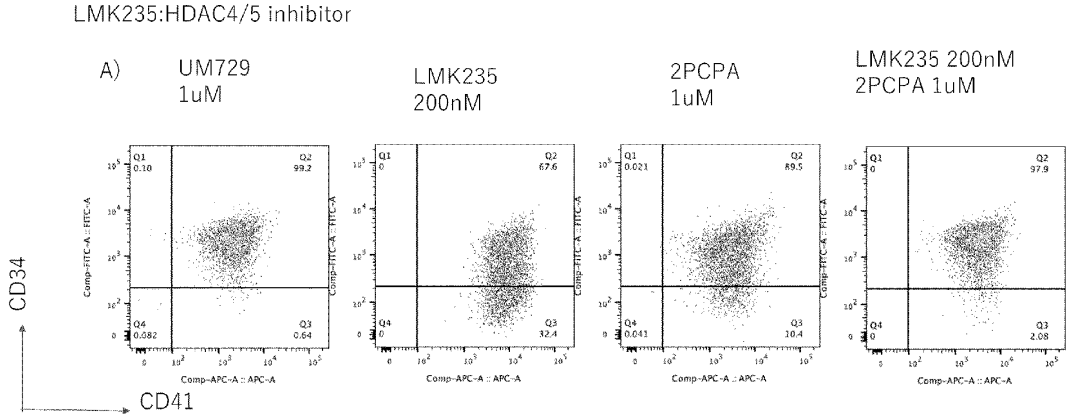
[図18-1]



[図18-2]


B)
QHJI 14s04-AB II -KO-3
QHJI 14s04-AB II -KO-11
PLT(per MK)
200
150
100
50
0
UQCRC2
Tet BACH
+ + + +
+ +
PLT(per MK)
200
150
100
50
0
26.0 28.0 32.0 36.0 39.0 46.0
Day

[図19]


LMK235:HDAC4/5 inhibitor
A)
UM729 1uM
LMK235 200nM
2PCPA 1uM
LMK235 200nM 2PCPA 1uM
CD34
CD41
Q1 0.10
Q2 99.2
Q4 0.082
Q3 0.64
Q1
Q2 67.6
Q4
Q3 32.4
Q1 0.021
Q2 89.5
Q4 0.041
Q3 10.4
Q1
Q2 97.9
Q4
Q3 2.08
Comp-APC-A :: APC-A
Comp-FITC-A :: FITC-A