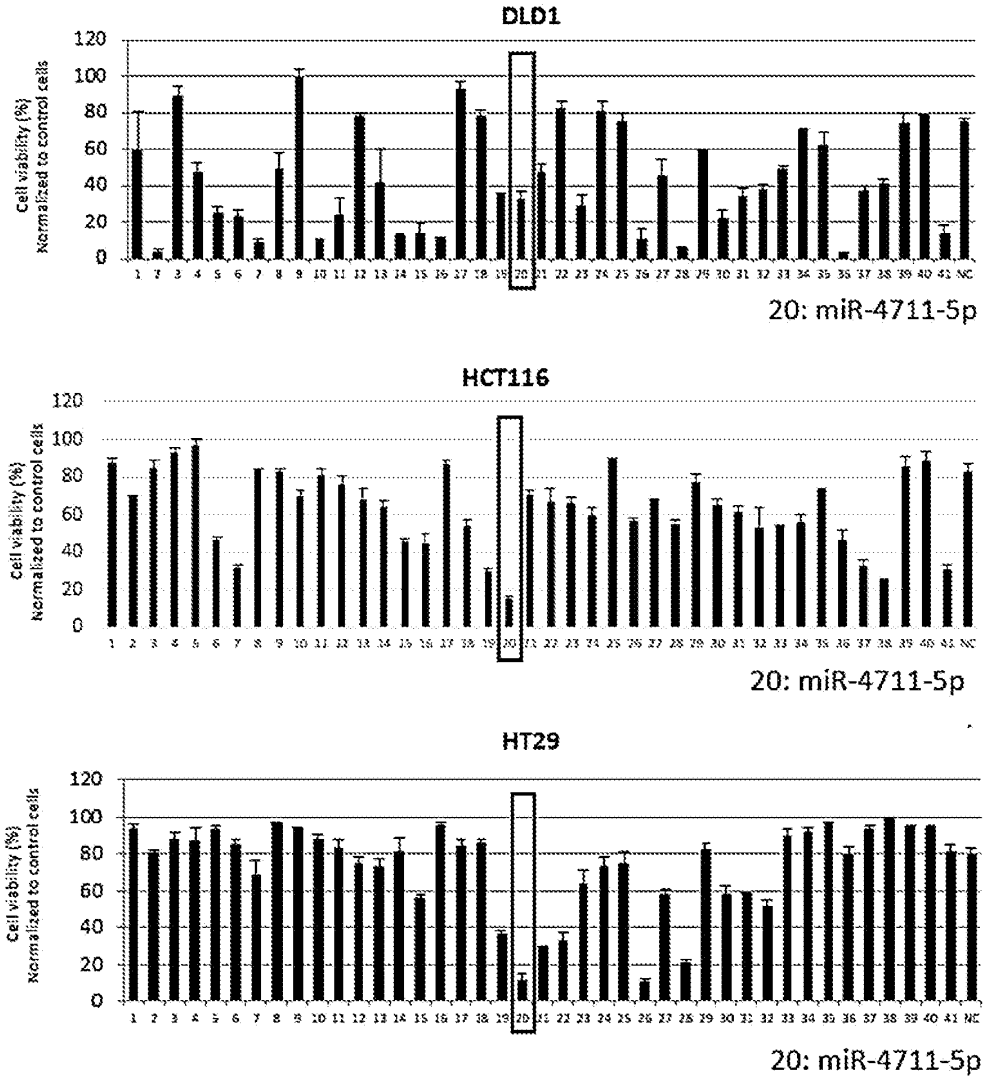
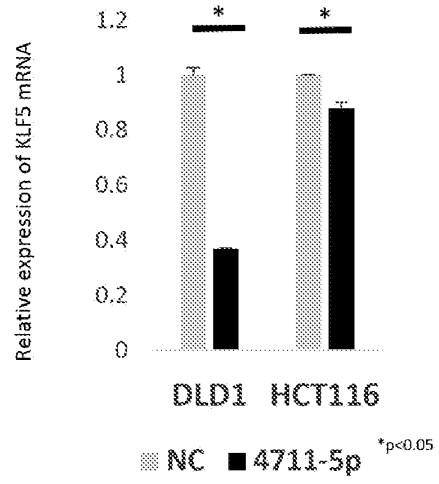
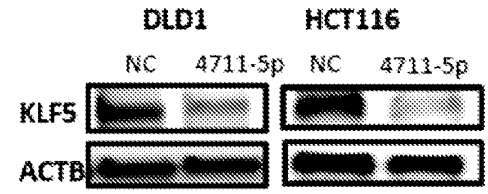
[図1]


DLD1
Cell viability (%)
Normalized to control cells
120
100
80
60
40
20
0
20: miR-4711-5p
HCT116
Cell viability (%)
Normalized to control cells
20: miR-4711-5p
HT29
Cell viability (%)
Normalized to control cells
20: miR-4711-5p

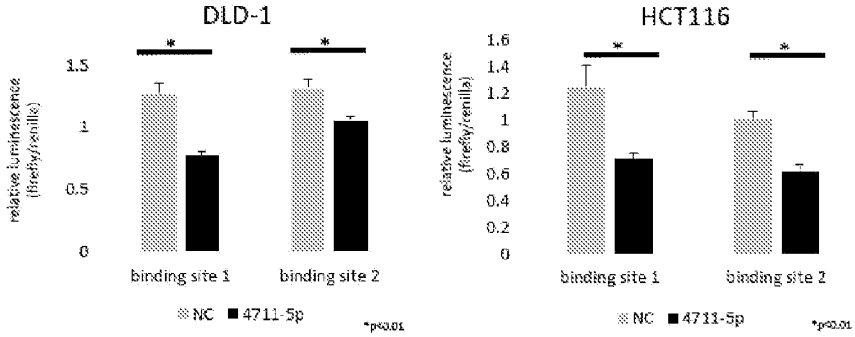
[図2]


Relative expression of KLF5 mRNA
1.2
1
0.8
0.6
0.4
0.2
0
*
*
DLD1 HCT116
NC
4711-5p
*p<0.05

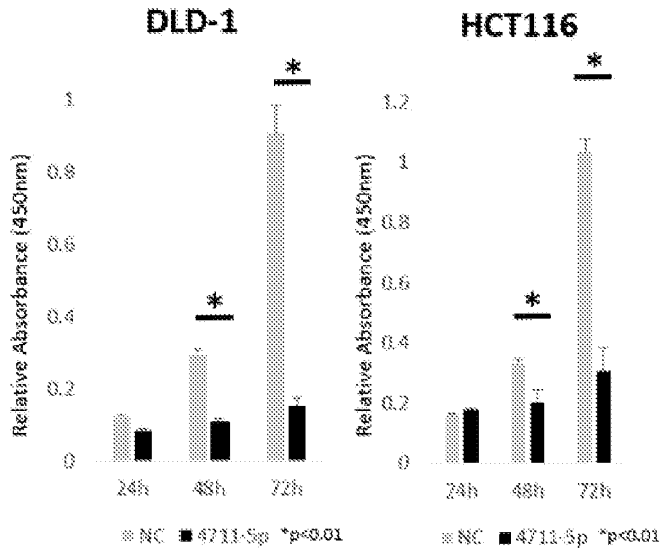
[図3]


DLD1
HCT116
NC
4711-5p
NC
4711-5p
KLF5
ACTB

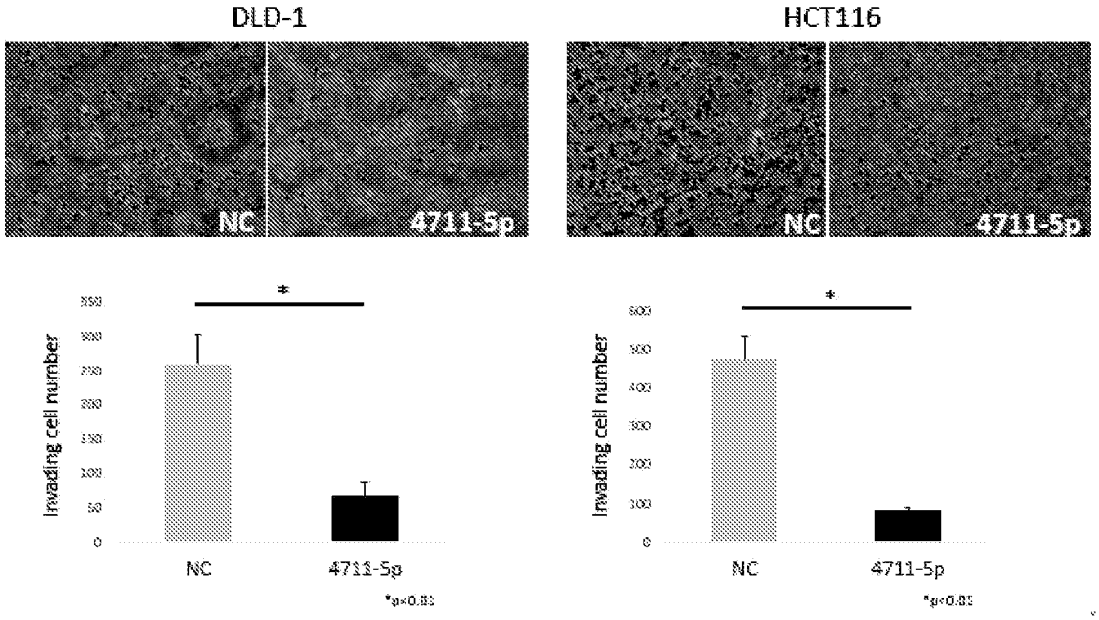
[図4]


DLD-1
HCT116
relative luminescence (firefly/renilla)
binding site 1
binding site 2
NC
4711-5p
*p<0.01

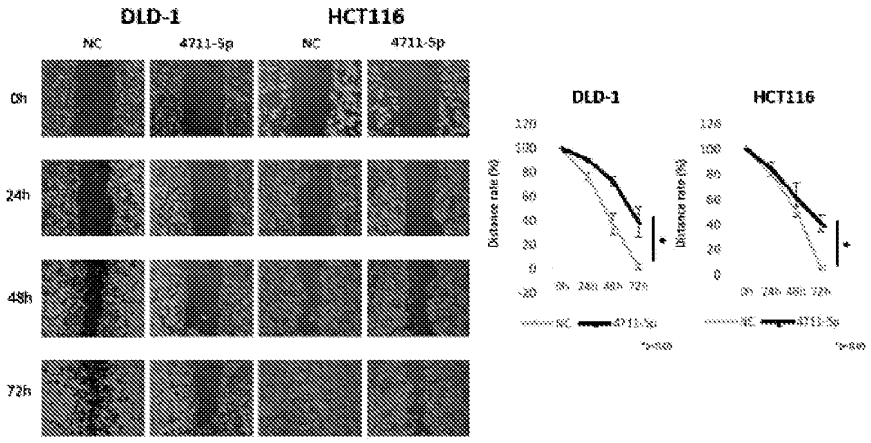
[図5]


DLD-1
HCT116
Relative Absorbance (450nm)
24h
48h
72h
NC
4711-5p
*p<0.01

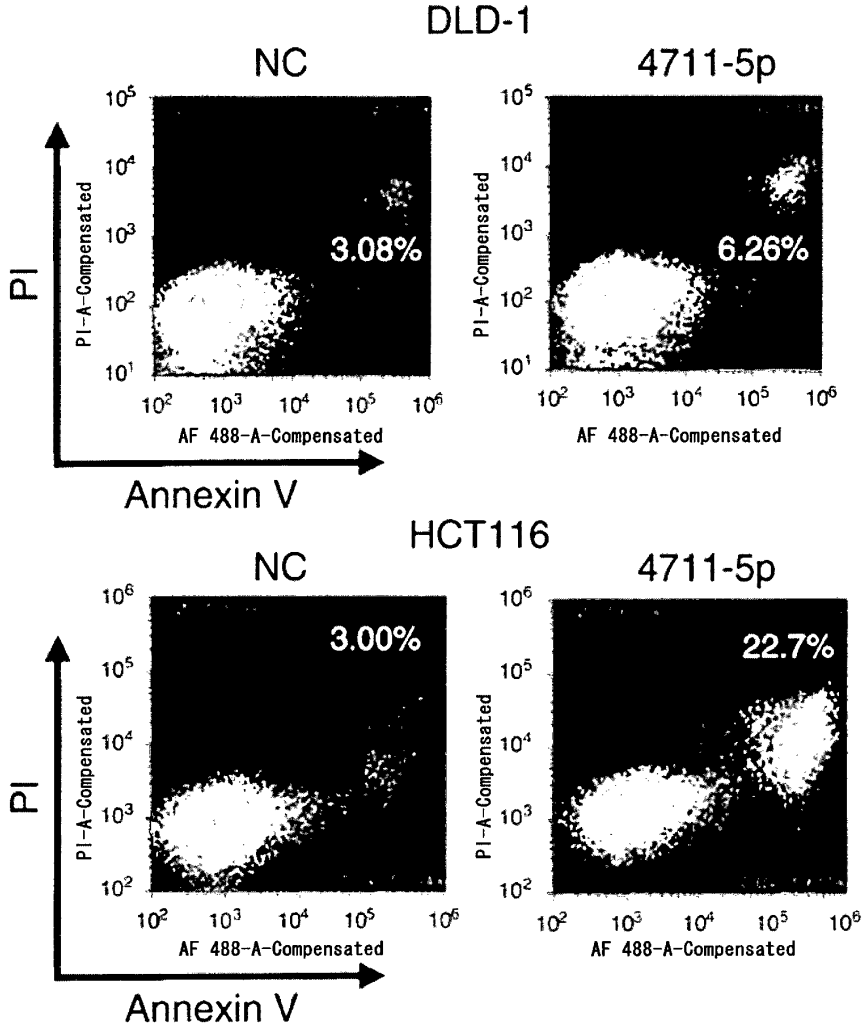
[図6]


DLD-1
HCT116
NC
4711-5p
NC
4711-5p
Invading cell number
*
NC
4711-5p
Invading cell number
*
NC
4711-5p

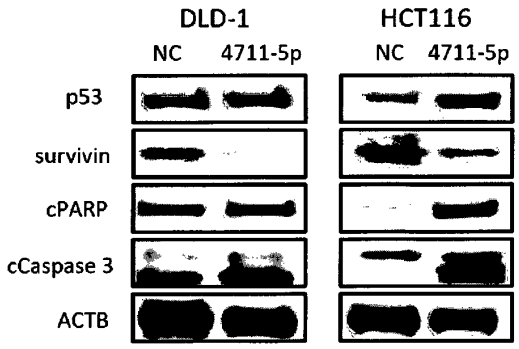
[図7]


DLD-1
HCT116
NC
4711-5p
NC
4711-5p
0h
24h
48h
72h
DLD-1
HCT116
Distance rate (%)
Distance rate (%)

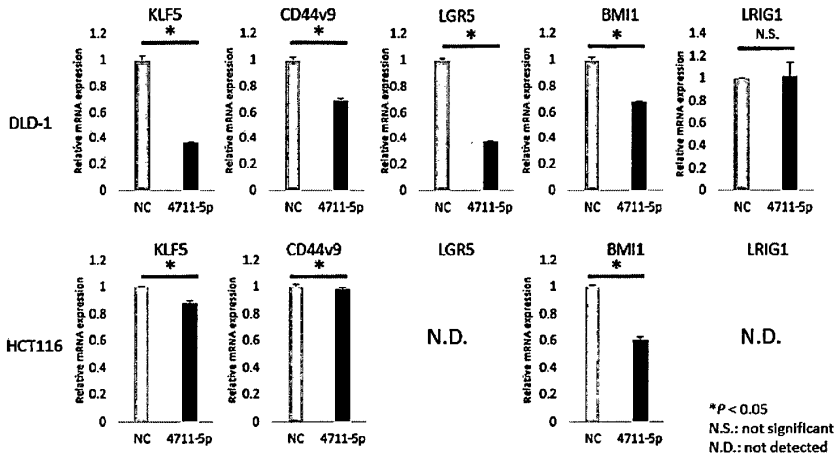
[図8]


DLD-1
NC
4711-5p
3.08%
6.26%
PI
PI-A-Compensated
AF 488-A-Compensated
Annexin V
HCT116
NC
4711-5p
3.00%
22.7%
PI
PI-A-Compensated
AF 488-A-Compensated
Annexin V

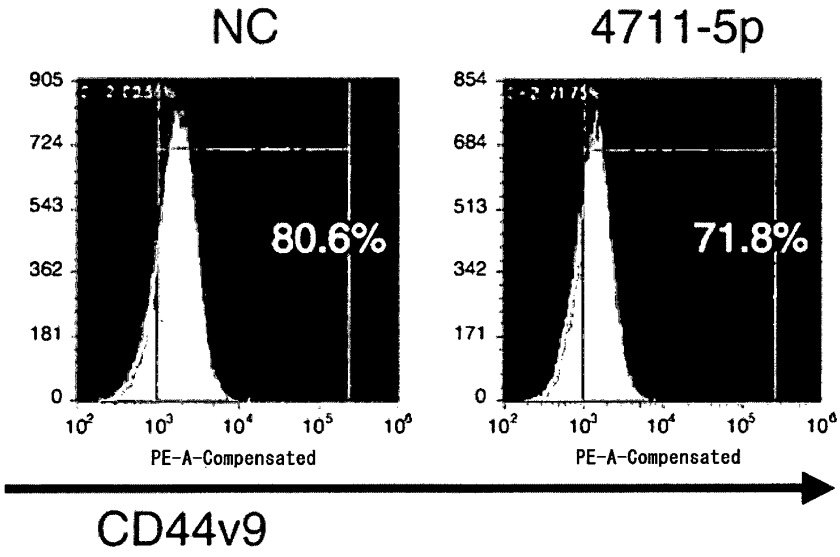
[図9]


DLD-1
HCT116
NC
4711-5p
NC
4711-5p
p53
survivin
cPARP
cCaspase 3
ACTB

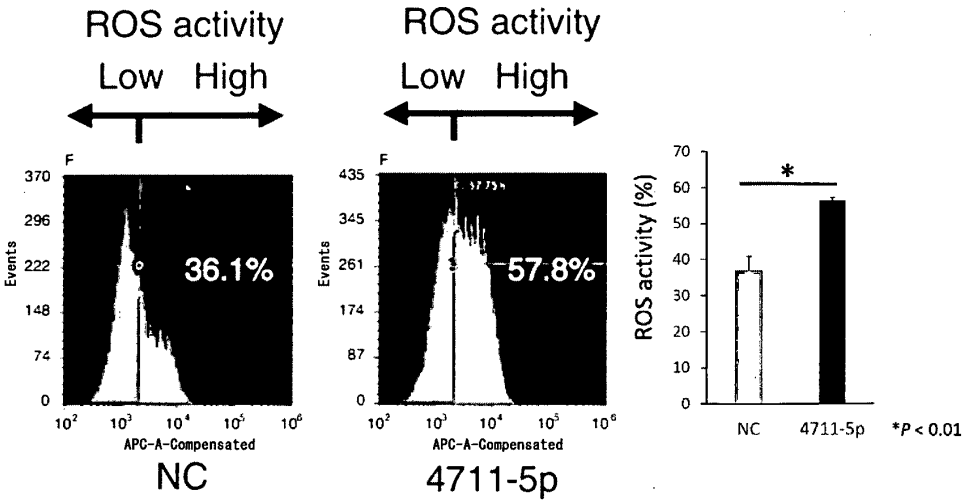
[図10]


KLF5
CD44v9
LGR5
BMI1
LRIG1
DLD-1
HCT116
Relative mRNA expression
NC
4711-5p
N.S.
N.D.
*P < 0.05
N.S.: not significant
N.D.: not detected

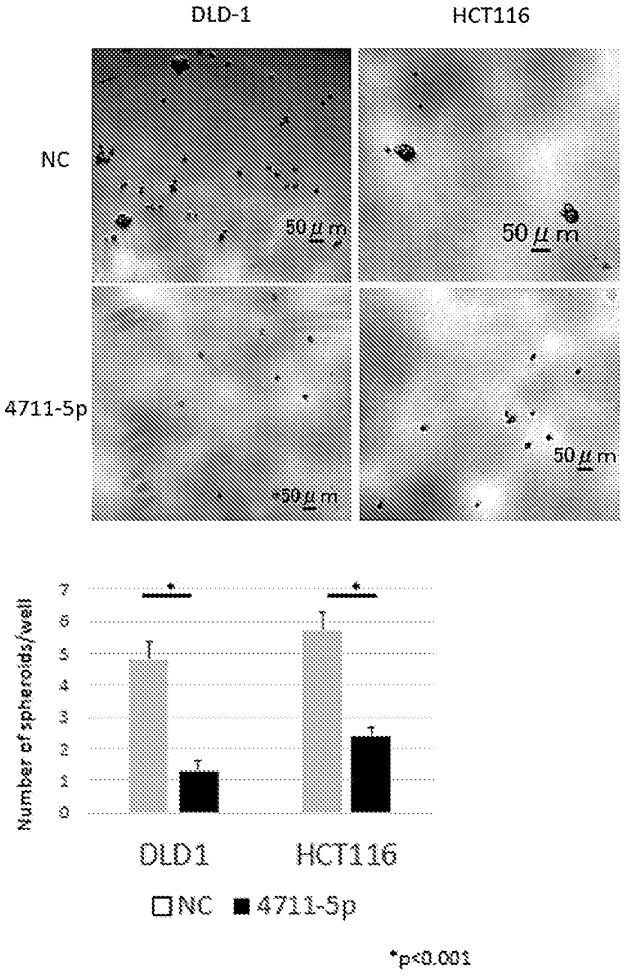
[図11]


NC
4711-5p
80.6%
71.8%
PE-A-Compensated
CD44v9

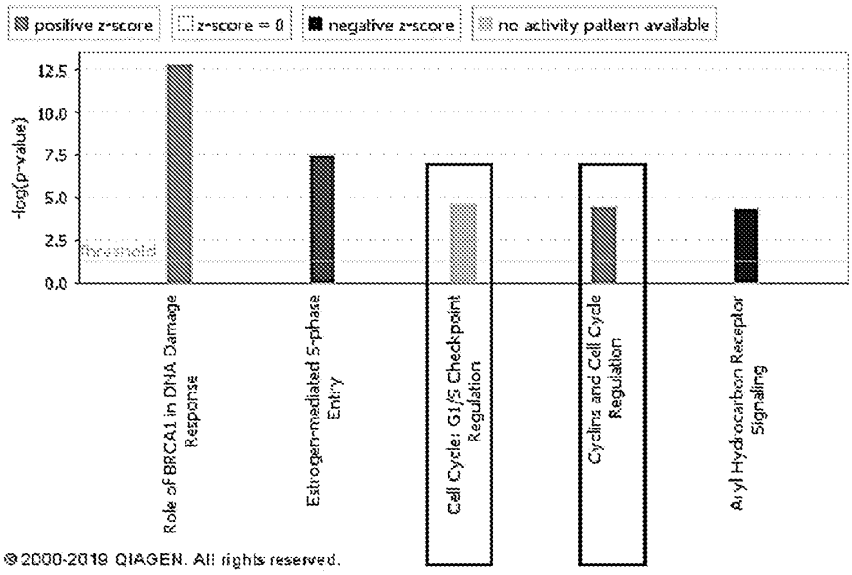
[図12]


ROS activity
Low High
36.1%
57.8%
Events
APC-A-Compensated
NC
4711-5p
ROS activity (%)
*P < 0.01

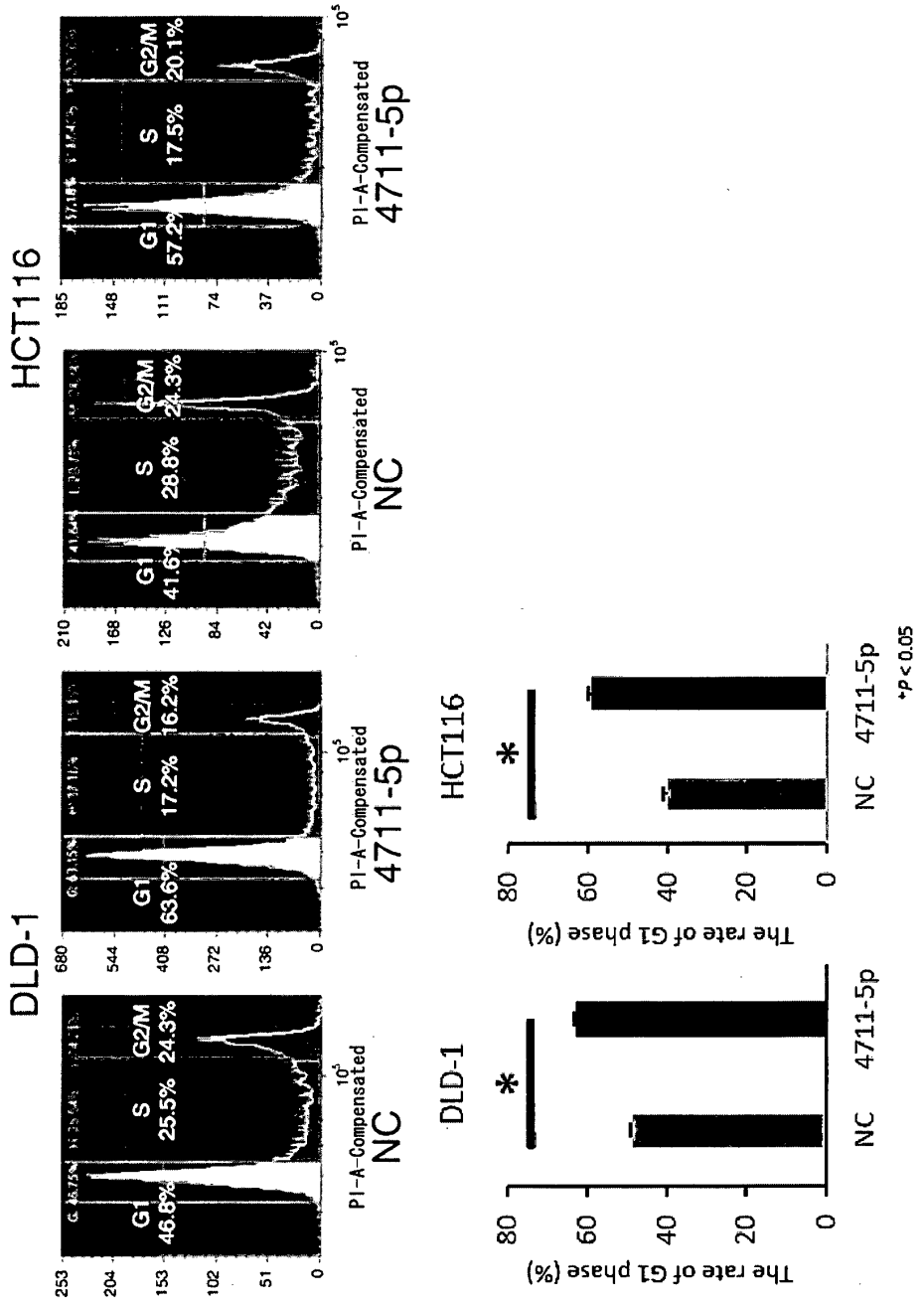
[図13]


DLD-1
HCT116
NC
4711-5p
50μm
Number of spheroids/well
DLD1
HCT116
NC
4711-5p
*p<0.001

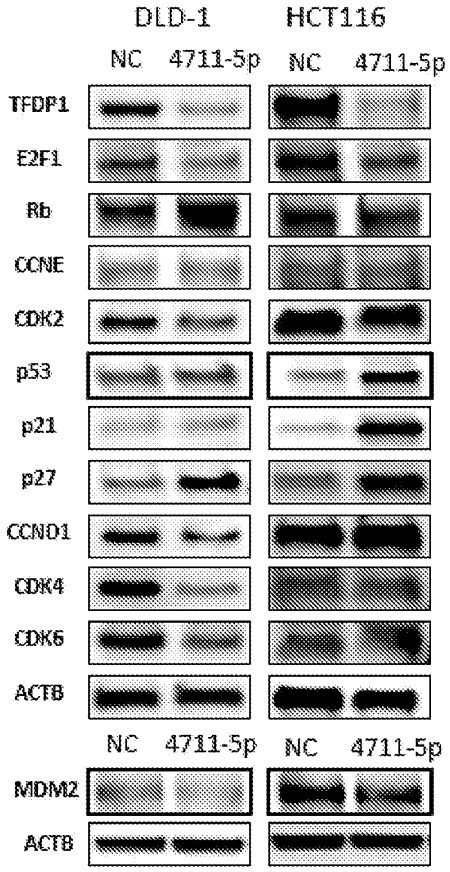
[図14]


positive z-score
z-score = 0
negative z-score
no activity pattern available
-log(p-value)
Threshold
Role of BRCA1 in DNA Damage Response
Estrogen-mediated S-phase Entry
Cell Cycle: G1/S Checkpoint Regulation
Cyclins and Cell Cycle Regulation
Aryl Hydrocarbon Receptor Signaling
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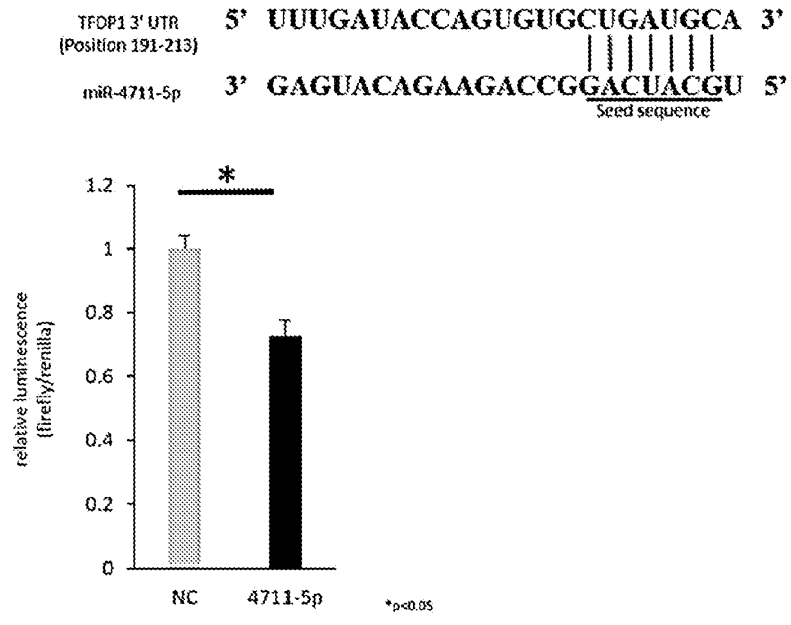
[図15]


DLD-1
HCT116
NC
4711-5p
PI-A-Compensated
G1
S
G2/M
46.8%
25.5%
24.3%
63.6%
17.2%
16.2%
41.6%
28.8%
24.3%
57.2%
17.5%
20.1%
The rate of G1 phase (%)
*P < 0.05

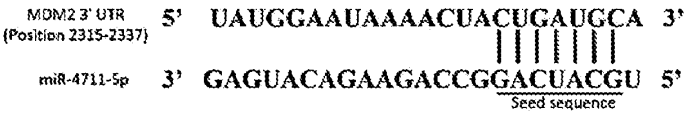
[図16]

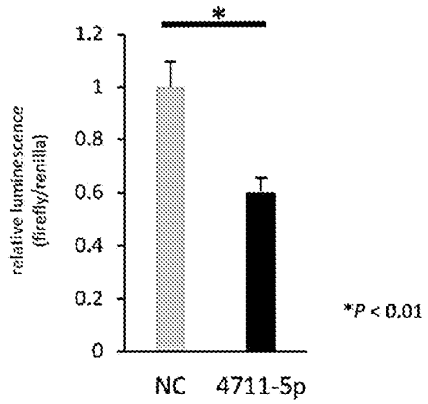

DLD-1
HCT116
NC
4711-5p
NC
4711-5p
TFDP1
E2F1
Rb
CCNE
CDK2
p53
p21
p27
CCND1
CDK4
CDK6
ACTB
NC
4711-5p
NC
4711-5p
MDM2
ACTB

[図17]

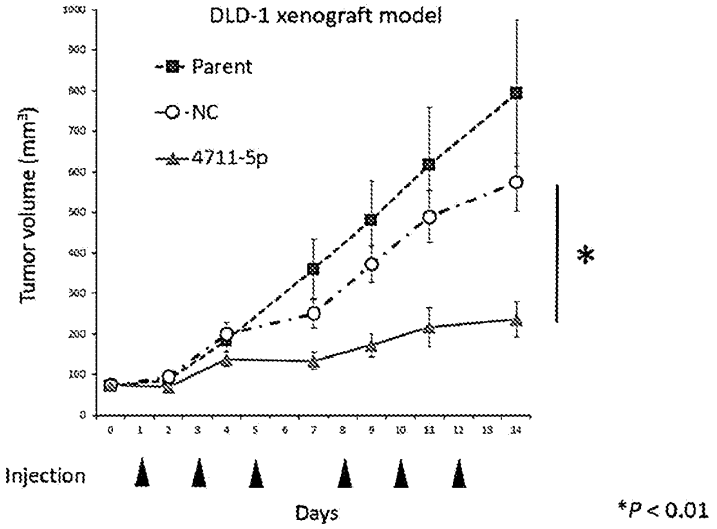

TFDP1 3' UTR
(Position 191-213)
5' UUUGAUACCAGUGUGCUGAUGCA 3'
miR-4711-5p
3' GAGUACAGAAGACCGGACUACGU 5'
Seed sequence
relative luminescence
(firefly/renilla)
1.2
1
0.8
0.6
0.4
0.2
0
*
NC
4711-5p
*p<0.05

[図18]

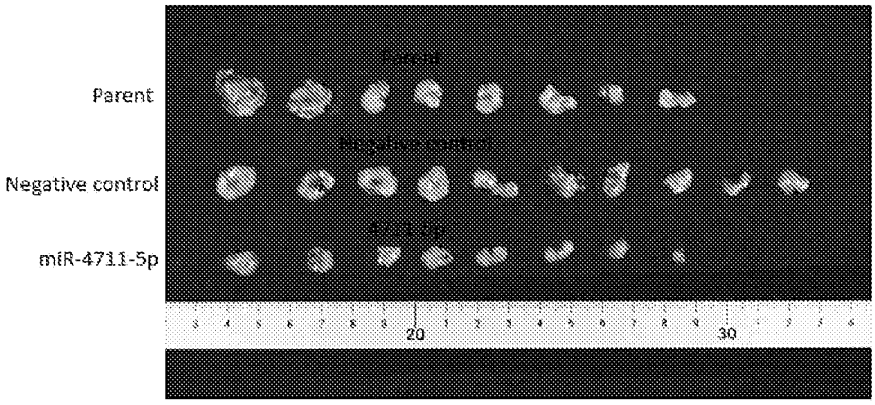

MDM2 3' UTR
(Position 2315-2337)
5' UAUGGAAUAAAACUACUGAUGCA 3'
miR-4711-5p
3' GAGUACAGAAGACCGGACUACGU 5'
Seed sequence


relative luminescence
(firefly/renilla)
1.2
1
0.8
0.6
0.4
0.2
0
*
*P < 0.01
NC
4711-5p

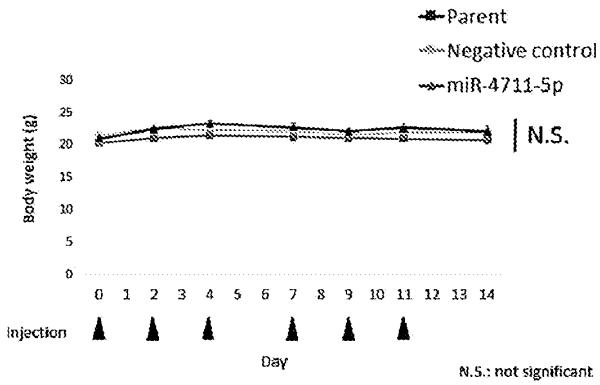
[図19]


DLD-1 xenograft model
Parent
NC
4711-5p
Tumor volume (mm³)
*
Injection
Days
*P < 0.01

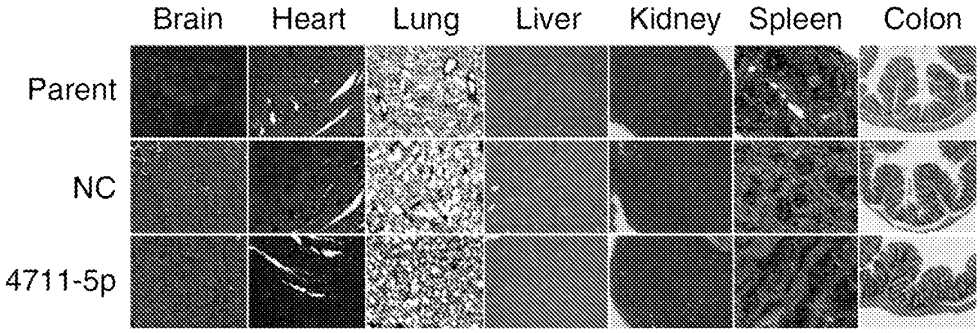
[図20]


Parent
Negative control
miR-4711-5p
20
30

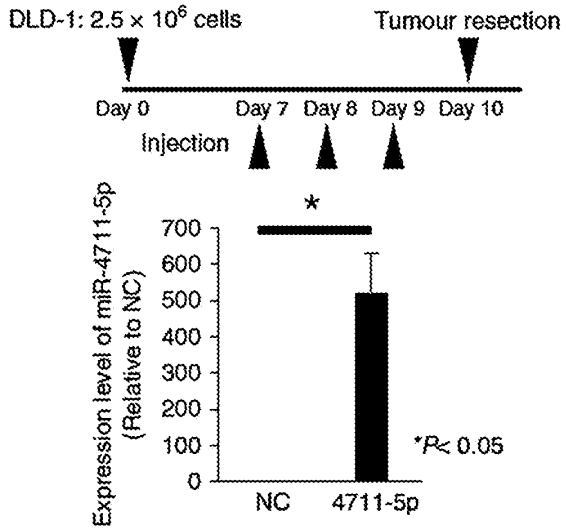
[図21]


Parent
Negative control
miR-4711-5p
Body weight (g)
30
25
20
15
10
5
0
N.S.
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Injection
Day
N.S.: not significant

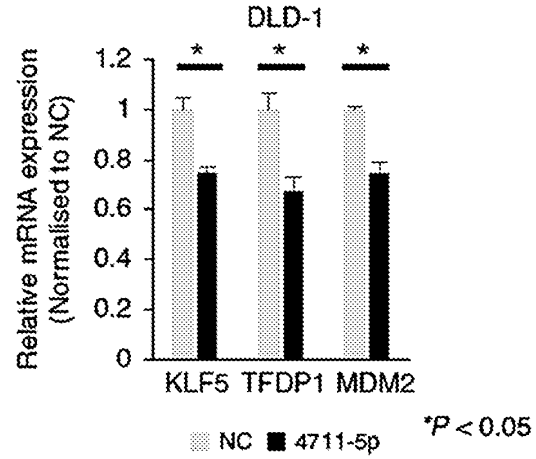
[図22]


Brain
Heart
Lung
Liver
Kidney
Spleen
Colon
Parent
NC
4711-5p

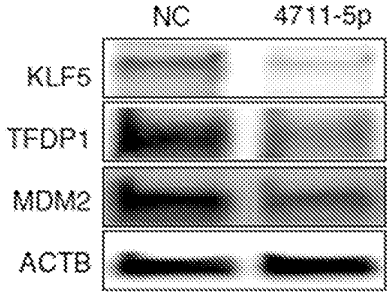
[図23]


DLD-1: 2.5 × 10^6 cells
Tumour resection
Day 0
Day 7
Day 8
Day 9
Day 10
Injection
*
Expression level of miR-4711-5p (Relative to NC)
700
600
500
400
300
200
100
0
*P< 0.05
NC
4711-5p

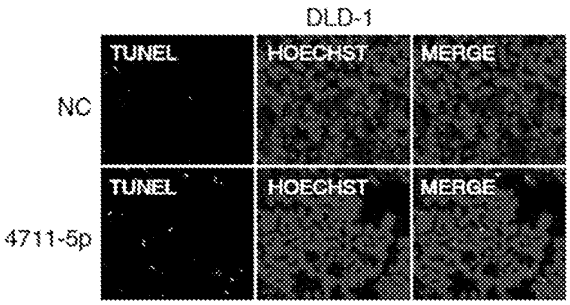
[図24]



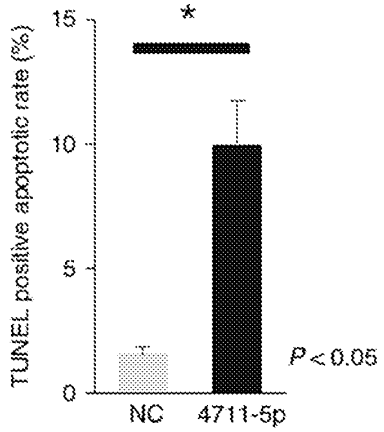
[図25]



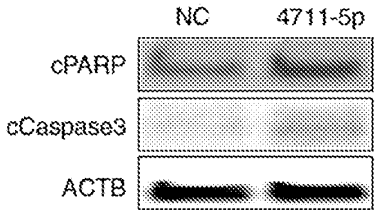
[図26]



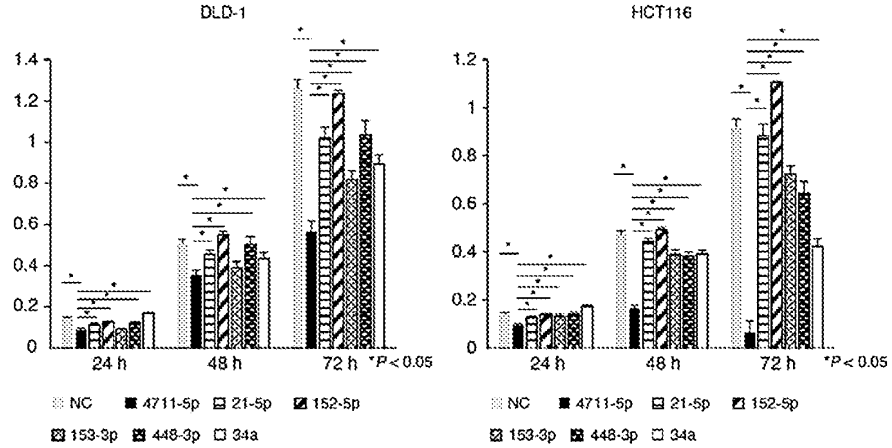
[図27]



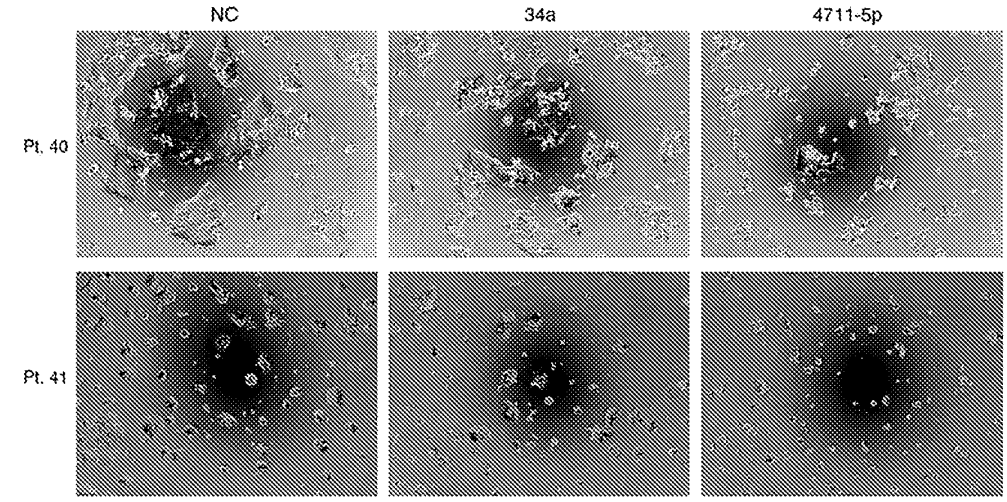
[図28]


NC
4711-5p
cPARP
cCaspase3
ACTB

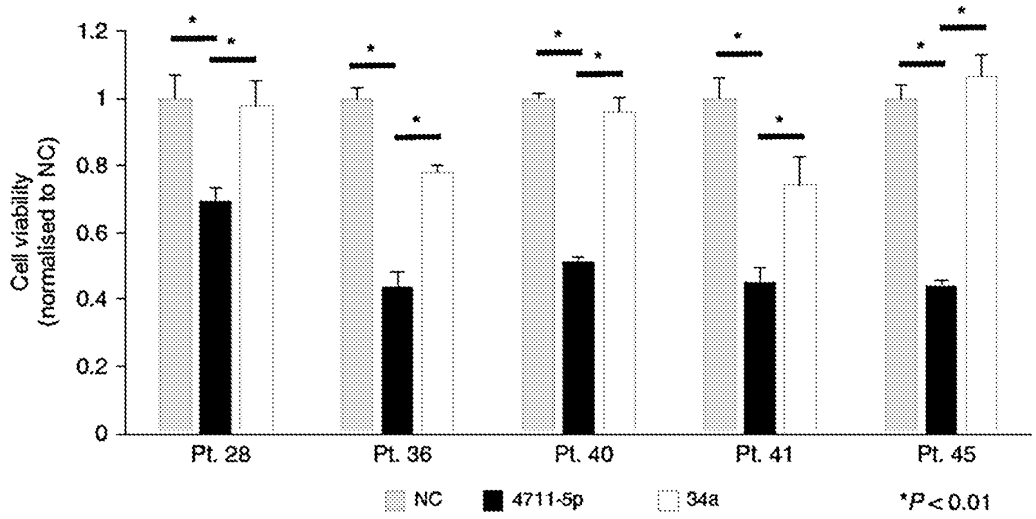
[図29]


DLD-1
HCT116
1.4
1.2
1
0.8
0.6
0.4
0.2
0
24 h
48 h
72 h
*P < 0.05
NC
4711-5p
21-5p
152-5p
153-3p
448-3p
34a

[図30]


NC
34a
4711-5p
Pt. 40
Pt. 41

[図31]


Cell viability
(normalised to NC)
1.2
1
0.8
0.6
0.4
0.2
0
Pt. 28
Pt. 36
Pt. 40
Pt. 41
Pt. 45
NC
4711-5p
34a
*P < 0.01