FIG.1A

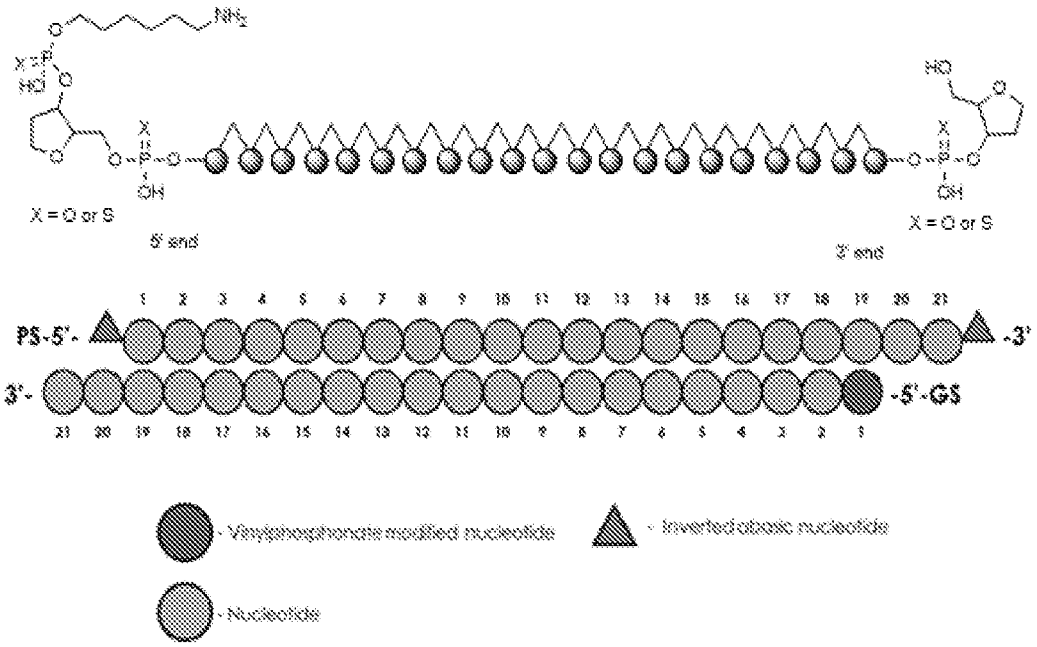

X = O or S
5' end
3' end
X = O or S
PS-5'-
-3'
3'-
-5'-GS
- Vinylphosphonate modified nucleotide
- Inverted abasic nucleotide
- Nucleotide

FIG. 1B

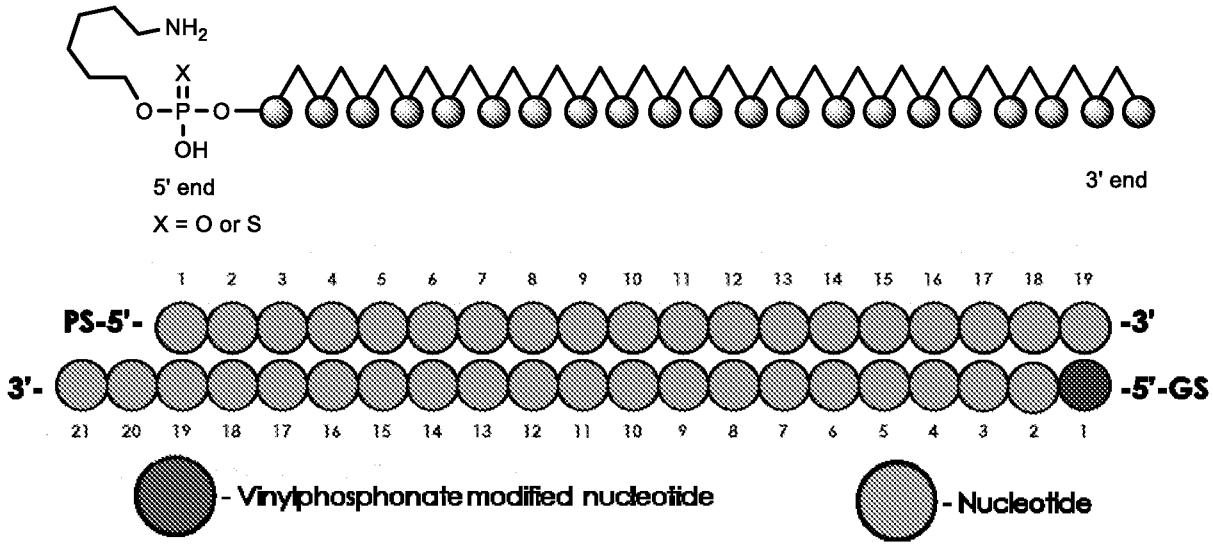

NH2
X
O-P-O
OH
5' end
X = O or S
3' end
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
PS-5'-
-3'
3'-
-5'-GS
21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1
- Vinylphosphonate modified nucleotide
- Nucleotide

FIG. 2

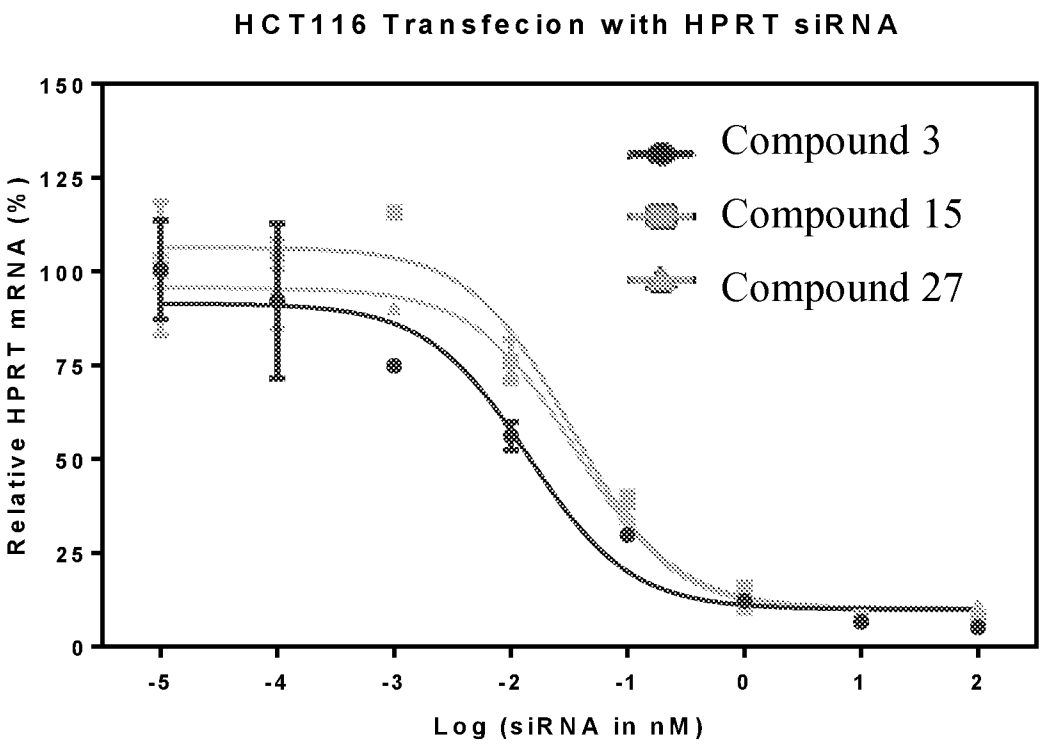

HCT116 Transfecion with HPRT siRNA
Relative HPRT mRNA (%)
150
125
100
75
50
25
0
-5
-4
-3
-2
-1
0
1
2
Log (siRNA in nM)
Compound 3
Compound 15
Compound 27

FIG. 3

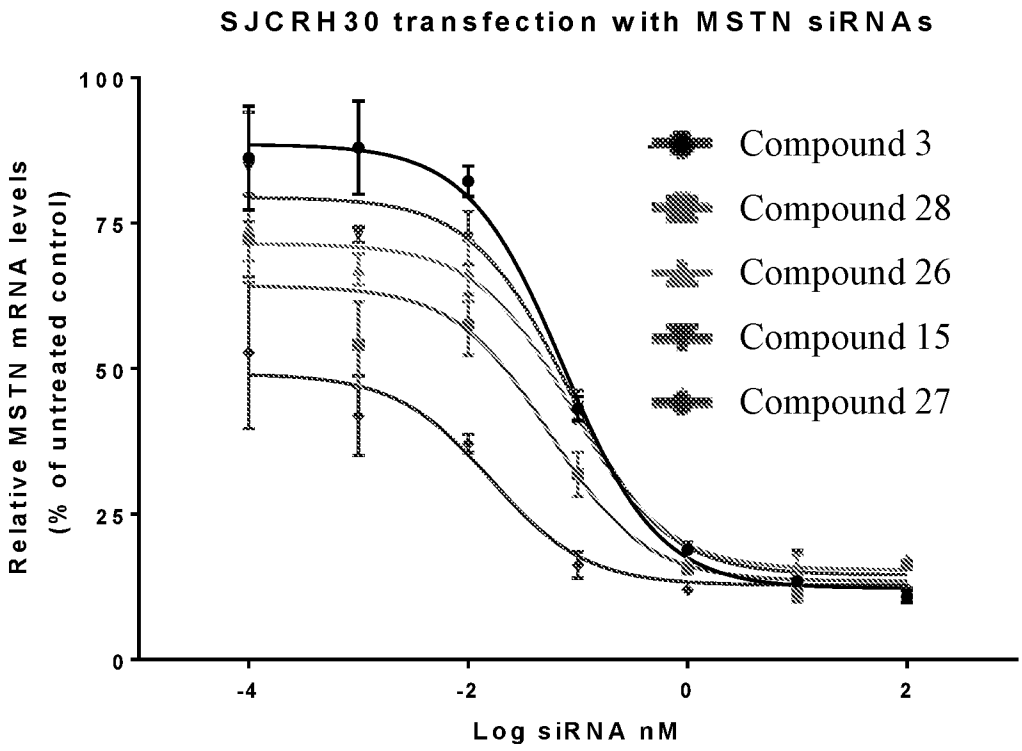

SJCRH30 transfection with MSTN siRNAs
Relative MSTN mRNA levels
(% of untreated control)
100
75
50
25
0
-4
-2
0
2
Log siRNA nM
Compound 3
Compound 28
Compound 26
Compound 15
Compound 27

FIG. 4

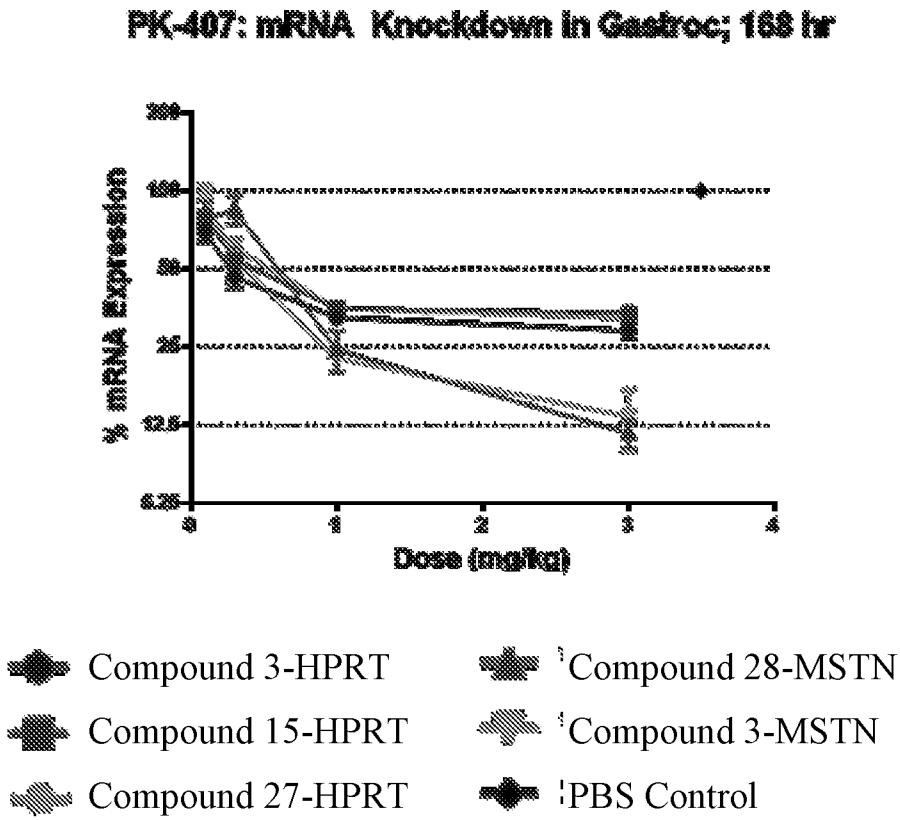
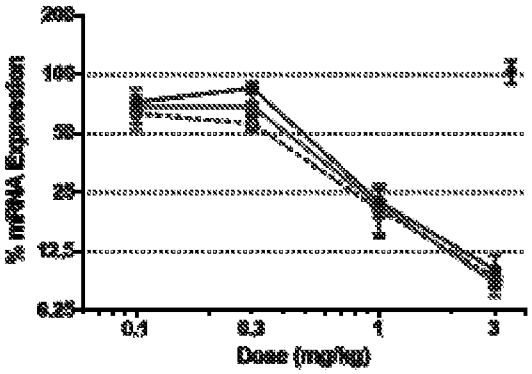
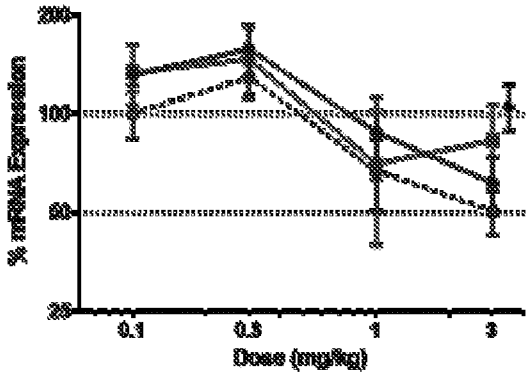

PK-407: mRNA Knockdown in Gastroc; 168 hr
% mRNA Expression
Dose (mg/kg)
Compound 3-HPRT
Compound 15-HPRT
Compound 27-HPRT
Compound 28-MSTN
Compound 3-MSTN
PBS Control

FIG. 5

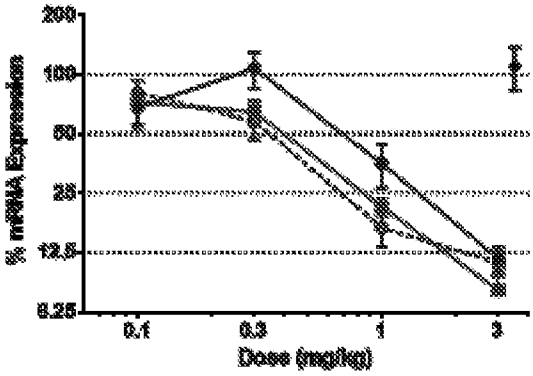
(A) Gastroc



(B) Heart



(C) Quad

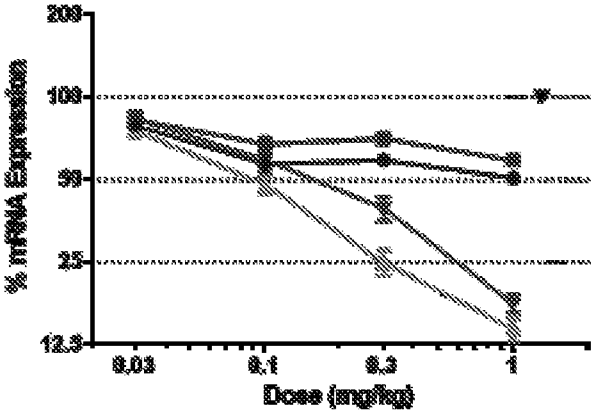


Compound 26 PBS Control

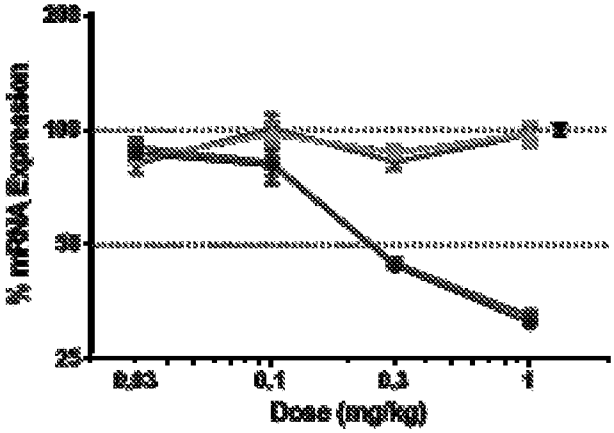
Compound 15 Compound 3

FIG. 6

(A) Gastroc



(B) Liver



TfR1-mAb-Compound 23-HPRT
TfR1-mAb-Compound 26-HPRT
PBS Control
ASGR-mAb-compound 3-HPRT
ASGR-mAb-compound 26-HPRT

FIG. 7

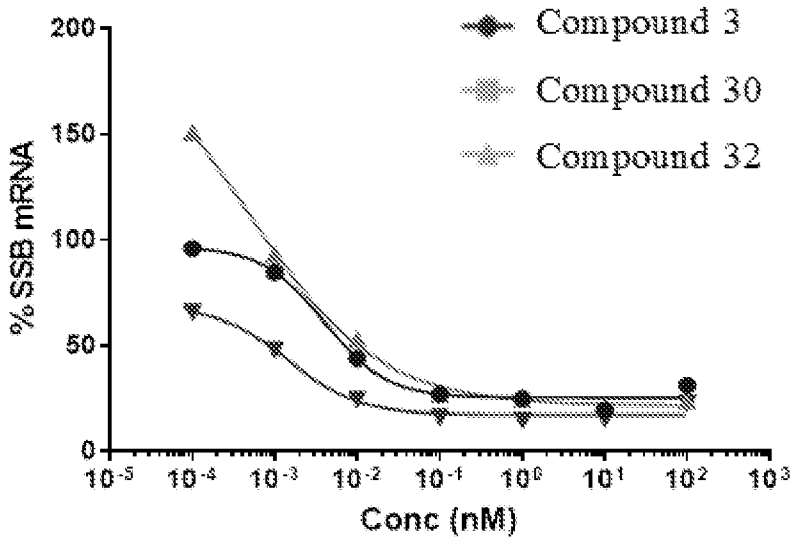

Compound 3
Compound 30
Compound 32
% SSB mRNA
200
150
100
50
0
10-5
10-4
10-3
10-2
10-1
100
101
102
103
Conc (nM)

FIG. 8

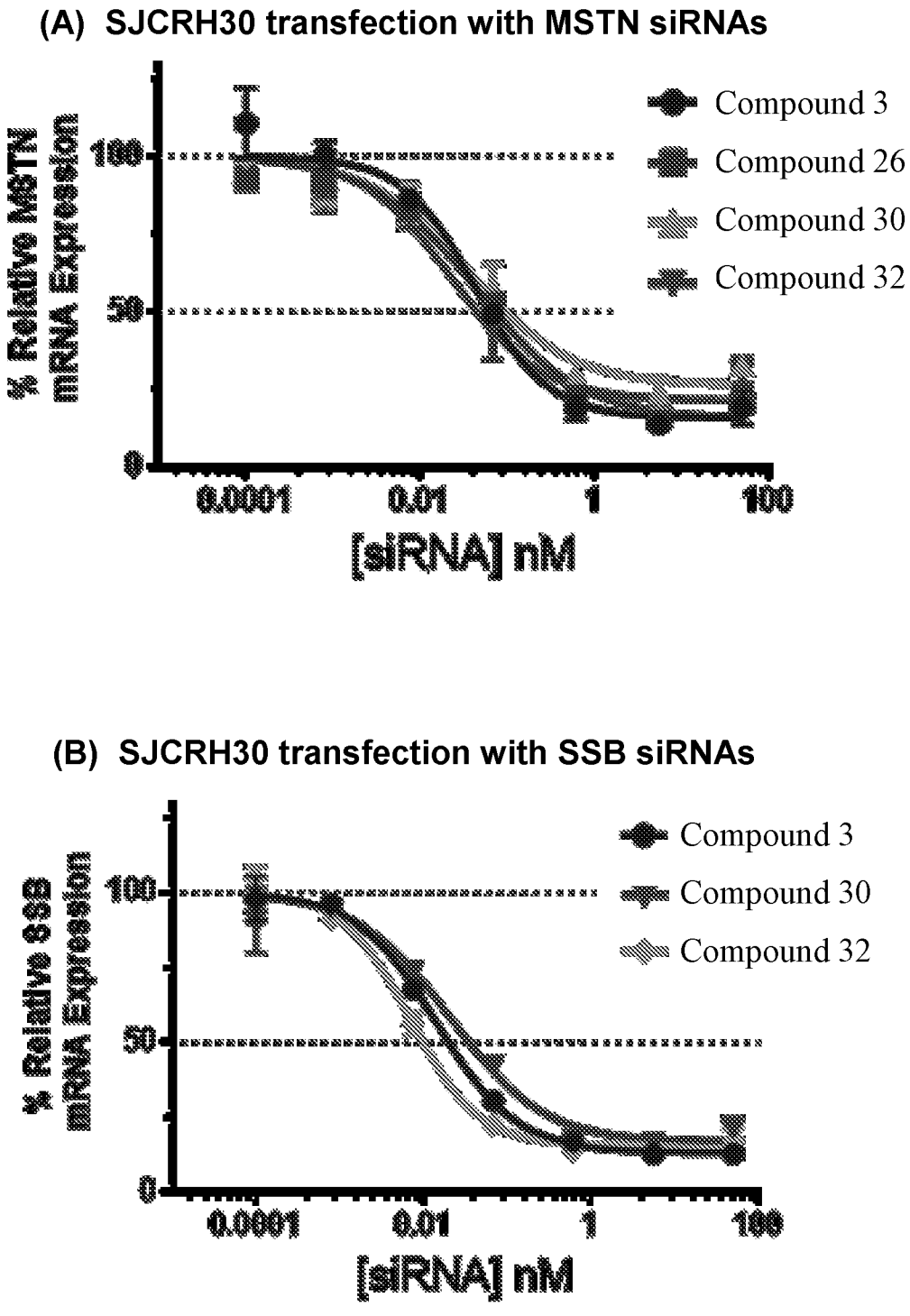
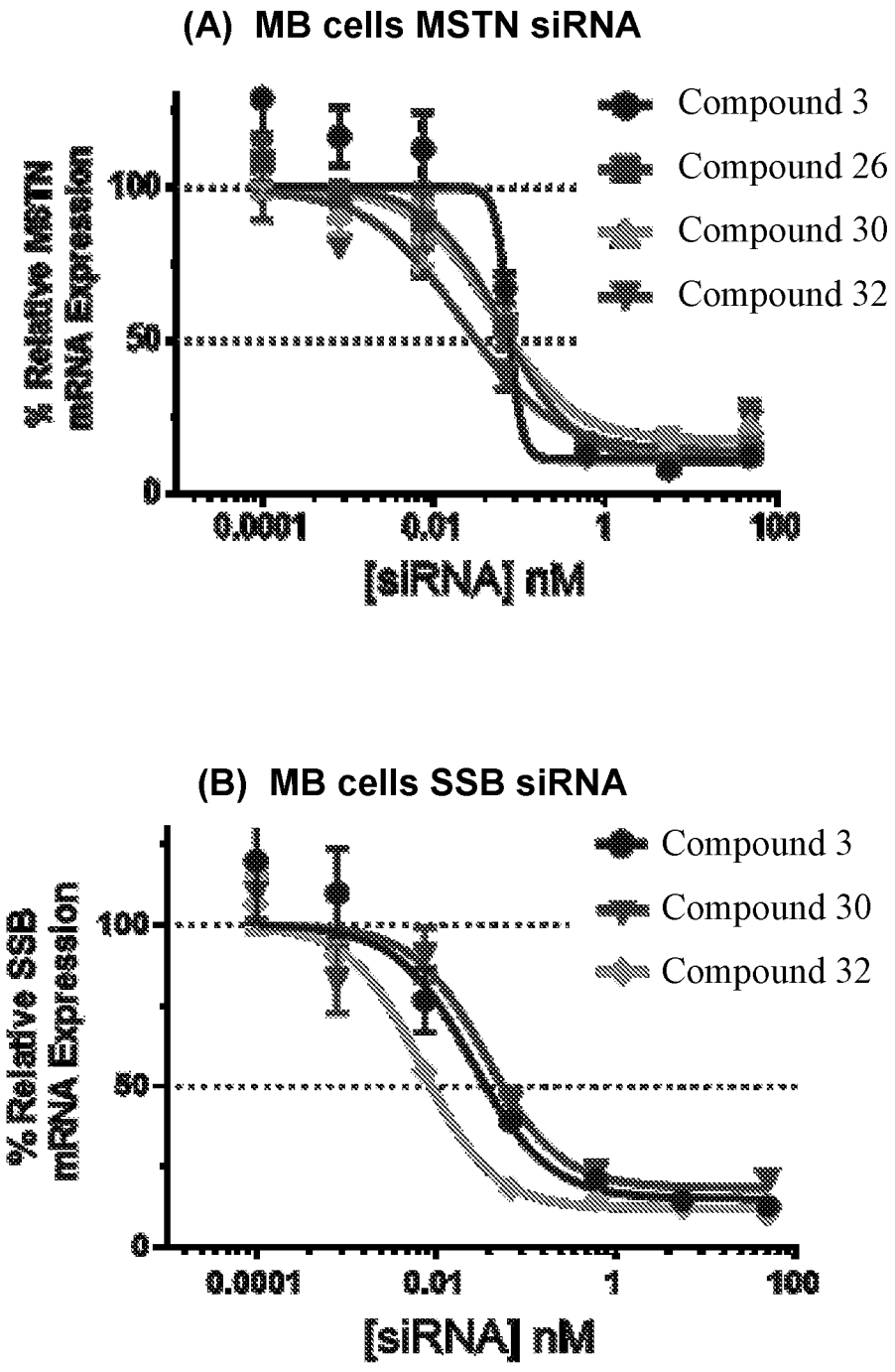

(A) SJCRH30 transfection with MSTN siRNAs
% Relative MSTN mRNA Expression
100
50
0
0.0001
0.01
1
100
[siRNA] nM
Compound 3
Compound 26
Compound 30
Compound 32
(B) SJCRH30 transfection with SSB siRNAs
% Relative SSB mRNA Expression
100
50
0
0.0001
0.01
1
100
[siRNA] nM
Compound 3
Compound 30
Compound 32

FIG. 9


(A) MB cells MSTN siRNA
% Relative MSTN mRNA Expression
100
50
0
0.0001
0.01
1
100
[siRNA] nM
Compound 3
Compound 26
Compound 30
Compound 32
(B) MB cells SSB siRNA
% Relative SSB mRNA Expression
100
50
0
0.0001
0.01
1
100
[siRNA] nM
Compound 3
Compound 30
Compound 32