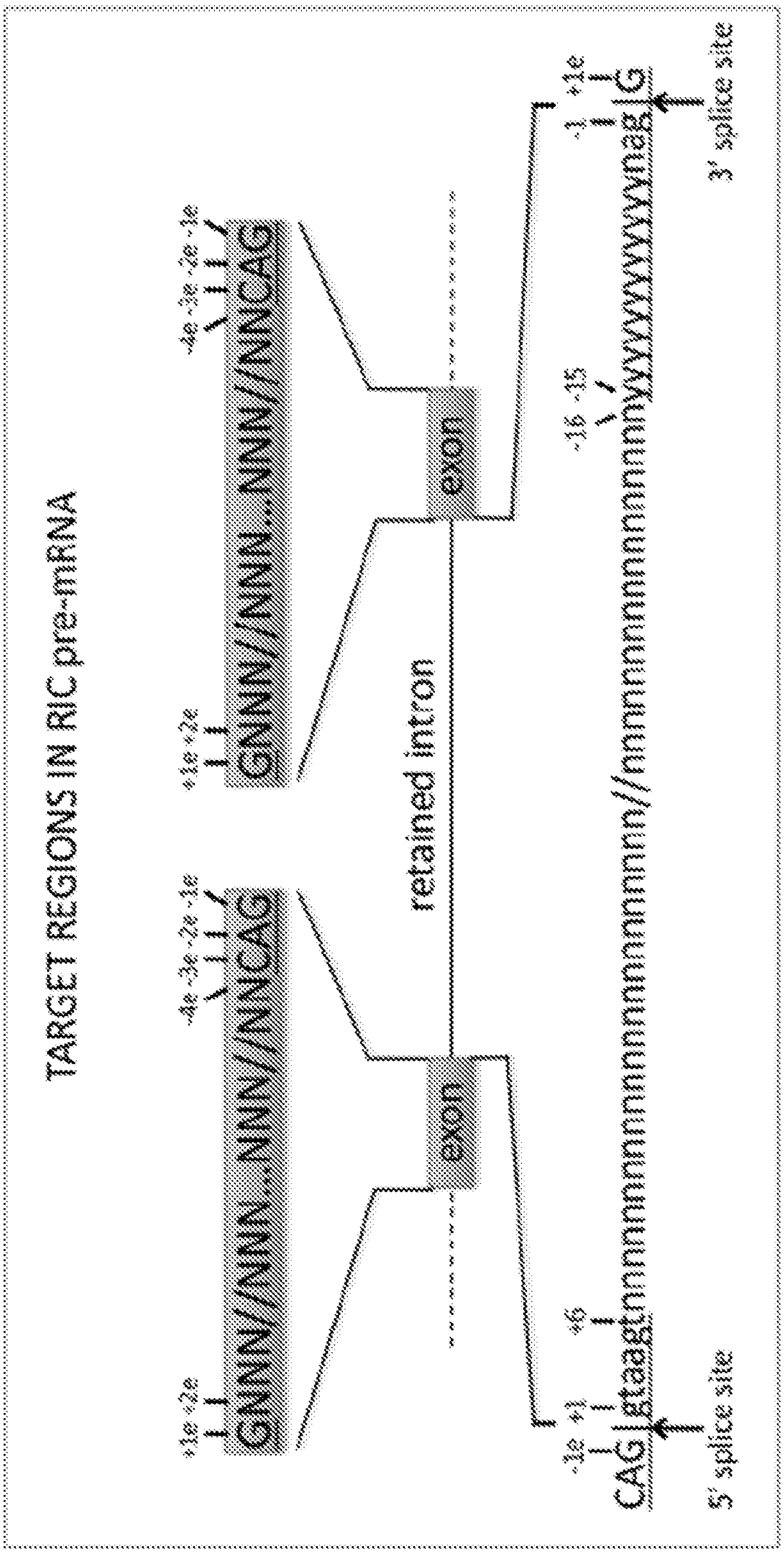

TARGET REGIONS IN RIC pre-mRNA
GNNN/NNN...NNN/NNCAG
GNNN/NNN...NNN/NNCAG
exon
exon
retained intron
CAG|gtaagtnnnnnnnnnnnnnnnnnn//nnnnnnnnnnnnnnnnyyyyyyyyyyyynag|G
5' splice site
3' splice site

FIG. 1

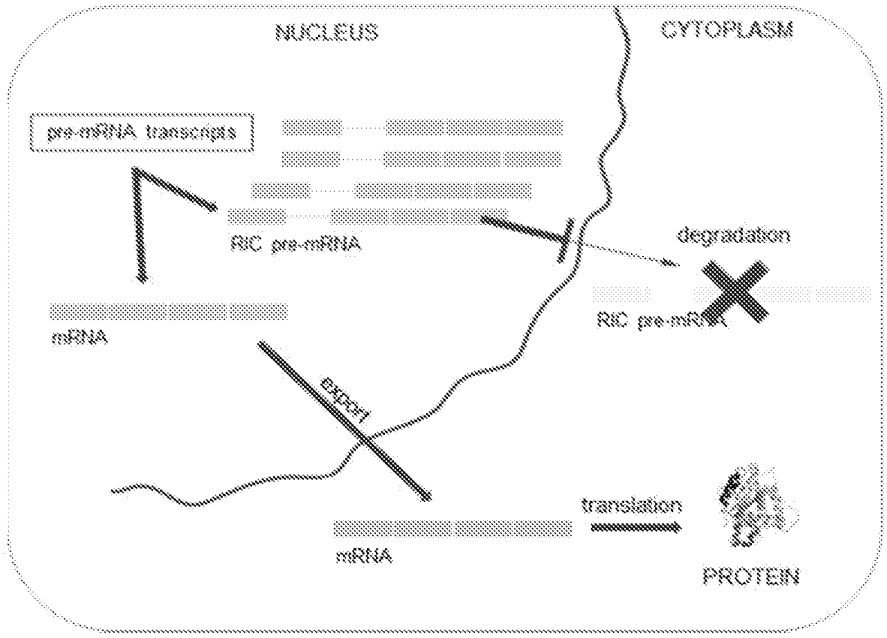

NUCLEUS
CYTOPLASM
pre-mRNA transcripts
RIC pre-mRNA
degradation
RIC pre-mRNA
mRNA
export
translation
mRNA
PROTEIN

FIG. 2A

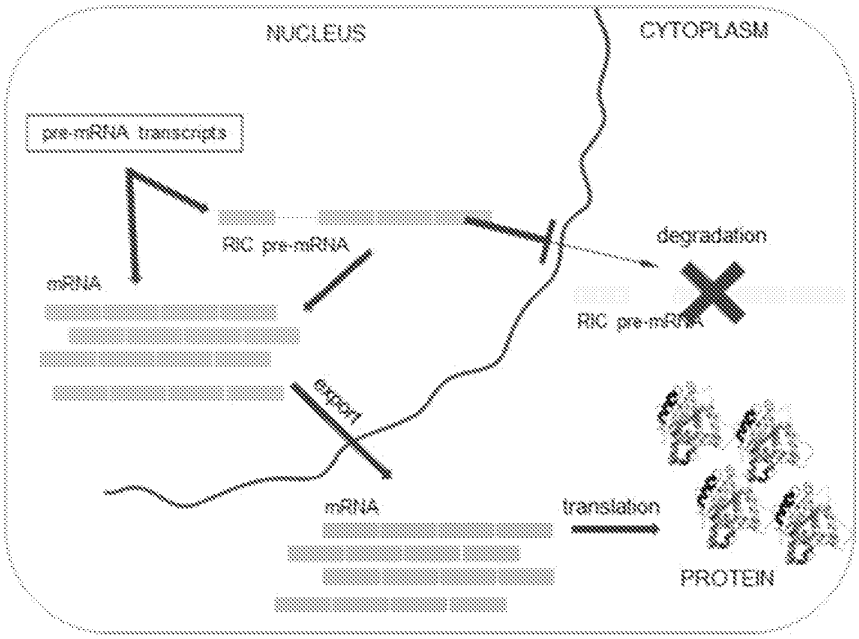

NUCLEUS
CYTOPLASM
pre-mRNA transcripts
RIC pre-mRNA
degradation
RIC pre-mRNA
mRNA
export
mRNA
translation
PROTEIN

FIG. 2B

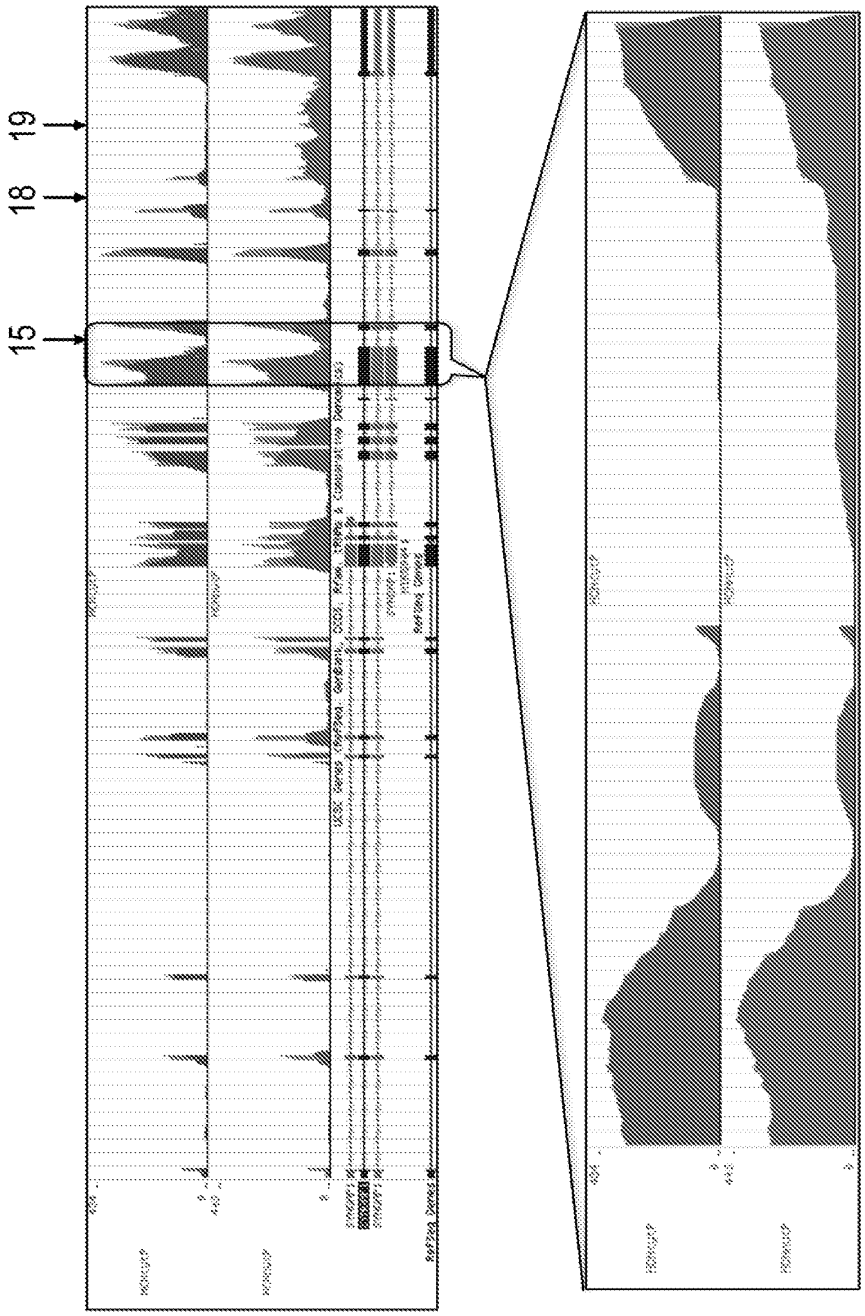


FIG. 3

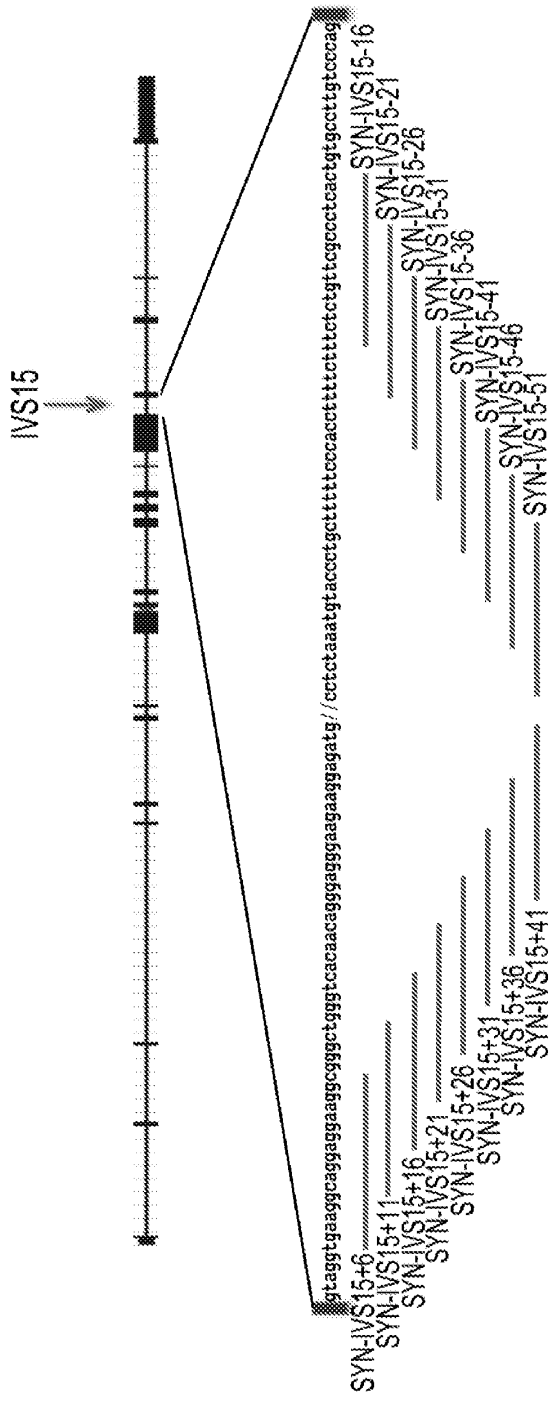

IVS15
SYN-IVS15+6
SYN-IVS15+11
SYN-IVS15+16
SYN-IVS15+21
SYN-IVS15+26
SYN-IVS15+31
SYN-IVS15+36
SYN-IVS15+41
SYN-IVS15-16
SYN-IVS15-21
SYN-IVS15-26
SYN-IVS15-31
SYN-IVS15-36
SYN-IVS15-41
SYN-IVS15-46
SYN-IVS15-51

FIG. 4

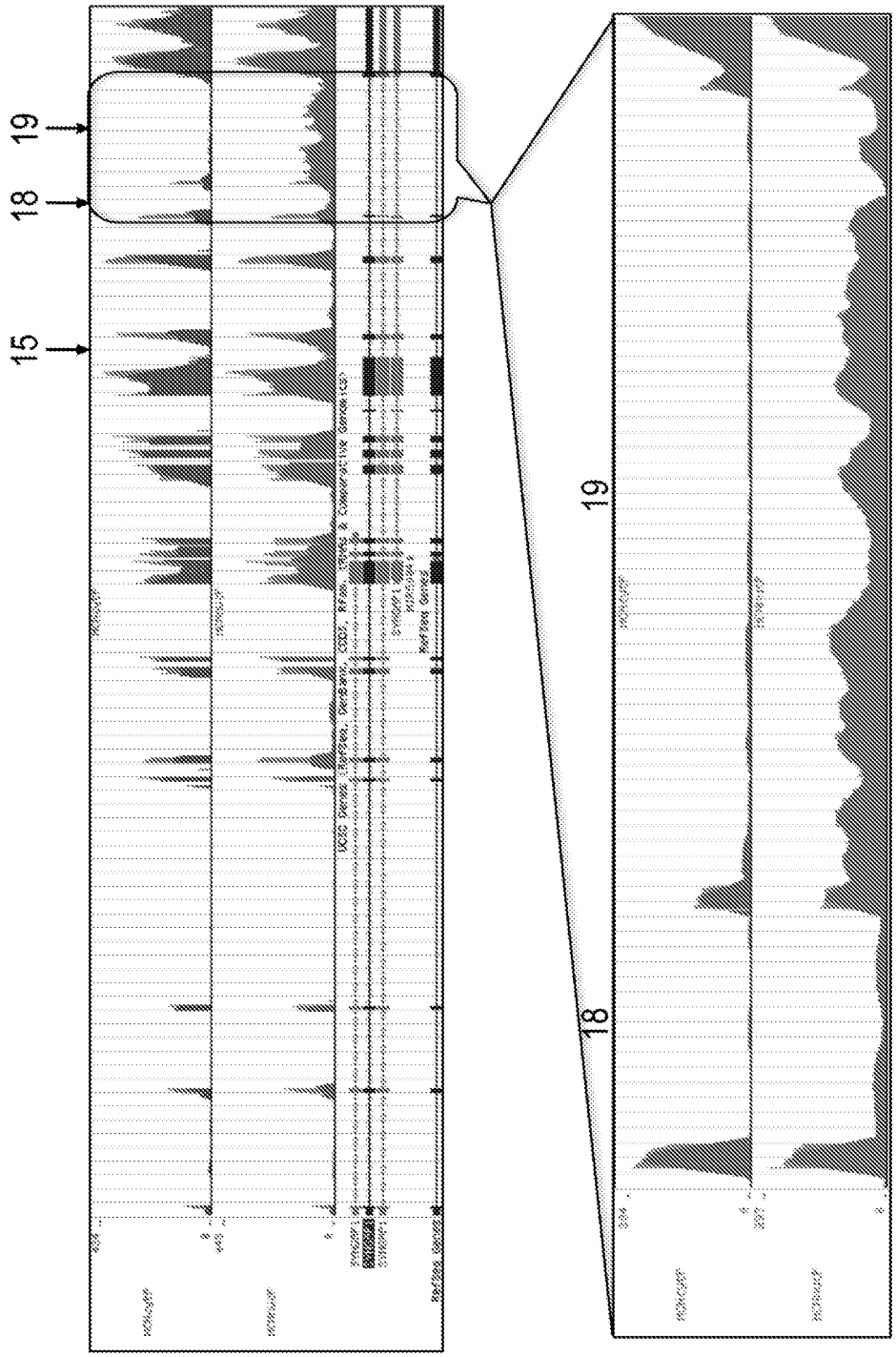


FIG. 5

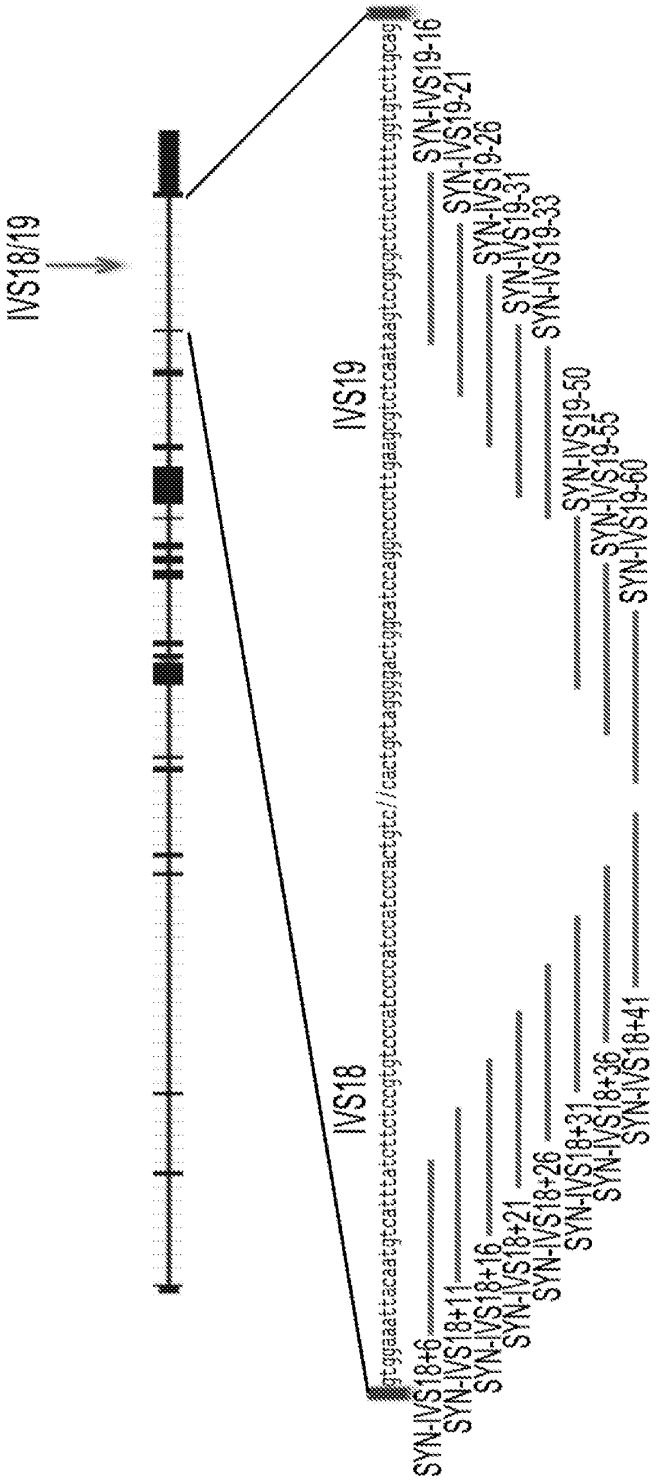

IVS18/19
IVS19
IVS18
SYN-IVS19-16
SYN-IVS19-21
SYN-IVS19-26
SYN-IVS19-31
SYN-IVS19-33
SYN-IVS19-50
SYN-IVS19-55
SYN-IVS19-60
SYN-IVS18+6
SYN-IVS18+11
SYN-IVS18+16
SYN-IVS18+21
SYN-IVS18+26
SYN-IVS18+31
SYN-IVS18+36
SYN-IVS18+41

FIG. 6

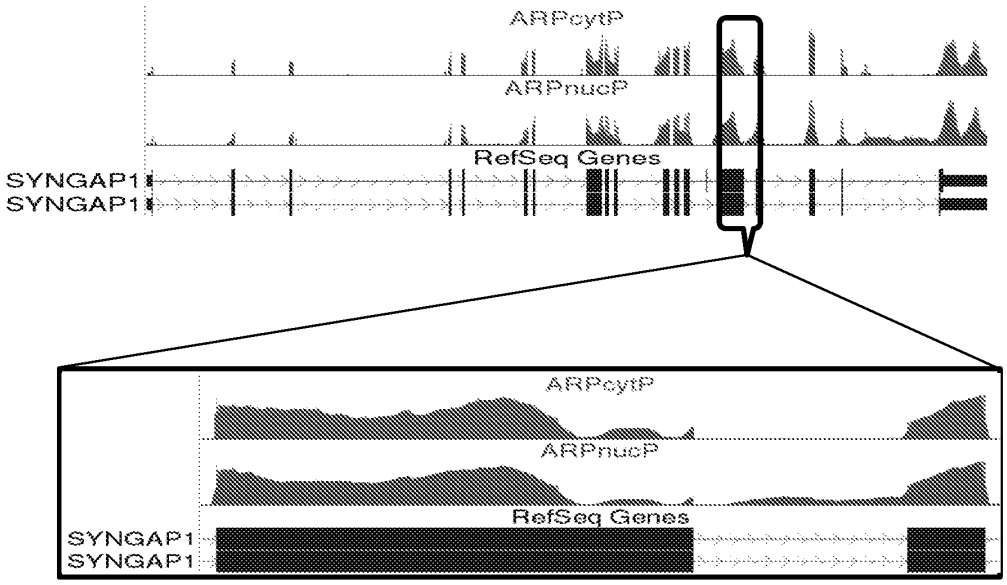

ARPcytP
ARPnucP
RefSeq Genes
SYNGAP1
SYNGAP1
ARPcytP
ARPnucP
RefSeq Genes
SYNGAP1
SYNGAP1

FIG. 7A

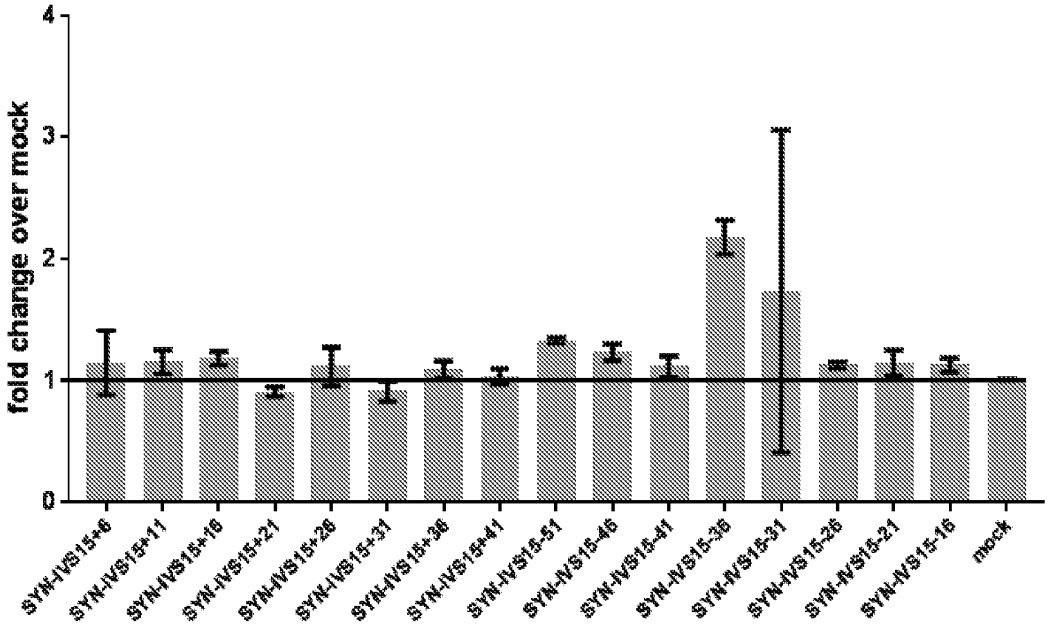

fold change over mock
0
1
2
3
4
SYN-IVS15+6
SYN-IVS15+11
SYN-IVS15+16
SYN-IVS15+21
SYN-IVS15+26
SYN-IVS15+31
SYN-IVS15+36
SYN-IVS15+41
SYN-IVS15-51
SYN-IVS15-46
SYN-IVS15-41
SYN-IVS15-36
SYN-IVS15-31
SYN-IVS15-26
SYN-IVS15-21
SYN-IVS15-16
mock

FIG. 7B

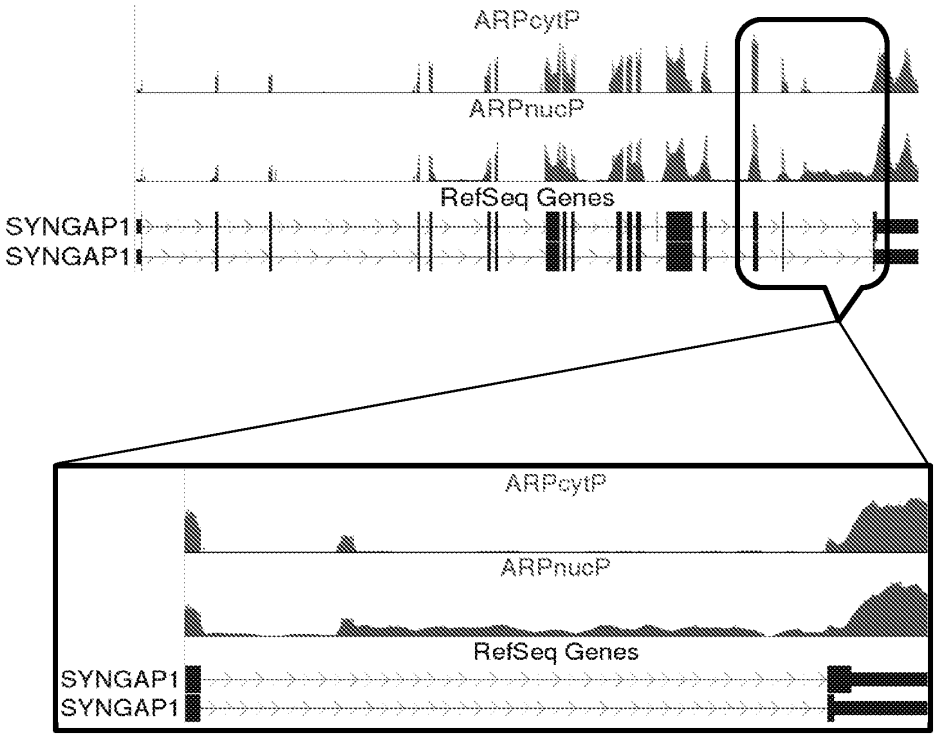

ARPcytP
ARPnucP
RefSeq Genes
SYNGAP1
SYNGAP1
ARPcytP
ARPnucP
RefSeq Genes
SYNGAP1
SYNGAP1

FIG. 7C

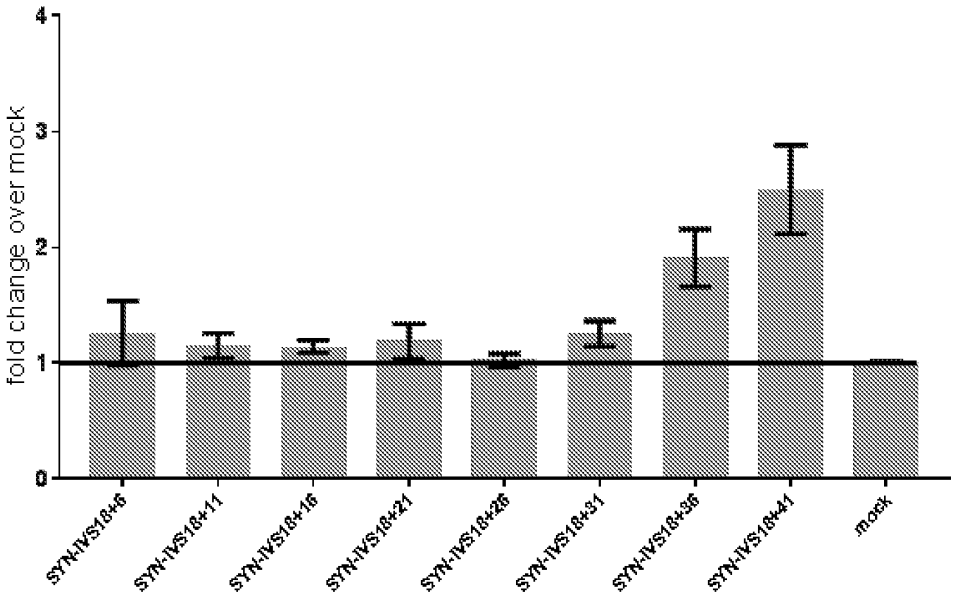

fold change over mock
0
1
2
3
4
SYN-IVS18+6
SYN-IVS18+11
SYN-IVS18+16
SYN-IVS18+21
SYN-IVS18+26
SYN-IVS18+31
SYN-IVS18+36
SYN-IVS18+41
mock

FIG. 7D

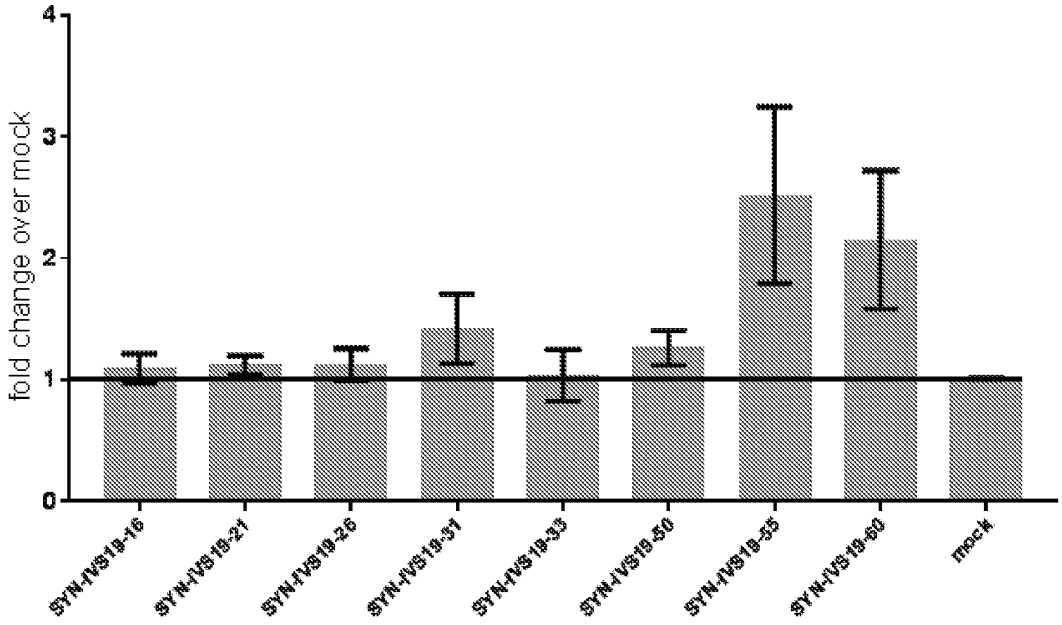

fold change over mock
4
3
2
1
0
SYN-IVS19-16
SYN-IVS19-21
SYN-IVS19-26
SYN-IVS19-31
SYN-IVS19-33
SYN-IVS19-50
SYN-IVS19-55
SYN-IVS19-60
mock

FIG. 7E

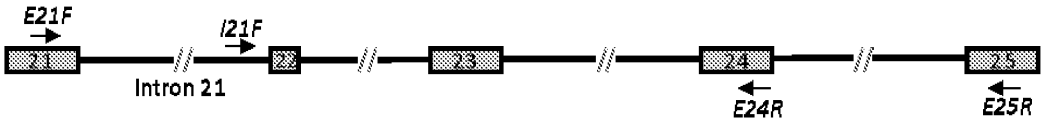


FIG. 8A

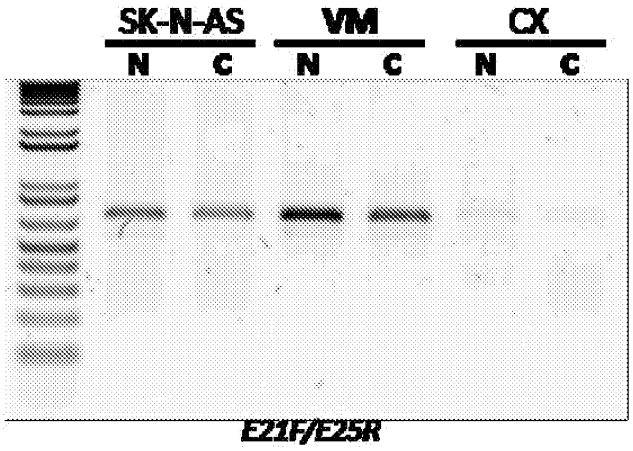


FIG. 8B

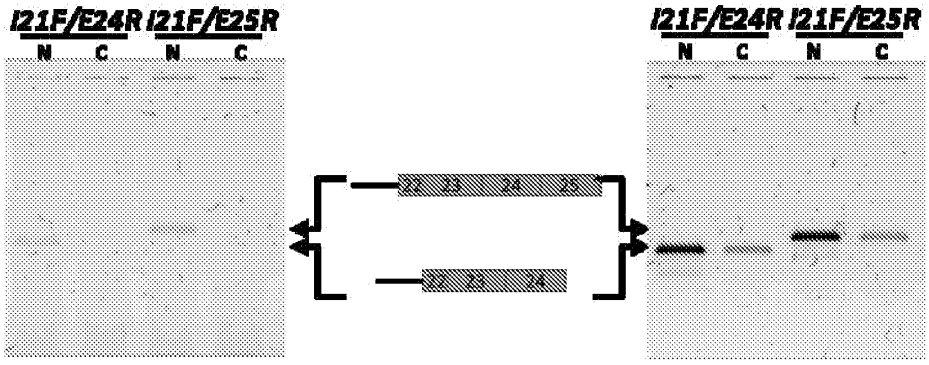


FIG. 8C

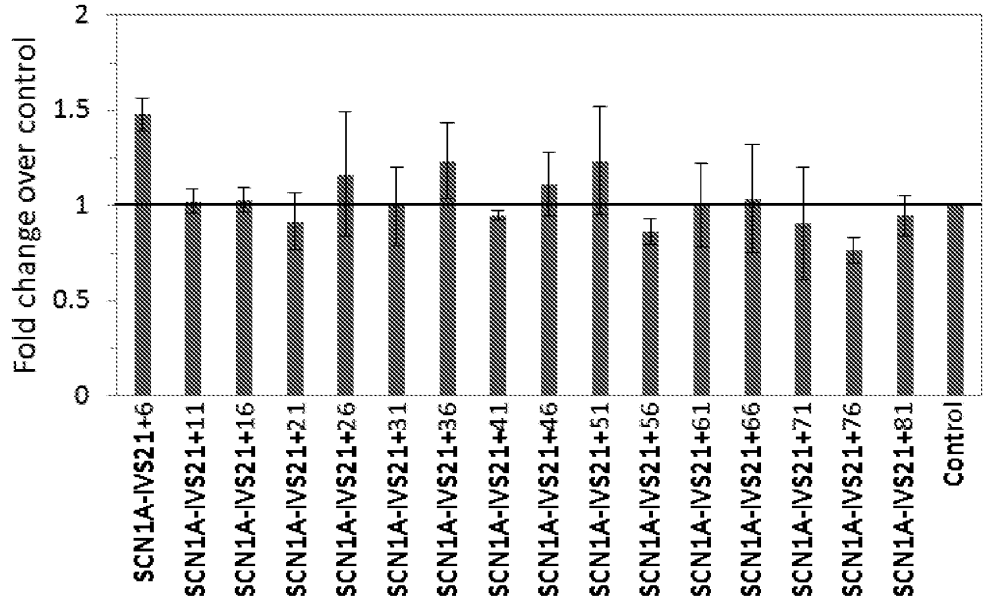

Fold change over control
2
1.5
1
0.5
0
SCN1A-IVS21+6
SCN1A-IVS21+11
SCN1A-IVS21+16
SCN1A-IVS21+21
SCN1A-IVS21+26
SCN1A-IVS21+31
SCN1A-IVS21+36
SCN1A-IVS21+41
SCN1A-IVS21+46
SCN1A-IVS21+51
SCN1A-IVS21+56
SCN1A-IVS21+61
SCN1A-IVS21+66
SCN1A-IVS21+71
SCN1A-IVS21+76
SCN1A-IVS21+81
Control

FIG. 8D

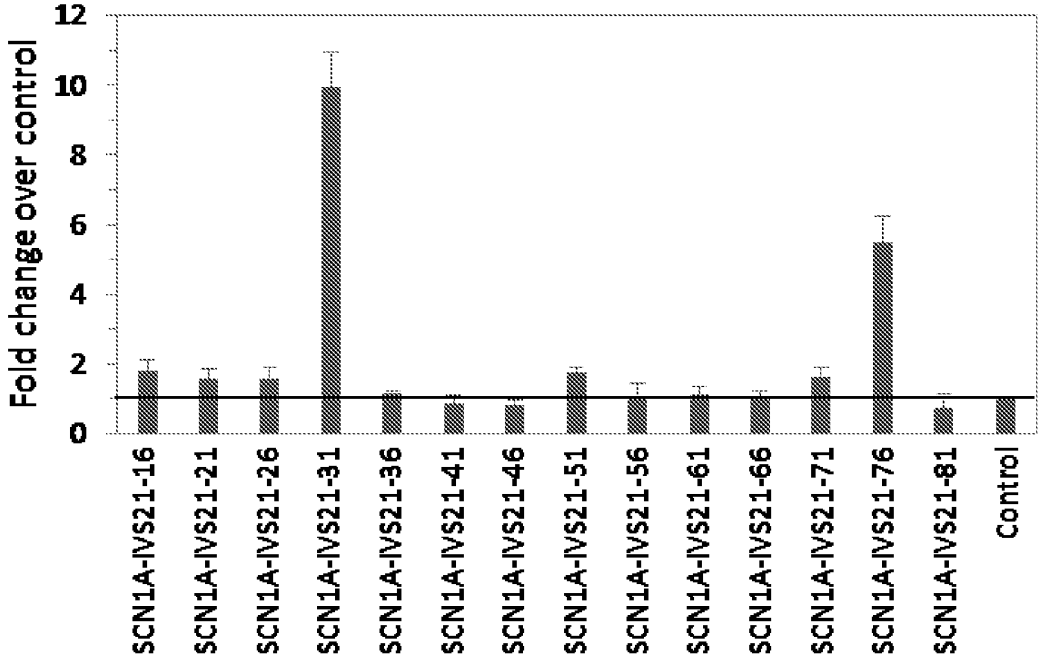

Fold change over control
12
10
8
6
4
2
0
SCN1A-IVS21-16
SCN1A-IVS21-21
SCN1A-IVS21-26
SCN1A-IVS21-31
SCN1A-IVS21-36
SCN1A-IVS21-41
SCN1A-IVS21-46
SCN1A-IVS21-51
SCN1A-IVS21-56
SCN1A-IVS21-61
SCN1A-IVS21-66
SCN1A-IVS21-71
SCN1A-IVS21-76
SCN1A-IVS21-81
Control

FIG. 8E

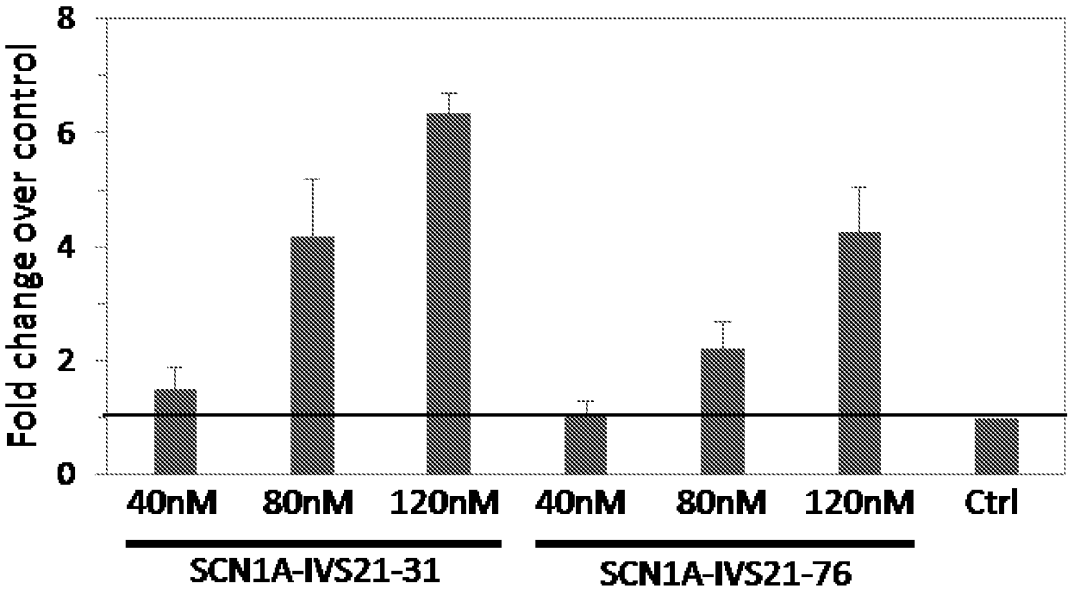

Fold change over control
8
6
4
2
0
40nM
80nM
120nM
40nM
80nM
120nM
Ctrl
SCN1A-IVS21-31
SCN1A-IVS21-76

FIG. 8F

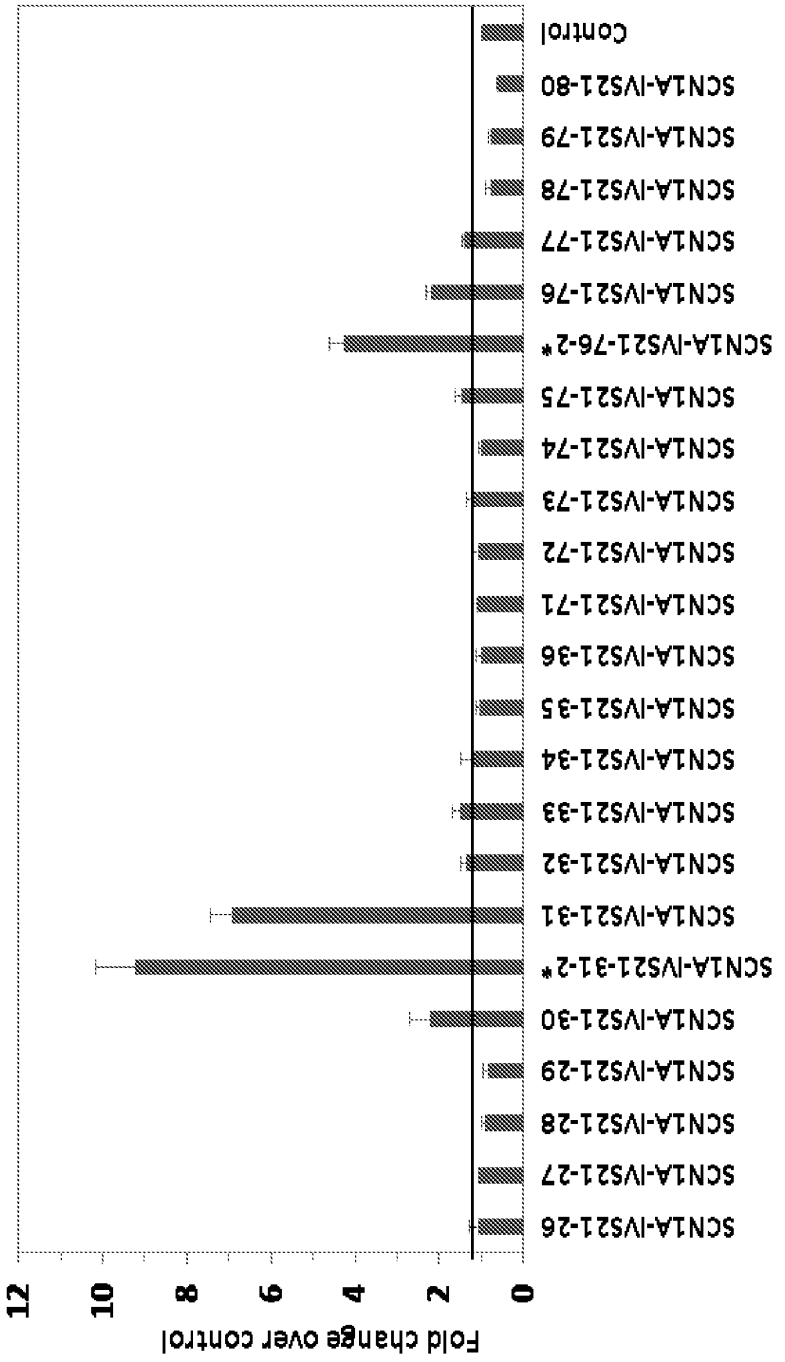

Fold change over control
0
2
4
6
8
10
12
SCN1A-IVS21-26
SCN1A-IVS21-27
SCN1A-IVS21-28
SCN1A-IVS21-29
SCN1A-IVS21-30
SCN1A-IVS21-31-2*
SCN1A-IVS21-31
SCN1A-IVS21-32
SCN1A-IVS21-33
SCN1A-IVS21-34
SCN1A-IVS21-35
SCN1A-IVS21-36
SCN1A-IVS21-71
SCN1A-IVS21-72
SCN1A-IVS21-73
SCN1A-IVS21-74
SCN1A-IVS21-75
SCN1A-IVS21-76-2*
SCN1A-IVS21-76
SCN1A-IVS21-77
SCN1A-IVS21-78
SCN1A-IVS21-79
SCN1A-IVS21-80
Control

FIG. 8G

ID	Sequence (5′–3′)
SCN1A-IVS21+6	CAGAGAAAAUAGUGUUCA
SCN1A-IVS21+11	AUAUUCAGAGAAAAUAGU
SCN1A-IVS21+16	UAAAAAUAUUCAGAGAAA
SCN1A-IVS21+21	AACAAUAAAAAUAUUCAG
SCN1A-IVS21+26	UUCCAAACAAUAAAAAUA
SCN1A-IVS21+31	UAUUAUUCCAAACAAUAA
SCN1A-IVS21+36	UUUGUUAUUAUUCCAAAC
SCN1A-IVS21+41	AUUAUUUUGUUAUUAUUC
SCN1A-IVS21+46	AUGUCAUUAUUUUGUUAU
SCN1A-IVS21+51	GAUGUAUGUCAUUAUUUU
SCN1A-IVS21+56	UAAUAGAUGUAUGUCAUU
SCN1A-IVS21+61	CUAAAUAAUAGAUGUAUG
SCN1A-IVS21+66	AGGAACUAAAUAAUAGAU
SCN1A-IVS21+71	UUCUUAGGAACUAAAUAA
SCN1A-IVS21+76	ACUUUUUCUUAGGAACUA
SCN1A-IVS21+81	UAUAUACUUUUUCUUAGG
SCN1A-IVS21-16	UGCAUGUUUUUACUUUGGA
SCN1A-IVS21-21	GUUUUUACUUUGGAGUAAA
SCN1A-IVS21-26	ACUUUGGAGUAAAAAAUAA
SCN1A-IVS21-31	GGAGUAAAAAUAAAUUUAG
SCN1A-IVS21-36	AAAAAUAAUUUAGACCUG
SCN1A-IVS21-41	UAAUUUAGACCUGAUGUU
SCN1A-IVS21-46	UAGACCUGAUGUUUAAUA
SCN1A-IVS21-51	CUGAUGUUUAAUAAAAUAU
SCN1A-IVS21-56	GUUUAAUAAAAUAUUCUUA
SCN1A-IVS21-61	AUAAAUAUUCUUACUGAU
SCN1A-IVS21-66	UAUUCUUACUGAUAUAAU
SCN1A-IVS21-71	UUACUGAUAUAAUUUUCA
SCN1A-IVS21-76	GAUAUAAUUUUCAAAAGG
SCN1A-IVS21-81	AAUUUUCAAAAGGGAAUA

FIG. 8H

ID	Sequence (5′–3′)
SCN1A-IVS21-27	CUUUGGAGUAAAAAUAAU
SCN1A-IVS21-28	UUUGGAGUAAAAAUAAUU
SCN1A-IVS21-29	UUGGAGUAAAAAUAAUUU
SCN1A-IVS21-30	UGGAGUAAAAAUAAUUUA
SCN1A-IVS21-32	GAGUAAAAAUAAUUUAGA
SCN1A-IVS21-33	AGUAAAAAUAAUUUAGAC
SCN1A-IVS21-34	GUAAAAAUAAUUUAGACC
SCN1A-IVS21-35	UAAAAAUAAUUUAGACCU
SCN1A-IVS21-72	UACUGAUAUAAUUUUCAA
SCN1A-IVS21-73	ACUGAUAUAAUUUUCAAA
SCN1A-IVS21-74	CUGAUAUAAUUUUCAAAA
SCN1A-IVS21-75	UGAUAUAAUUUUCAAAAG
SCN1A-IVS21-77	AUAUAAUUUUCAAAAGGG
SCN1A-IVS21-78	UAUAAUUUUCAAAAGGGA
SCN1A-IVS21-79	AUAAUUUUCAAAAGGGAA
SCN1A-IVS21-80	UAAUUUUCAAAAGGGAAU

FIG. 8I