FIGURE 1.

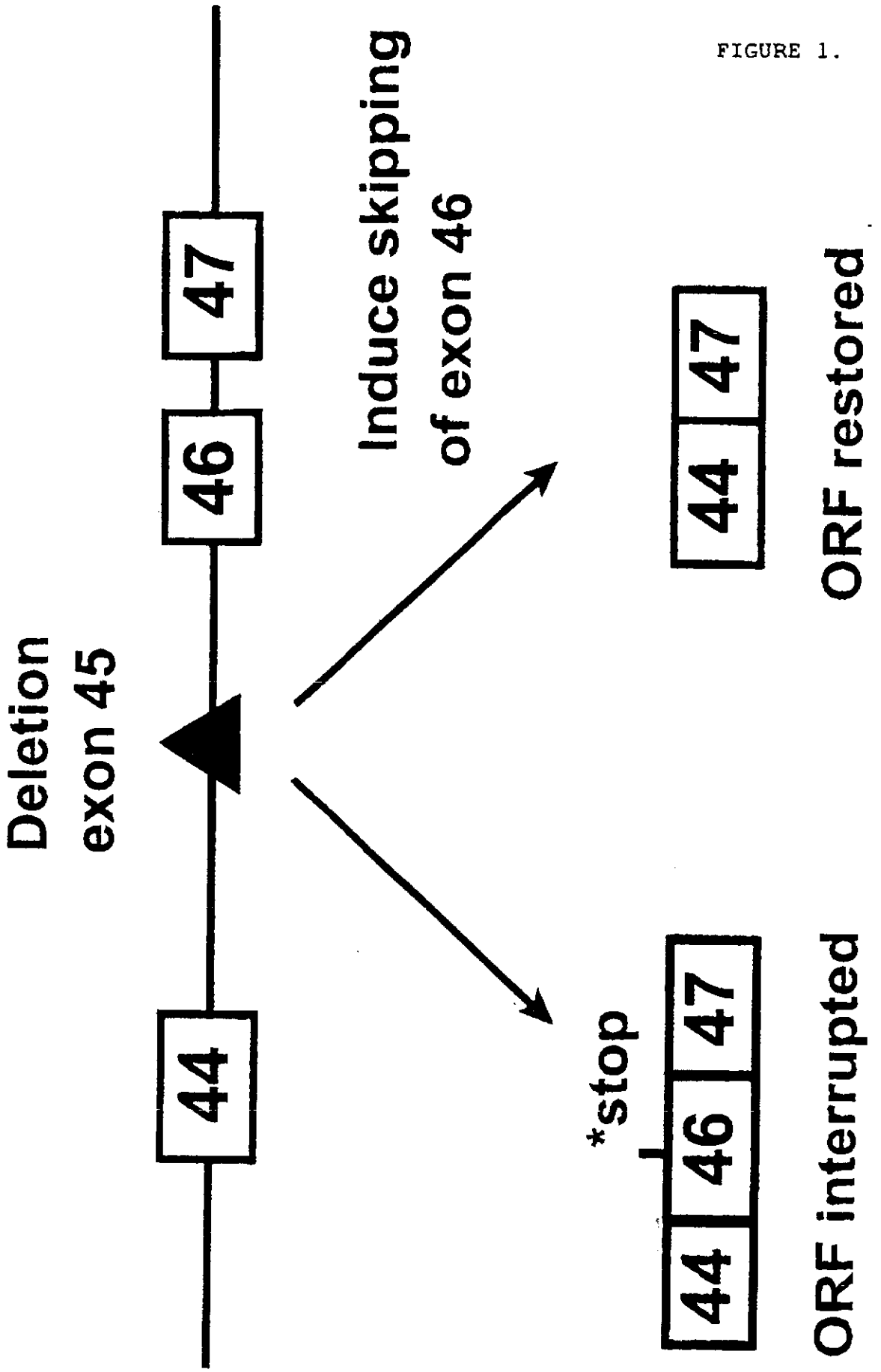

Deletion
exon 45
44
46
47
Induce skipping
of exon 46
44
47
ORF restored
*stop
44
46
47
ORF interrupted

FIGURE 2.

Dystrophin Exon 46
Potential
Splicing Regulatory Sequence
AON 6
AON 5
AON 4
AON 3
AON 2
AON 11
AON 10
AON 9
AON 8
AON 7
AONs: antisense oligoribonucleotides
1) 2' O-methyl phosphorothioate RNA
2) 5' Fluorescein group

FIGURE 3.

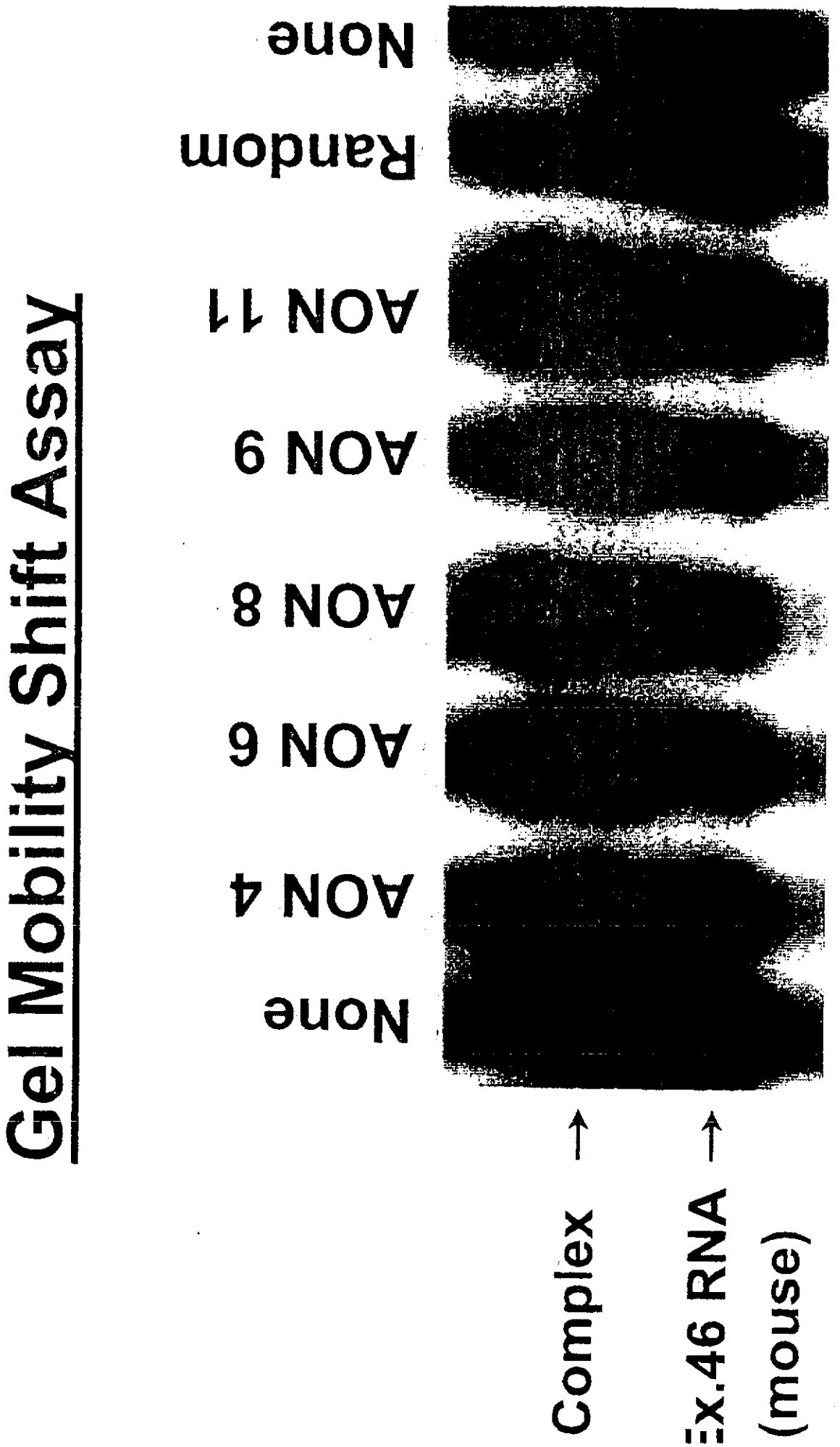

Gel Mobility Shift Assay
None
AON 4
AON 6
AON 8
AON 9
AON 11
Random
None
Complex
Ex.46 RNA
(mouse)

FIGURE 4.

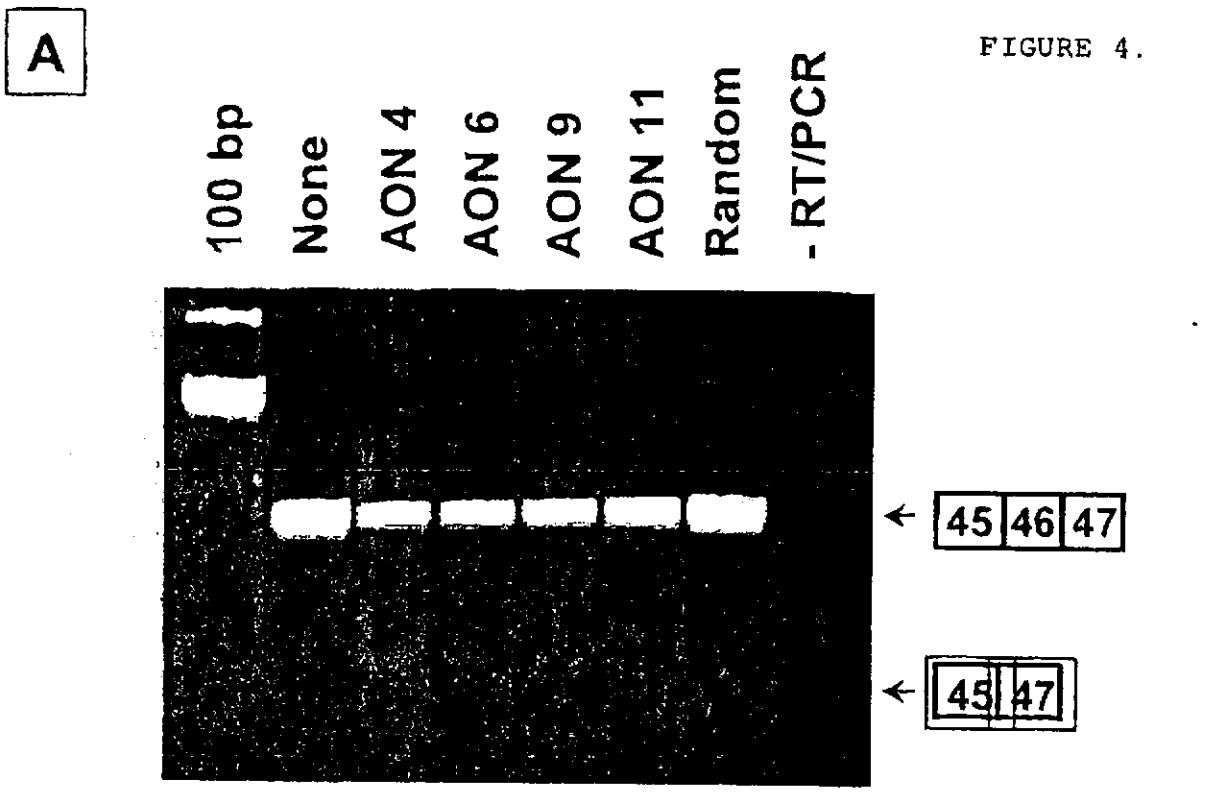

A
100 bp
None
AON 4
AON 6
AON 9
AON 11
Random
- RT/PCR
45 46 47
45 47
B
None
Random
hAON 4
hAON 8
M C P1P2 – C P1P2 – C P1P2 – C P1P2 – M
44 45 46 47
44 45 47
44 46 47
44 47

FIGURE 5.

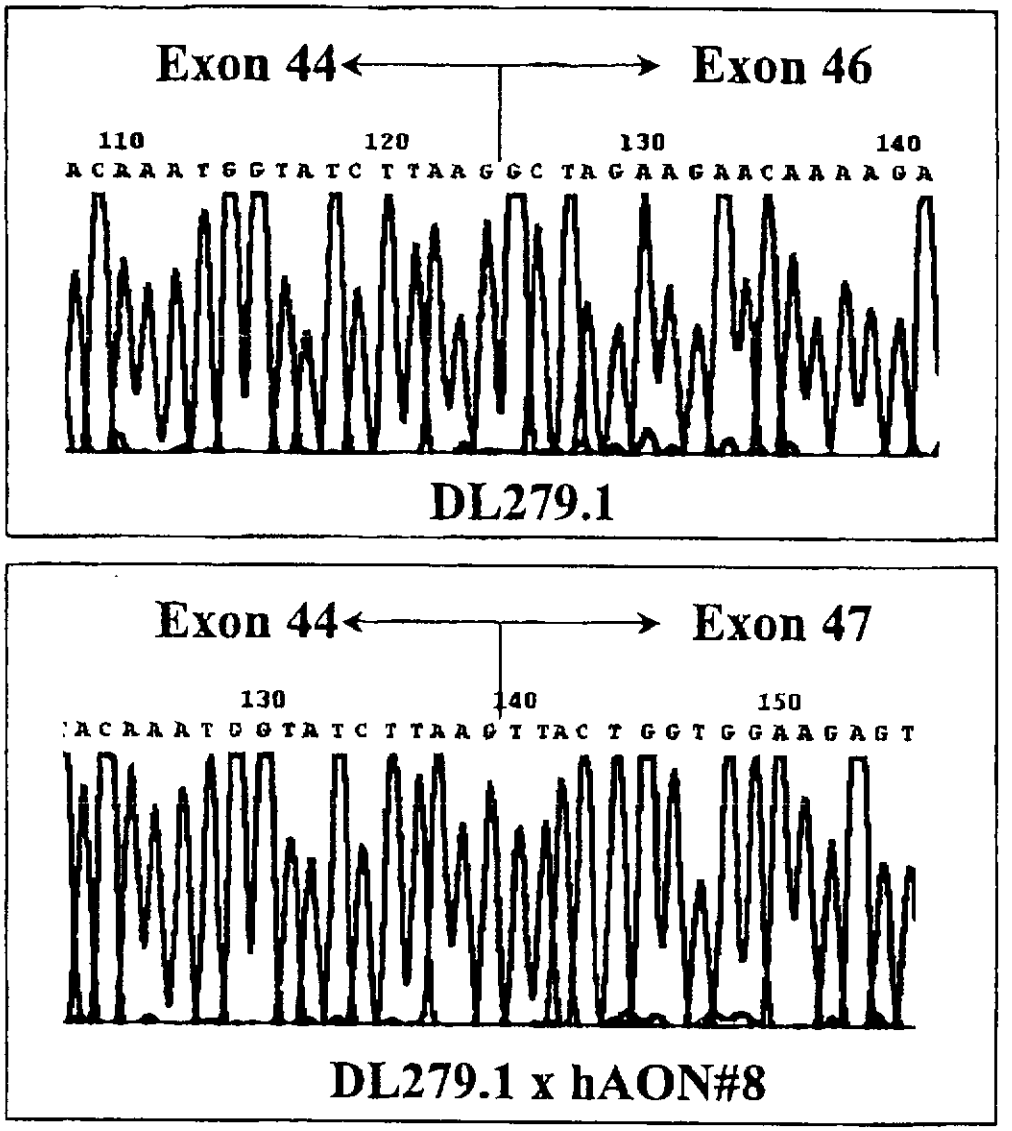

Exon 44
Exon 46
110
120
130
140
DL279.1
Exon 44
Exon 47
130
140
150
DL279.1 x hAON#8

FIGURE 6

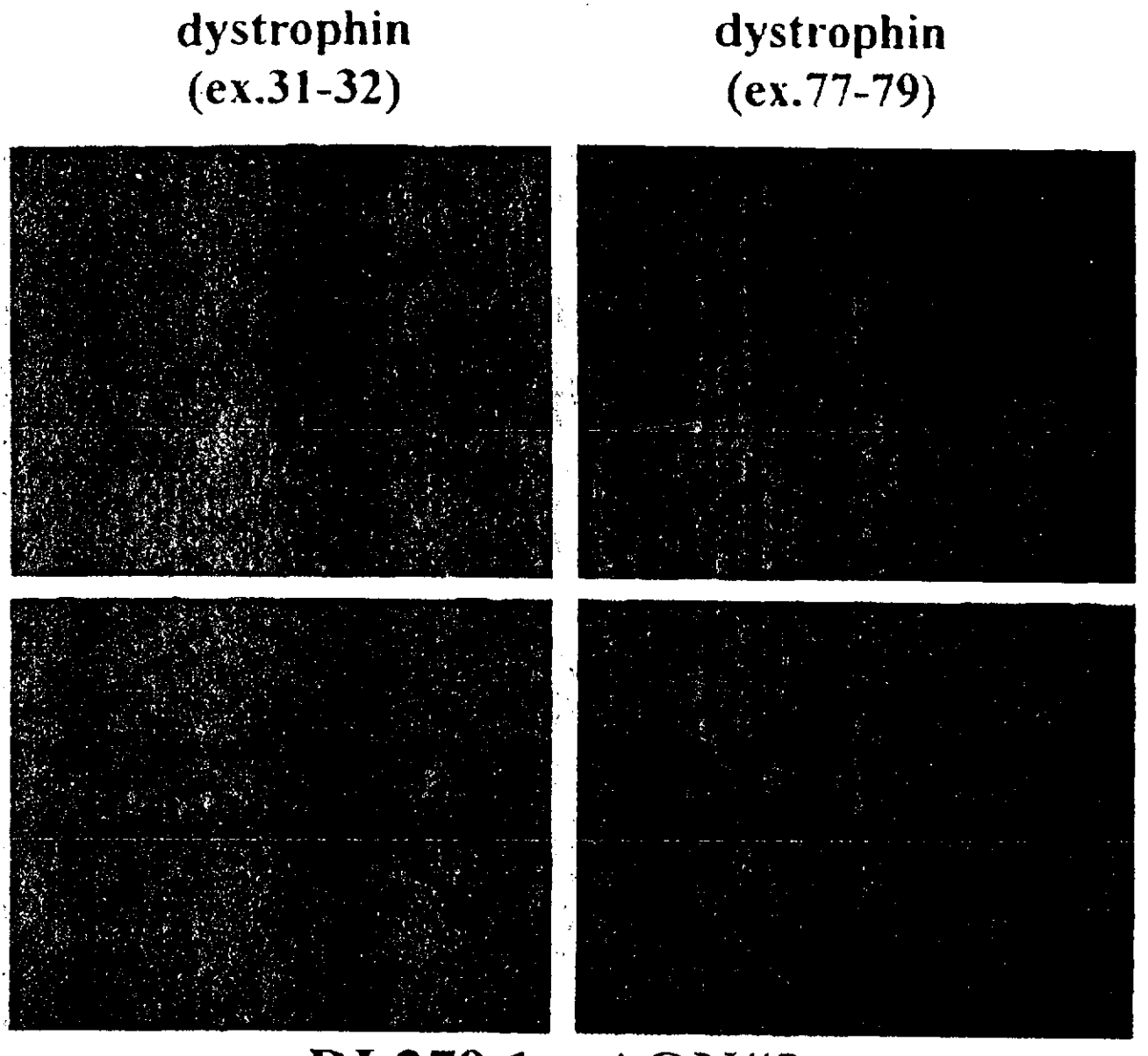
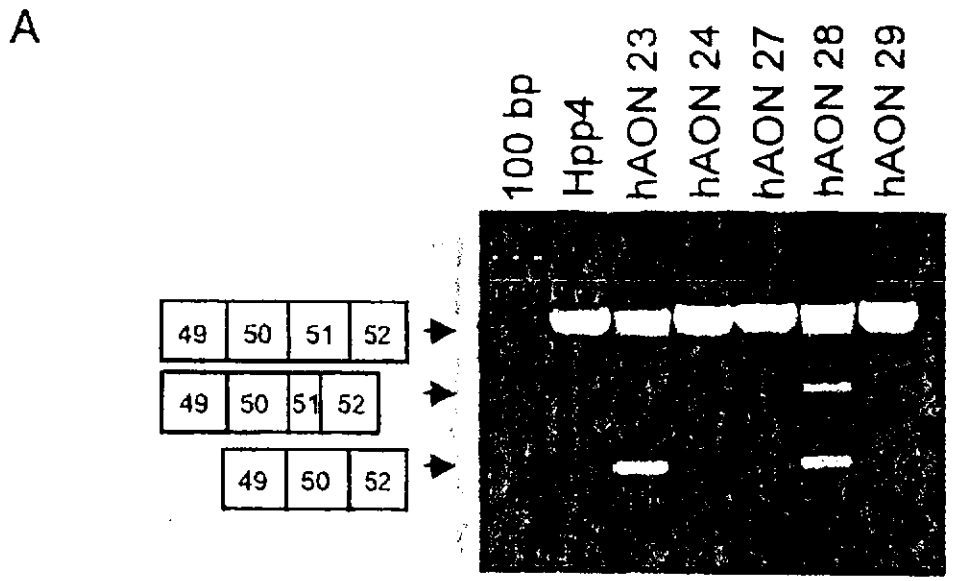


FIGURE 7.


A
100 bp
Hpp4
hAON 23
hAON 24
hAON 27
hAON 28
hAON 29
49 50 51 52
49 50 51 52
49 50 52

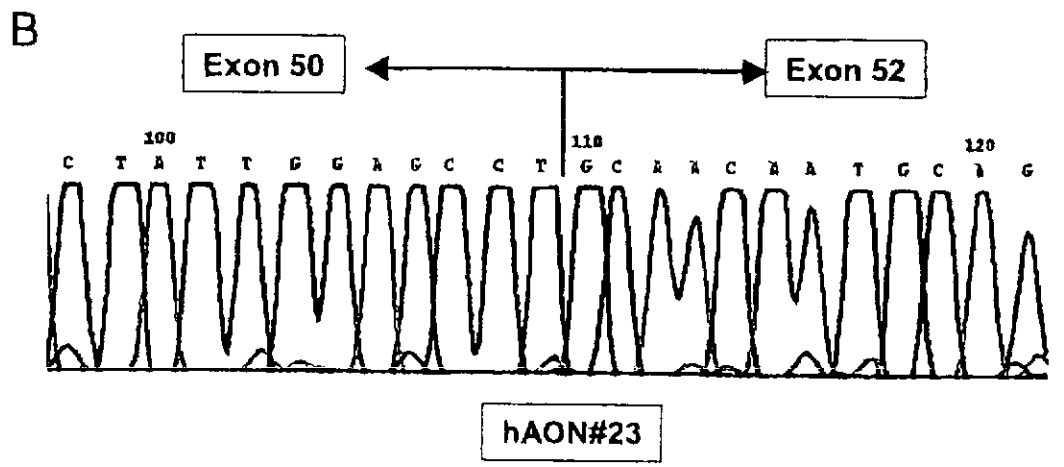
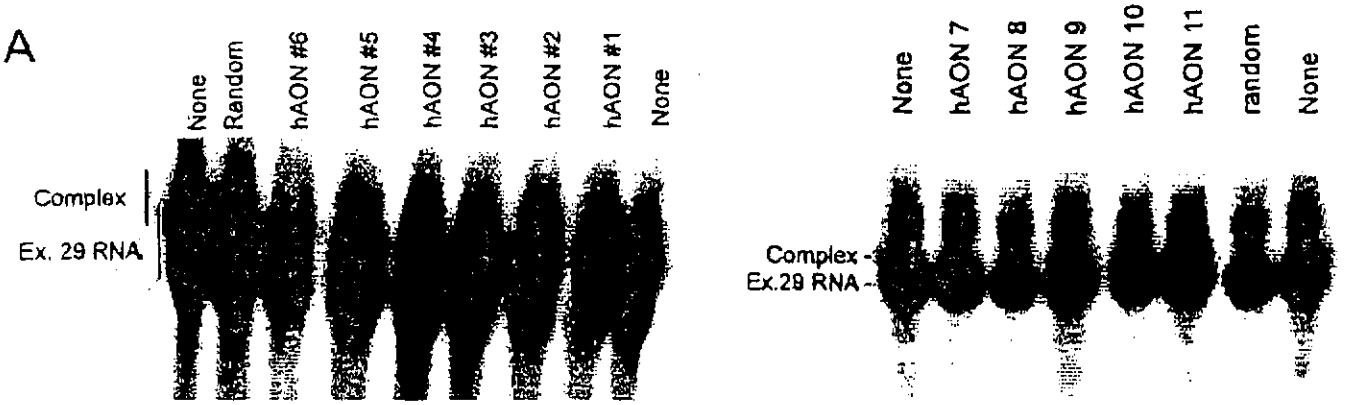
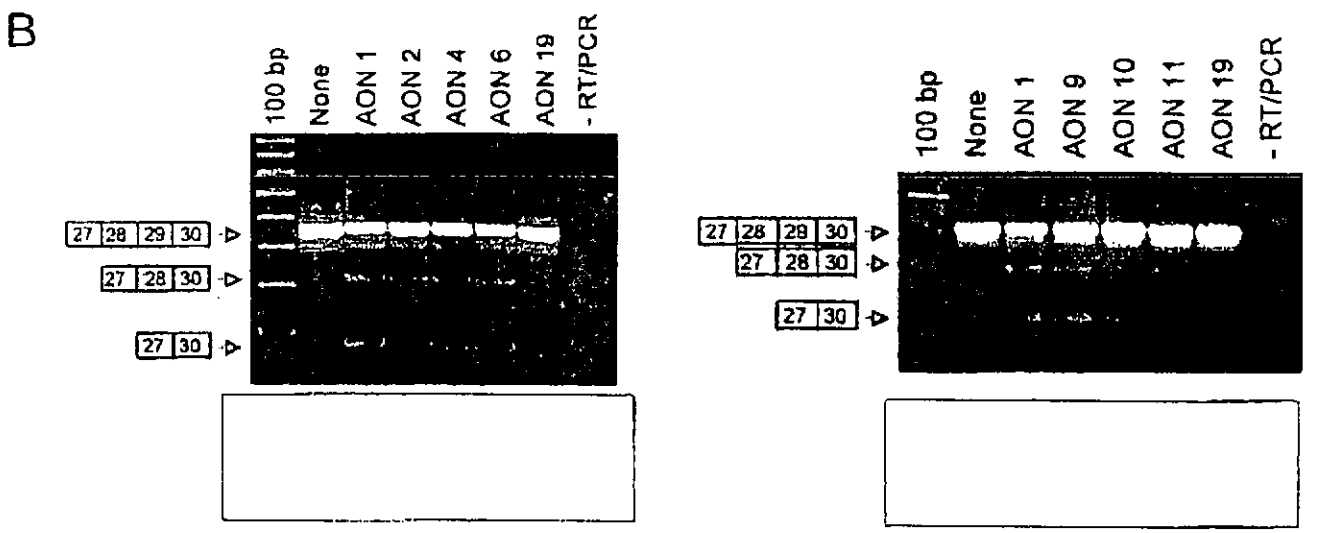

B
Exon 50
Exon 52
100
110
120
hAON#23

FIGURE 8.


A
None
Random
hAON #6
hAON #5
hAON #4
hAON #3
hAON #2
hAON #1
None
Complex
Ex. 29 RNA
None
hAON 7
hAON 8
hAON 9
hAON 10
hAON 11
random
None
Complex
Ex.29 RNA


B
100 bp
None
AON 1
AON 2
AON 4
AON 6
AON 19
- RT/PCR
27 28 29 30
27 28 30
27 30
100 bp
None
AON 1
AON 9
AON 10
AON 11
AON 19
- RT/PCR
27 28 29 30
27 28 30
27 30

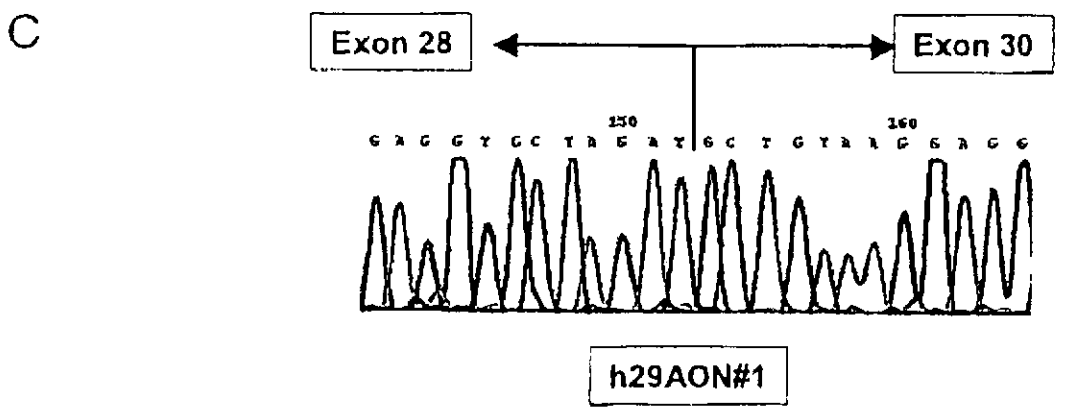
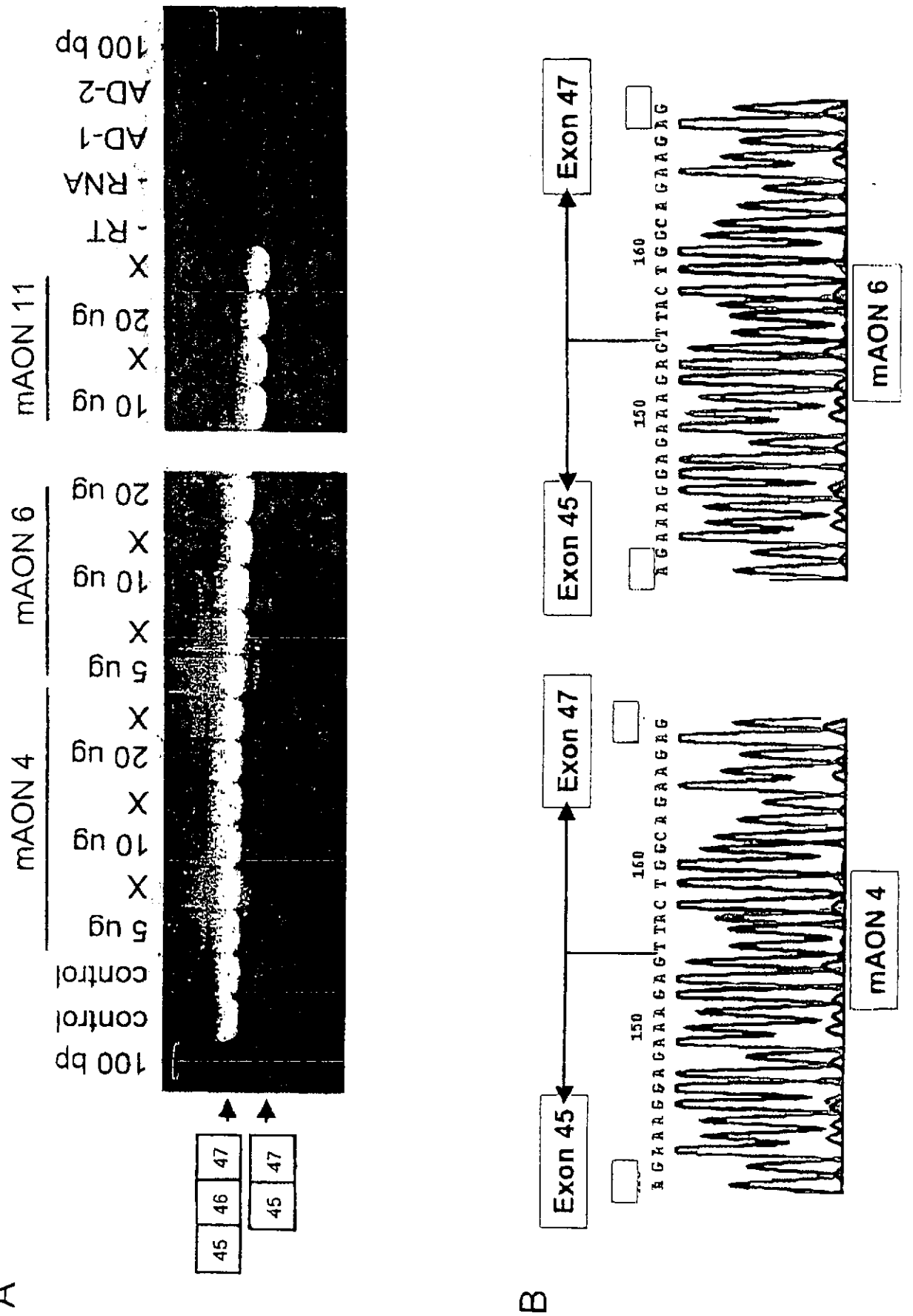

C
Exon 28
Exon 30
150
160
h29AON#1

FIGURE 9.


A
mAON 4
mAON 6
mAON 11
100 bp
control
control
5 ug
X
10 ug
X
20 ug
X
5 ug
X
10 ug
X
20 ug
10 ug
X
20 ug
- RT
+ RNA
AD-1
AD-2
100 bp
45
46
47
45
47
B
Exon 45
Exon 47
mAON 6
mAON 4
150
160