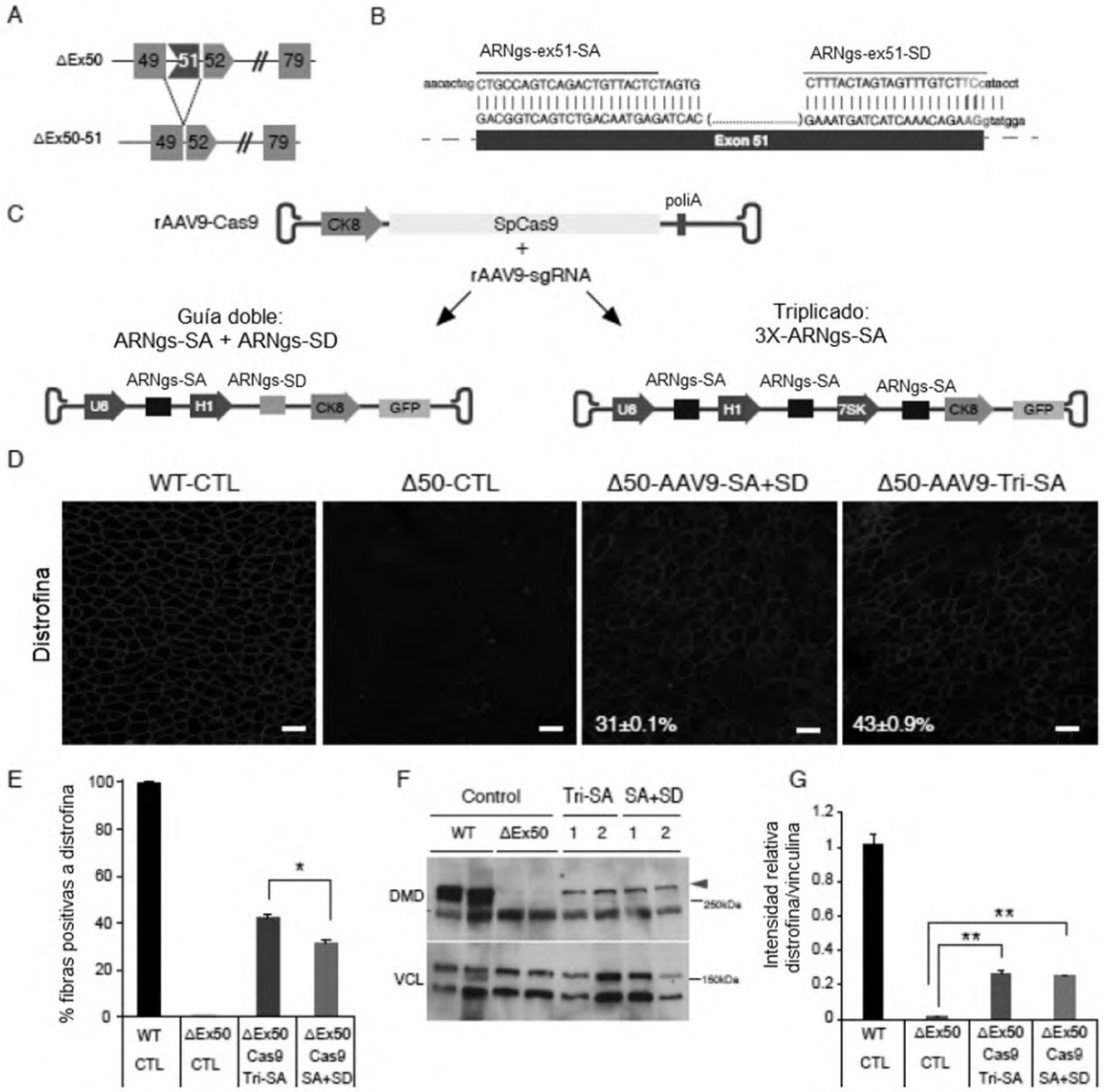
A
ΔEx50
49
51
52
79
ΔEx50-51
49
52
79
B
ARNgs-ex51-SA
ARNgs-ex51-SD
aacactag CTGCCAGTCAGACTGTTACTCTAGTG
CTTTACTAGTAGTTTGTCTTCcatacct
GACGGTCAGTCTGACAATGAGATCAC (.....)GAAATGATCATCAAACAGAAGgtatgga
Exon 51
C
rAAV9-Cas9
CK8
SpCas9
poliA
+
rAAV9-sgRNA
Guía doble:
ARNgs-SA + ARNgs-SD
Triplicado:
3X-ARNgs-SA
ARNgs-SA
ARNgs-SD
U6
H1
CK8
GFP
ARNgs-SA
ARNgs-SA
ARNgs-SA
U6
H1
7SK
CK8
GFP
D
WT-CTL
Δ50-CTL
Δ50-AAV9-SA+SD
Δ50-AAV9-Tri-SA
Distrofina
31±0.1%
43±0.9%
E
% fibras positivas a distrofina
100
80
60
40
20
0
*
WT CTL
ΔEx50 CTL
ΔEx50 Cas9 Tri-SA
ΔEx50 Cas9 SA+SD
F
Control
Tri-SA
SA+SD
WT
ΔEx50
1
2
1
2
DMD
VCL
250kDa
150kDa
G
Intensidad relativa distrofina/vinculina
1.2
1
0.8
0.6
0.4
0.2
0
**
**
WT CTL
ΔEx50 CTL
ΔEx50 Cas9 Tri-SA
ΔEx50 Cas9 SA+SD

FIGURAS 3A-G