

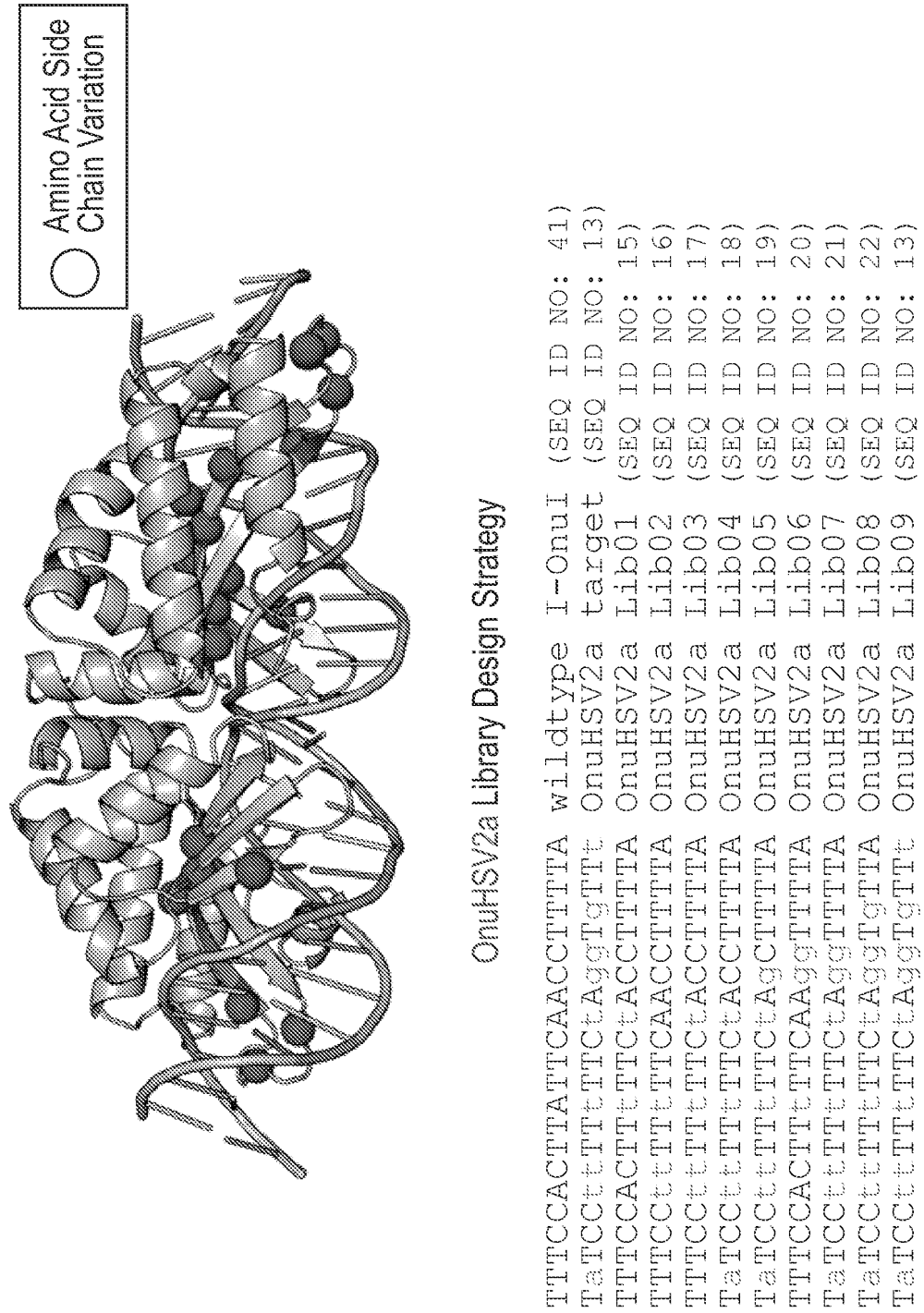


FIG. 1

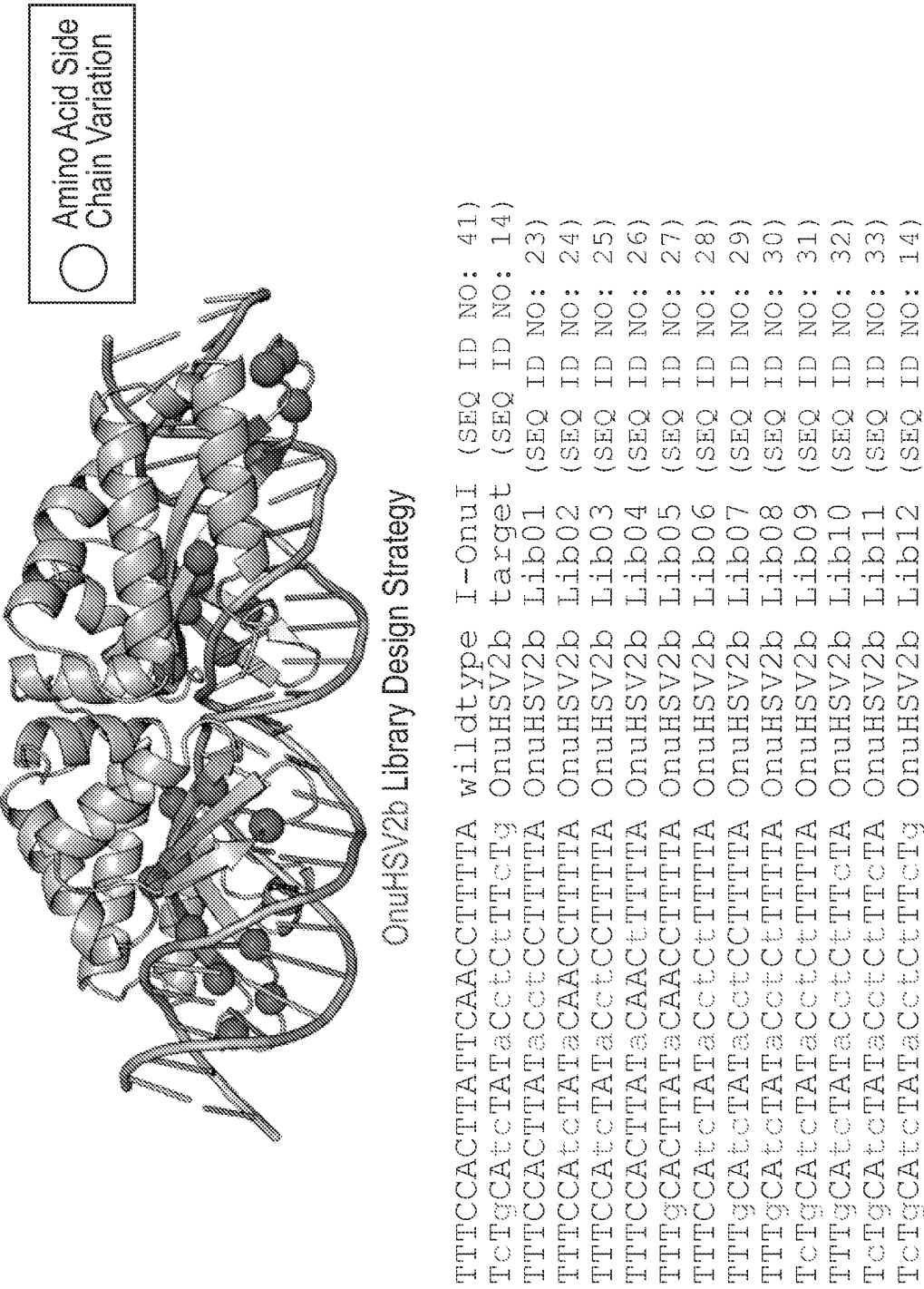


FIG. 2

3/30

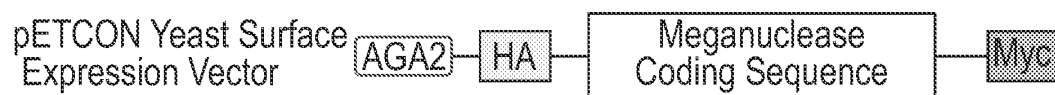


FIG. 3A

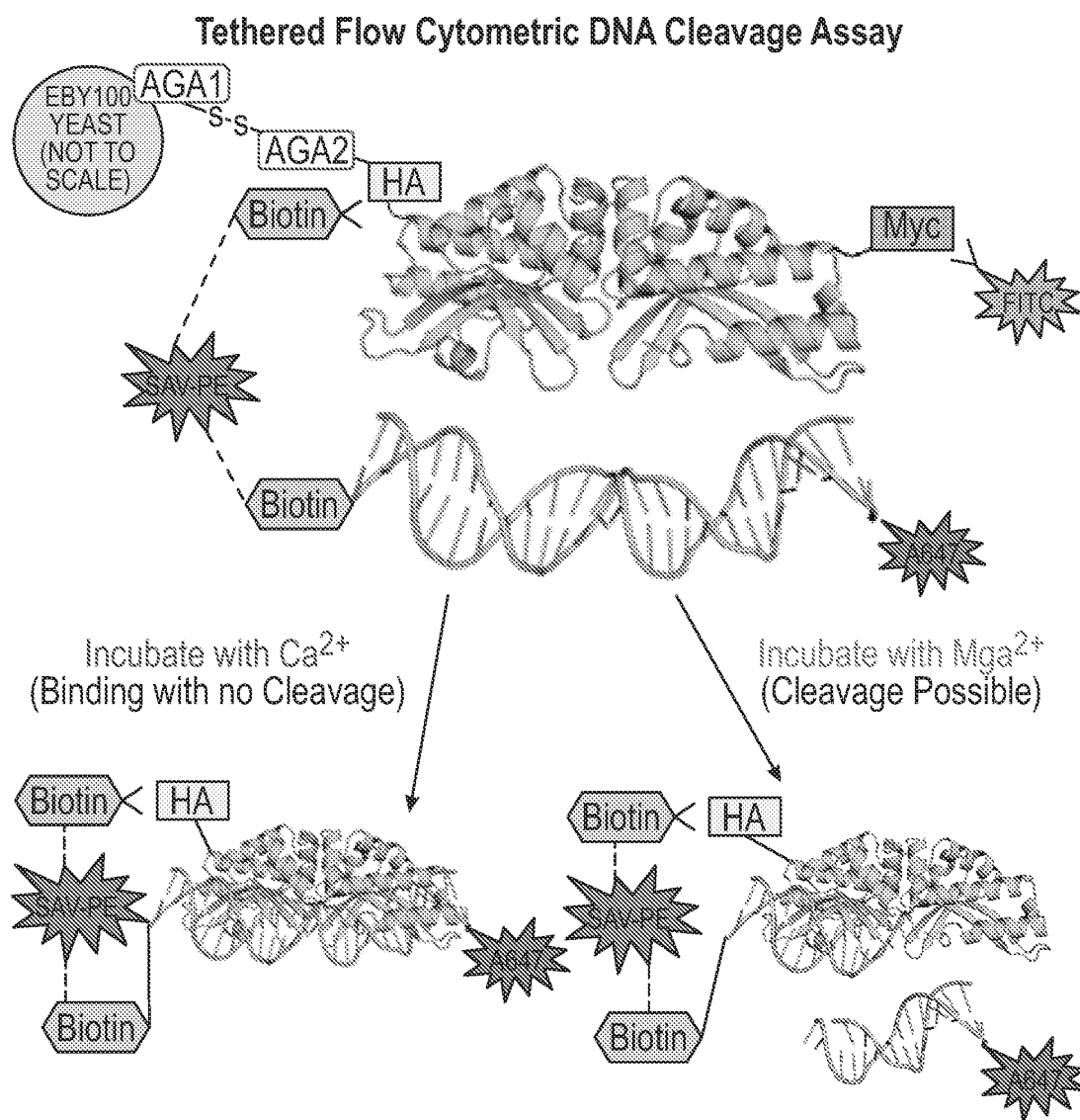
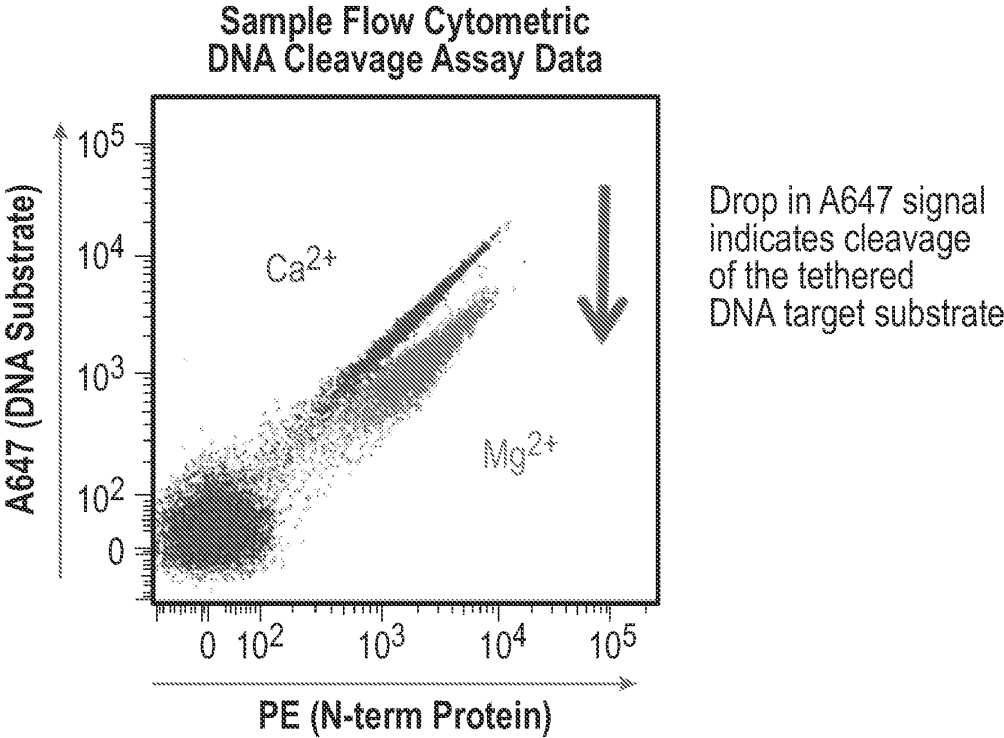


FIG. 3B

4/30



Sorting for DNA Cleavage Activity

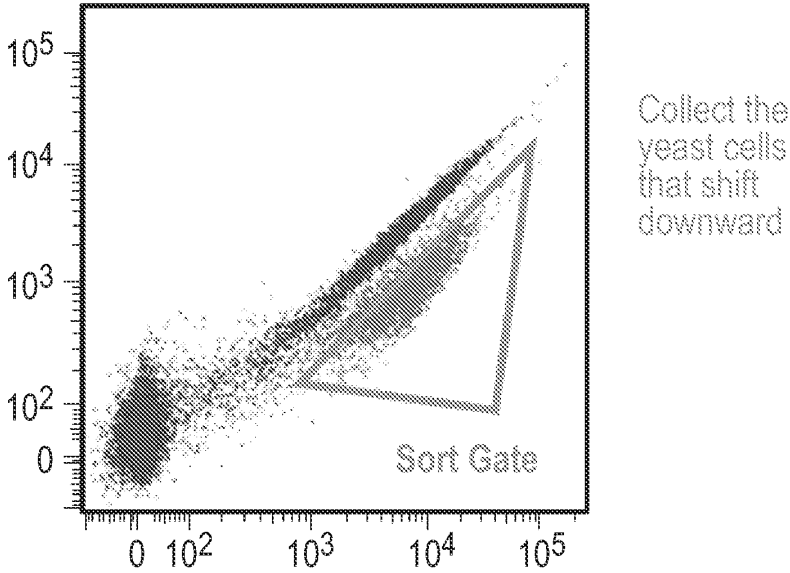


FIG. 3C

5/30

Activity of Sorted Populations for OnuHSV2a Libraries
Using the Tethered Flow Cytometric DNA Cleavage Assay

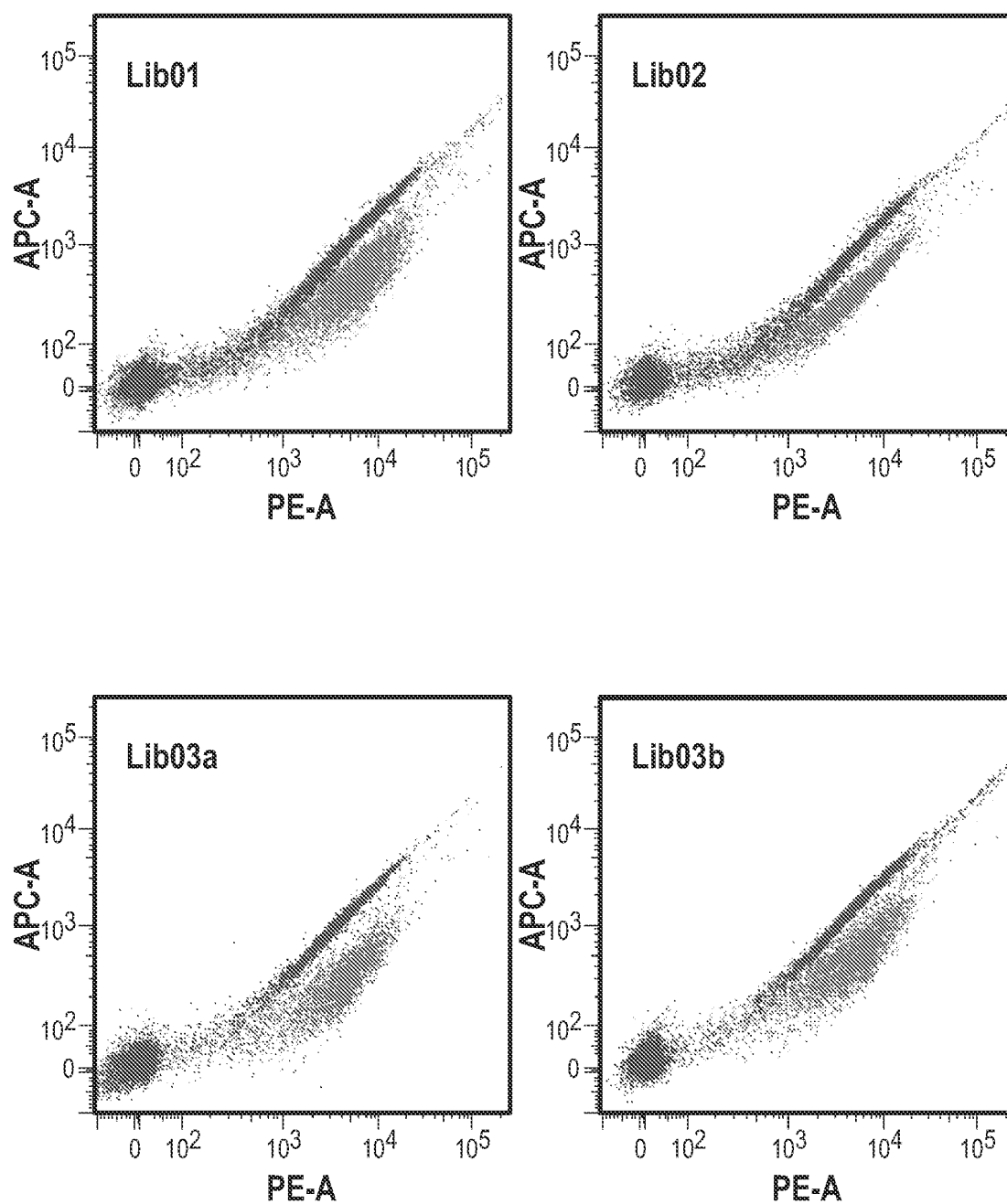


FIG. 4A

6/30

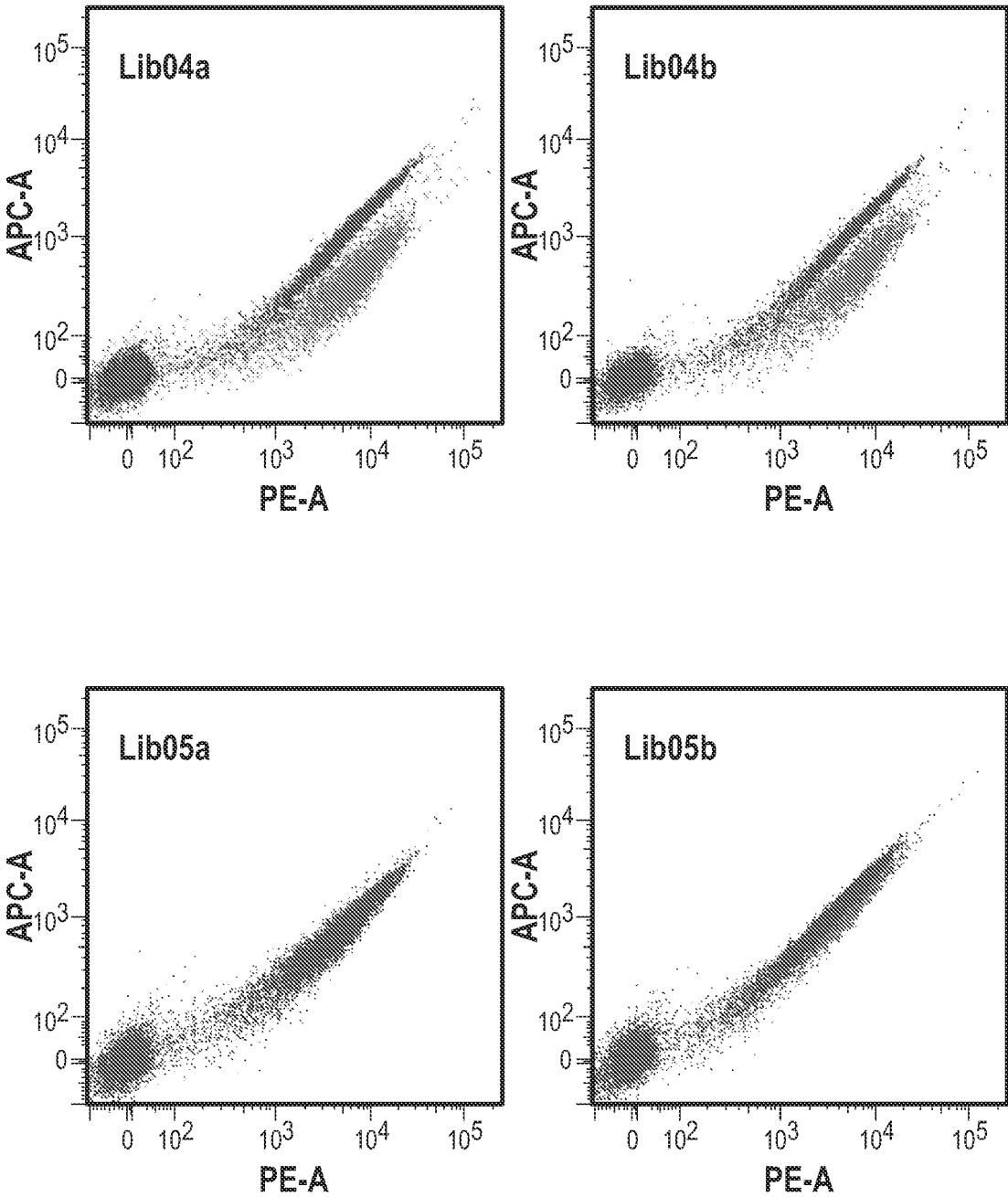
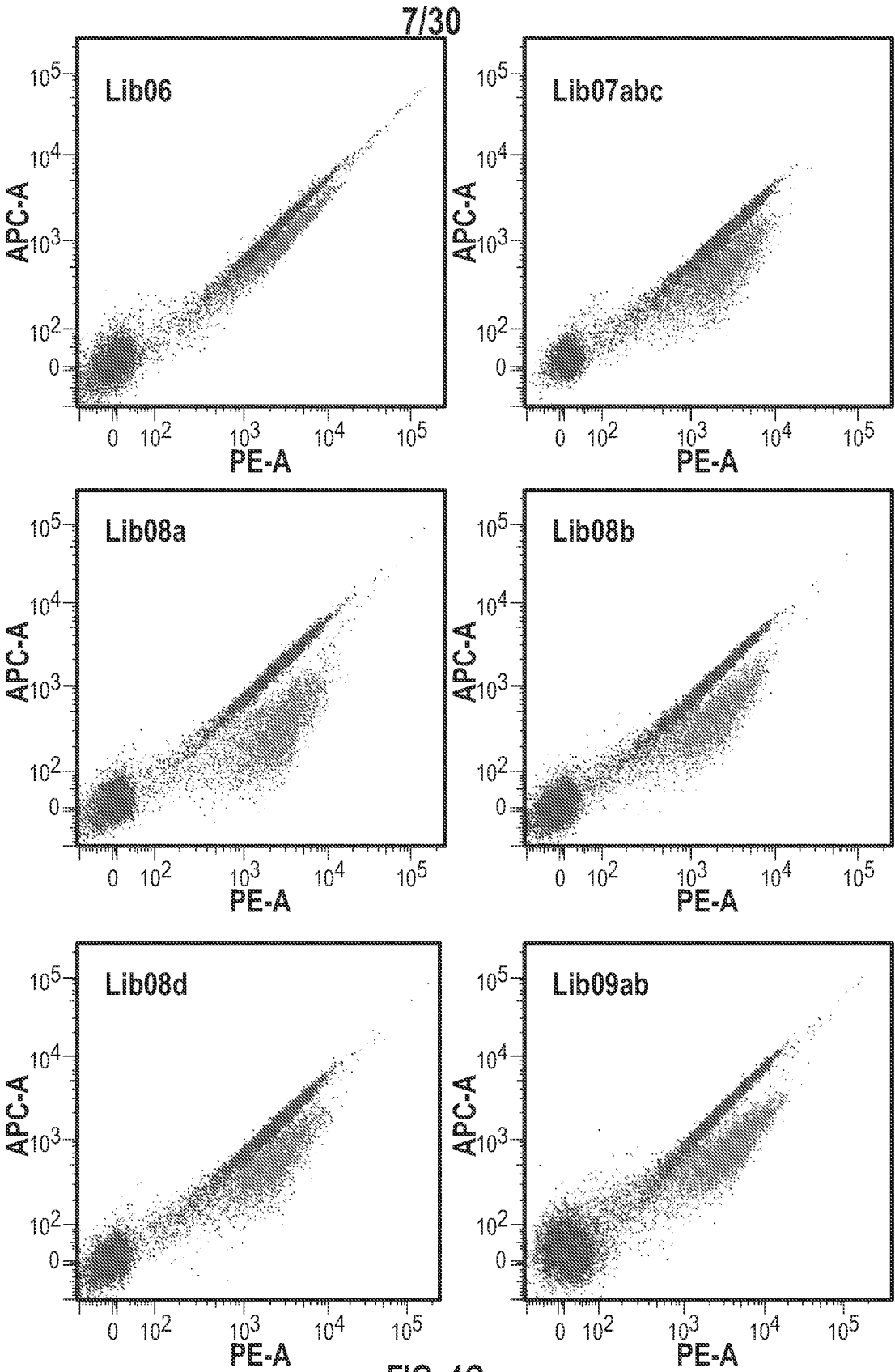


FIG. 4B



8/30

Activity of Sorted Populations for OnuHSV2b Libraries
Using the Tethered Flow Cytometric DNA Cleavage Assay

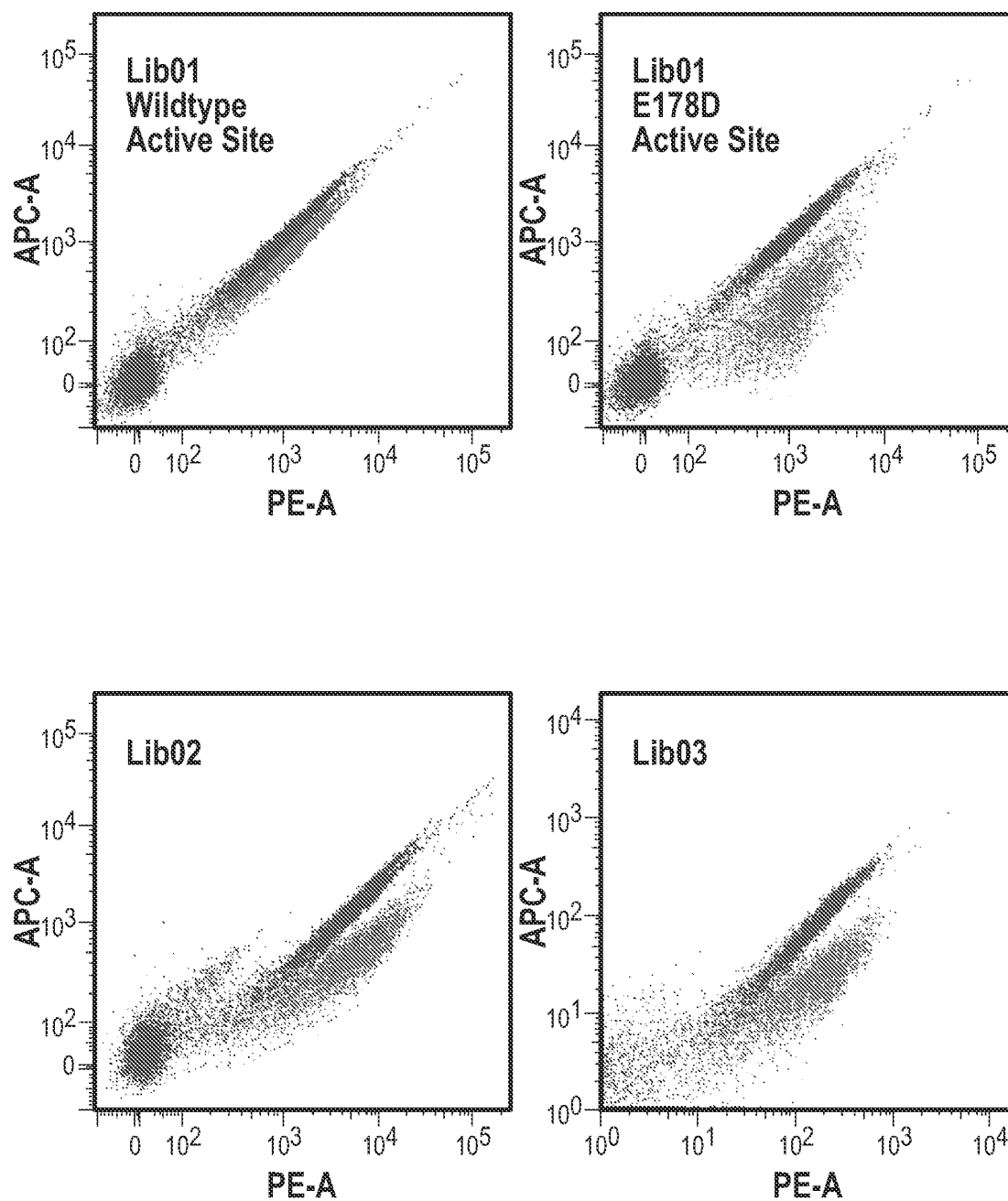


FIG. 5A

9/30

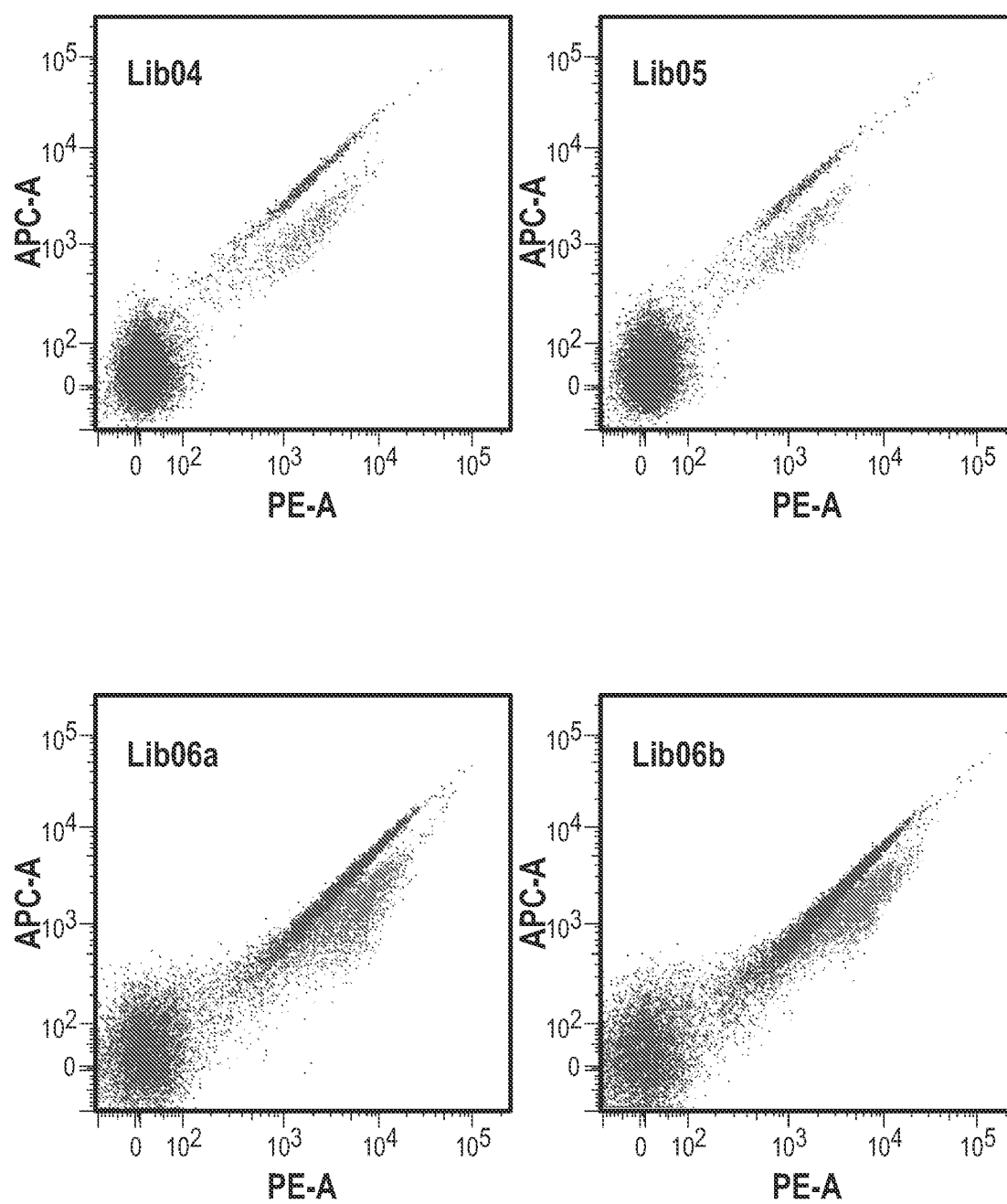


FIG. 5B

10/30

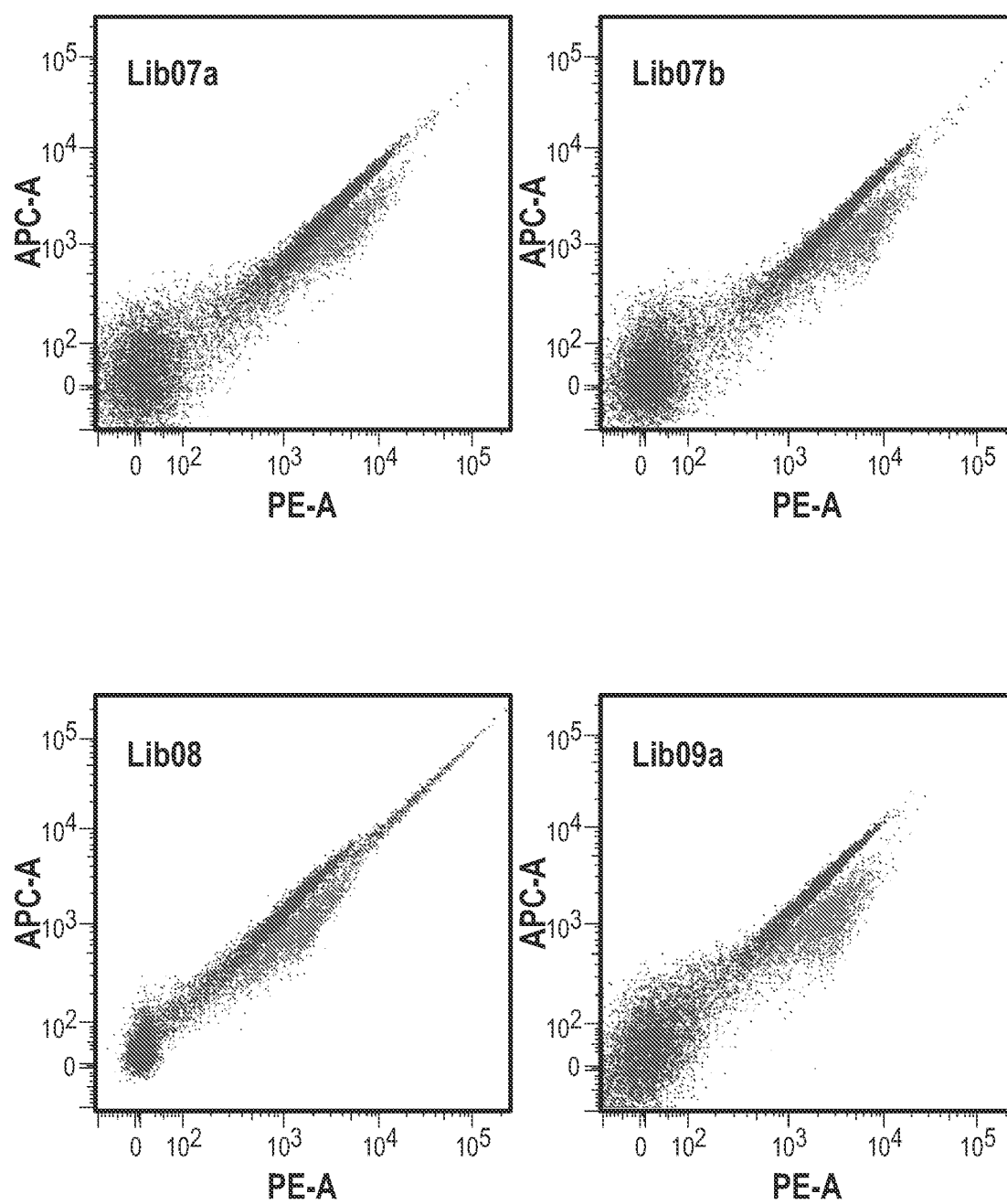


FIG. 5C

11/30

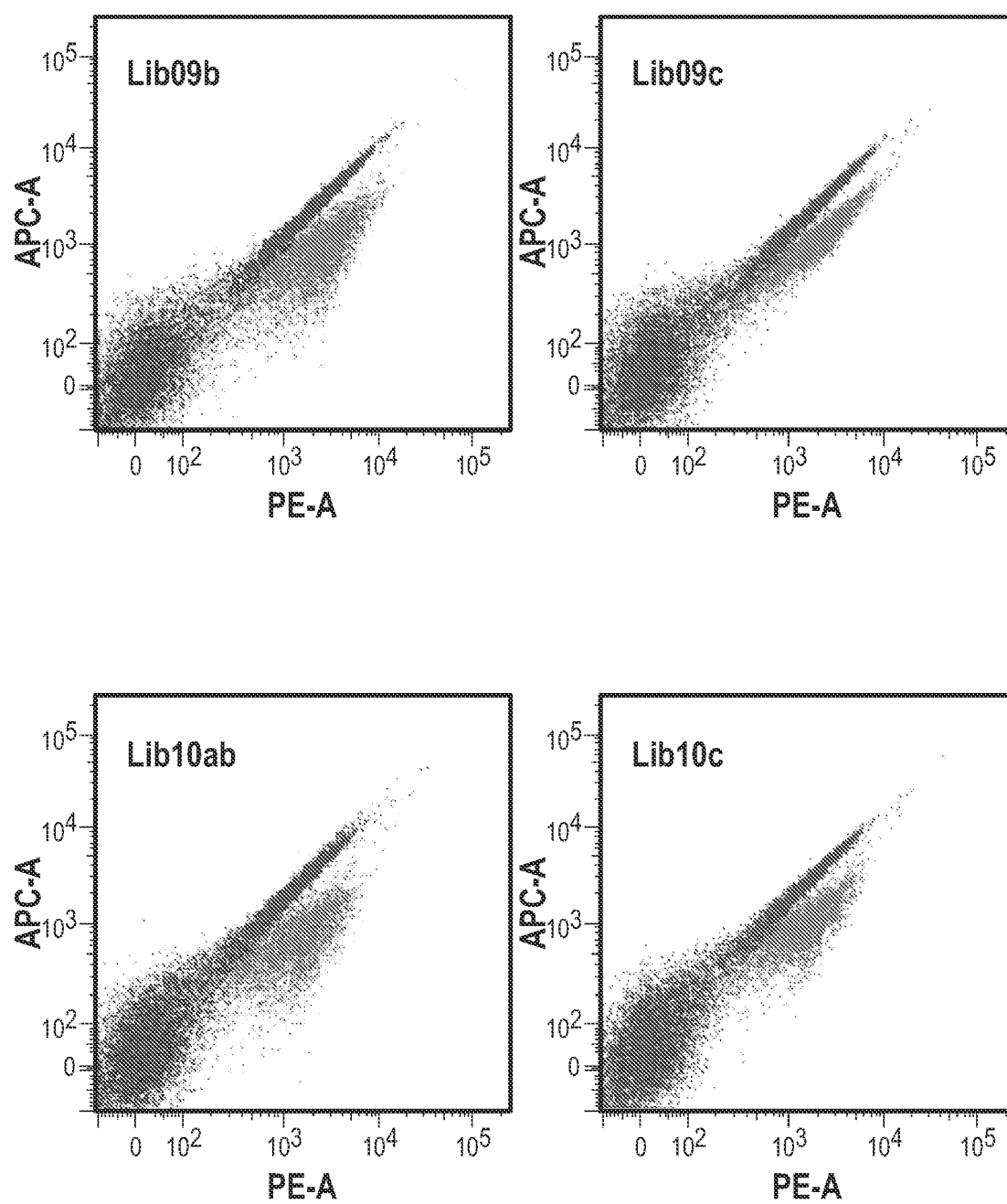


FIG. 5D

12/30

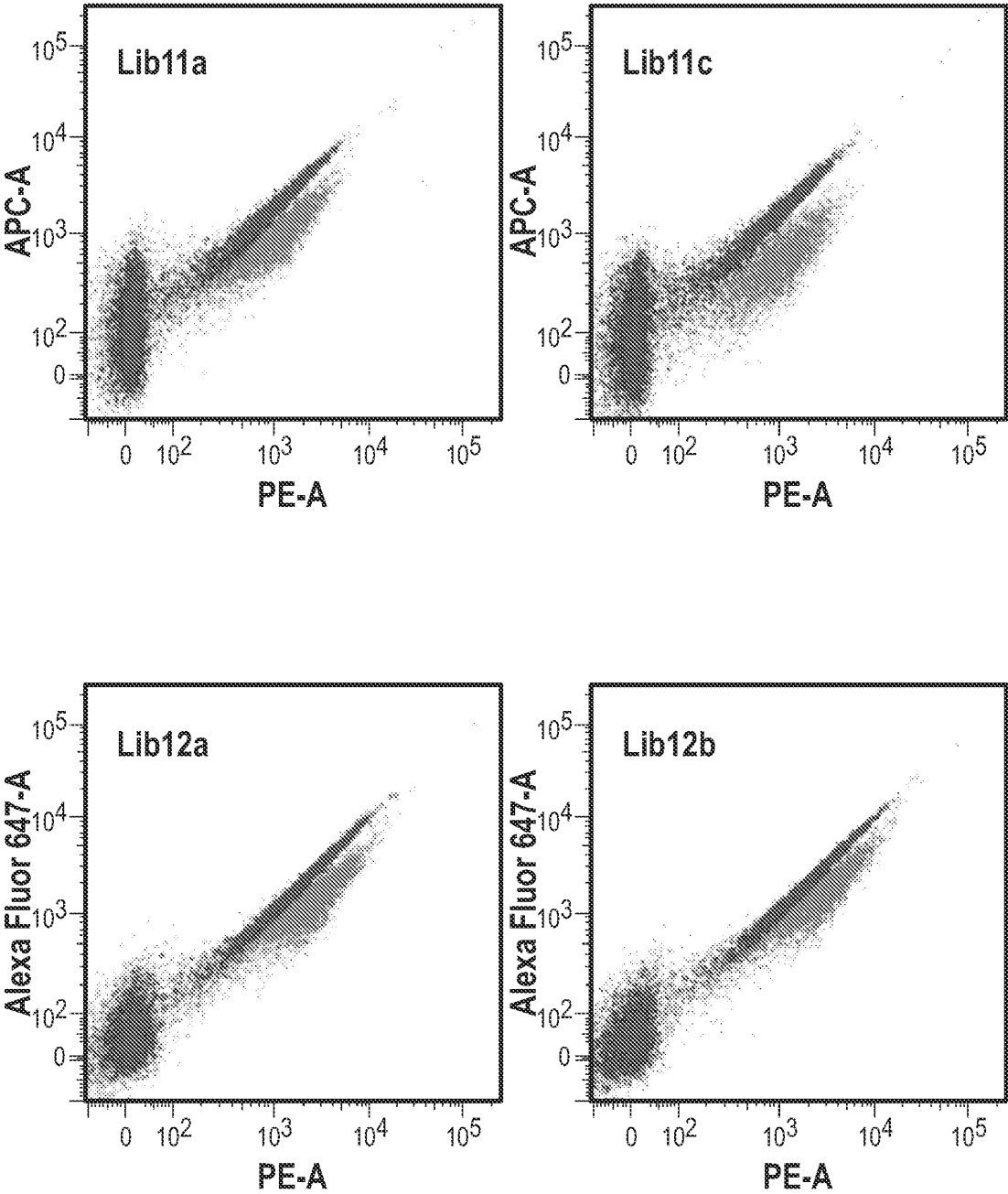


FIG. 5E

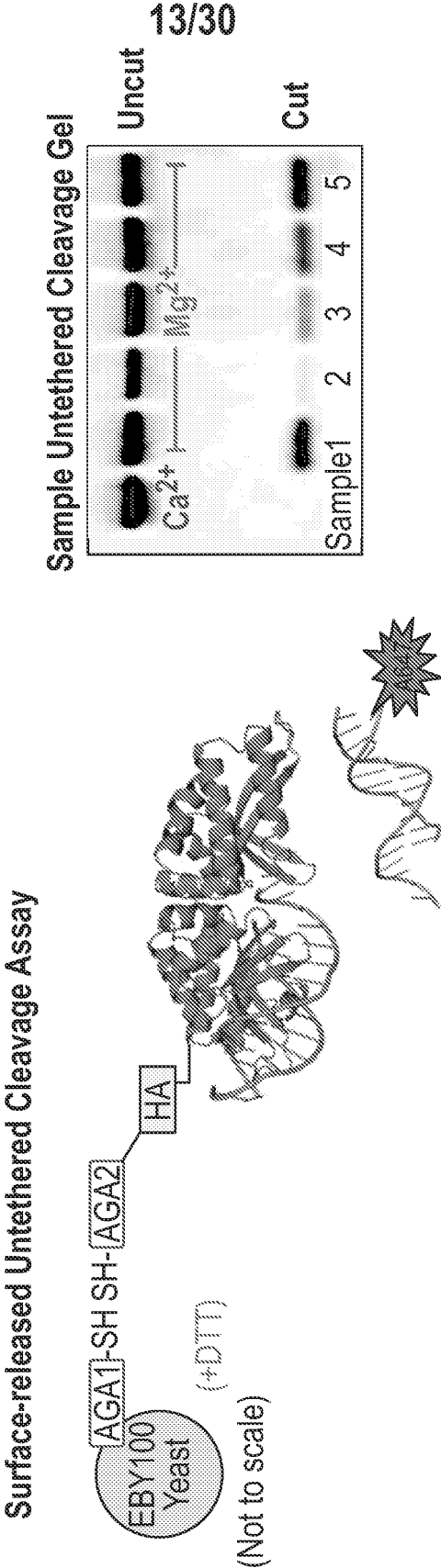


FIG. 6

14/30

OnuHSV2a Six Final Candidates: Tethered Flow Cytometric Activity Assay

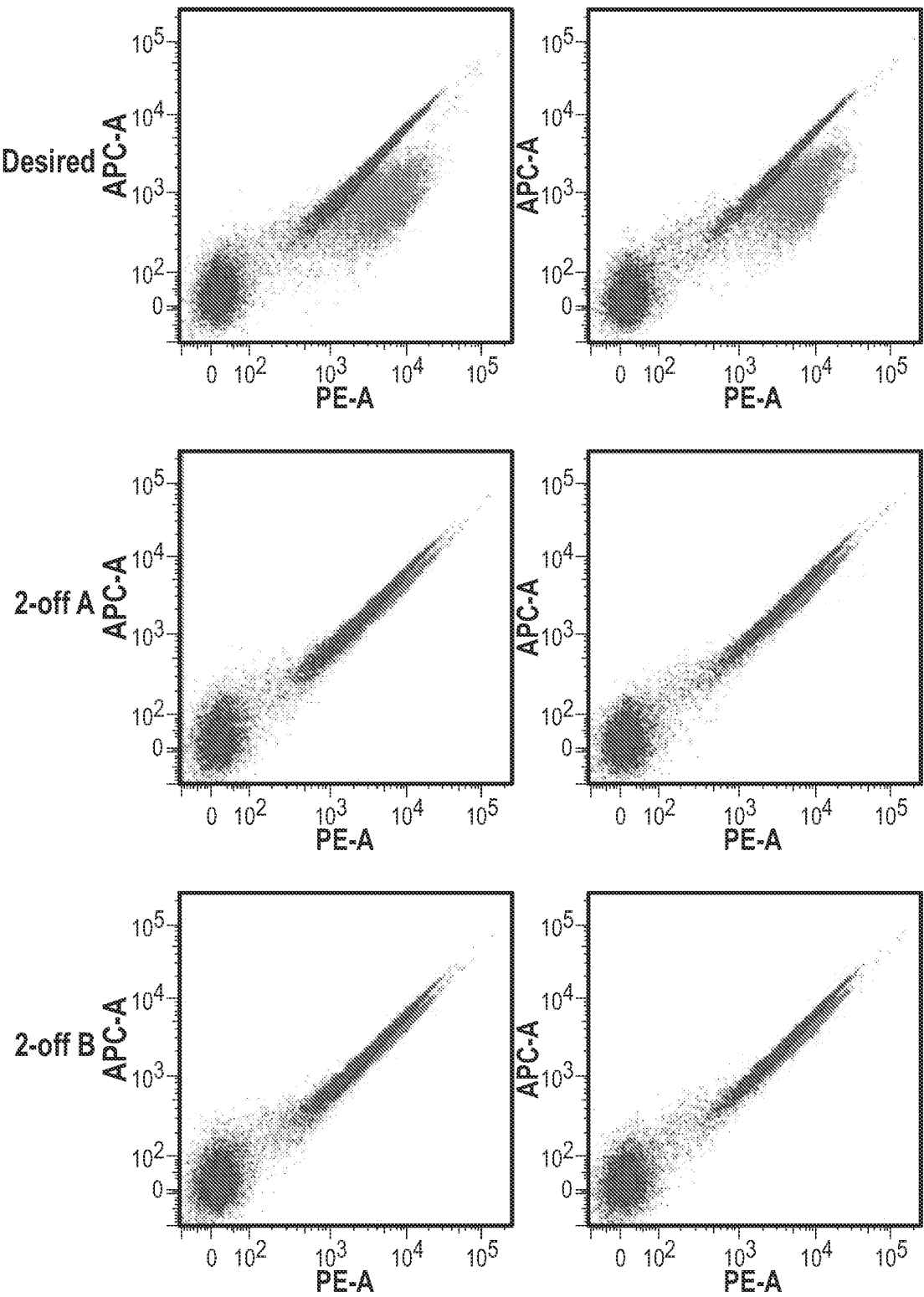
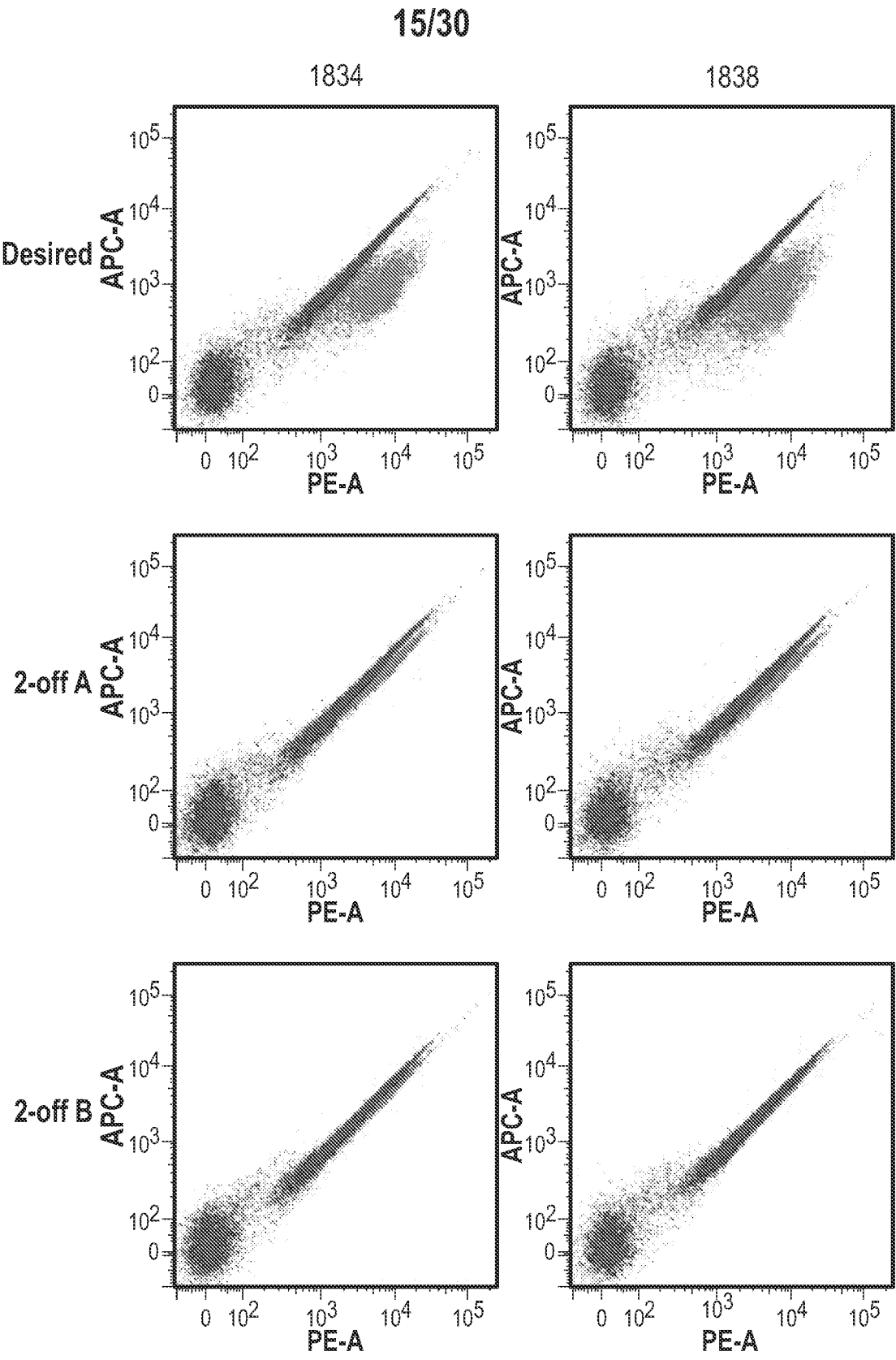


FIG. 7A



16/30

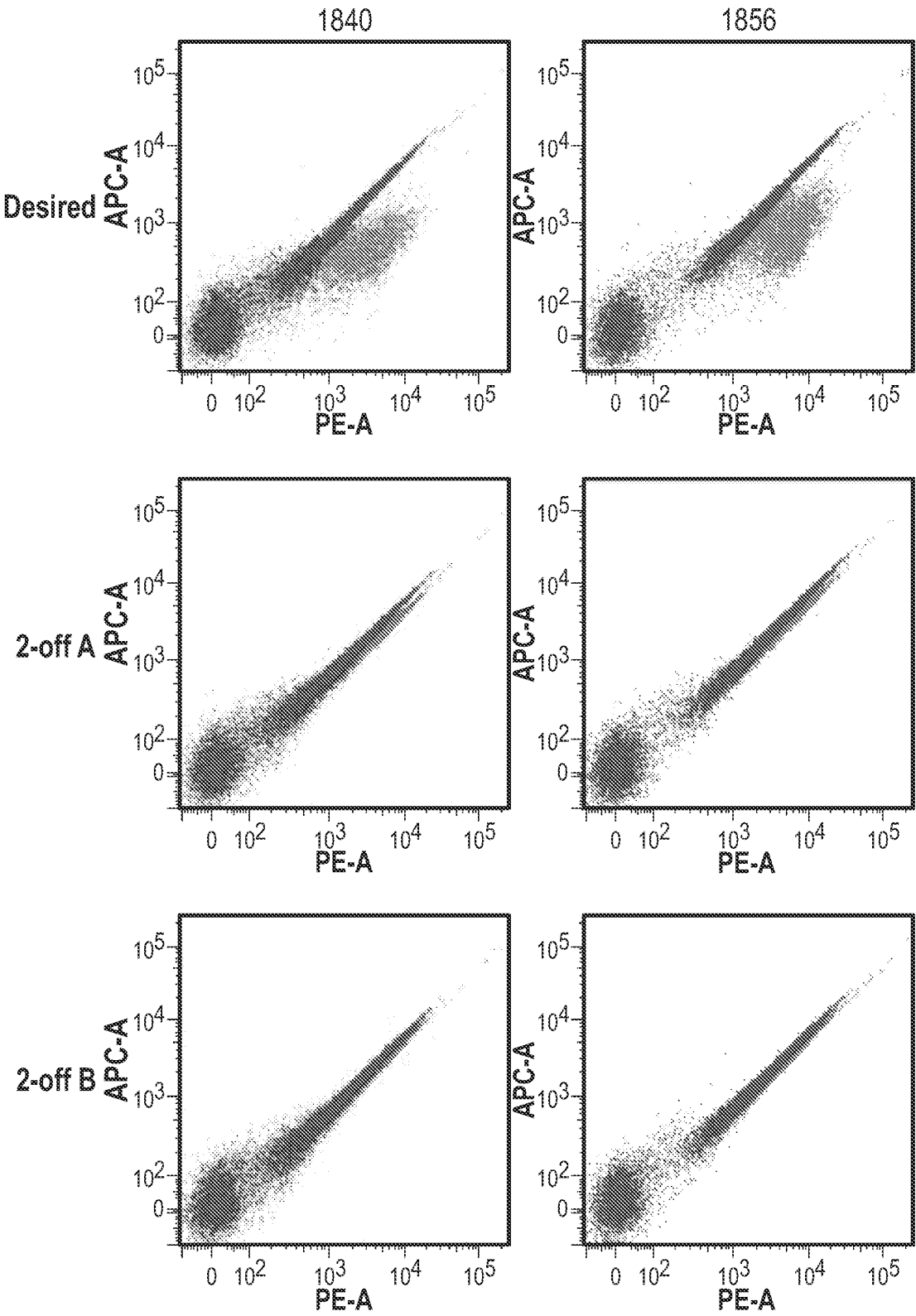


FIG. 7C

17/30

TaTCCtttTTtTTCtAggTgTTt OnuHSV2a Desired (SEQ ID NO: 13)
TaTCCtttTTtTTCtAggTTTTC Human 2-off A (SEQ ID NO: 34)
TtTCCtttTTtTTCtAggTTTGt Human 2-off B (SEQ ID NO: 35)

FIG. 7D

OnuHSV2a Six Final Candidates: Non-Tethered *In Vitro* Activity Assay

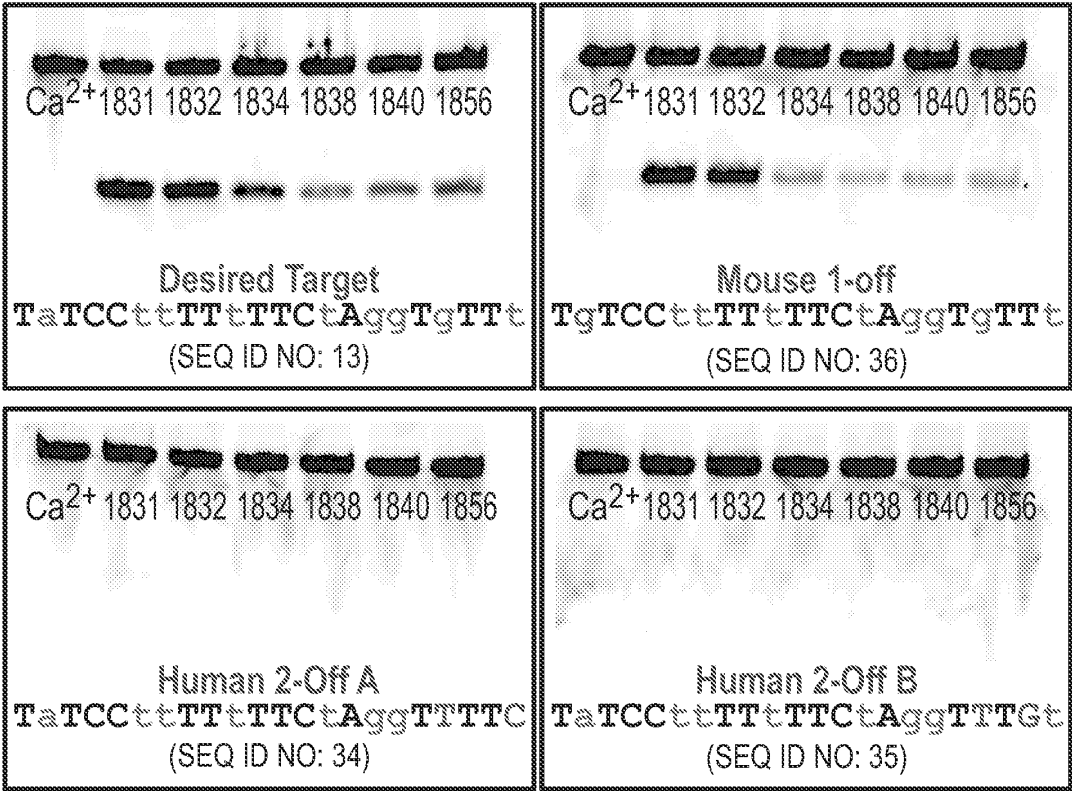
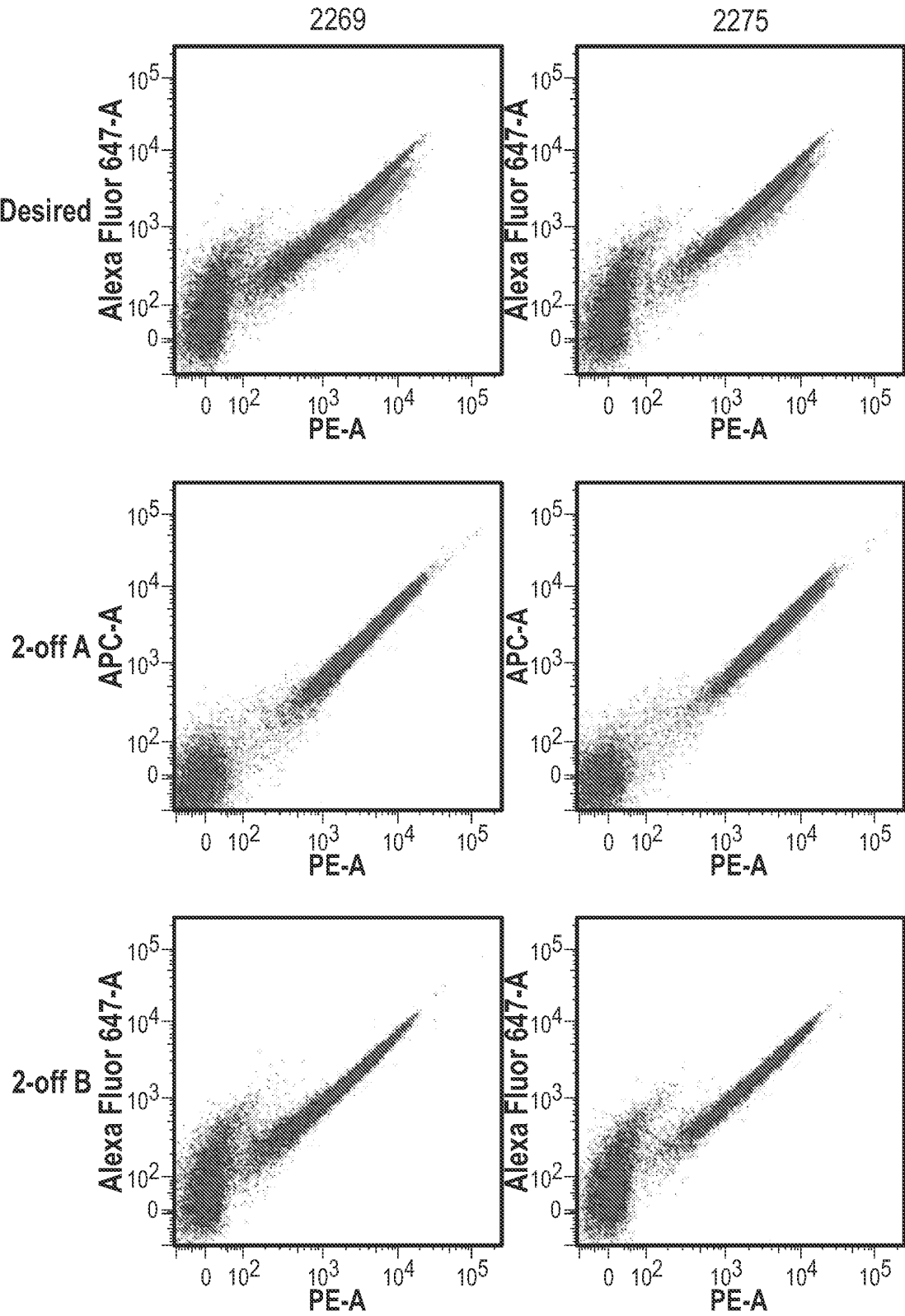


FIG. 8

18/30

OnuHSV2b Six Final Candidates: Tethered Flow Cytometric Activity Assay



19/30

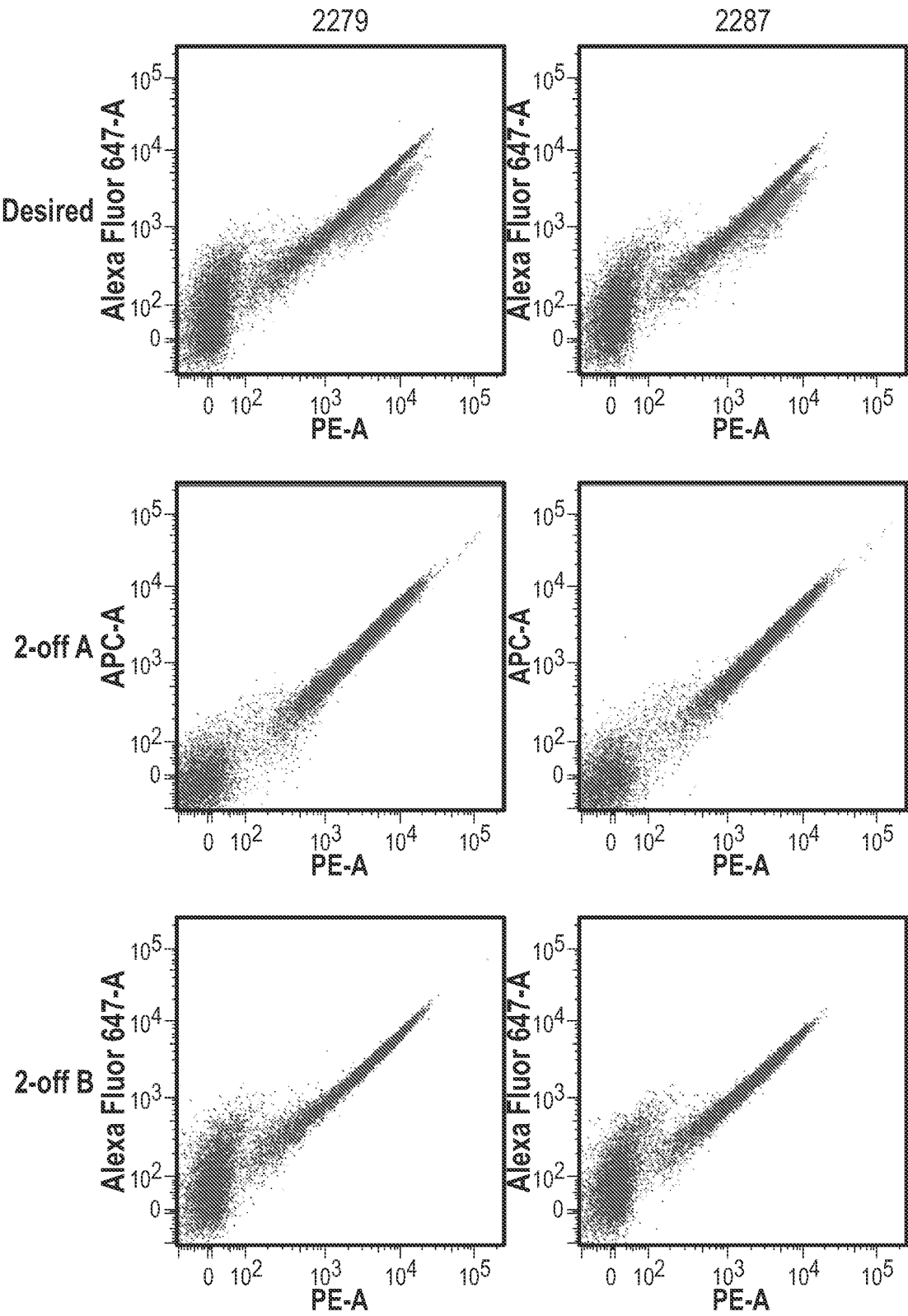


FIG. 9B

20/30

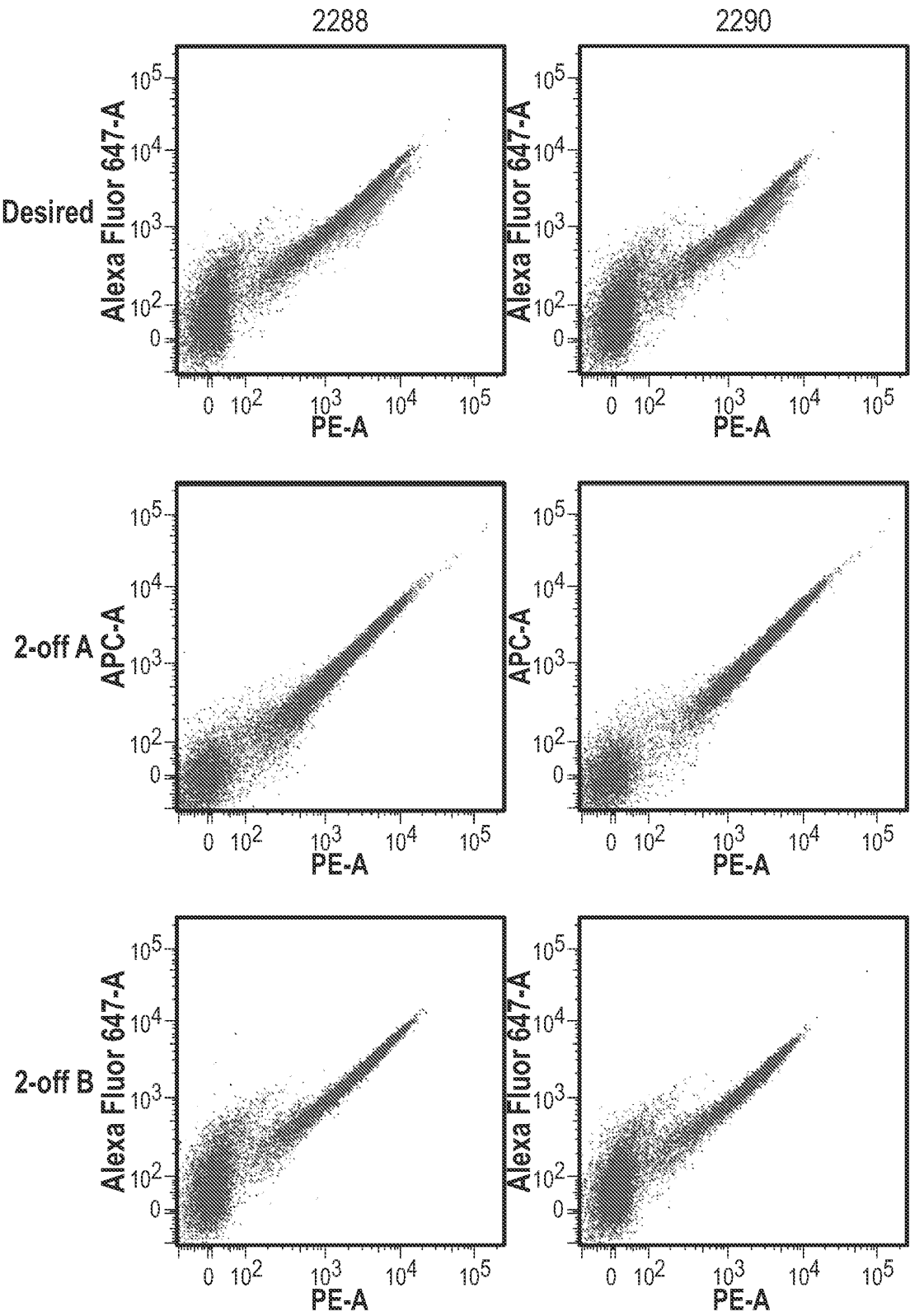


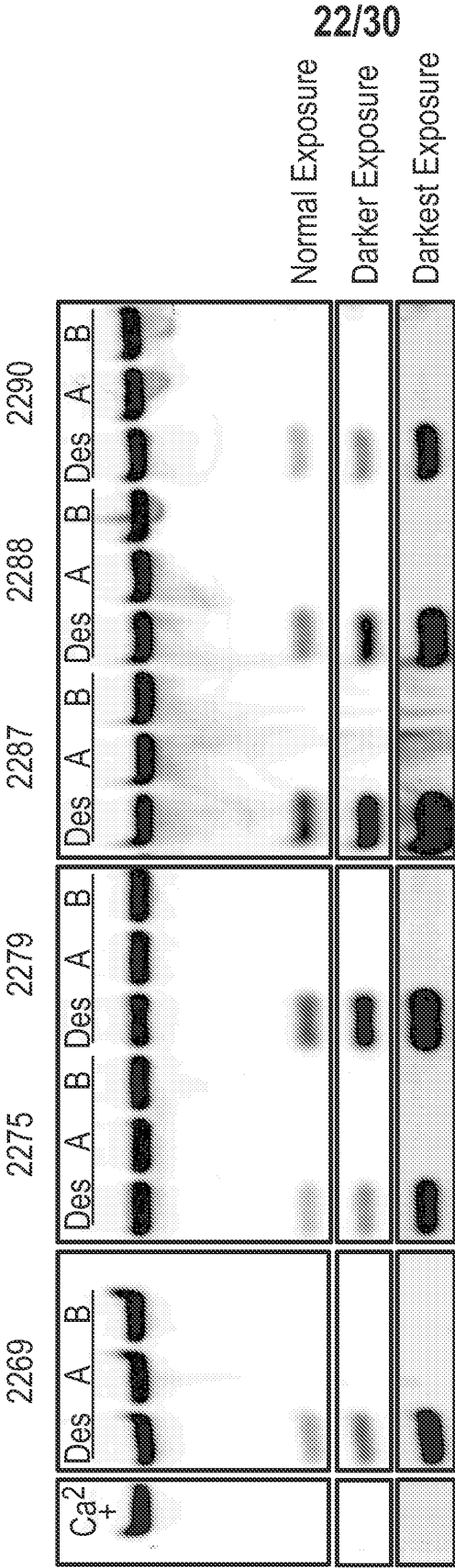
FIG. 9C

DNA Target Sequences

TcTgCAtcctATaCctCctTTcTg OnuHSV2b Desired (SEQ ID NO: 14)
TcTgCAtcctATaCctCctTTgAc Human 3-off A (SEQ ID NO: 37)
TcTgCAtcctATaCctCctTTtGz Human 3-off B (SEQ ID NO: 38)

FIG. 9D

OnuHSV2b Six Final Candidates: Non-Tethered In Vitro Activity Assay



(This figure is composed of sections from three separate gels all imaged simultaneously.)

DNA Target Sequences

TcTgCAtcTATaCctCtTtCg OnuHSV2b Desired (SEQ ID NO: 14)
TcTgCAtcTATaCctCtTtGAc Human 3-off A (SEQ ID NO: 37)
TcTgCAtcTATaCctCtTtGc Human 3-off B (SEQ ID NO: 38)

FIG. 10

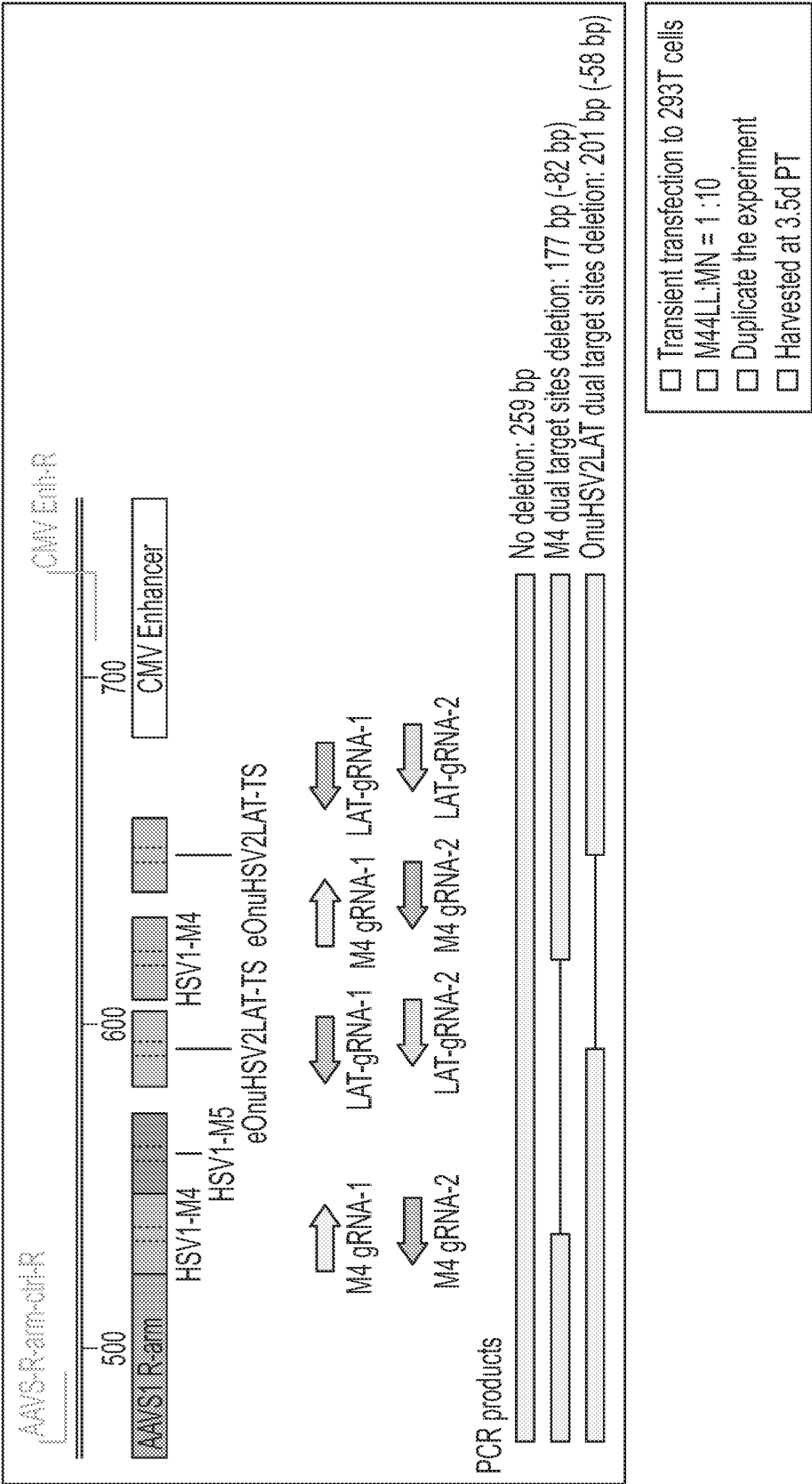


FIG. 11A

24/30

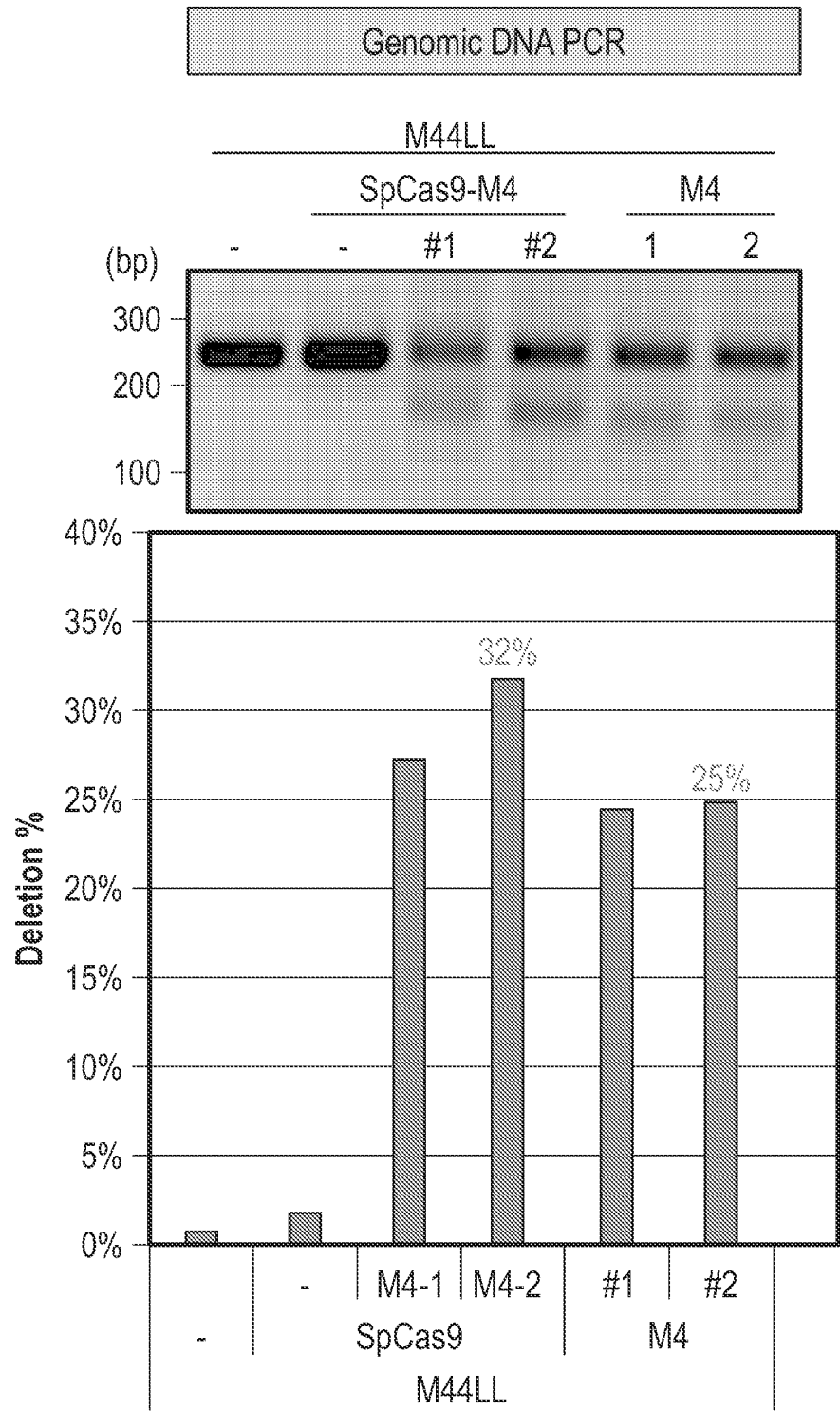
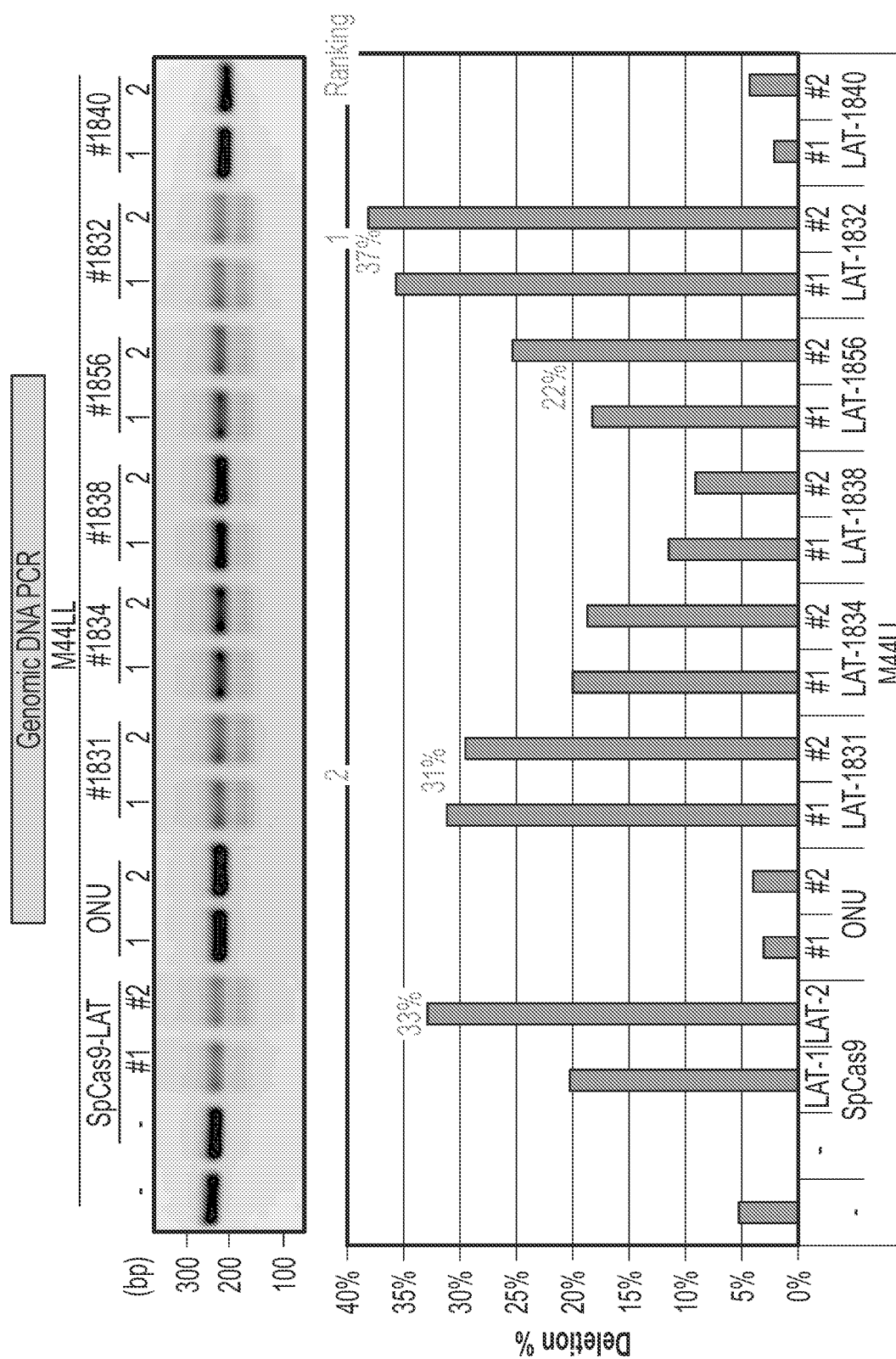


FIG. 11B



Detection of Indels by Sanger Sequencing

HSV2-LAT-TS

AAACACCTAGAAAAAAGGATA (SEQ ID NO: 39)

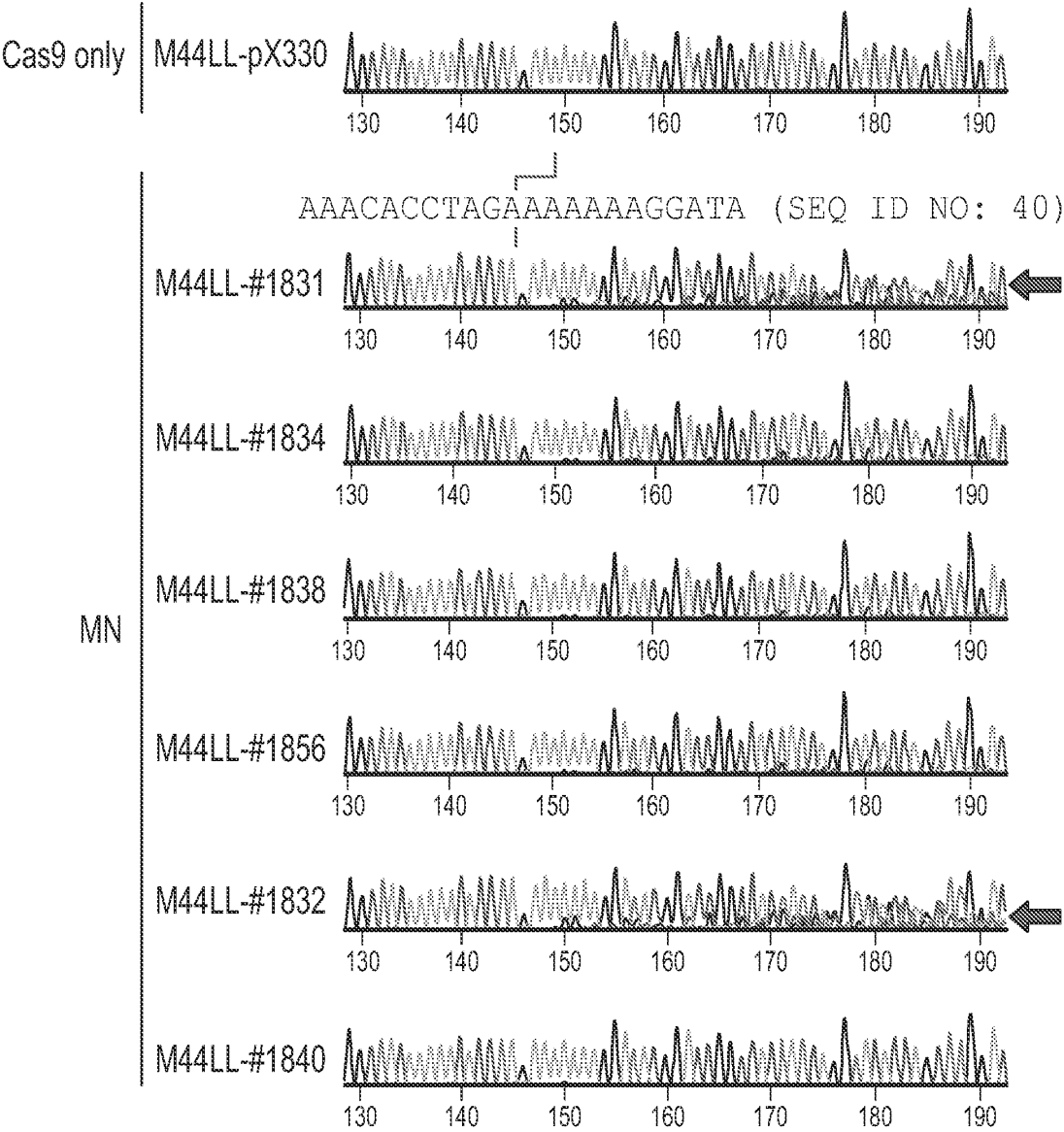


FIG. 12

27/30

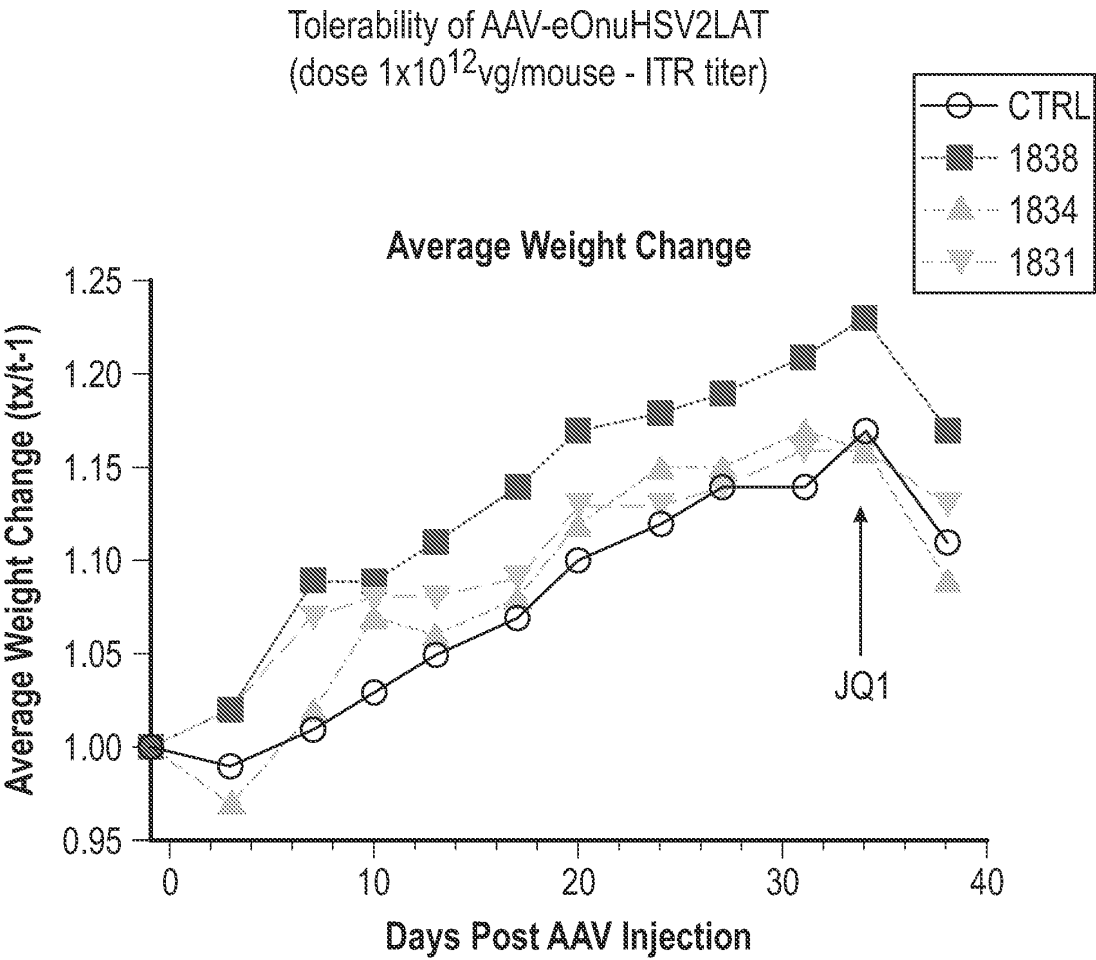
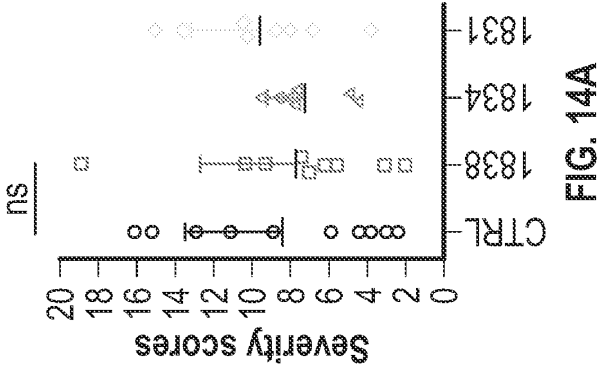


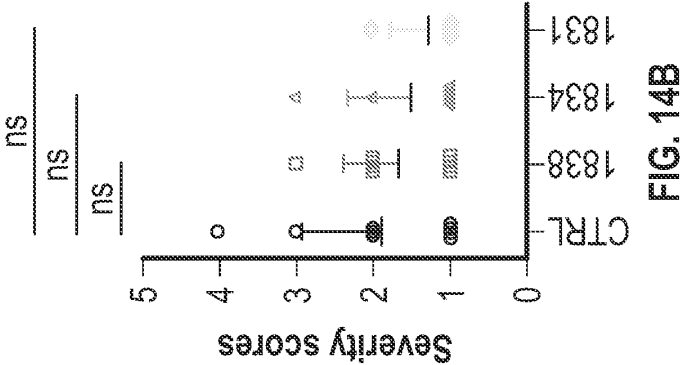
FIG. 13

Tolerability of AAV-eOnuHSV2LAT
(dose 1x10¹²vg/mouse - ITR titer)

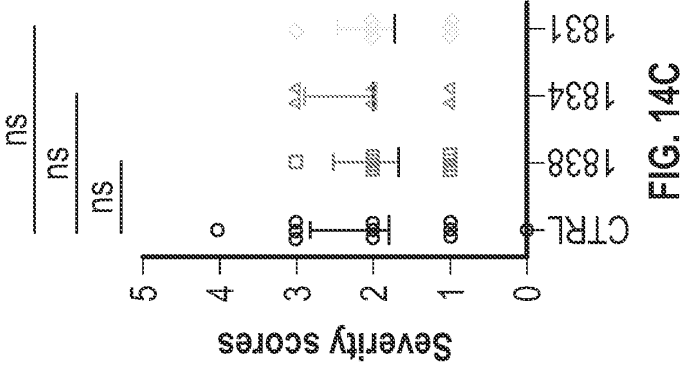
Liver IFC



TG axonopathy



TG inflammation



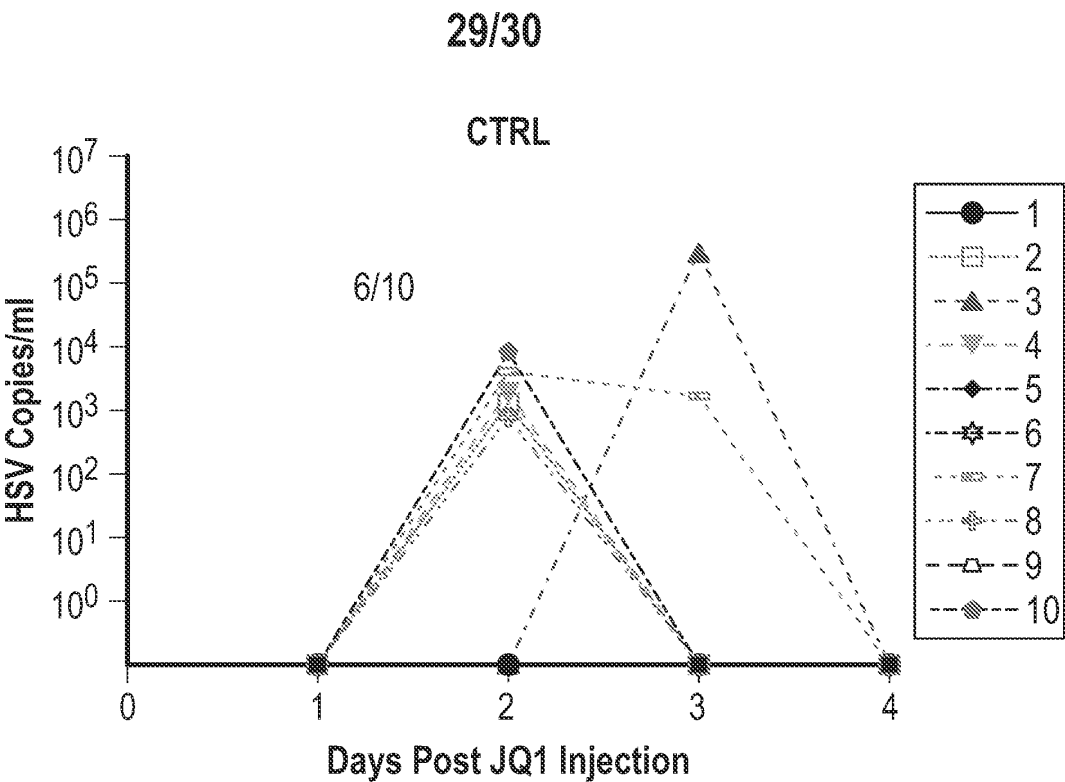


FIG. 15A

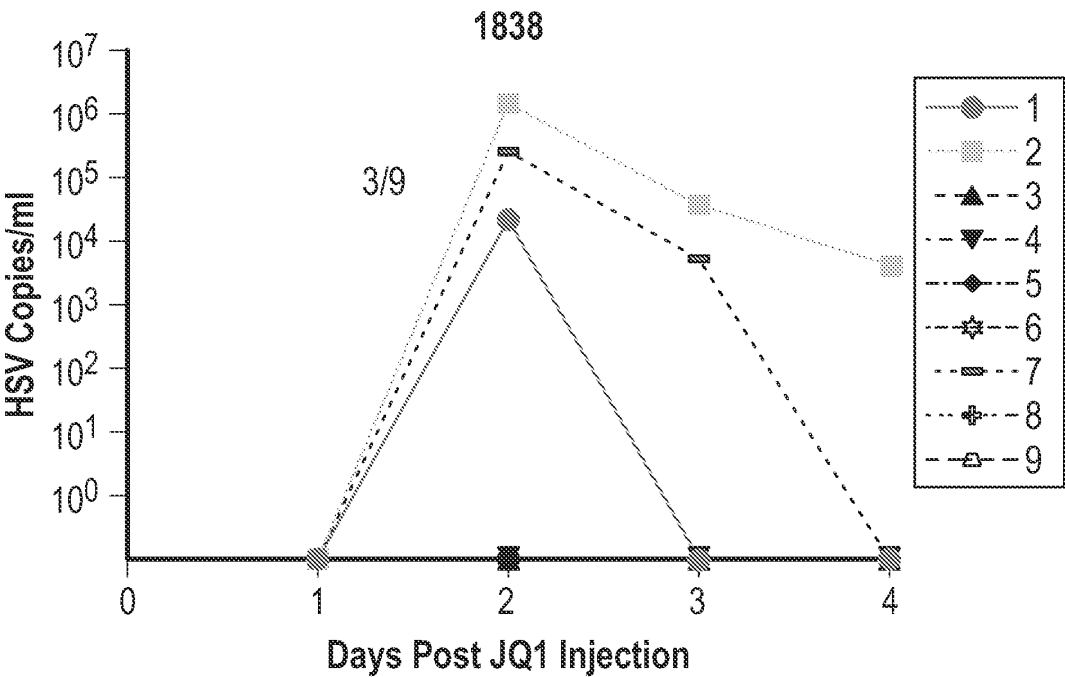


FIG. 15B

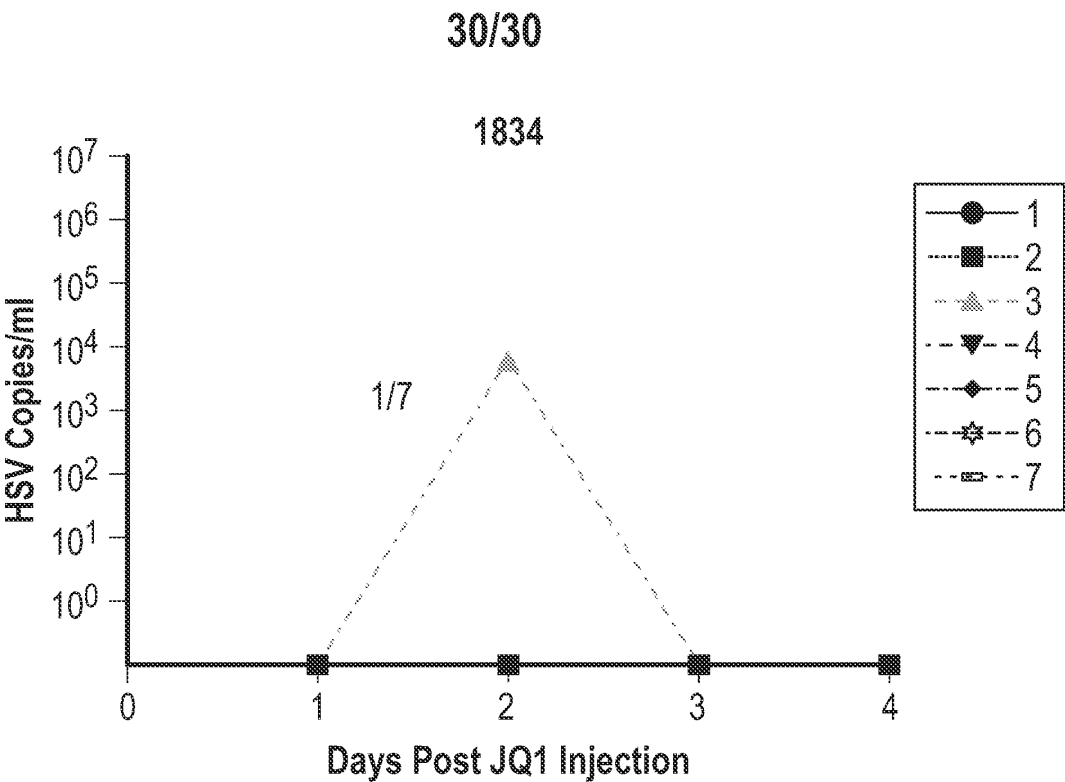


FIG. 15C

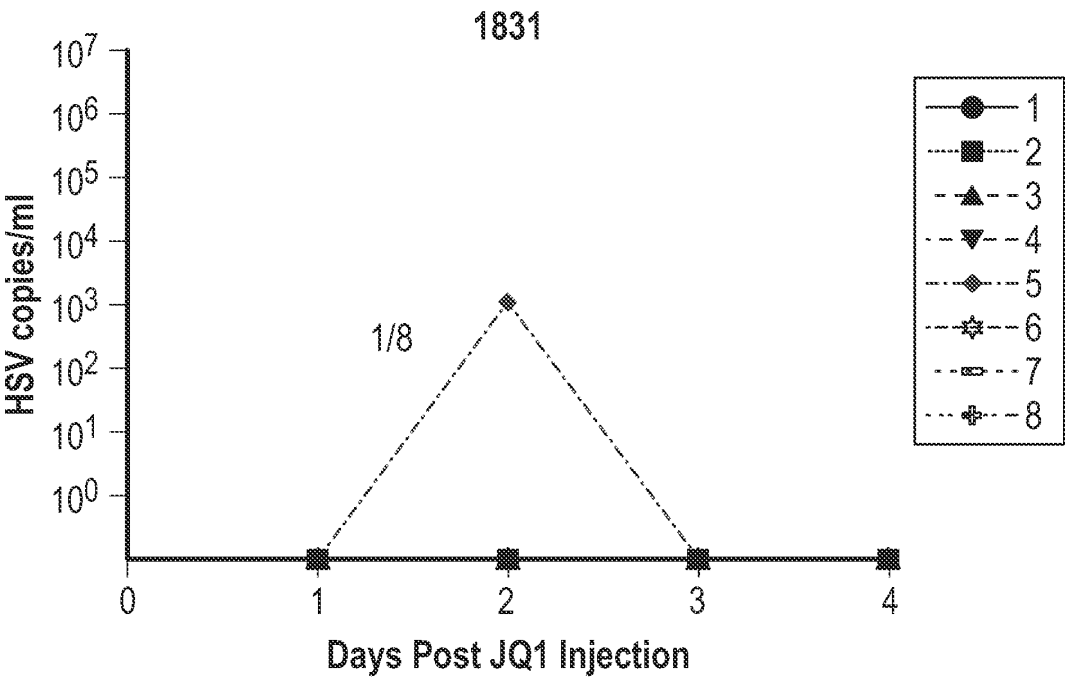


FIG. 15D