FIG. 1A

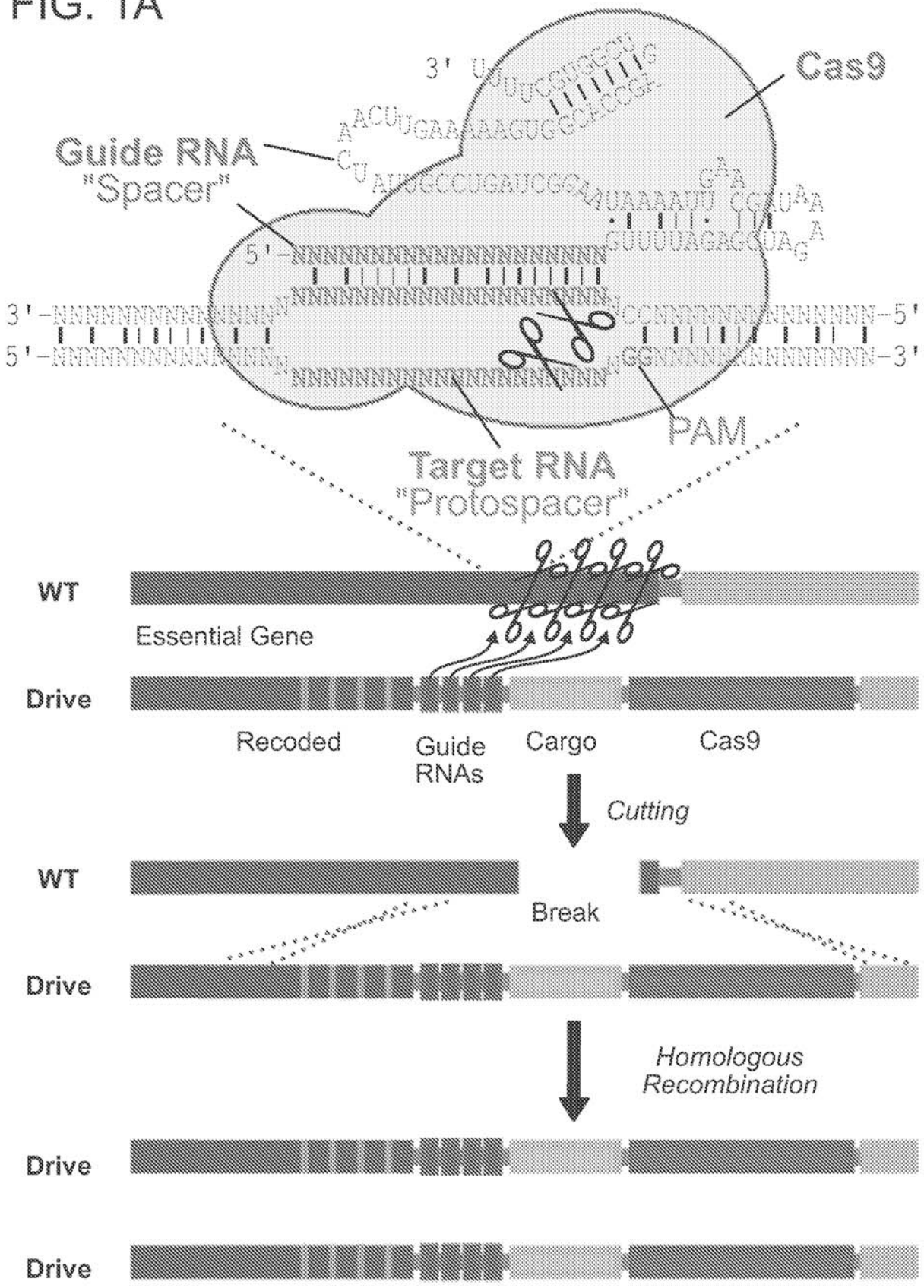
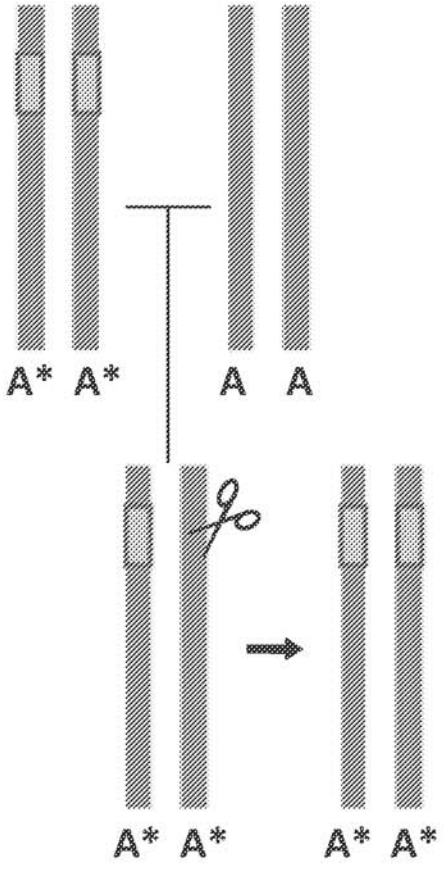
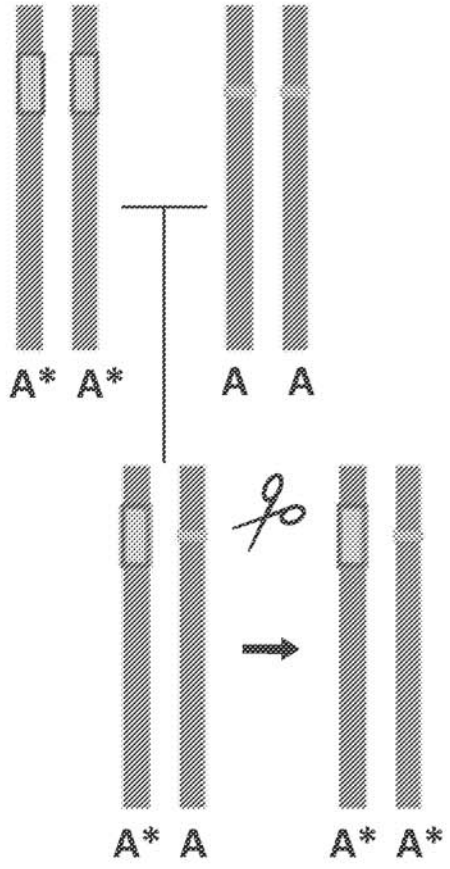

Cas9
Guide RNA
"Spacer"
5'-NNNNNNNNNNNNNNNNNNNN
3'-NNNNNNNNNNNNNNNNNNNN
5'-NNNNNNNNNNNNNNNNNNNN
3'-NNNNNNNNNNNNNNNNNNNN
PAM
Target RNA
"Protospacer"
WT
Essential Gene
Drive
Recoded
Guide RNAs
Cargo
Cas9
Cutting
WT
Break
Drive
Homologous Recombination
Drive
Drive

FIG. 1B



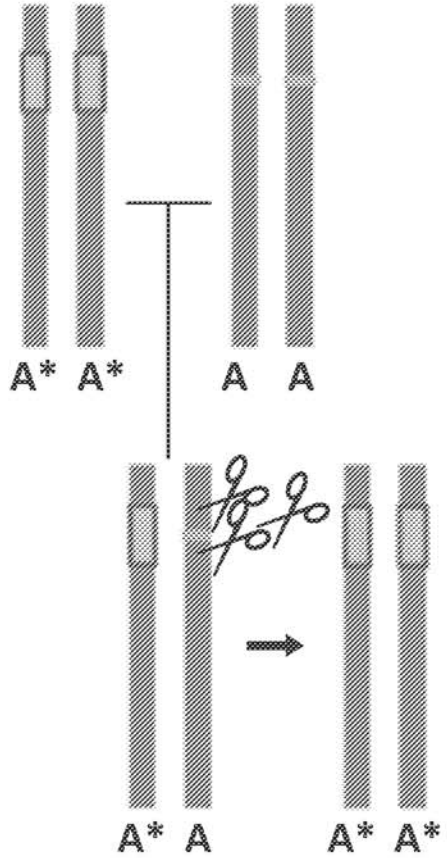
Drive Inheritance

FIG. 1C



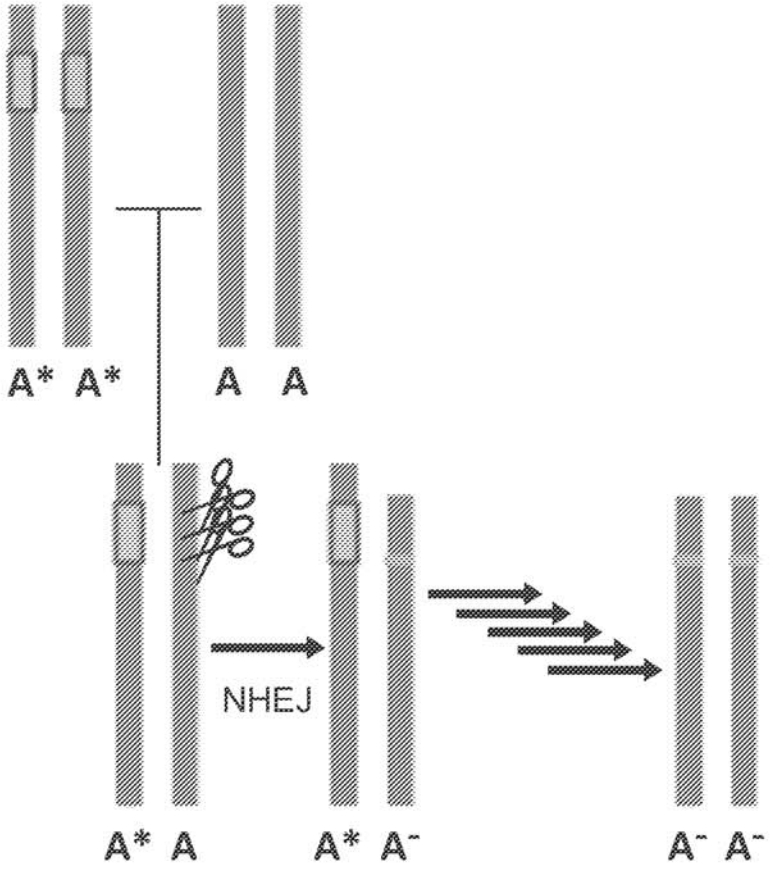
One Target vs Mutation

FIG. 1D



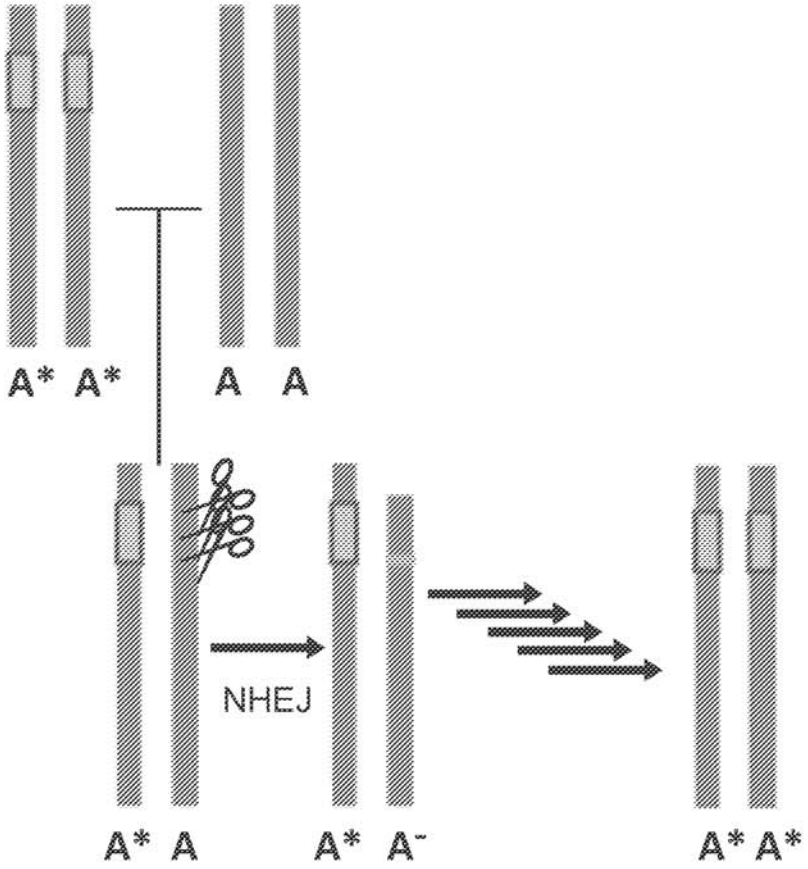
Many Targets vs Mutation

FIG. 1E



Neutral Target Sites: Deletion

FIG. 1F



Essential Target Sites: Deletion

FIG. 2A

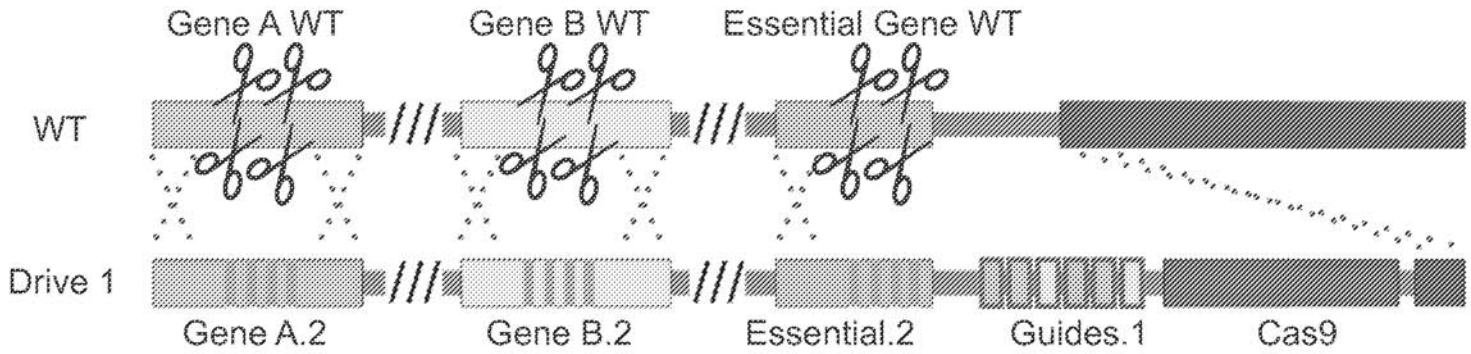


FIG. 2B

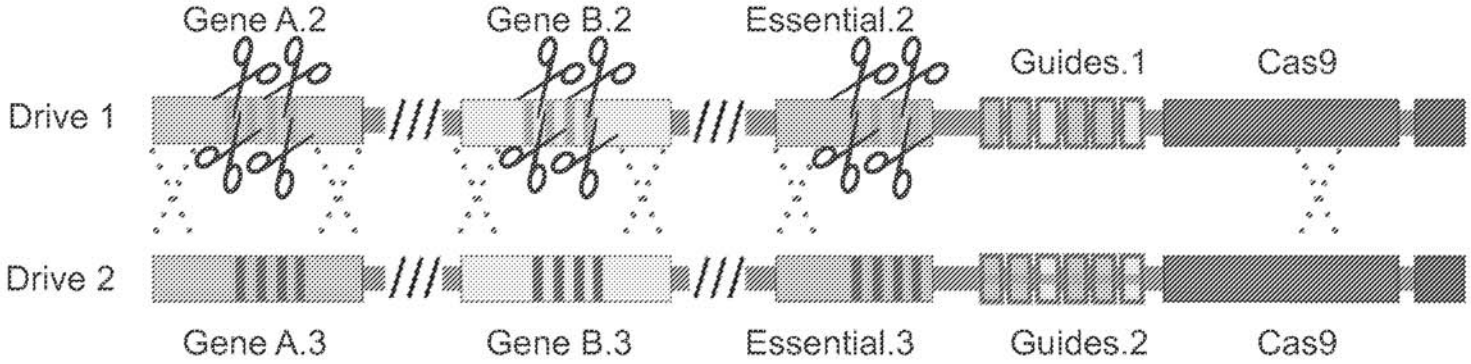


FIG. 2C

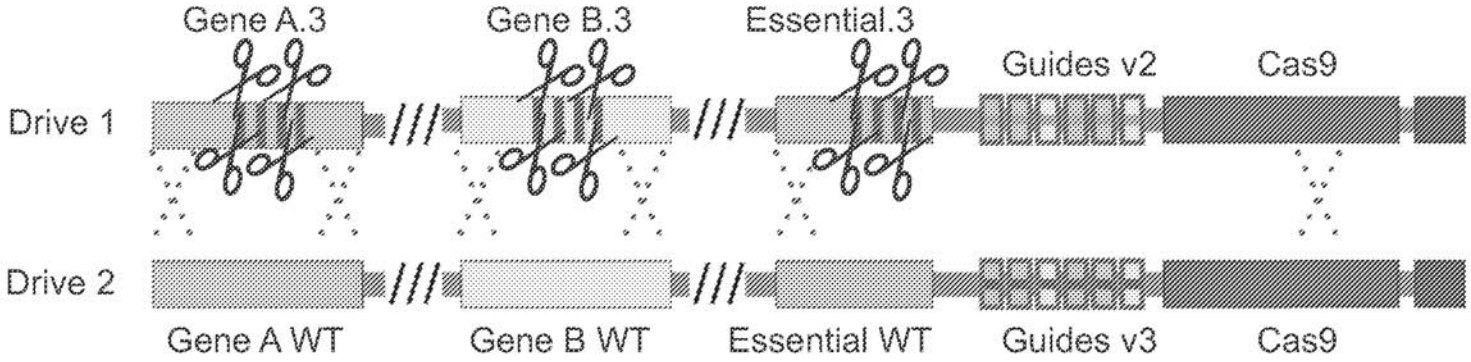


FIG. 3

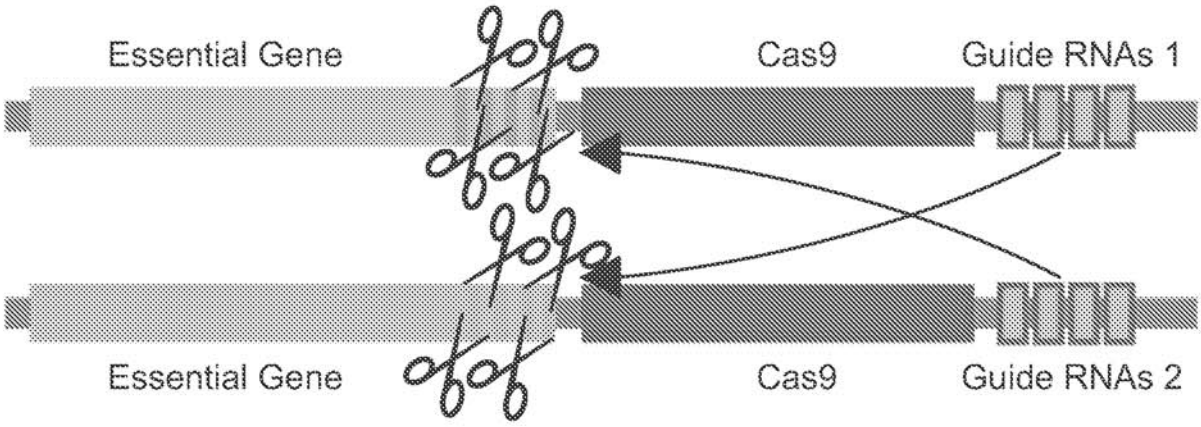

Essential Gene
Cas9
Guide RNAs 1
Essential Gene
Cas9
Guide RNAs 2

FIG. 4A

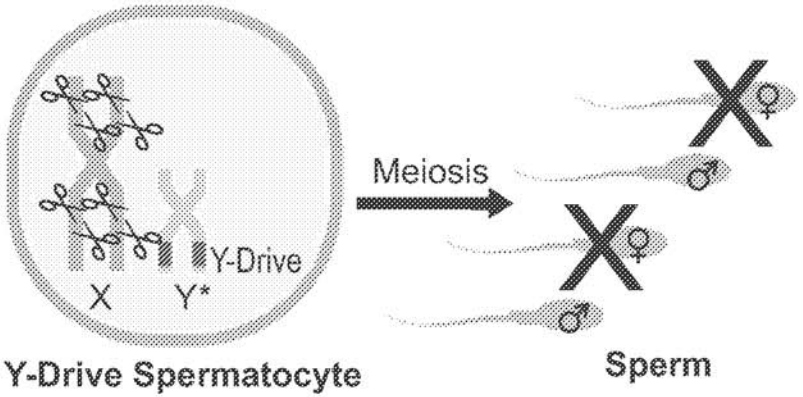


FIG.4B

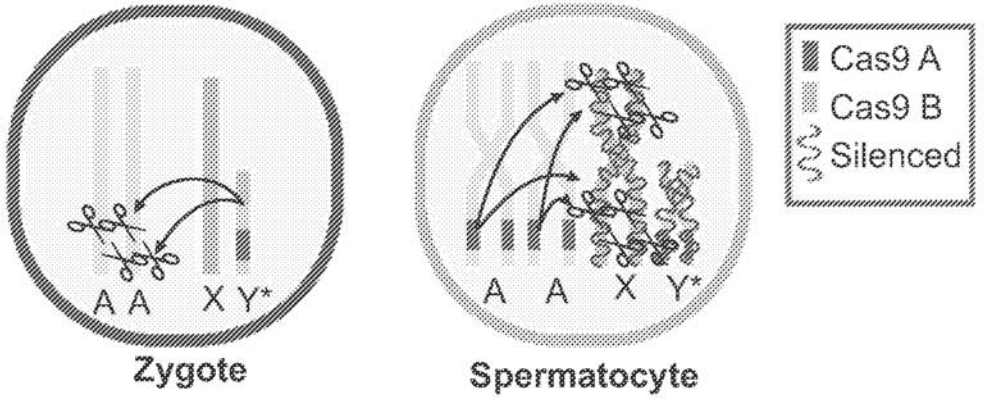


FIG. 4C

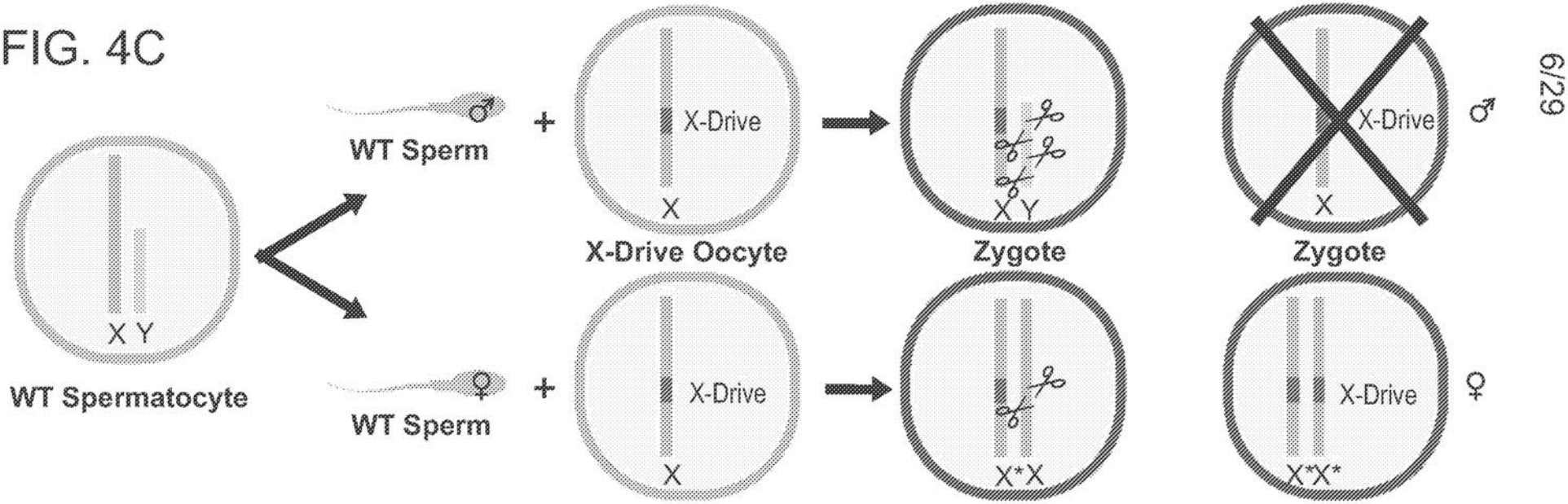


FIG. 4D

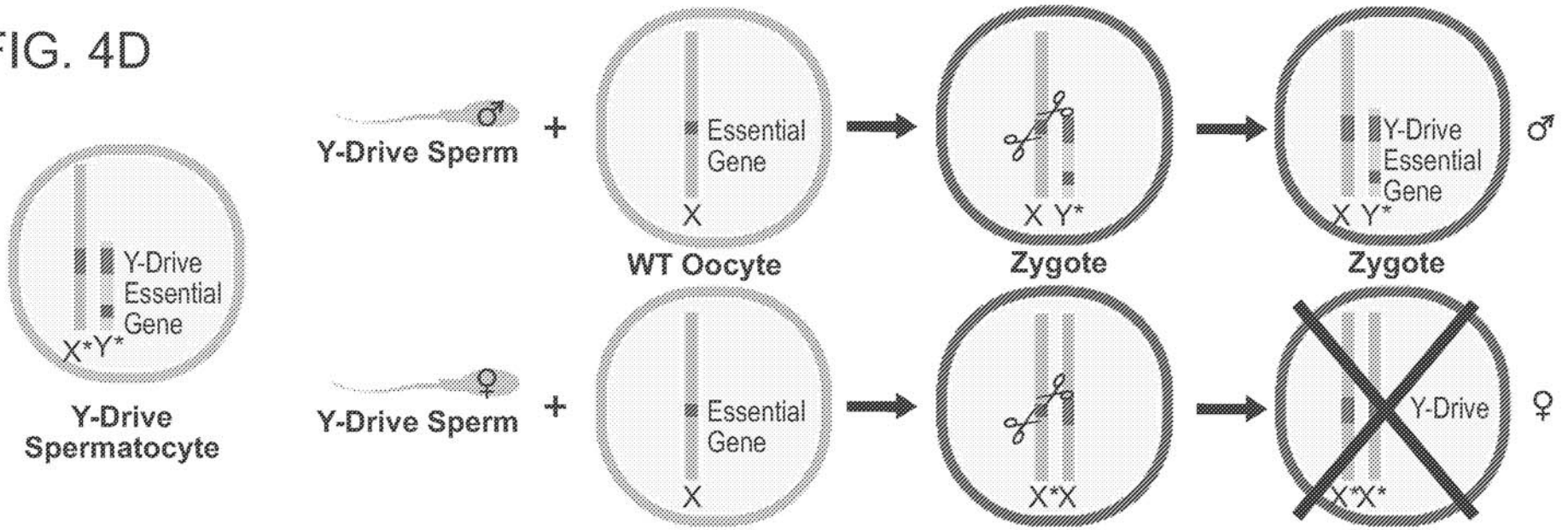


FIG. 5A

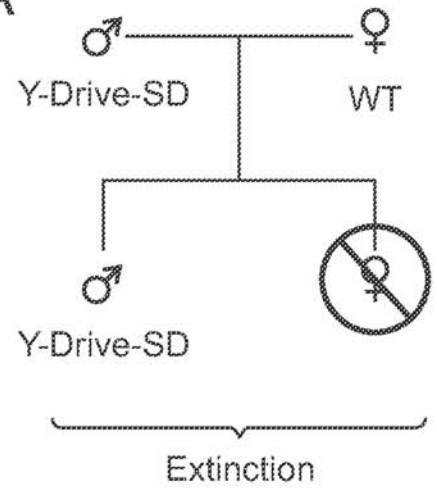
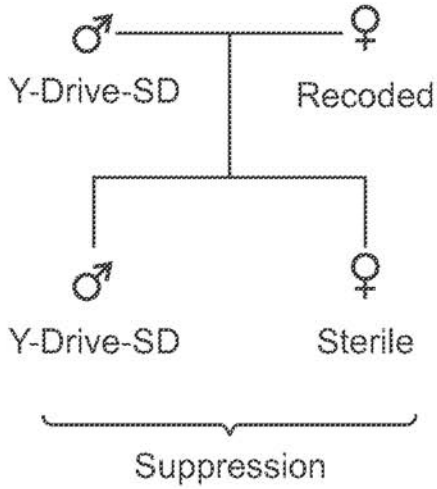


FIG. 5B



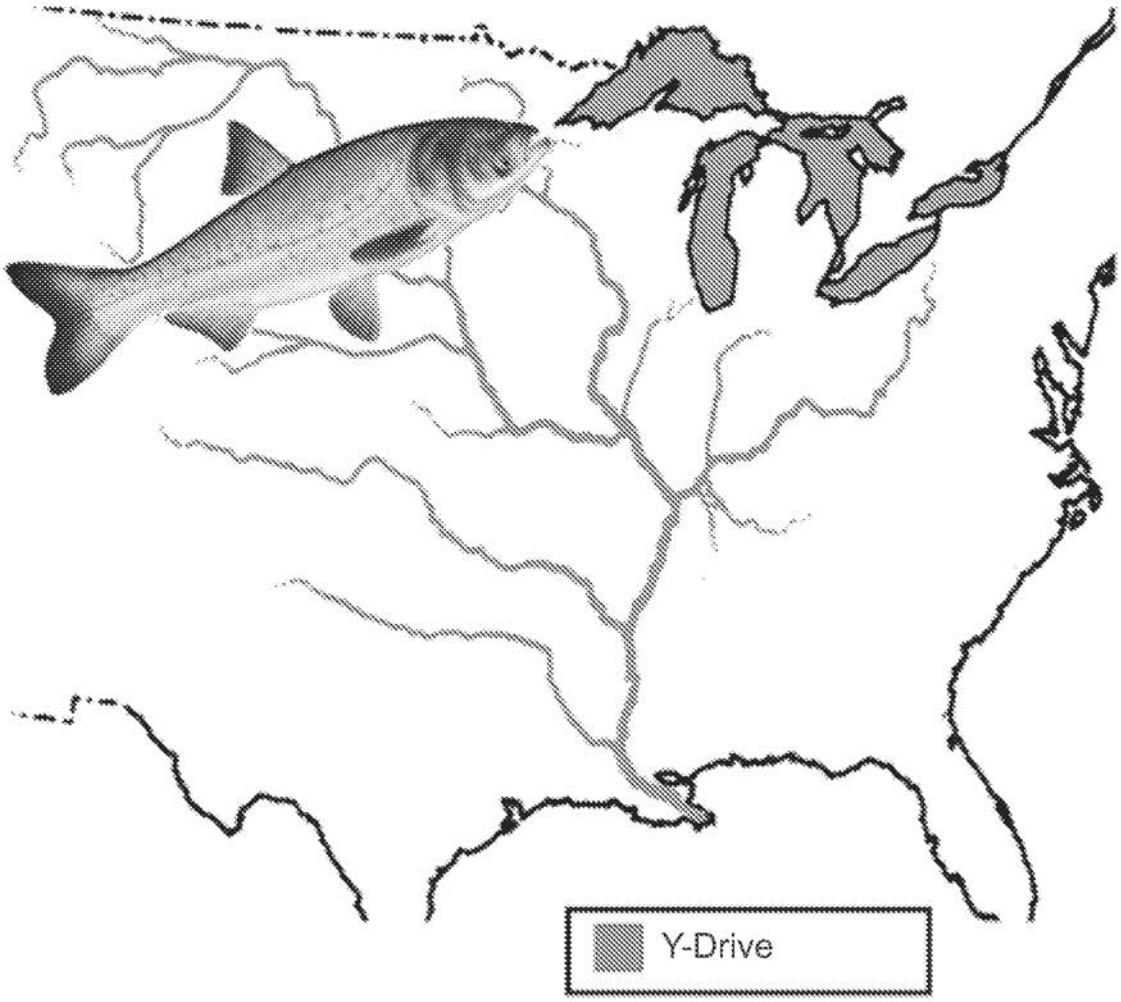


FIG. 6A

FIG.6B

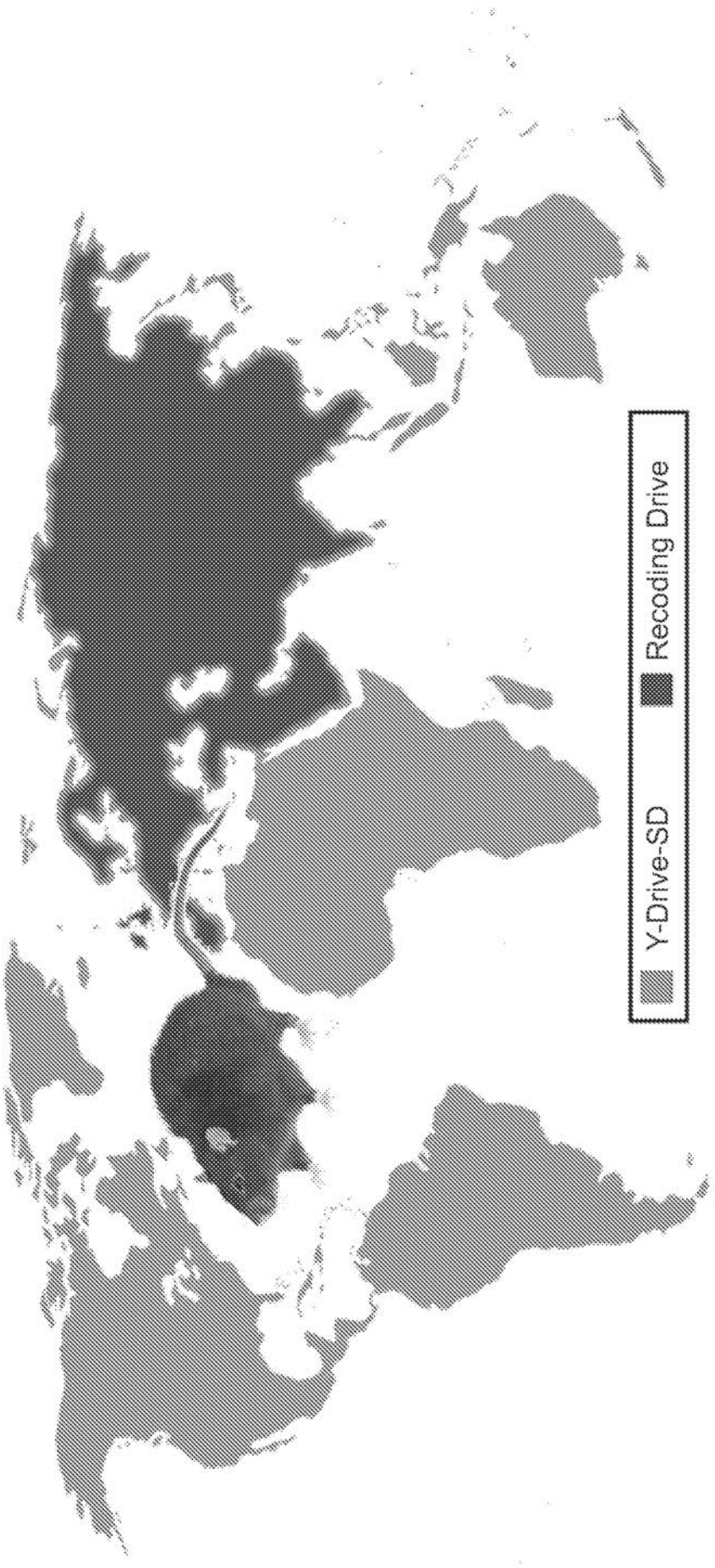


FIG. 7

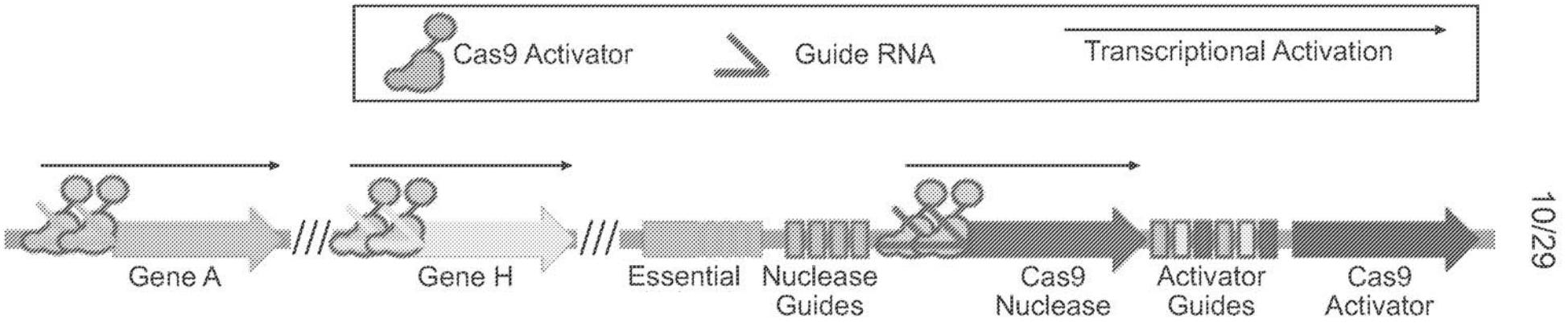

Cas9 Activator
Guide RNA
Transcriptional Activation
Gene A
Gene H
Essential
Nuclease Guides
Cas9 Nuclease
Activator Guides
Cas9 Activator

FIG. 8A

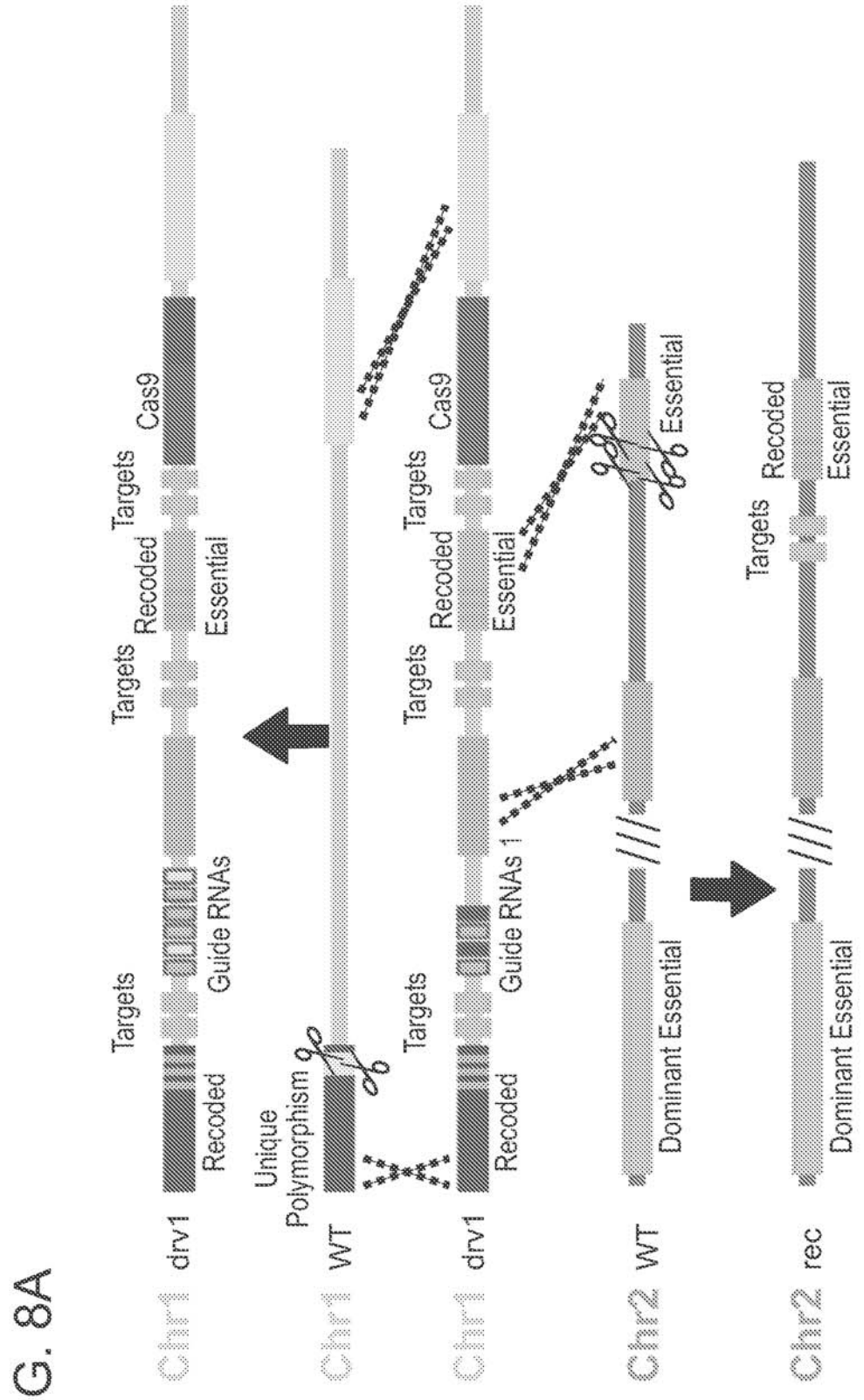

Chr1 drv1
Targets
Recoded
Guide RNAs
Targets
Recoded
Essential
Targets
Cas9
Chr1 WT
Unique Polymorphism
Targets
Chr1 drv1
Targets
Recoded
Guide RNAs 1
Targets
Recoded
Essential
Targets
Cas9
Chr2 WT
Dominant Essential
Essential
Chr2 rec
Targets
Recoded
Essential
Dominant Essential

FIG. 8B

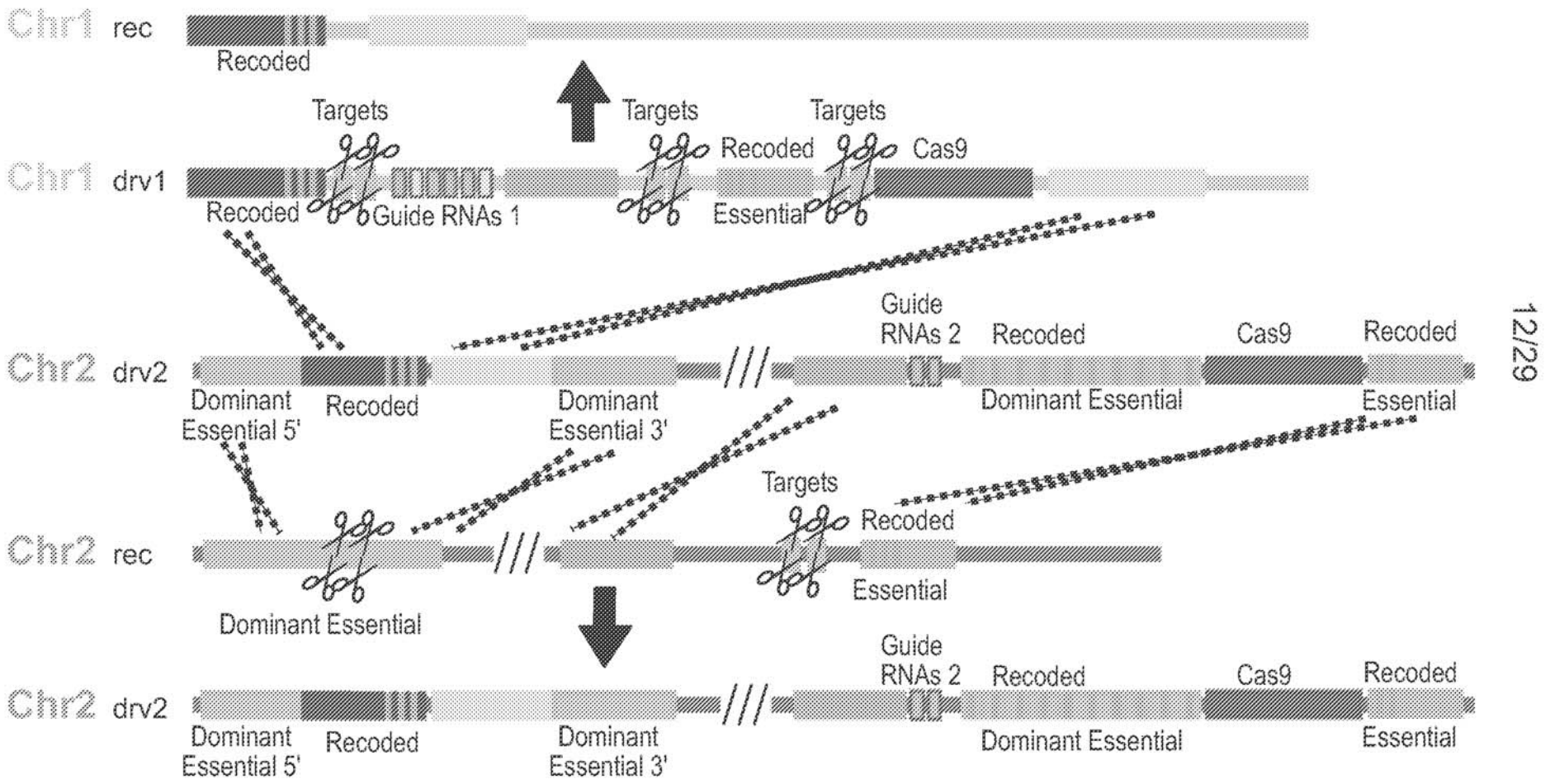

Chr1 rec
Recoded
Targets
Targets
Targets
Chr1 drv1
Recoded
Guide RNAs 1
Recoded
Cas9
Essential
Guide RNAs 2
Recoded
Cas9
Recoded
Chr2 drv2
Dominant Essential 5'
Recoded
Dominant Essential 3'
Dominant Essential
Essential
Targets
Recoded
Chr2 rec
Dominant Essential
Essential
Guide RNAs 2
Recoded
Cas9
Recoded
Chr2 drv2
Dominant Essential 5'
Recoded
Dominant Essential 3'
Dominant Essential
Essential

FIG. 8C

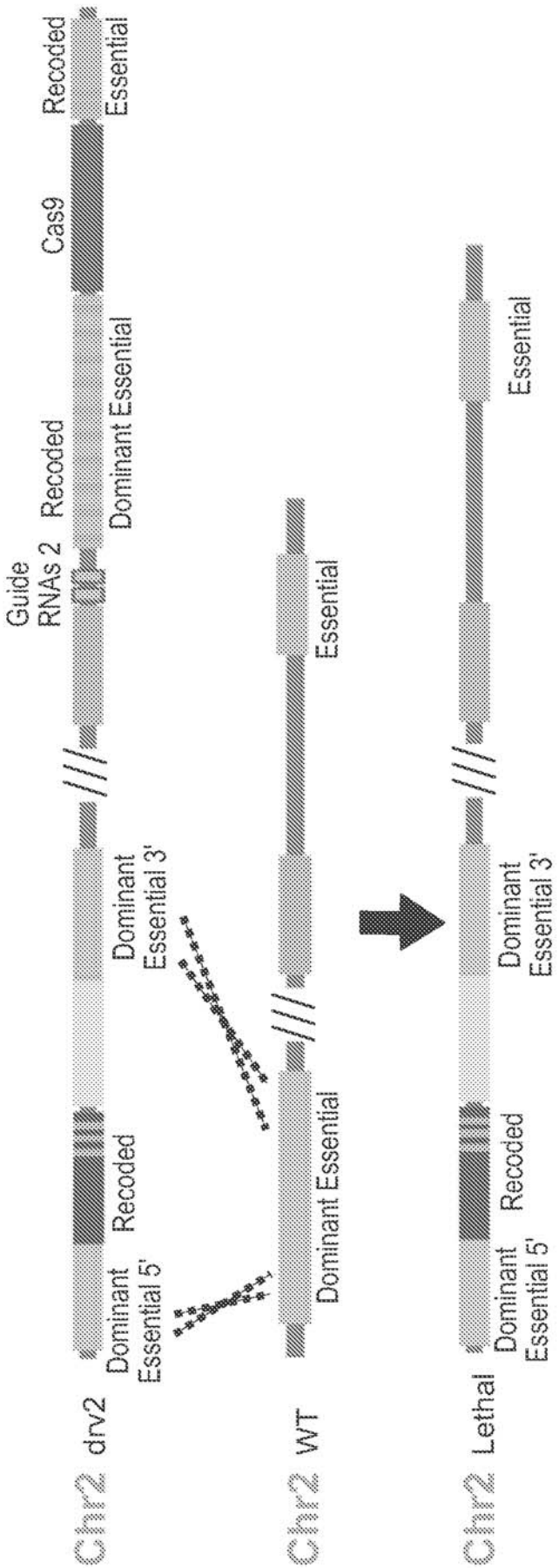
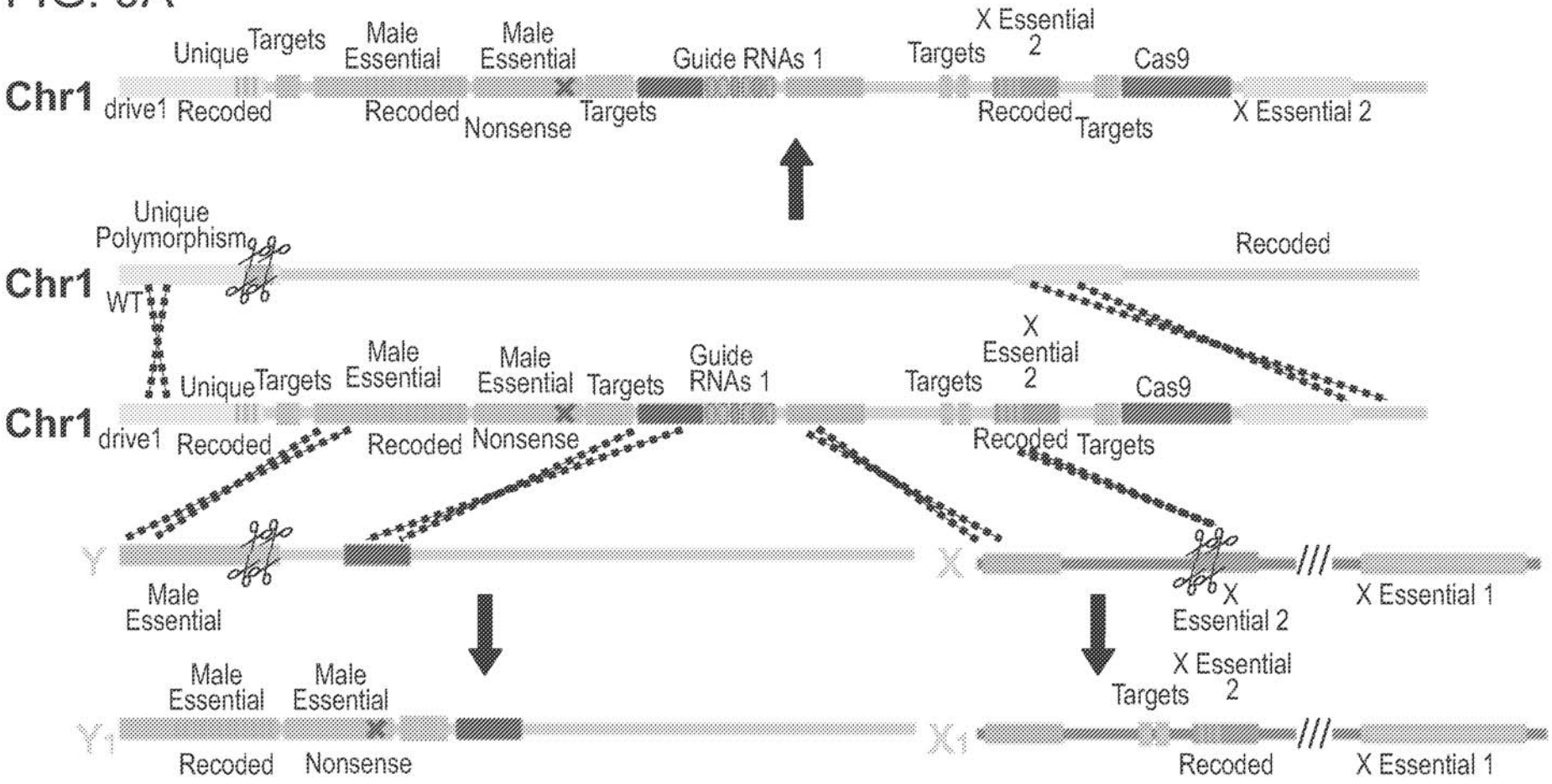

Chr2 drv2
Dominant Essential 5'
Recoded
Dominant Essential 3'
Guide RNAs 2
Recoded
Cas9
Recoded
Dominant Essential
Essential
Chr2 WT
Dominant Essential
Essential
Chr2 Lethal
Dominant Essential 5'
Recoded
Dominant Essential 3'
Essential

FIG. 9A


Chr1
drive1
Unique
Targets
Recoded
Male
Essential
Recoded
Male
Essential
Nonsense
Guide RNAs 1
Targets
X Essential
2
Targets
Recoded
Cas9
Targets
X Essential 2
Unique
Polymorphism
WT
Chr1
Recoded
X
Essential
2
Unique
Targets
Male
Essential
Male
Essential
Targets
Guide
RNAs 1
Targets
Cas9
Chr1
drive1
Recoded
Recoded
Nonsense
Recoded
Targets
Y
Male
Essential
X
X
Essential 2
X Essential 1
Male
Essential
Male
Essential
X Essential
2
Targets
Y1
Recoded
Nonsense
X1
Recoded
X Essential 1

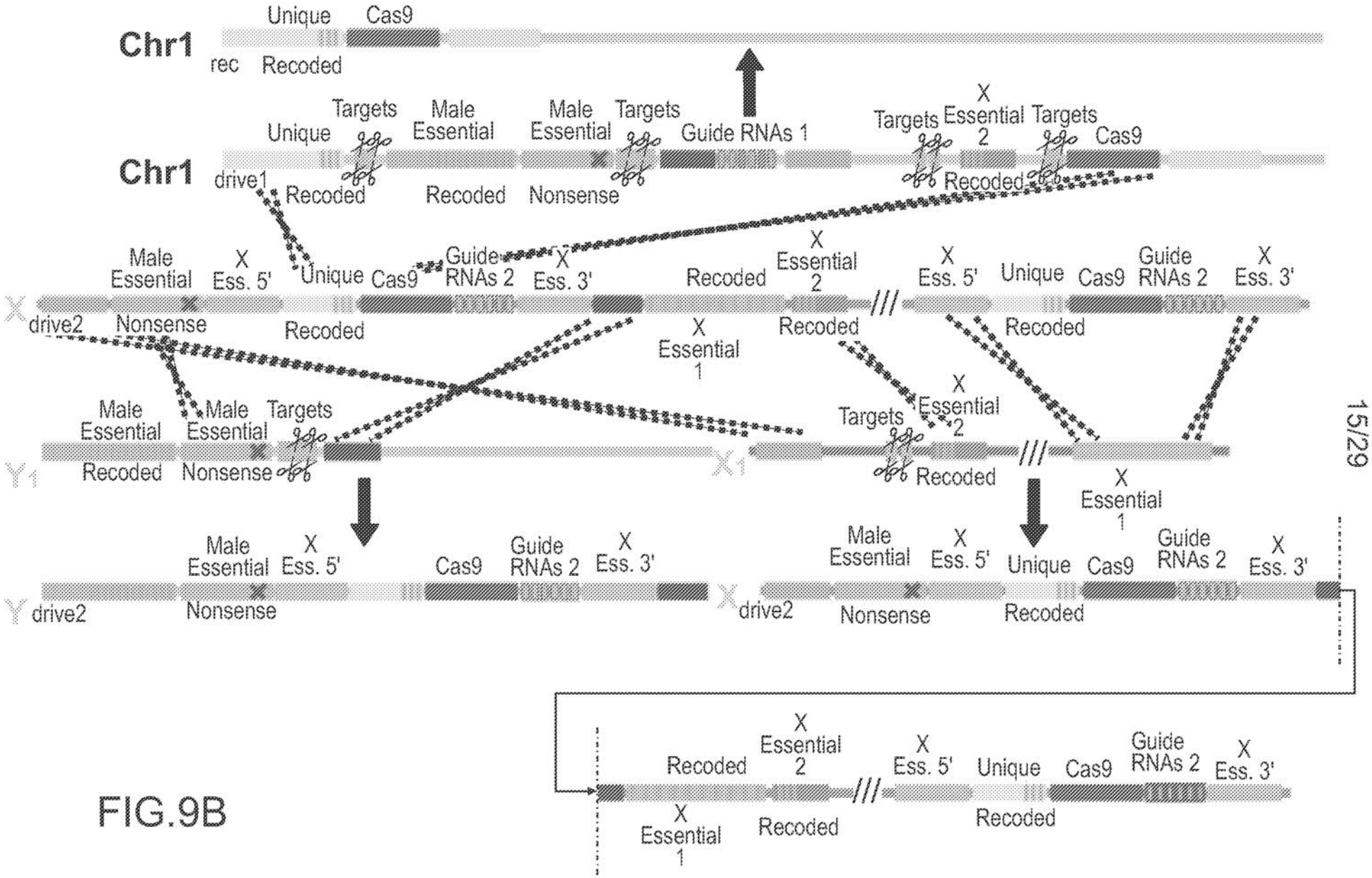

Chr1
Unique
Cas9
rec
Recoded
Chr1
drive1
Targets
Male Essential
Male Essential
Targets
Guide RNAs 1
Targets
X Essential 2
Targets
Cas9
Recoded
Recoded
Nonsense
Recoded
drive2
Male Essential
X Ess. 5'
Unique
Cas9
Guide RNAs 2
X Ess. 3'
Recoded
X Essential 2
X Ess. 5'
Unique
Cas9
Guide RNAs 2
X Ess. 3'
Recoded
Recoded
X Essential 1
Male Essential
Male Essential
Targets
Recoded
Nonsense
Targets
X Essential 2
Recoded
X Essential 1
Male Essential
X Ess. 5'
Cas9
Guide RNAs 2
X Ess. 3'
drive2
Nonsense
Male Essential
X Ess. 5'
Unique
Cas9
Guide RNAs 2
X Ess. 3'
drive2
Nonsense
Recoded
Recoded
X Essential 2
X Ess. 5'
Unique
Cas9
Guide RNAs 2
X Ess. 3'
X Essential 1
Recoded
Recoded

FIG.9B

FIG. 9C

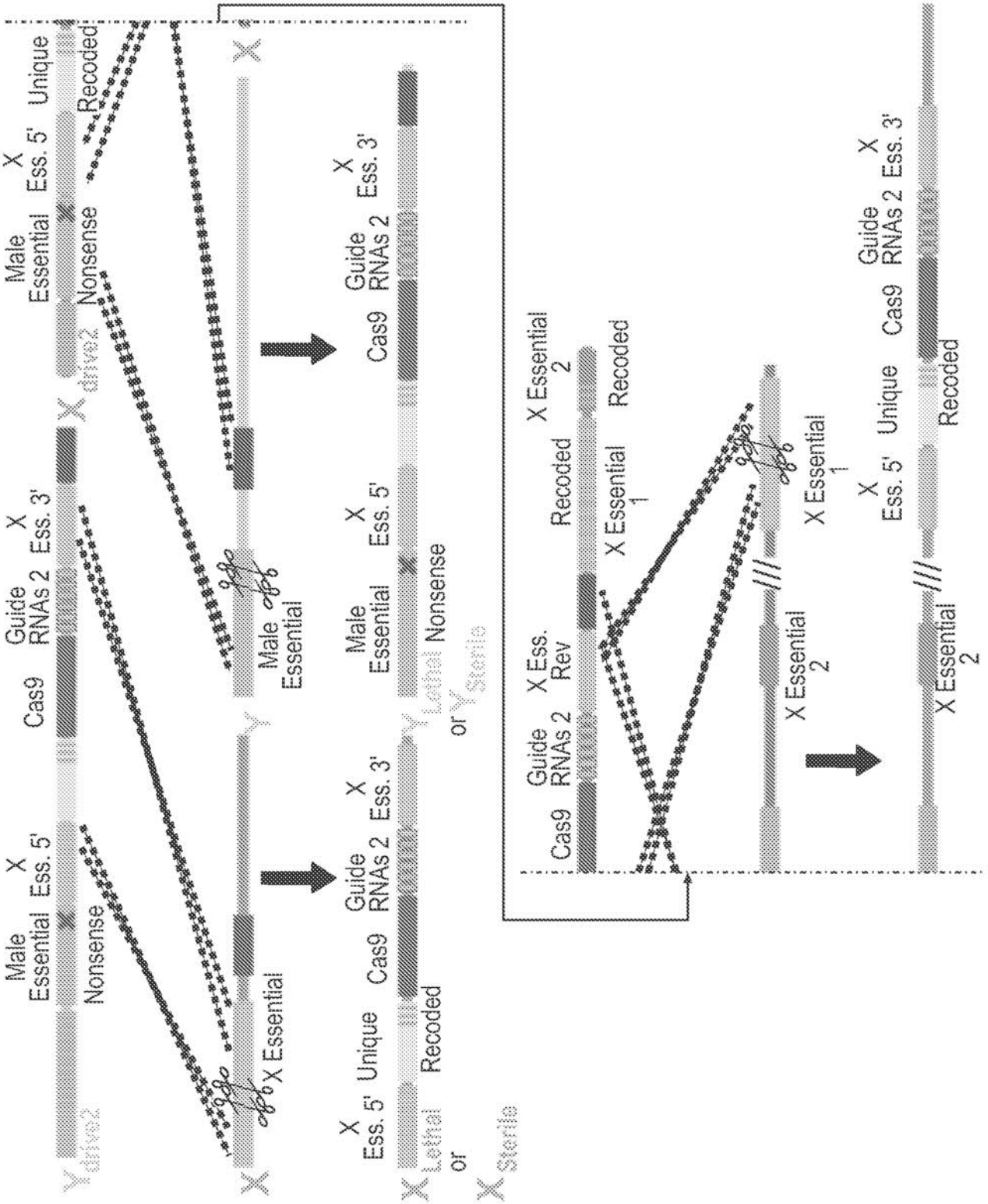

Male
Essential
X
Ess. 5'
Unique
Cas9
Guide
RNAs 2
X
Ess. 3'
Recoded
Nonsense
drive2
Y
X
Essential
Lethal
or
Sterile
X Ess.
Rev
Recoded
2
1

FIG. 10A



FIG.10B



FIG. 10C

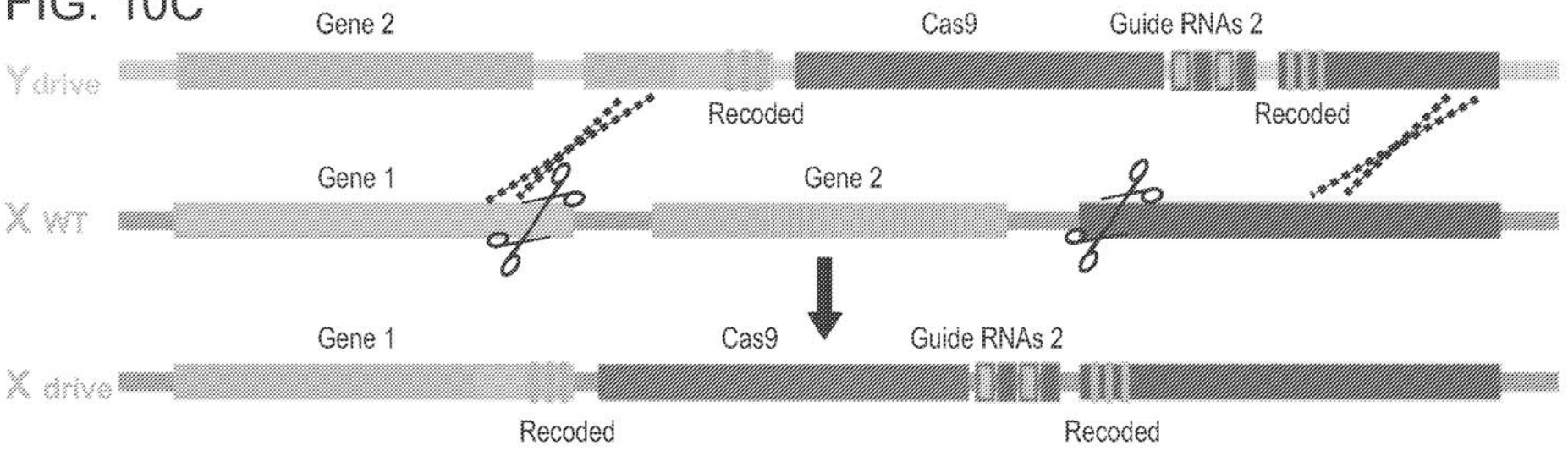


FIG. 10D

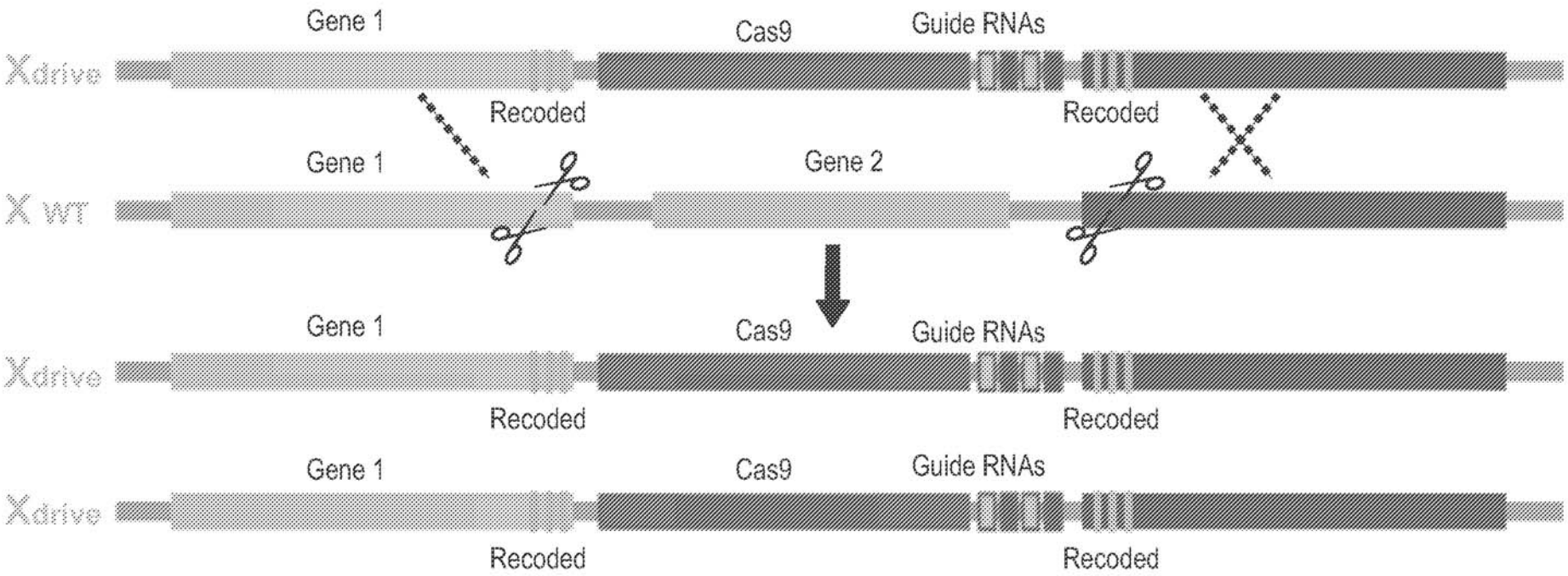

Gene 1
Cas9
Guide RNAs
Xdrive
Recoded
Recoded
Gene 1
Gene 2
X WT
Gene 1
Cas9
Guide RNAs
Xdrive
Recoded
Recoded
Gene 1
Cas9
Guide RNAs
Xdrive
Recoded
Recoded

FIG. 11A

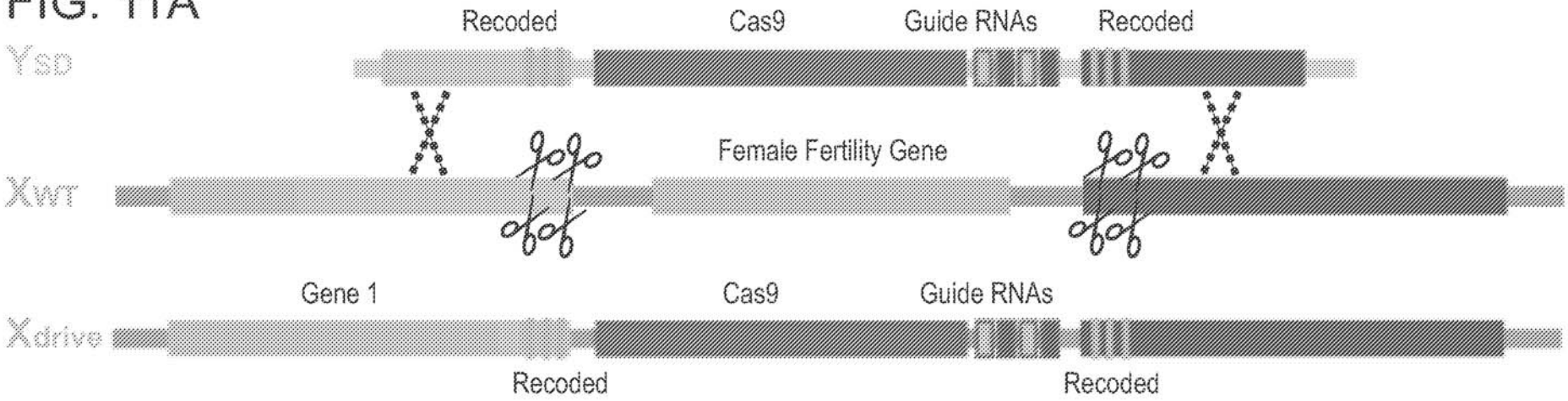


FIG.11B



FIG. 12A

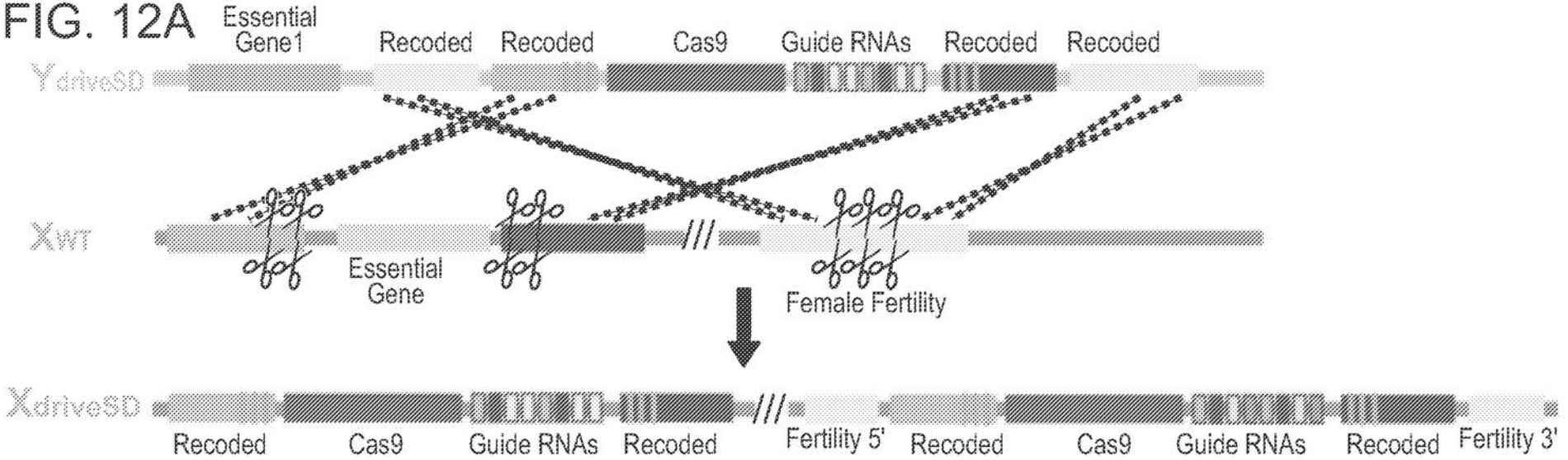


FIG.12B

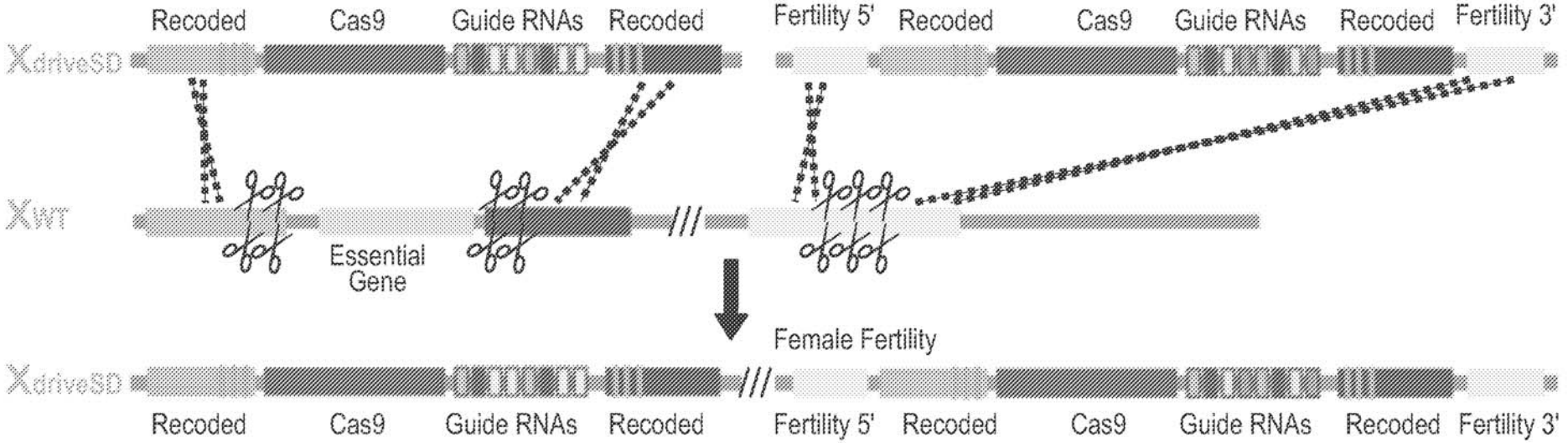


FIG. 12C

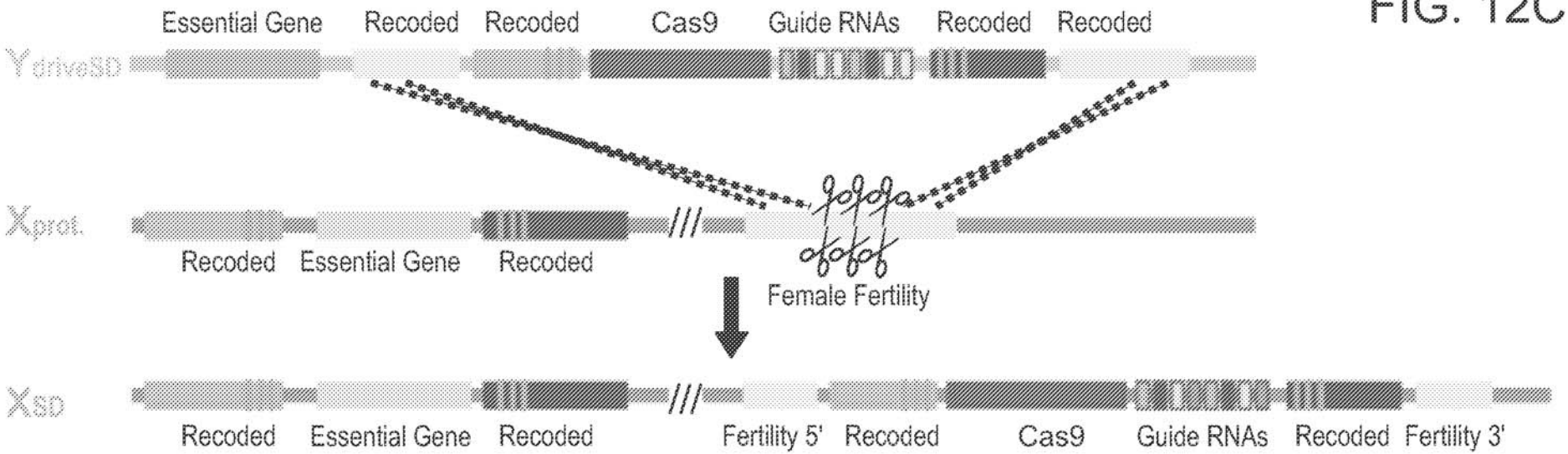


FIG. 12D

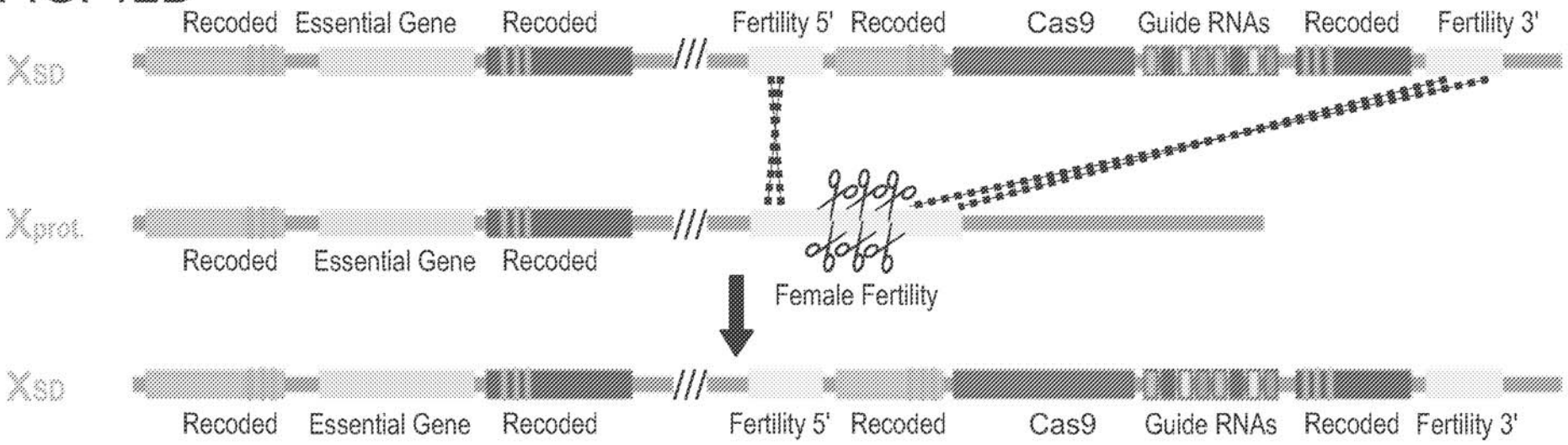


FIG. 13A

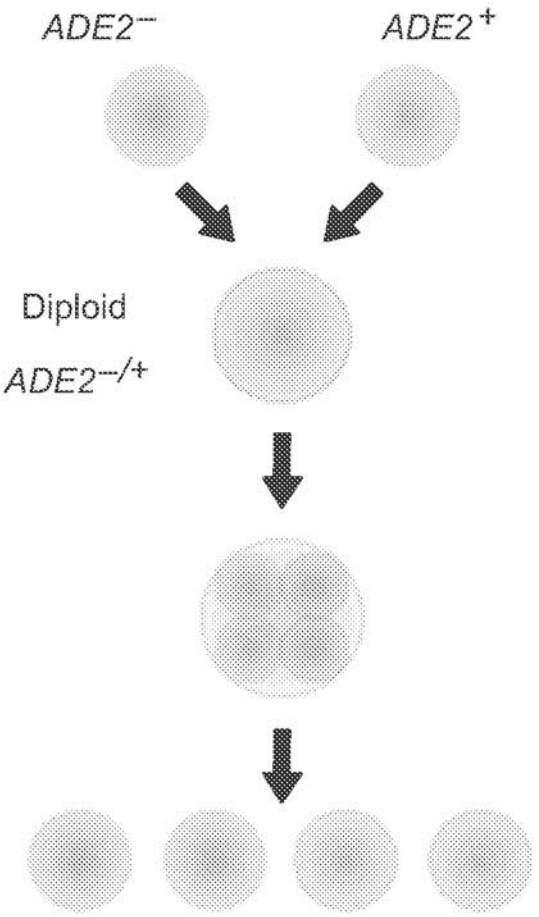


FIG.13B

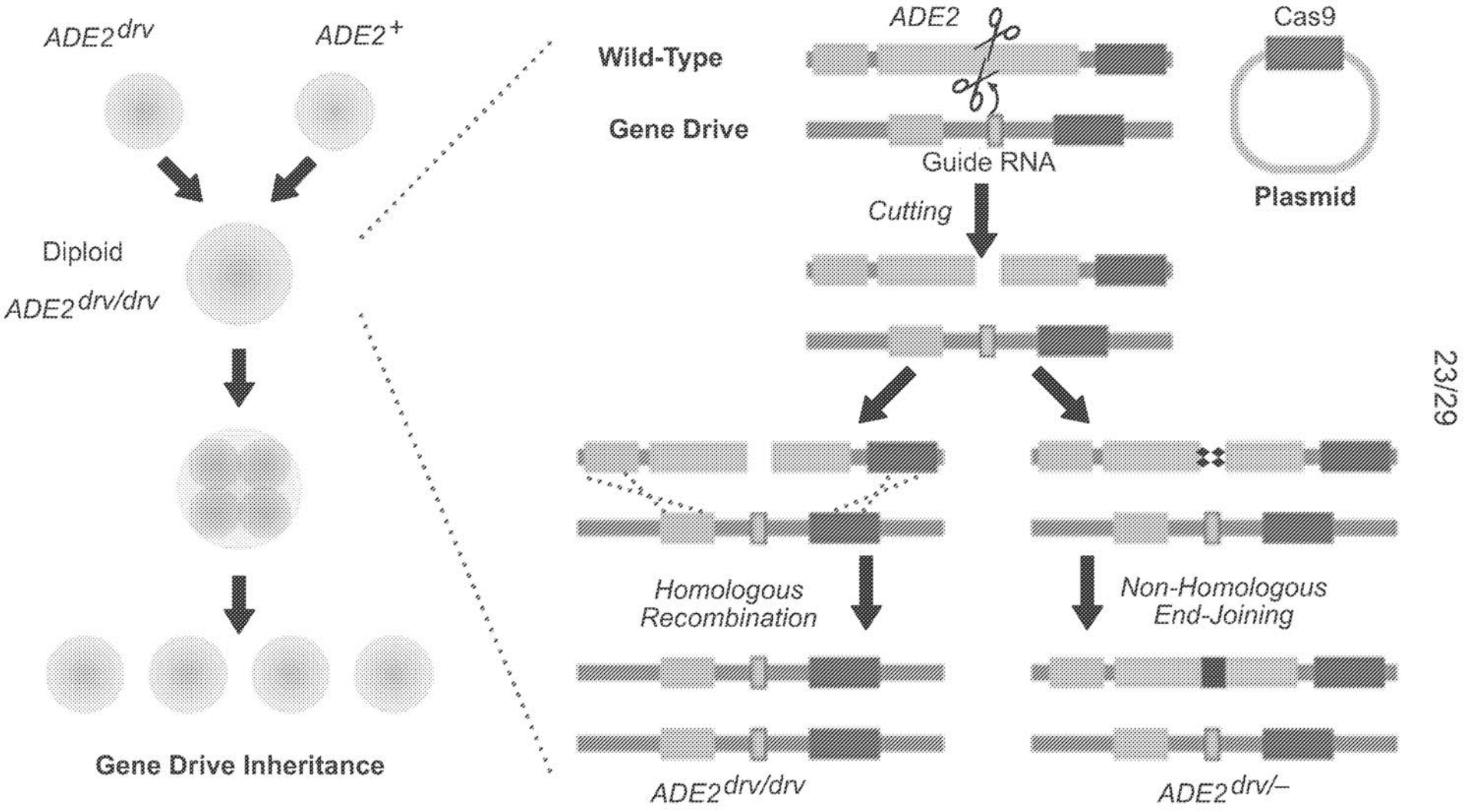

ADE2drv
ADE2+
Diploid
ADE2drv/drv
Gene Drive Inheritance
Wild-Type
Gene Drive
ADE2
Guide RNA
Cutting
Cas9
Plasmid
Homologous Recombination
Non-Homologous End-Joining
ADE2drv/drv
ADE2drv/–

FIG. 13C

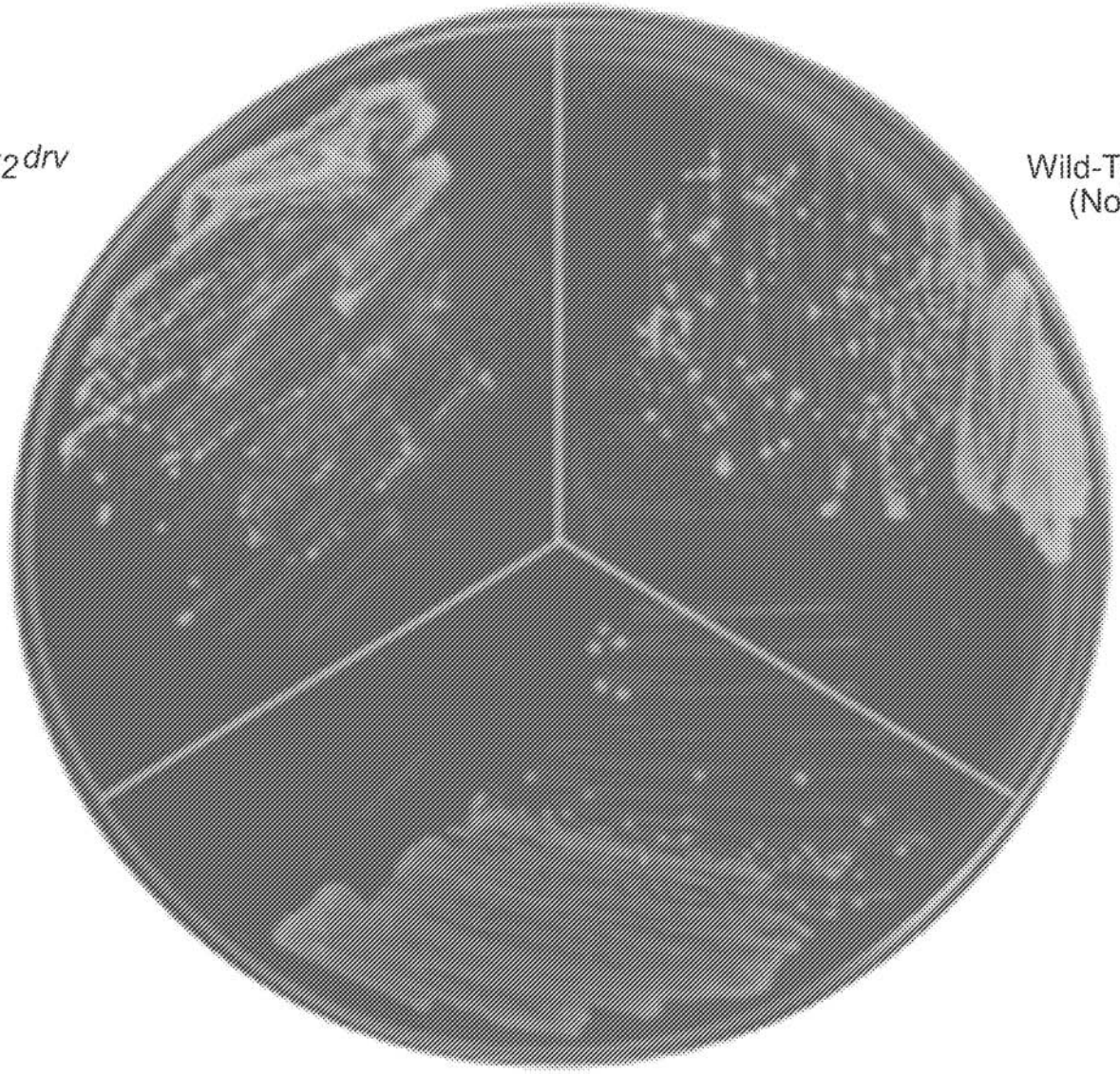

Wild-Type x *ADE2*^{drv}
(No Cas9)
Wild-Type x *ADE2*^{drv}
(No Target Site)
Wild-Type x *ADE2*^{drv}

FIG. 13D

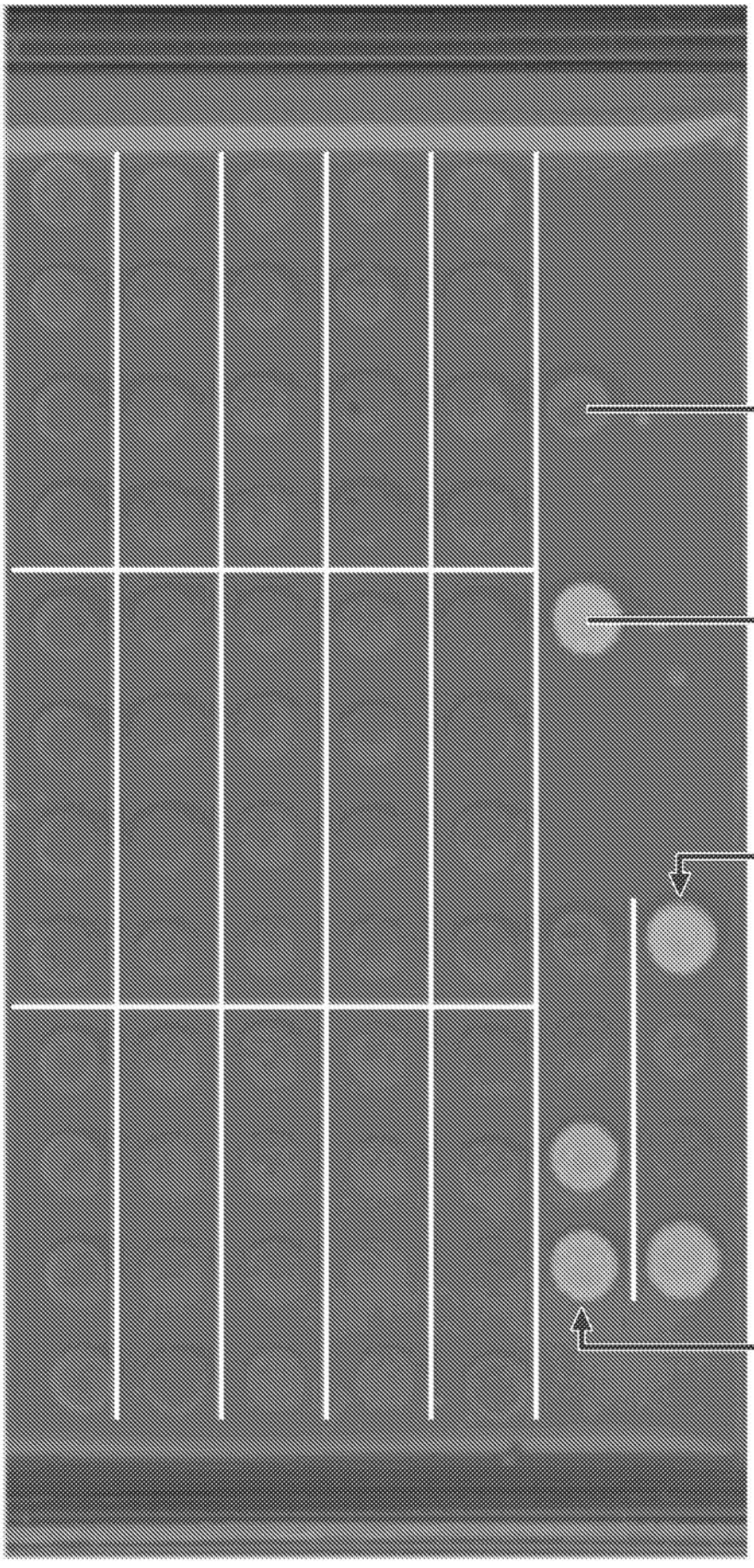


FIG. 14A

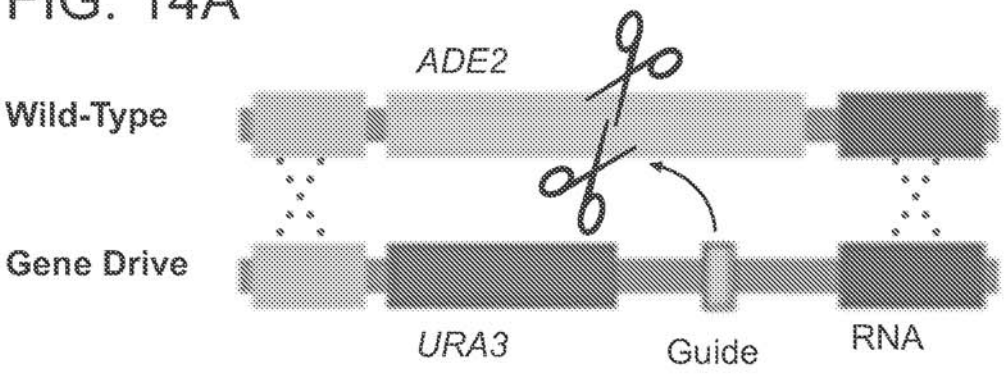


FIG. 14C

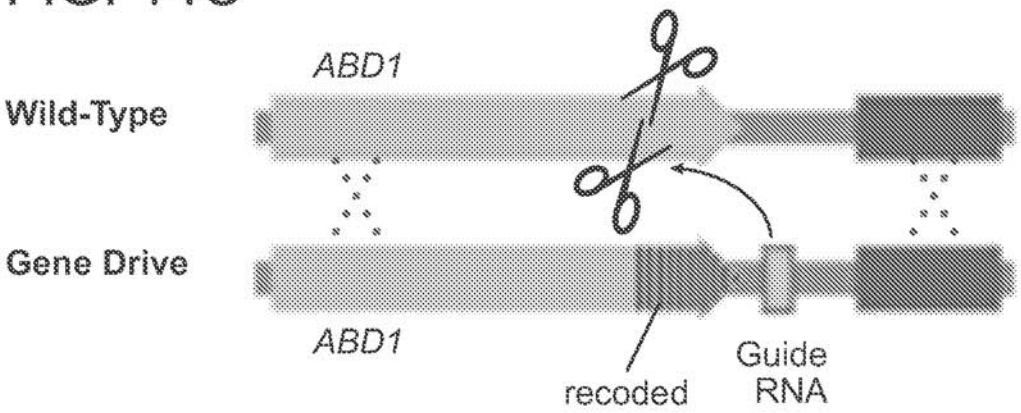


FIG. 14B

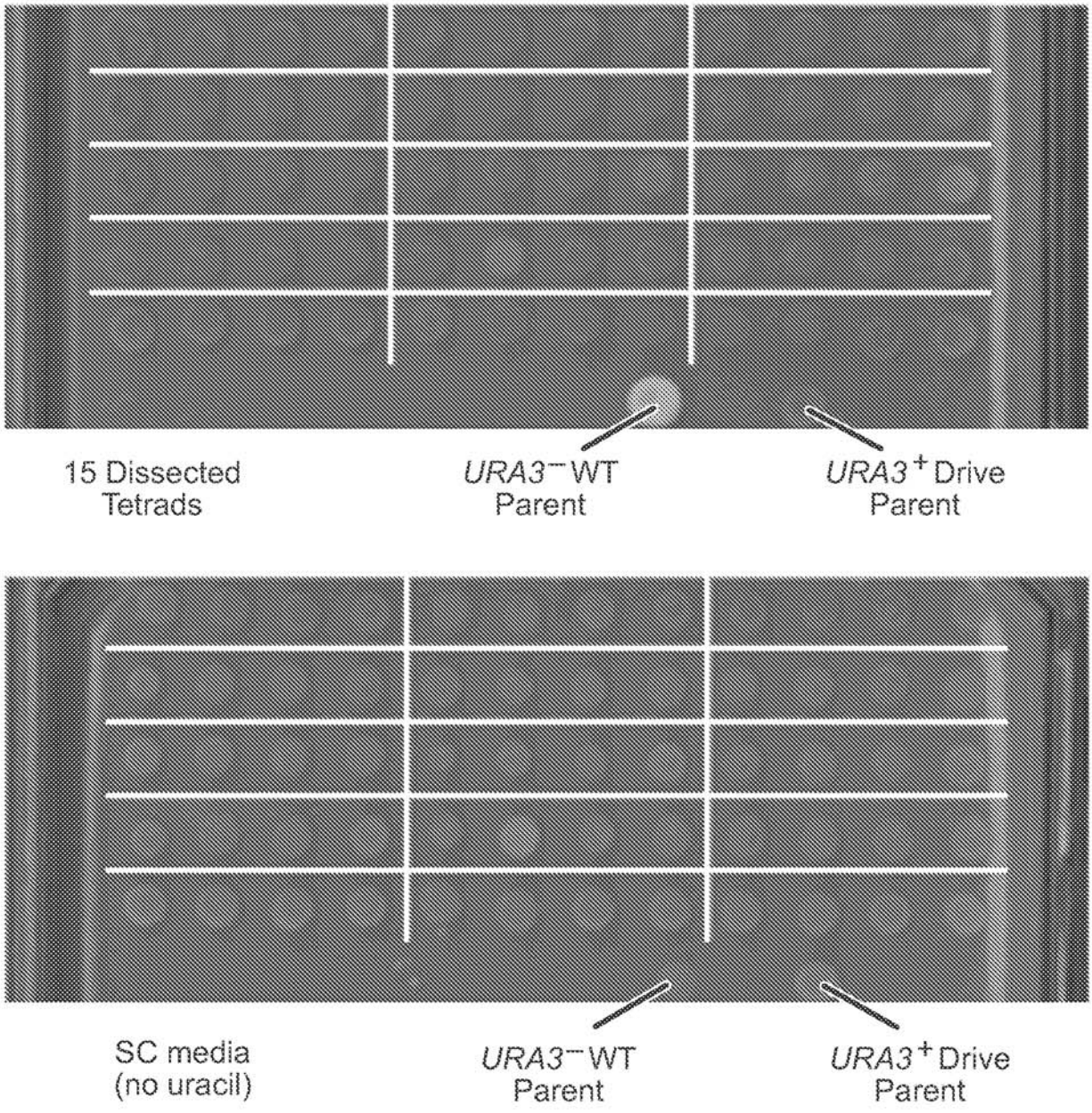

15 Dissected Tetrads
URA3⁻ WT Parent
URA3⁺ Drive Parent
SC media (no uracil)
URA3⁻ WT Parent
URA3⁺ Drive Parent

FIG. 15A

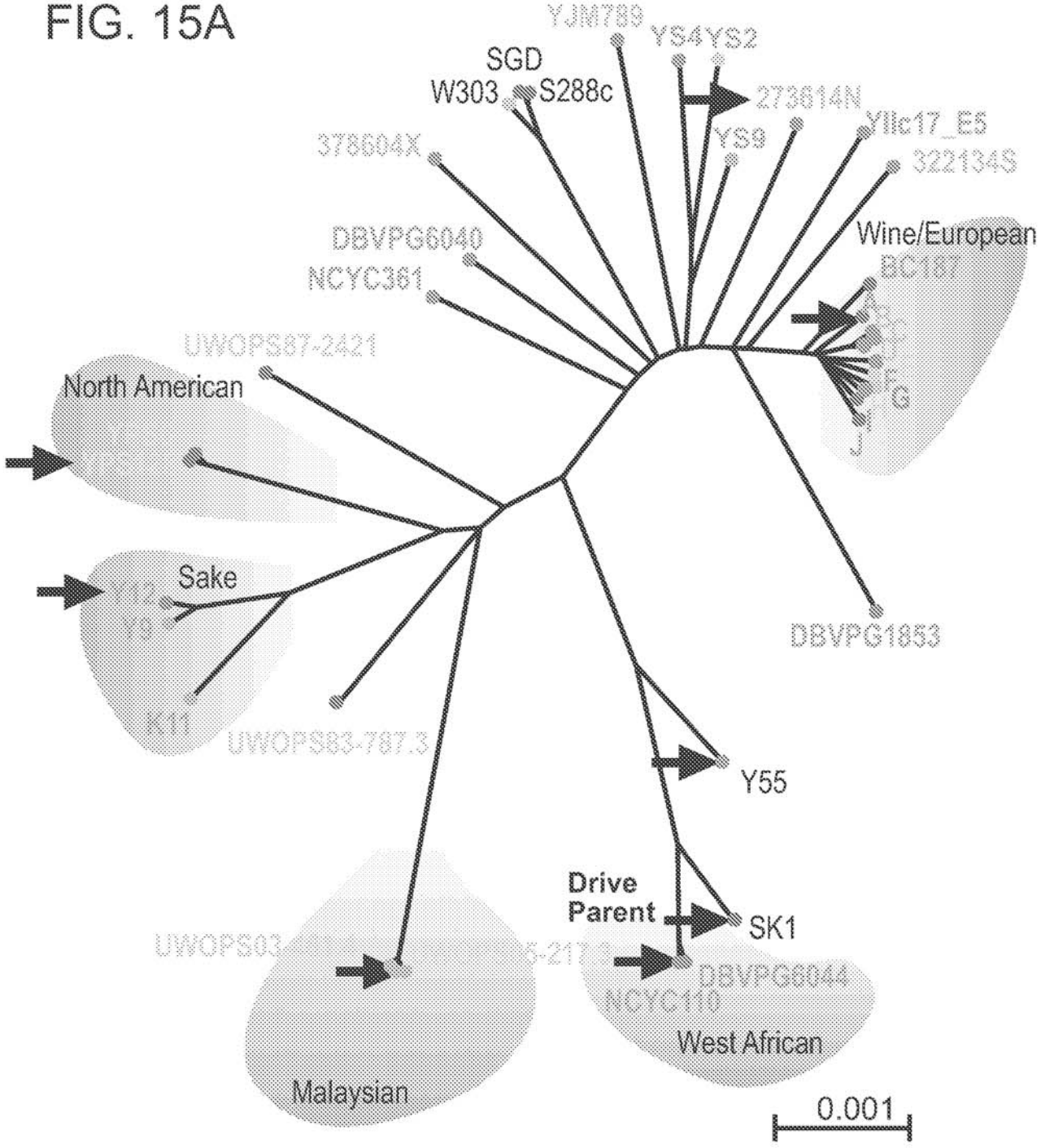
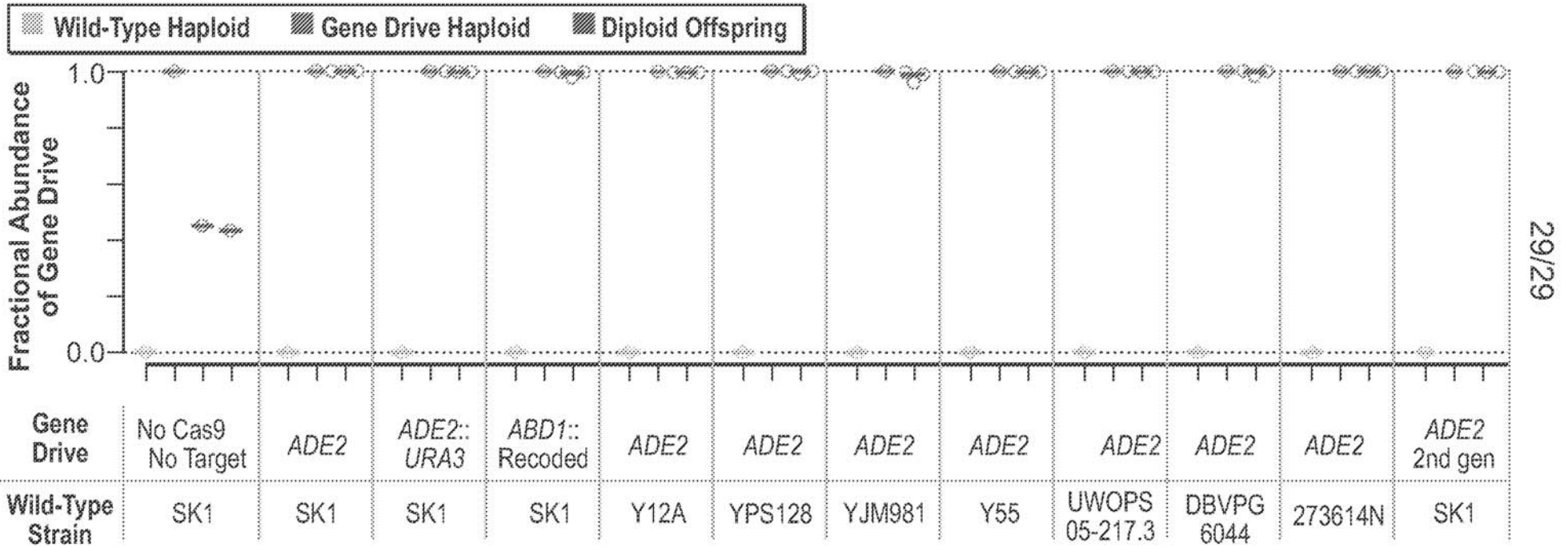

YJM789
YS4YS2
SGD
W303
S288c
273614N
YIIc17_E5
YS9
378604X
322134S
DBVPG6040
NCYC361
Wine/European
BC187
UWOPS87-2421
North American
Sake
K11
UWOPS83-787.3
DBVPG1853
Y55
Drive
Parent
SK1
DBVPG6044
NCYC110
West African
Malaysian
0.001
A, RM11_1A
B, YJM981
C, YJM978
D, YJM975
E, DBVPG1373
F, DBVPG1106
G, DBVPG6765
H, DBVPG1788
I, L-1374
J, L-1528
Europe
Americas
Asia
Oceania
Africa
Unknown
Laboratory
Wild
Fermentation
Clinical
Baking
Unknown

FIG.15B


Wild-Type Haploid
Gene Drive Haploid
Diploid Offspring
Fractional Abundance of Gene Drive
1.0
0.0
29/29
Gene Drive
No Cas9 No Target
ADE2
ADE2:: URA3
ABD1:: Recoded
ADE2
ADE2
ADE2
ADE2
ADE2
ADE2
ADE2
ADE2 2nd gen
Wild-Type Strain
SK1
SK1
SK1
SK1
Y12A
YPS128
YJM981
Y55
UWOPS 05-217.3
DBVPG 6044
273614N
SK1