

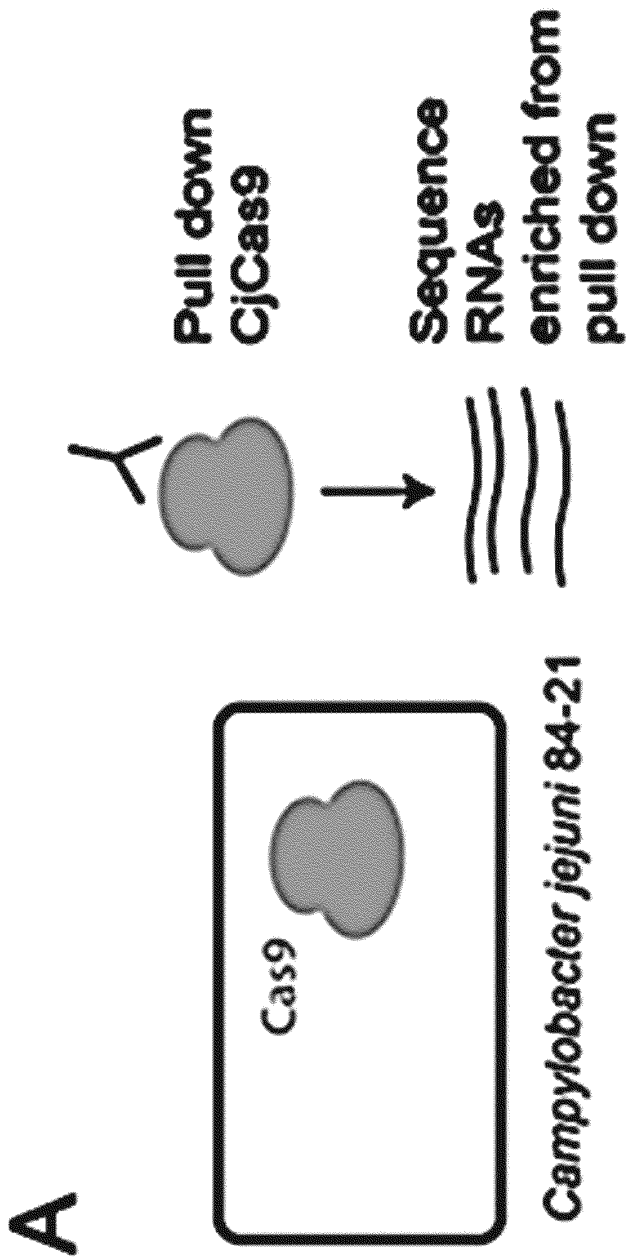


Figure 1

Figure 1 (continued)



C

The diagram illustrates the processing of tracrRNA. At the top, a Cas9 protein (grey cloud) is bound to a cellular RNA strand (black line) and a tracrRNA strand (black line with white boxes). The tracrRNA strand is shown with 5' and 3' ends. Below this, the tracrRNA strand is shown being cleaved by RNase III (grey cloud). The cleavage site is indicated by a vertical line. The bottom part shows the resulting products: ncrRNA (black line with white boxes) and processed tracrRNA (black line with white boxes). The processed tracrRNA is shown with 5' and 3' ends.

cellular RNA

Cas9

tracrRNA

5'

3'

5'

3'

cellular RNA

5'

3'

5'

3'

ncrRNA

processed tracrRNA

RNase III cleavage site

Figure 2

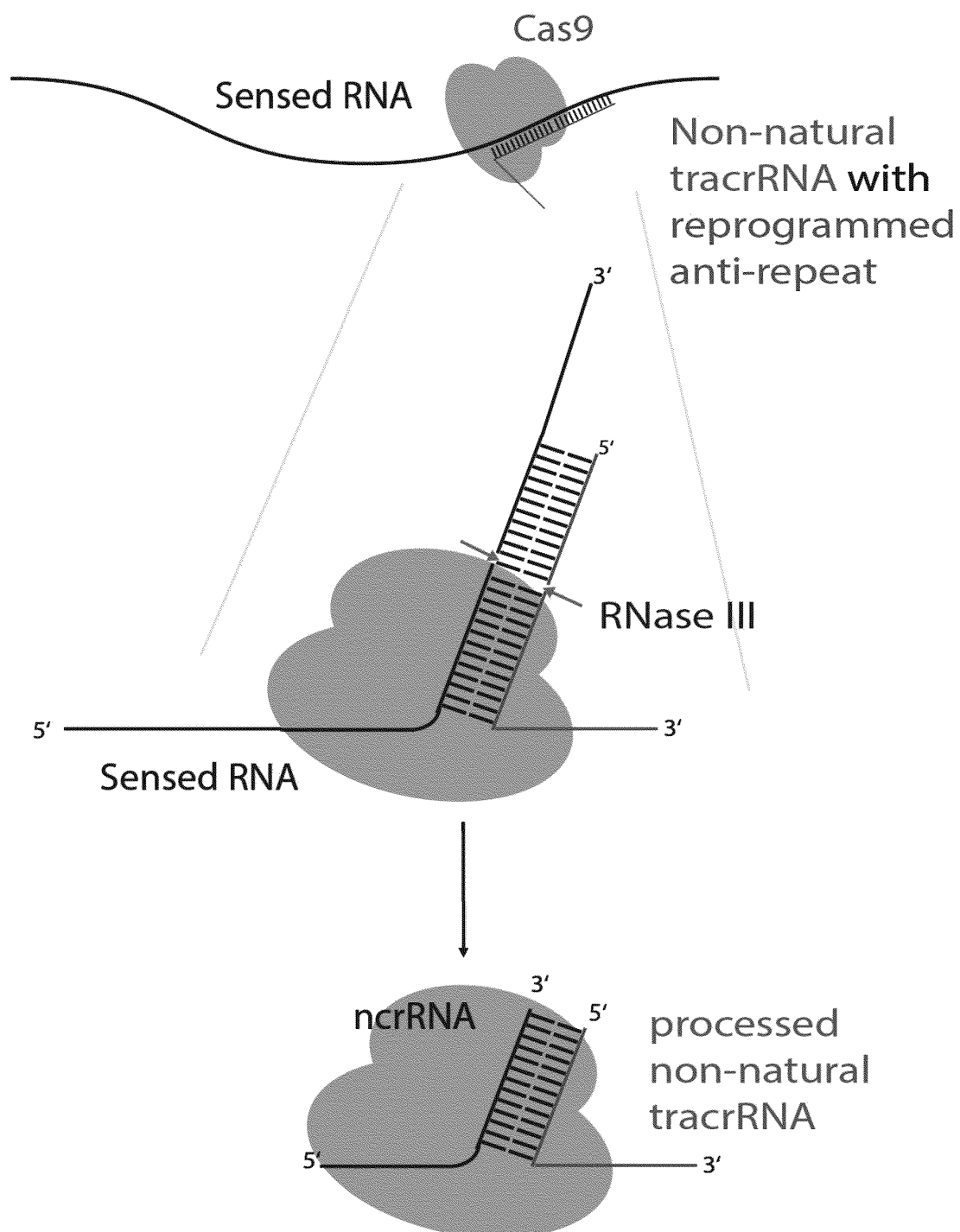
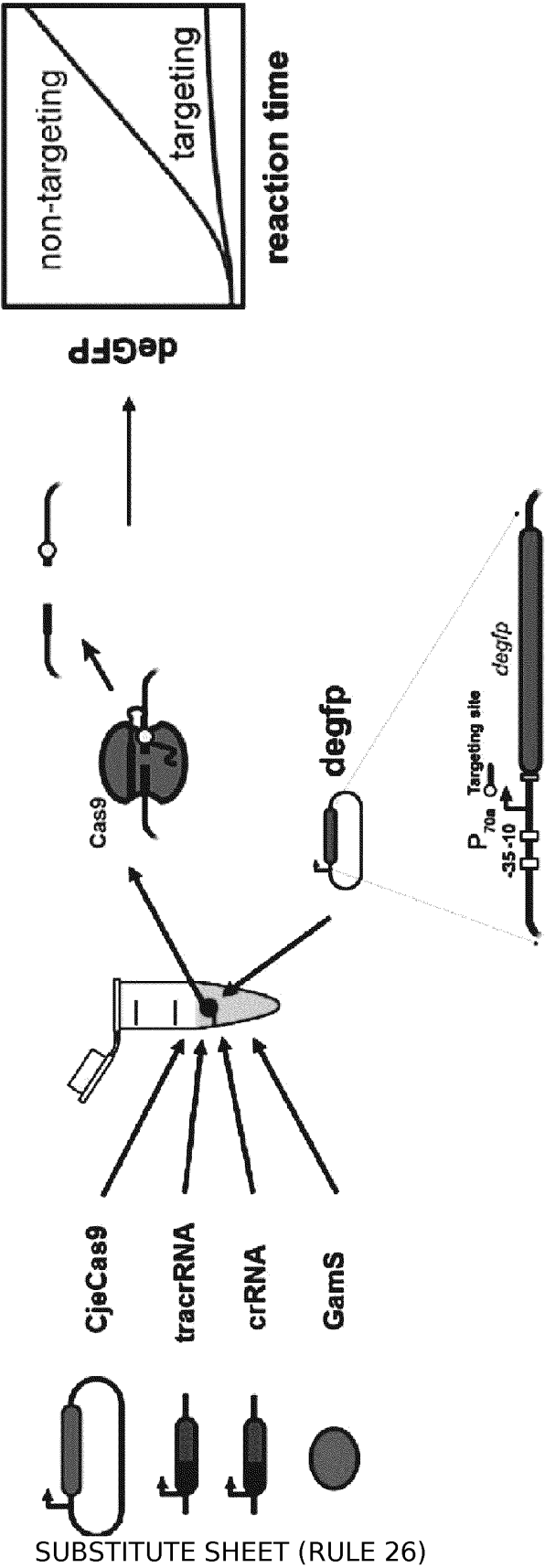


Figure 3



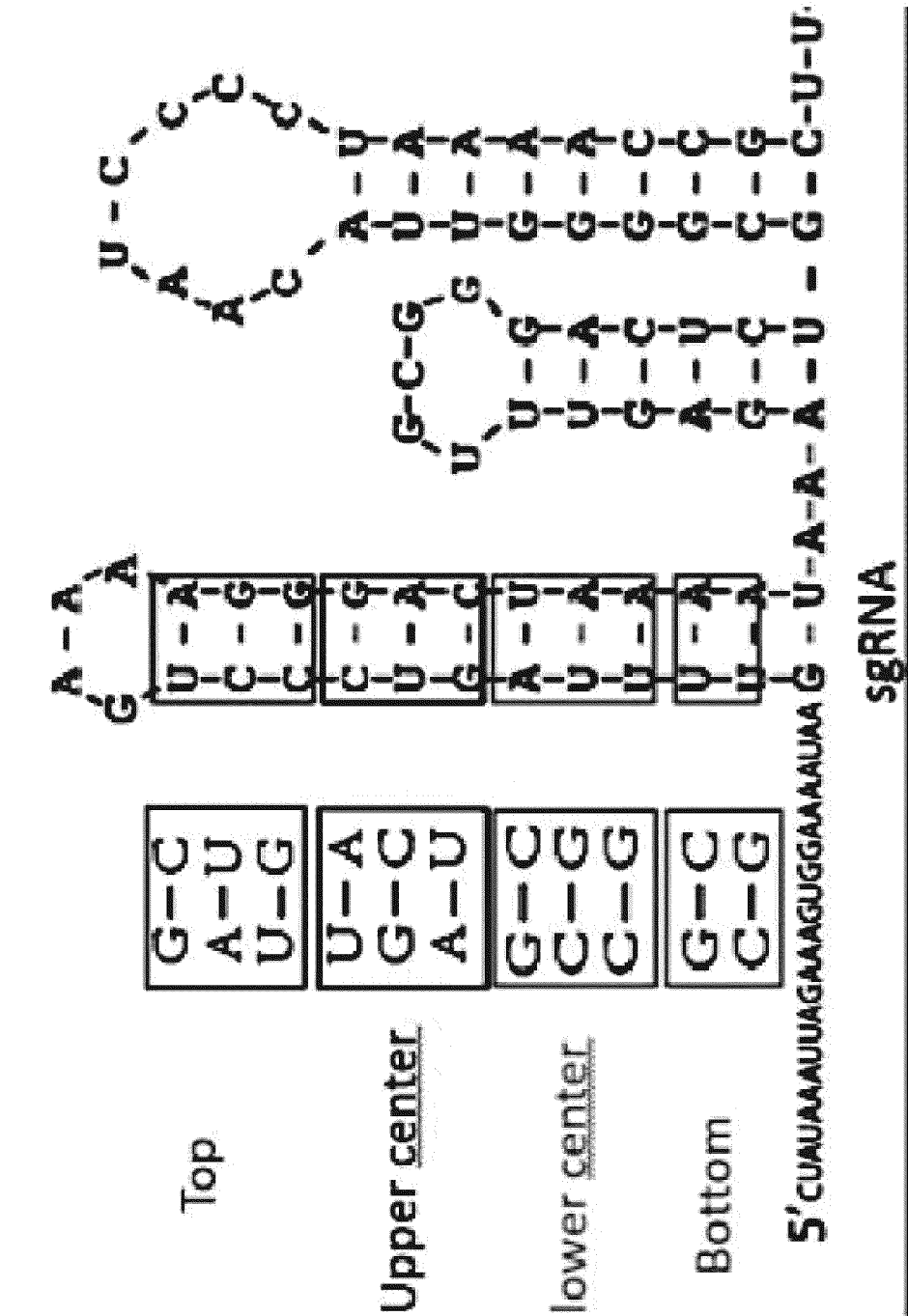
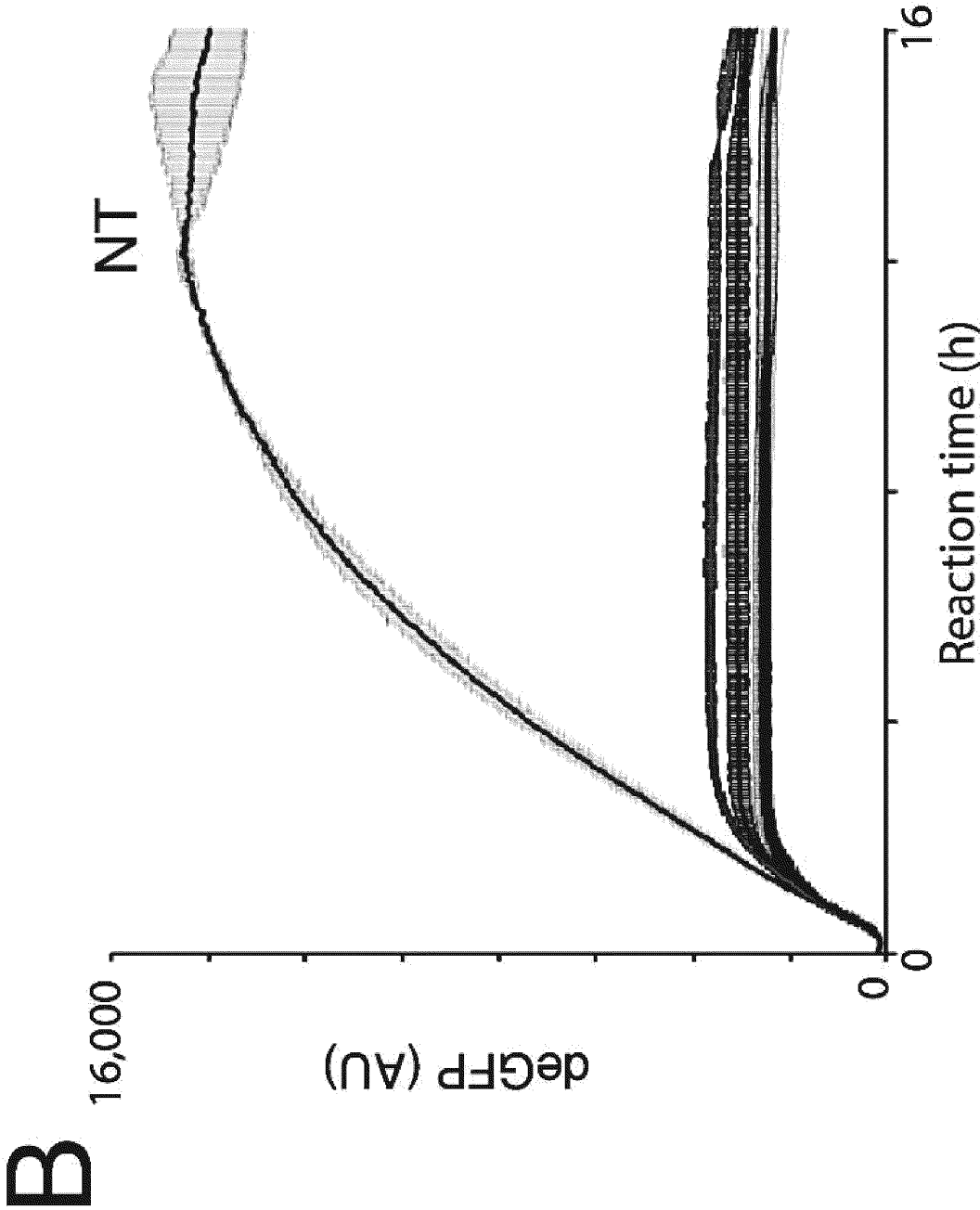


Figure 4 (continued)



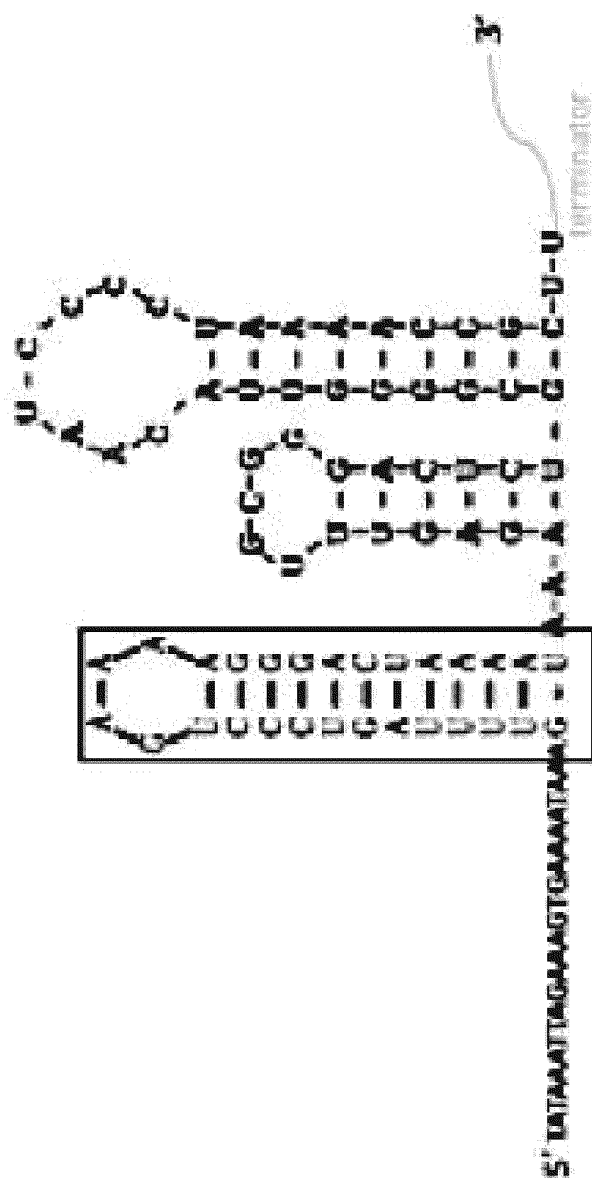


Figure 5

Figure 5 (continued)

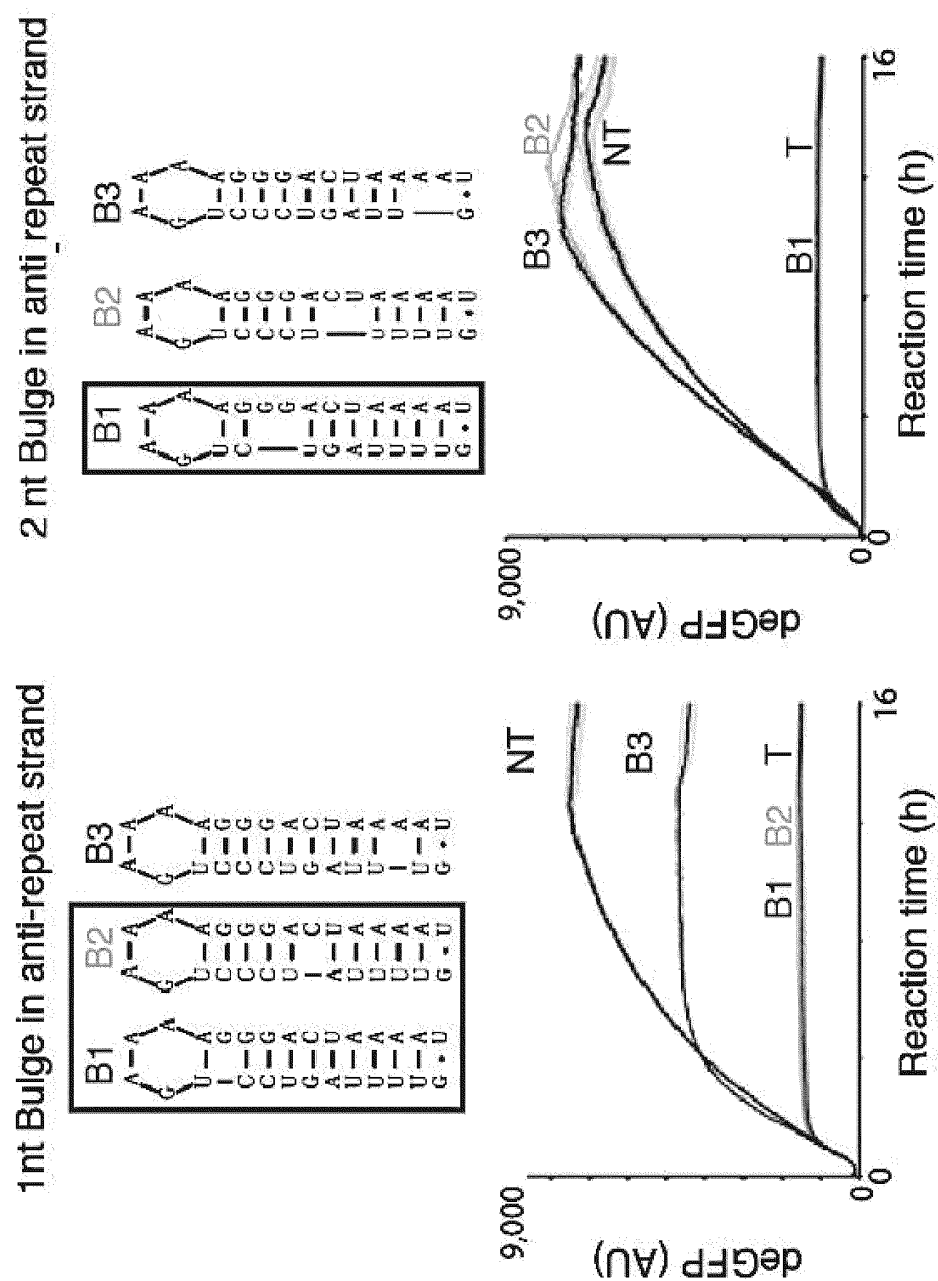
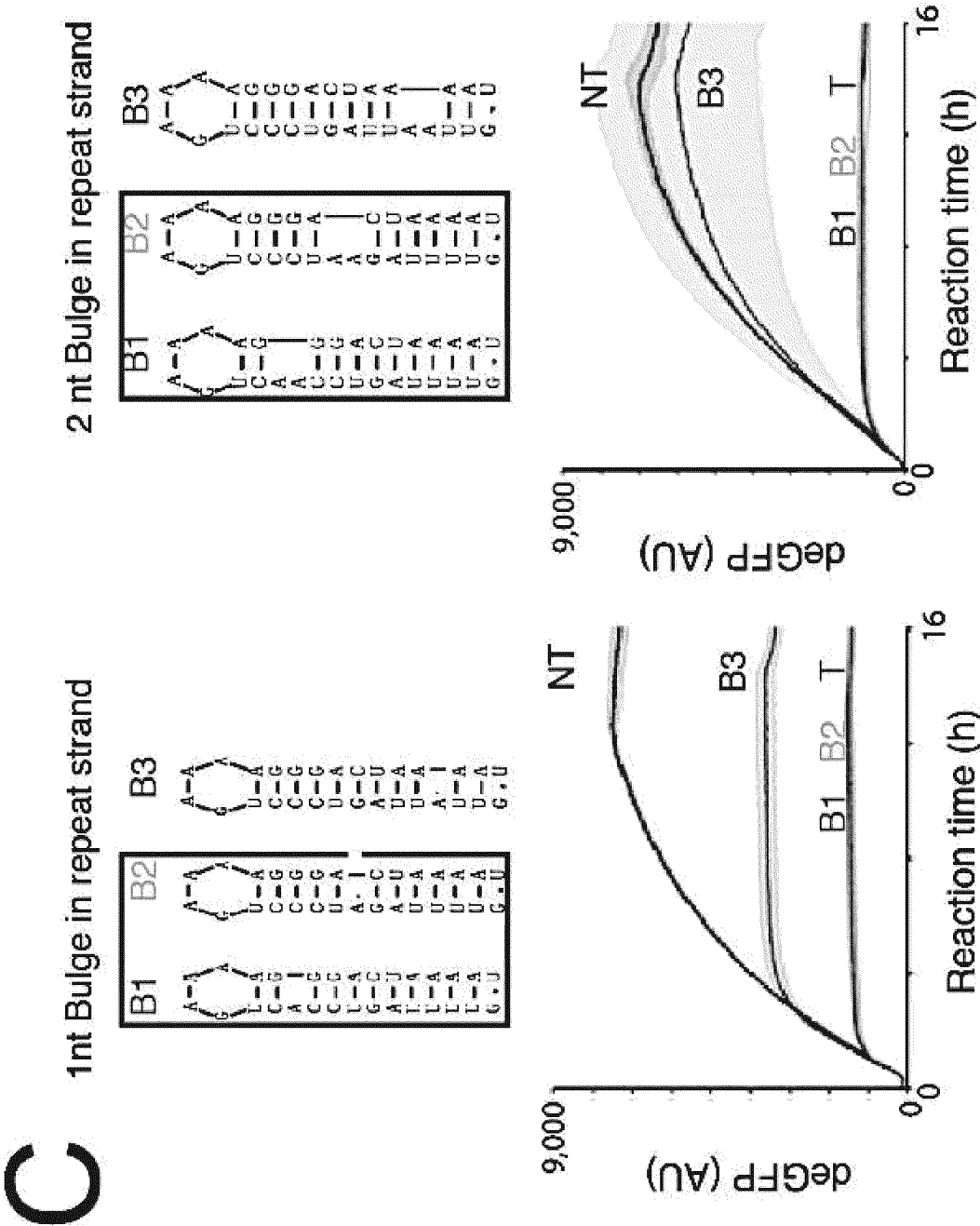


Figure 5 (continued)



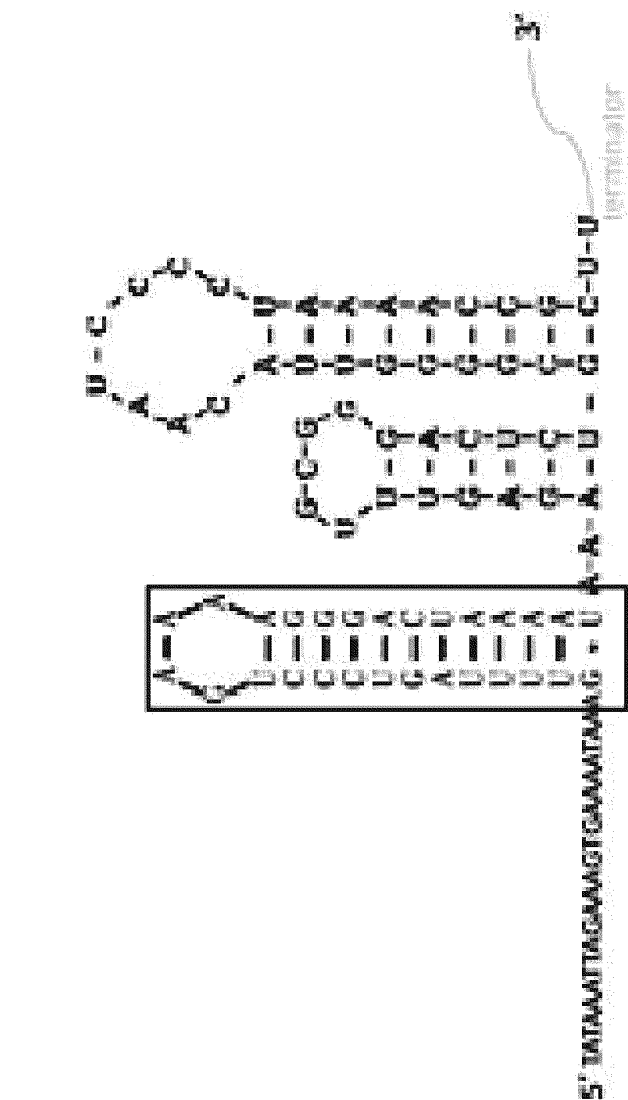
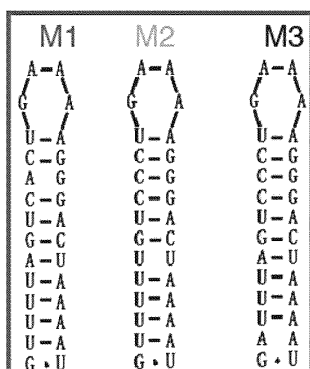
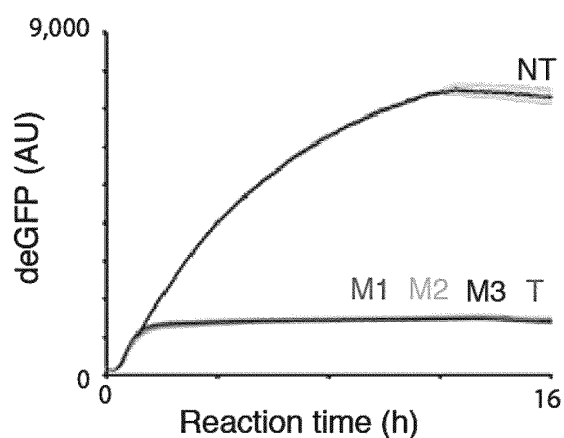


Figure 6

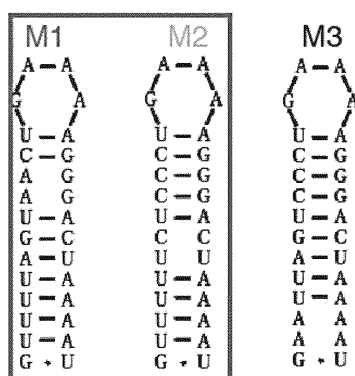
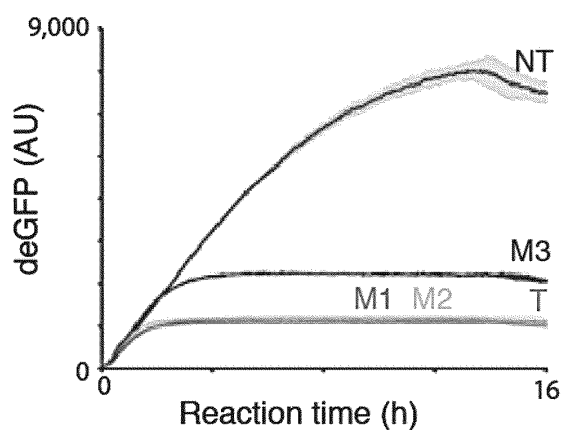
Figure 6 (continued)

B

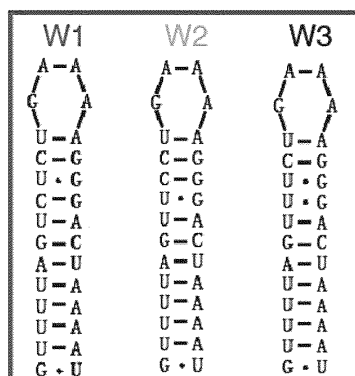
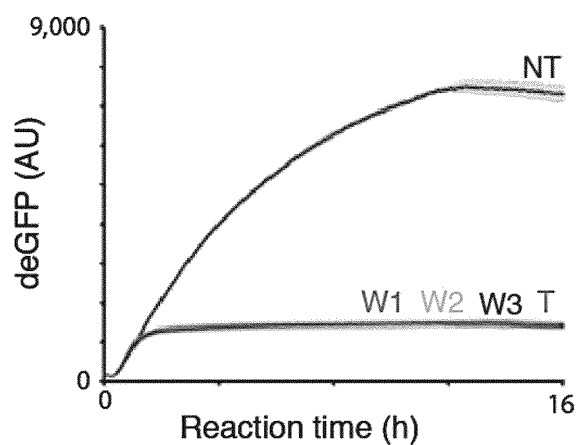
1 bp mismatch



2 bp mismatch



G:U wobble base pair



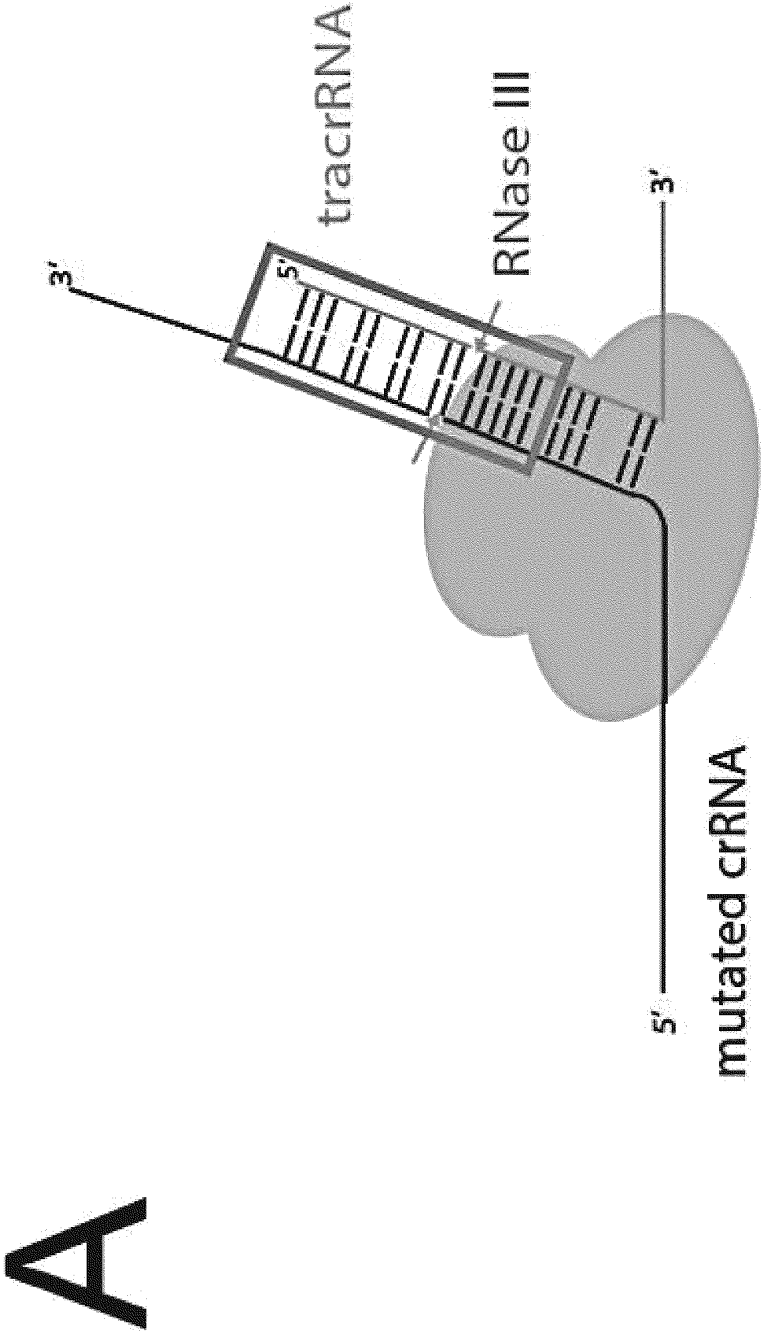
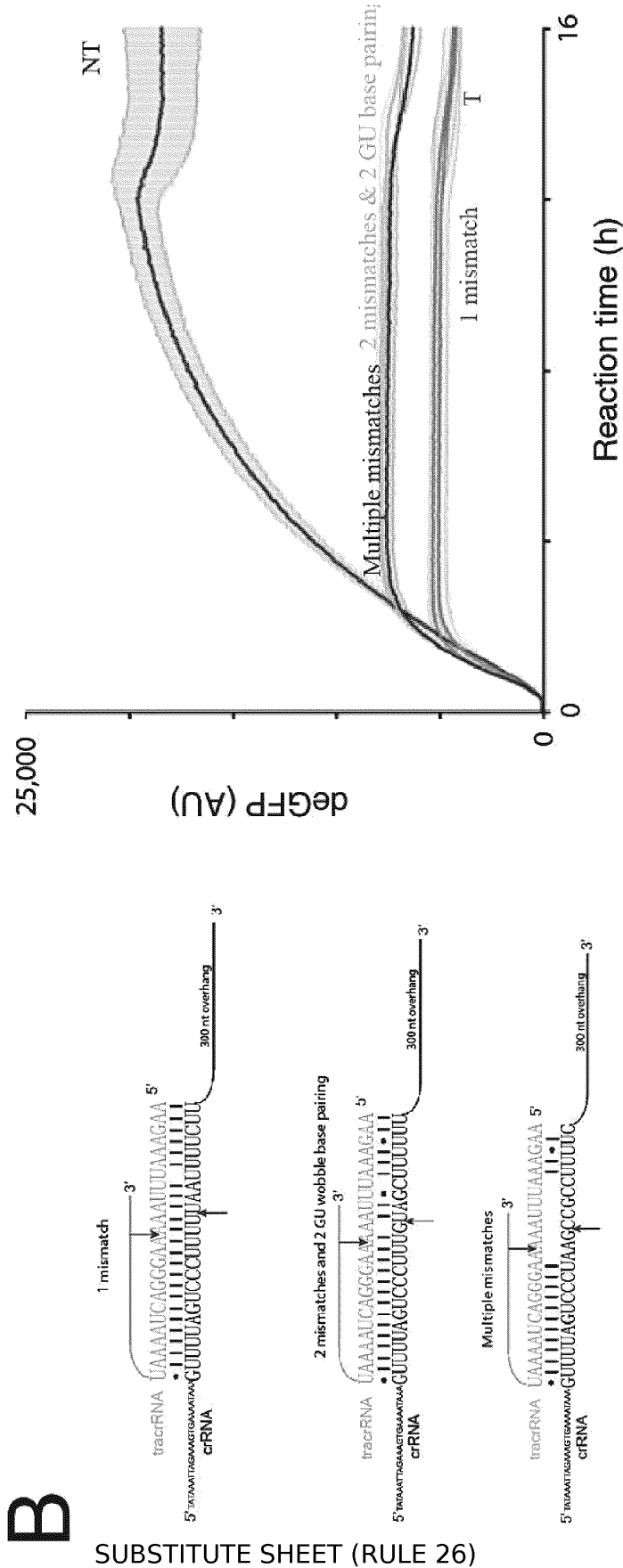


Figure 7

Figure 7 (continued)

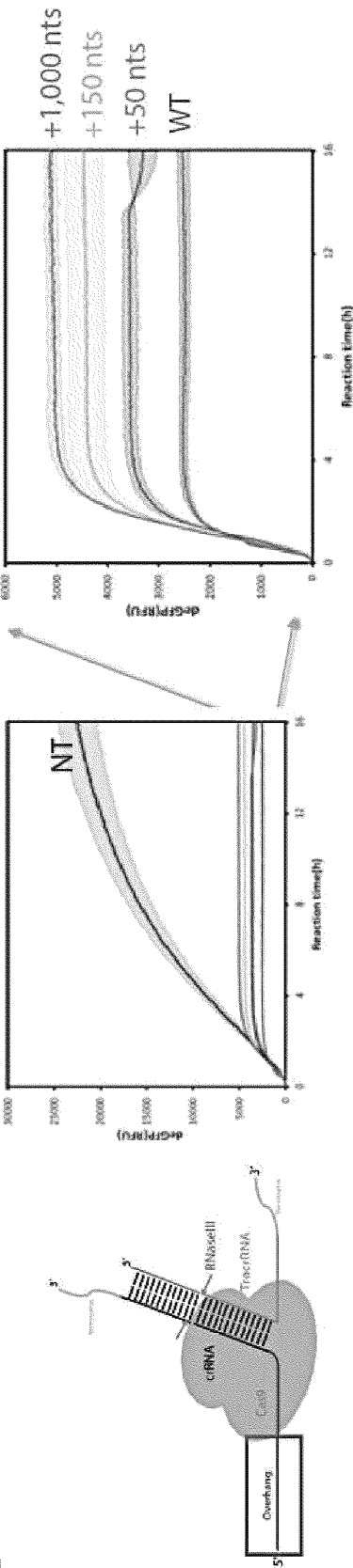


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Figure 8

A

SUBSTITUTE SHEET (RULE 26)



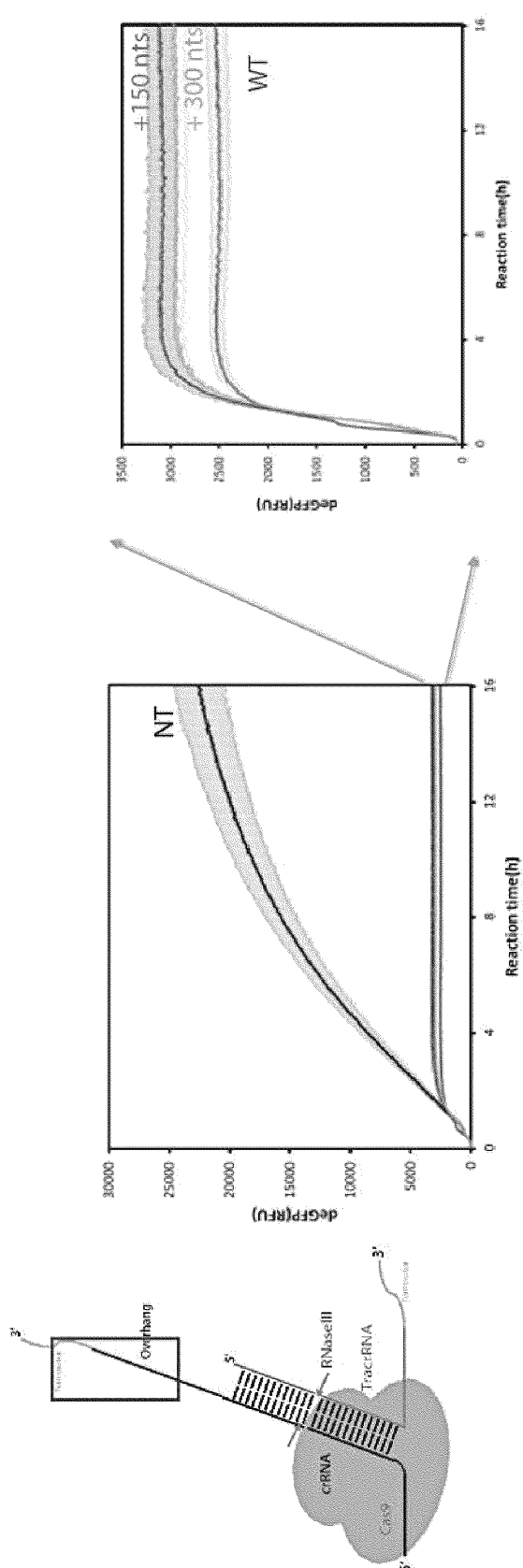


Figure 9 (continued)

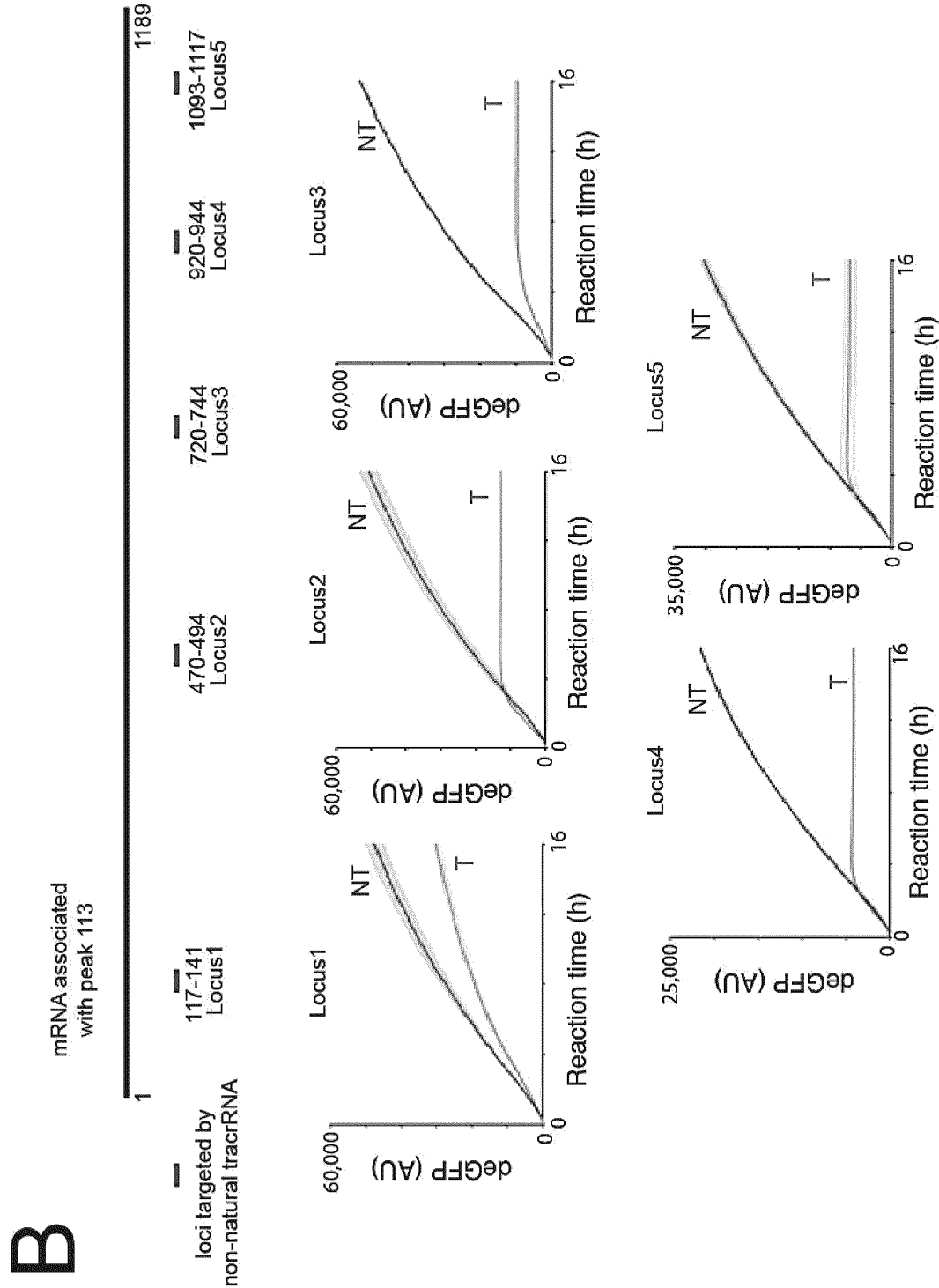


Figure 10

A

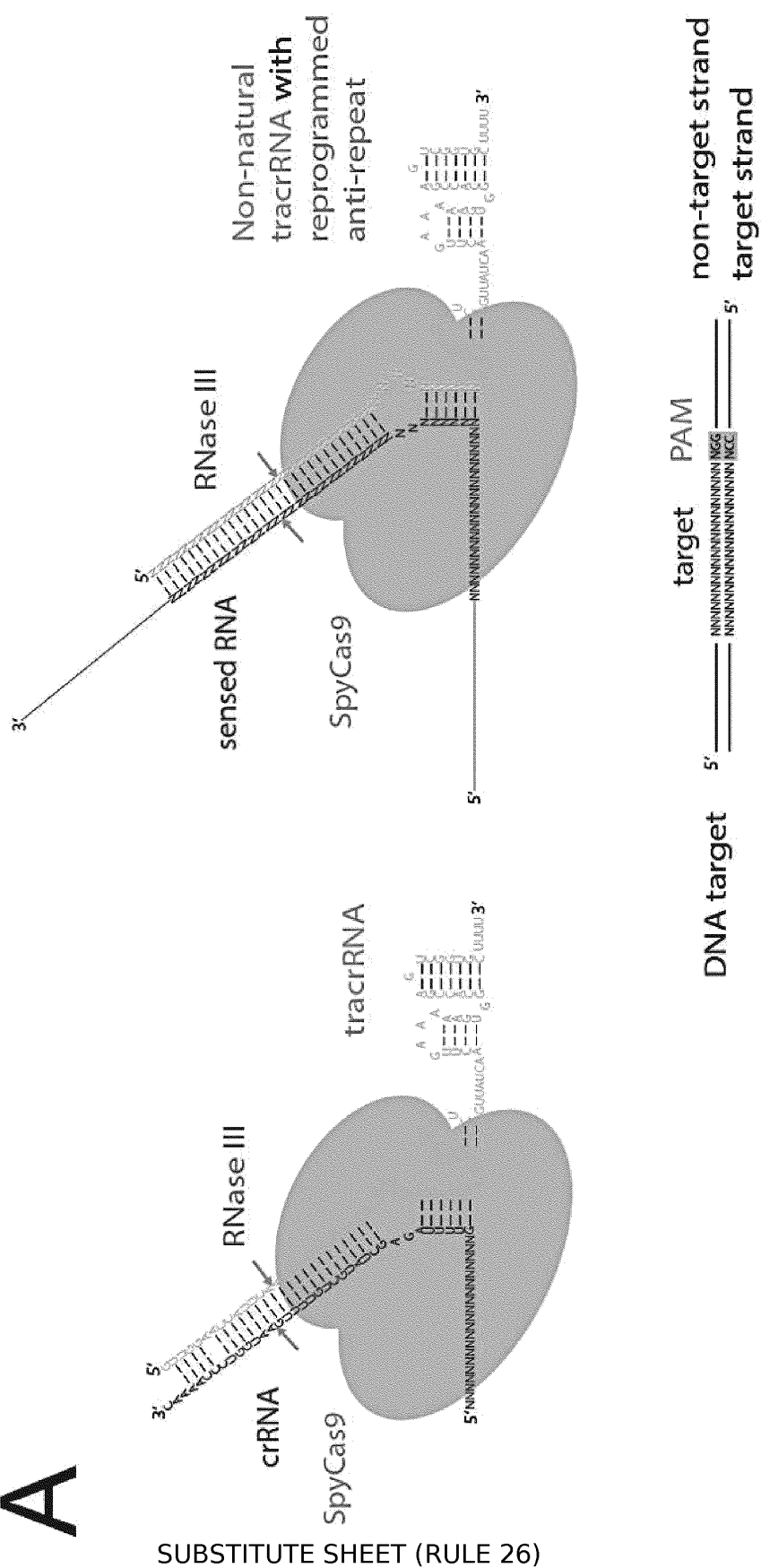


Figure 10 (continued)

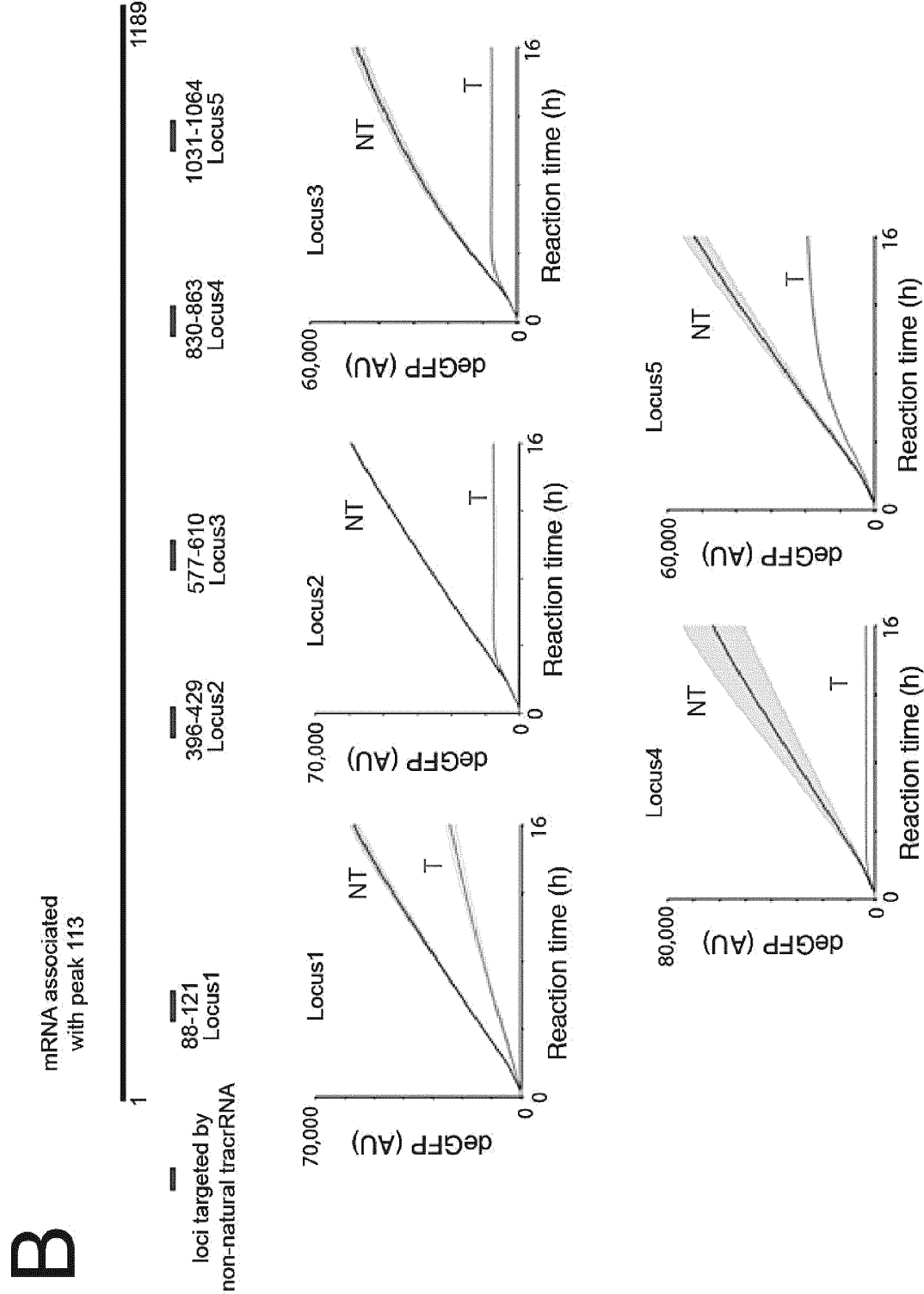
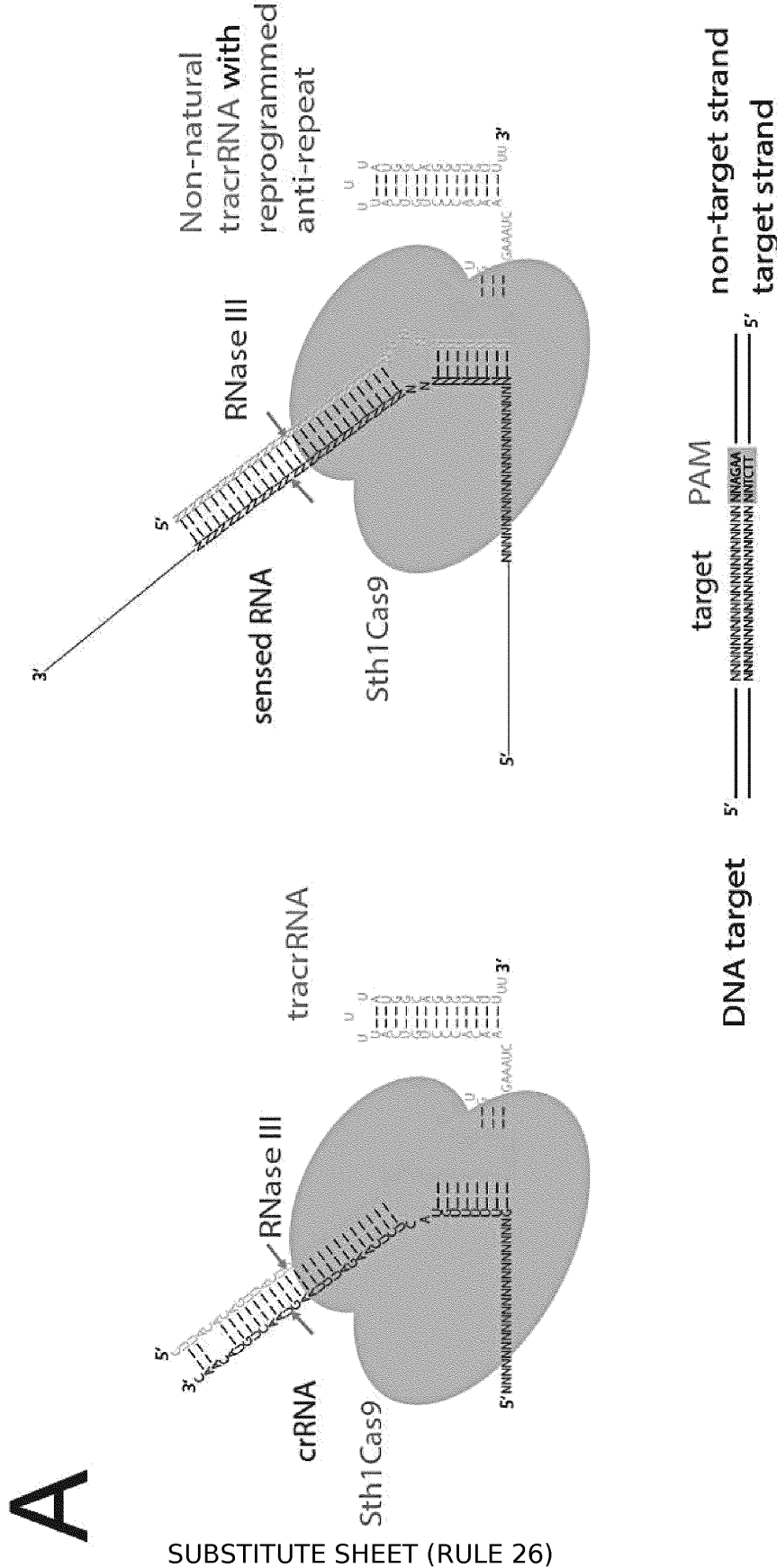


Figure 11



SUBSTITUTE SHEET (RULE 26)

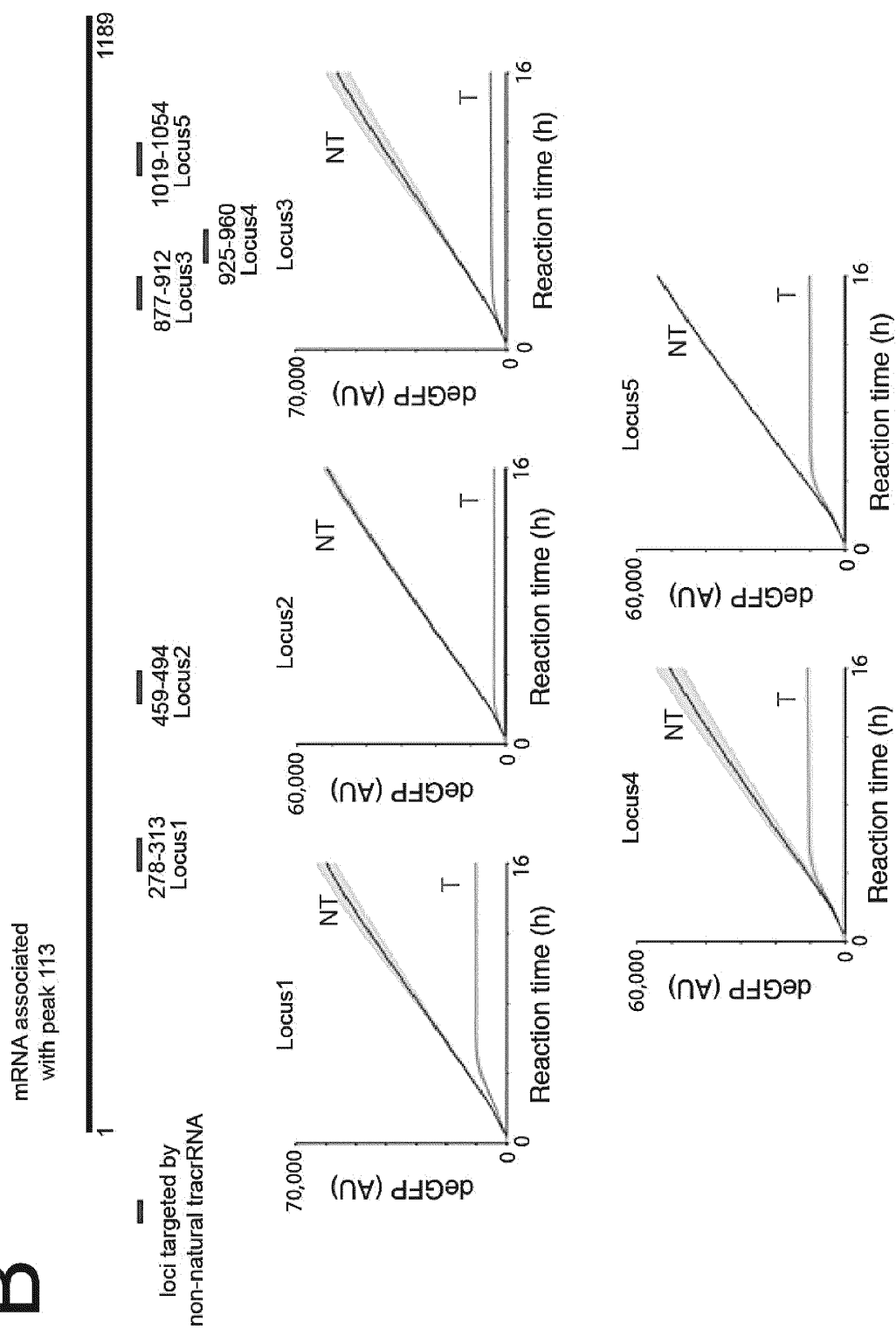
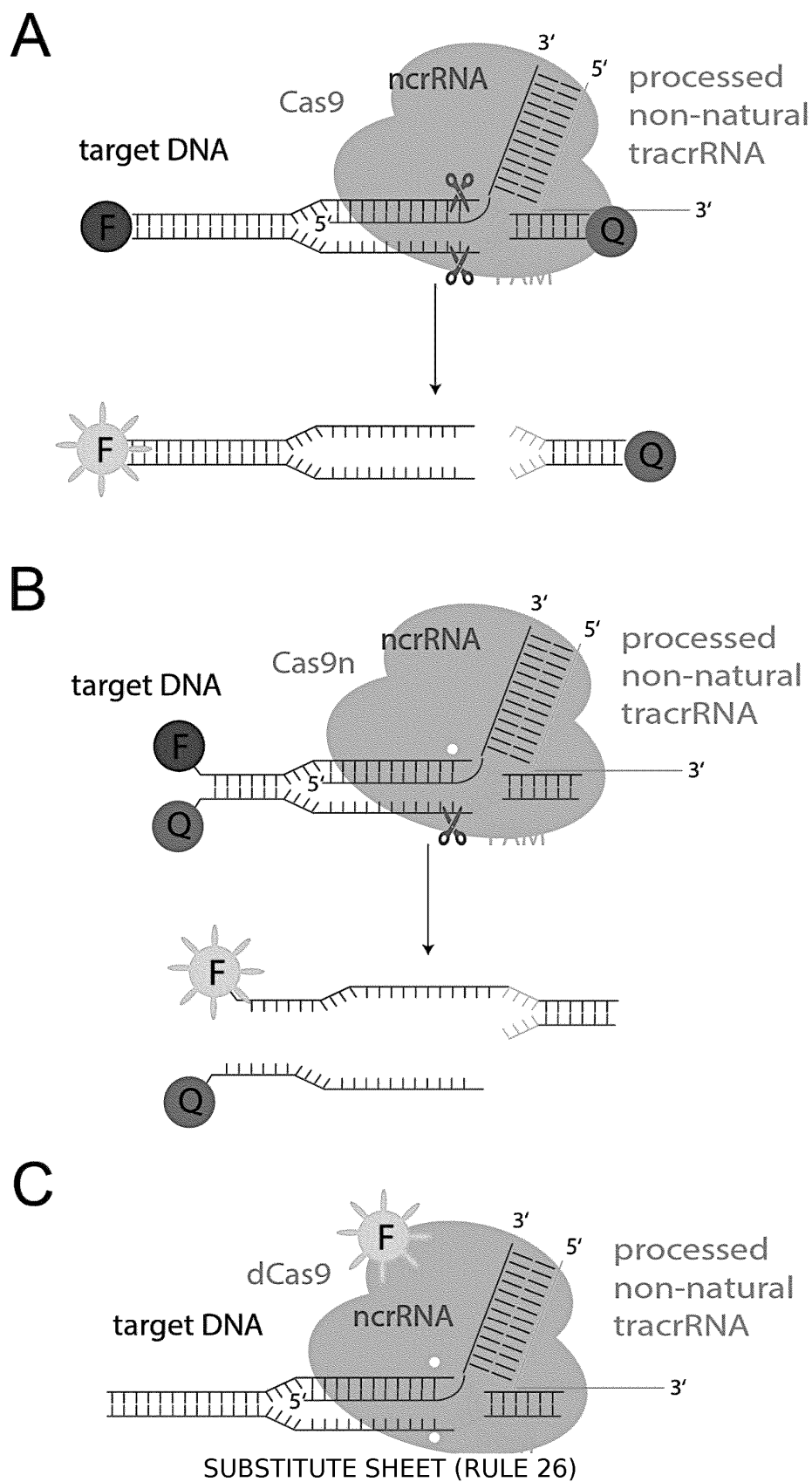


Figure 12



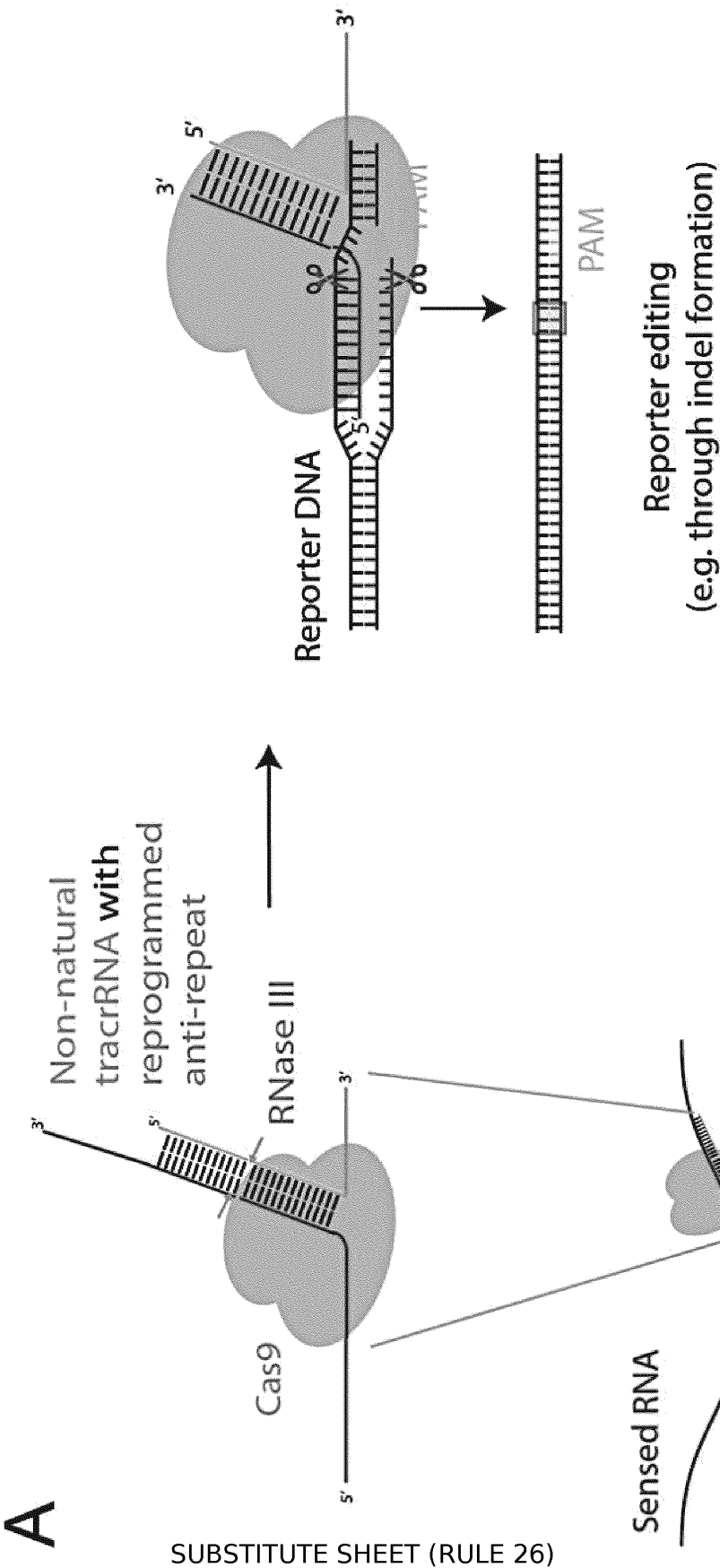
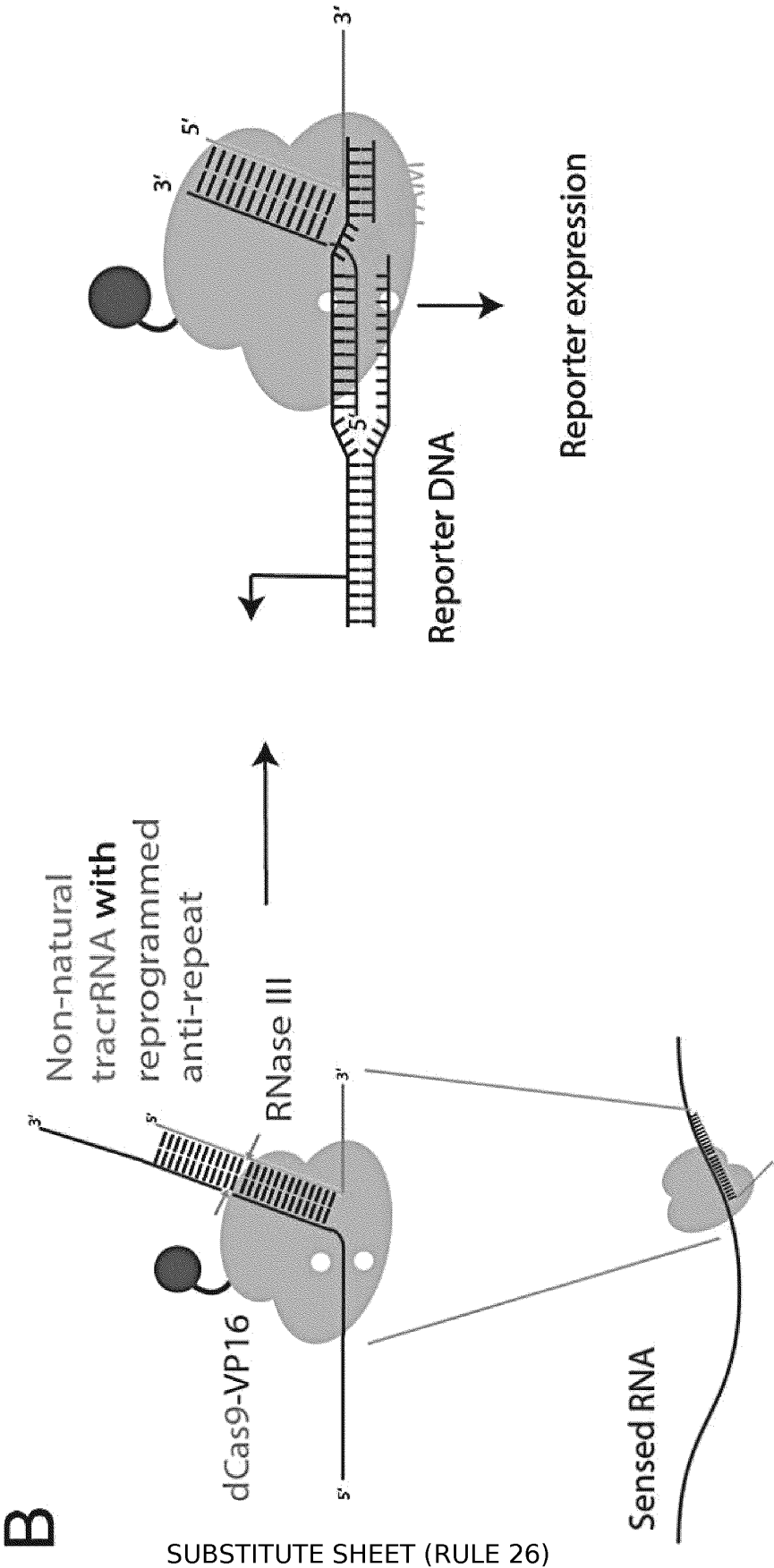


Figure 13

Figure 13 (continued)



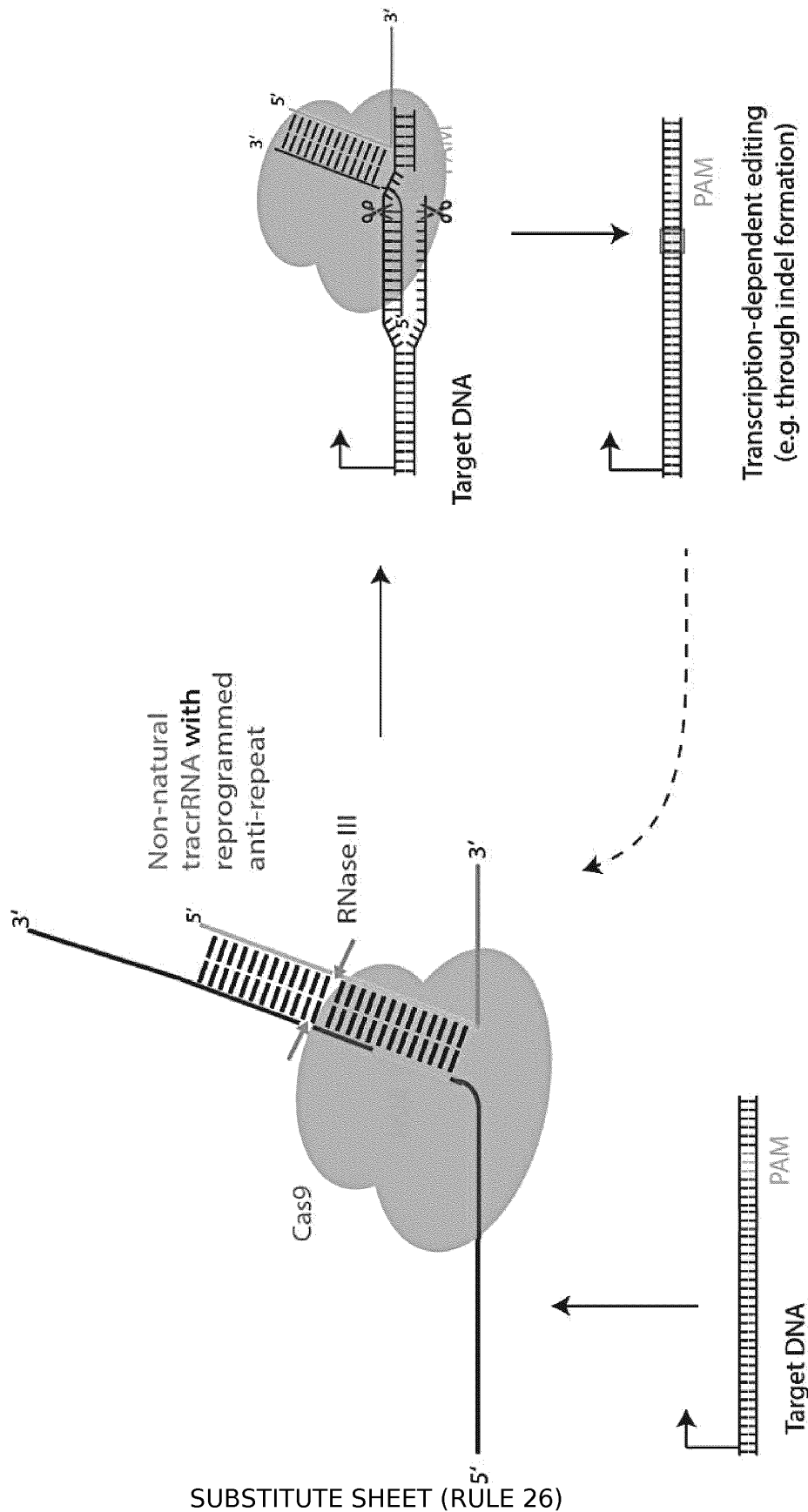


Figure 14

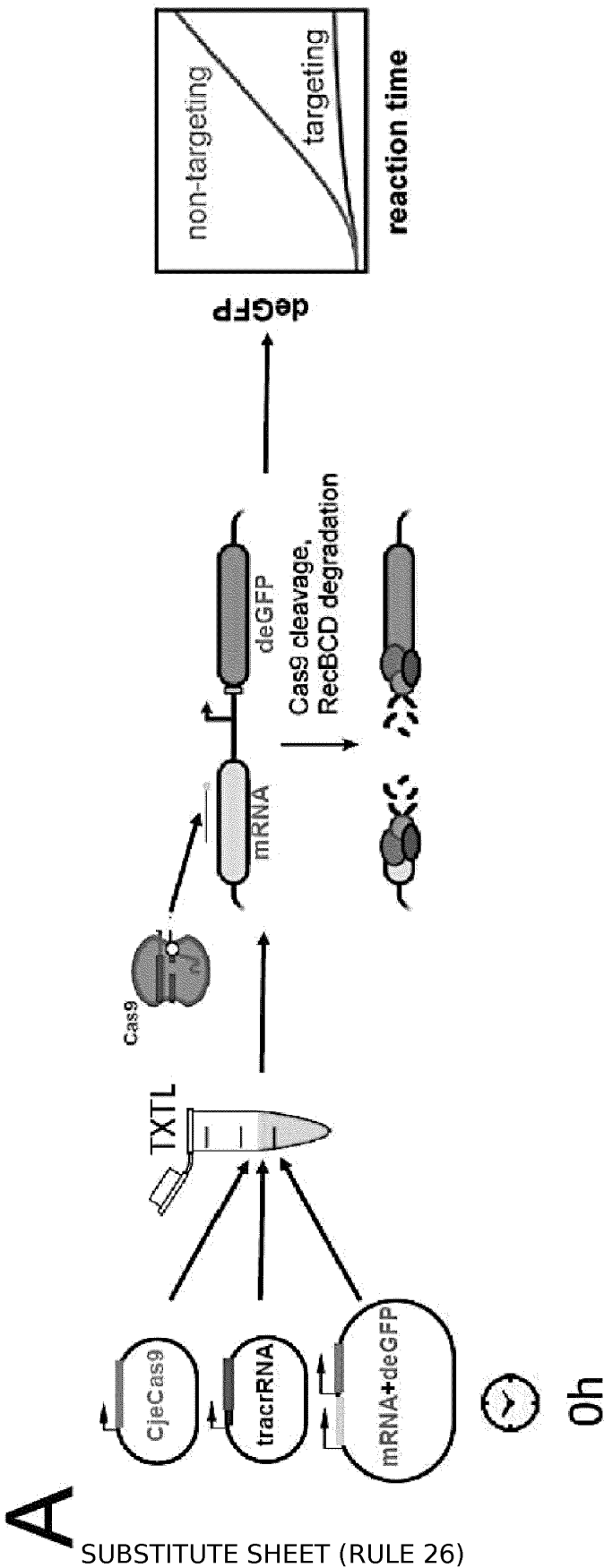


Figure 15

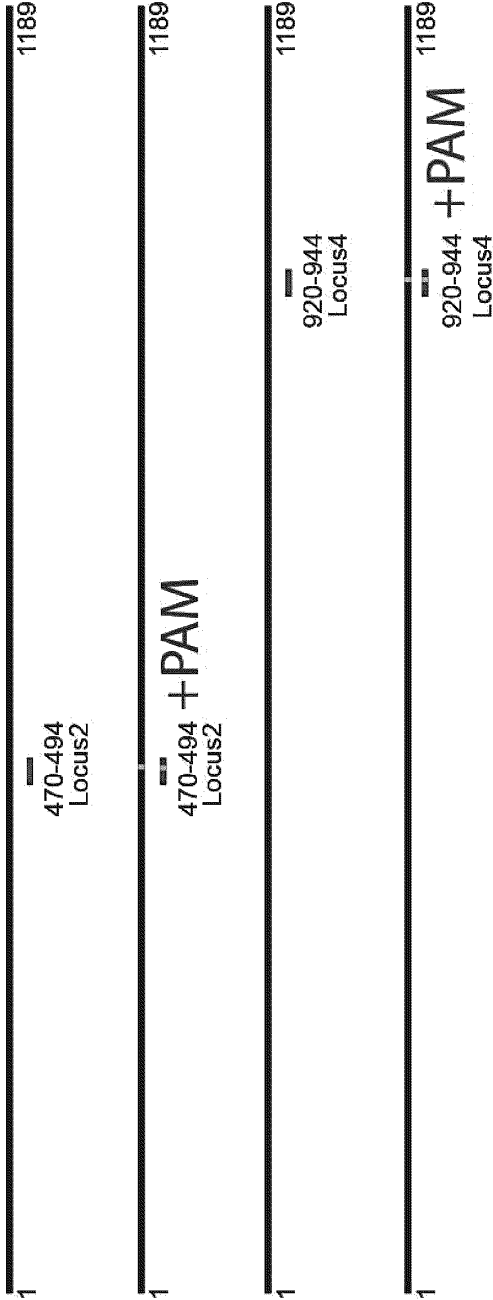
Figure 15 (continued)

B

mRNA associated
with peak 113

loci targeted by
non-natural tracrRNA

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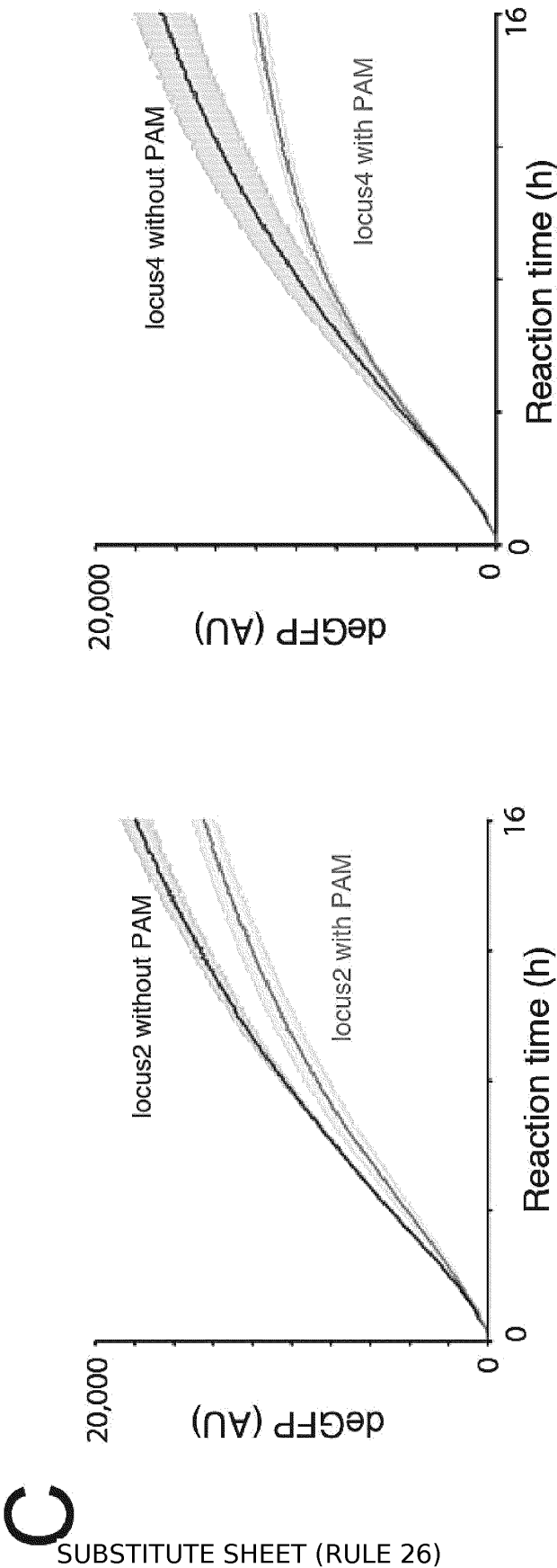


Figure 15 (continued)

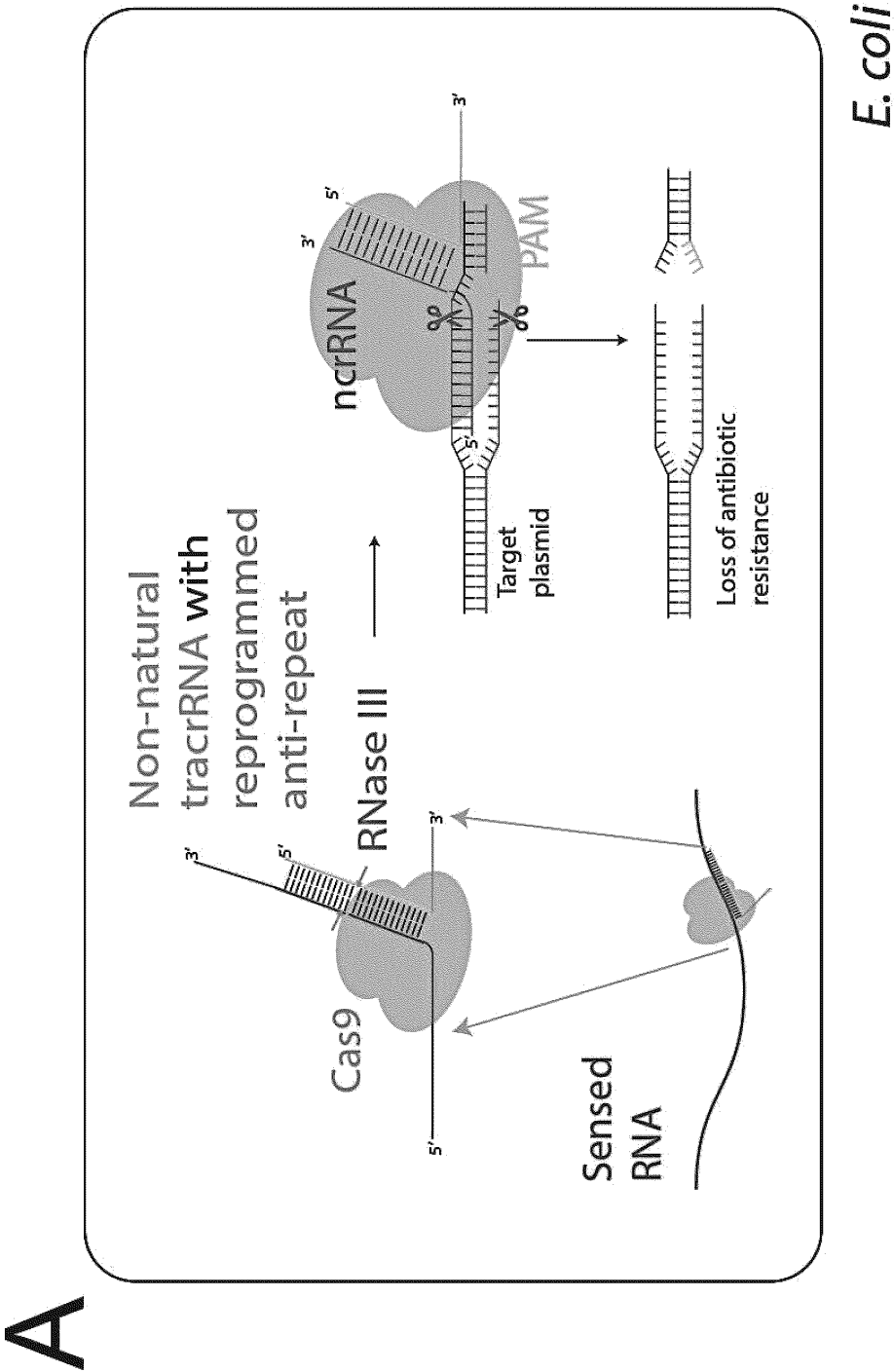


Figure 16

B

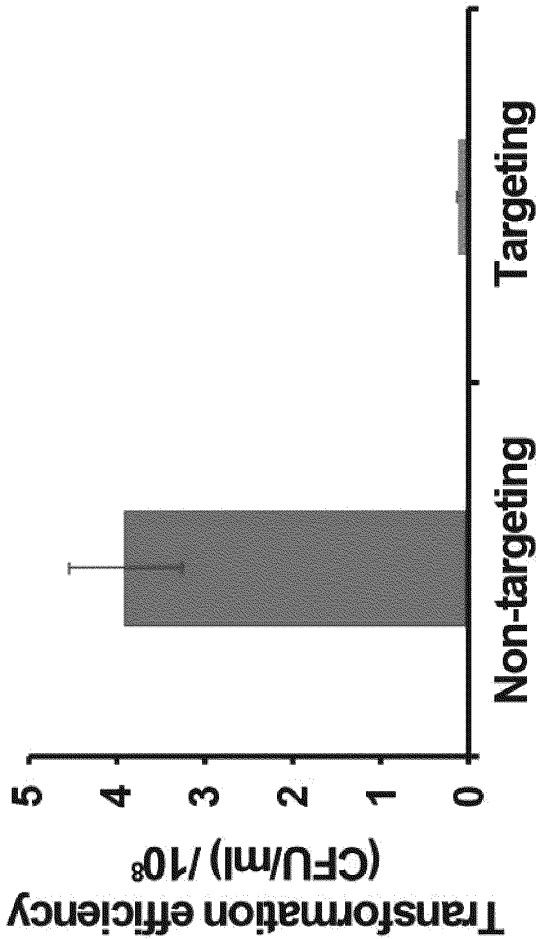
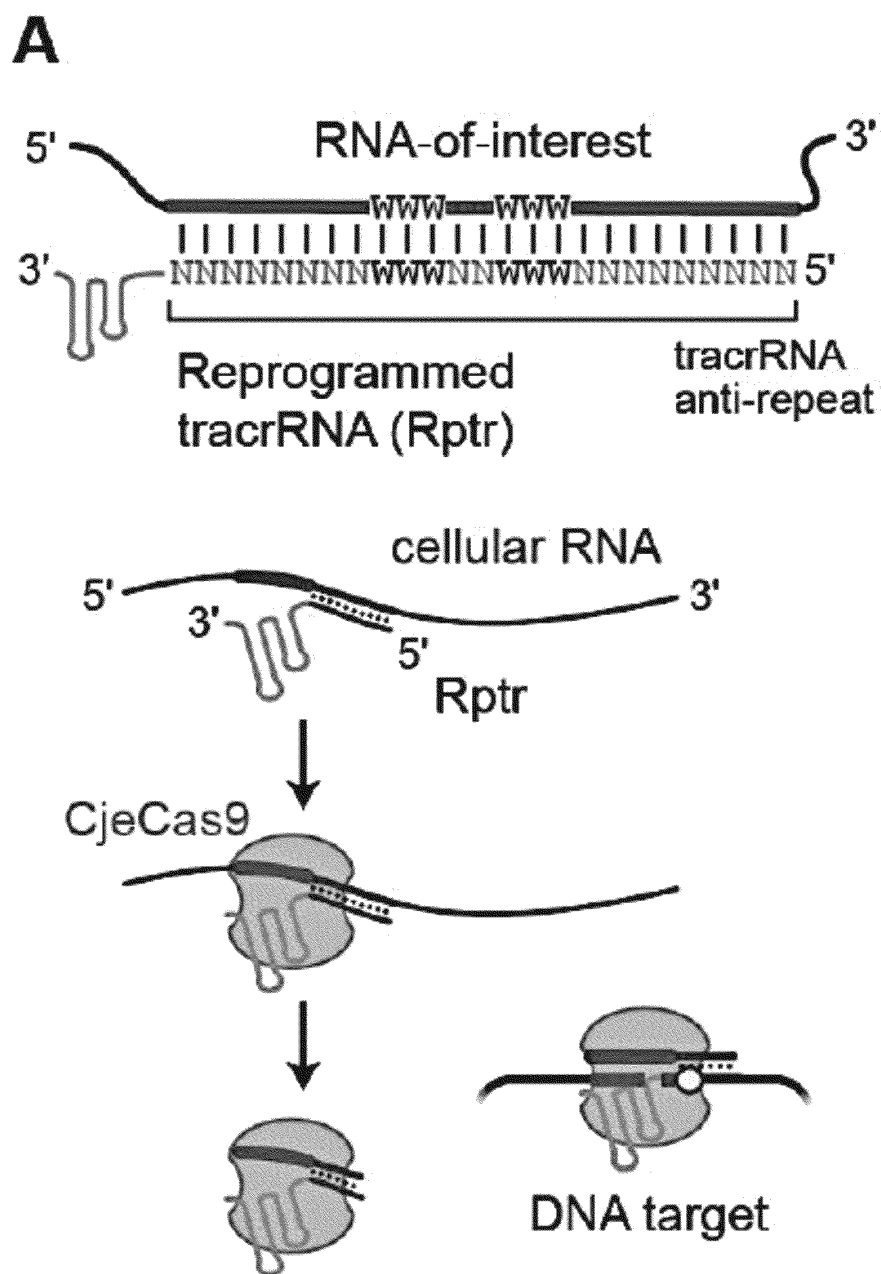


Figure 16 (continued)

Figure 17



SUBSTITUTE SHEET (RULE 26)

Figure 17 (continued)

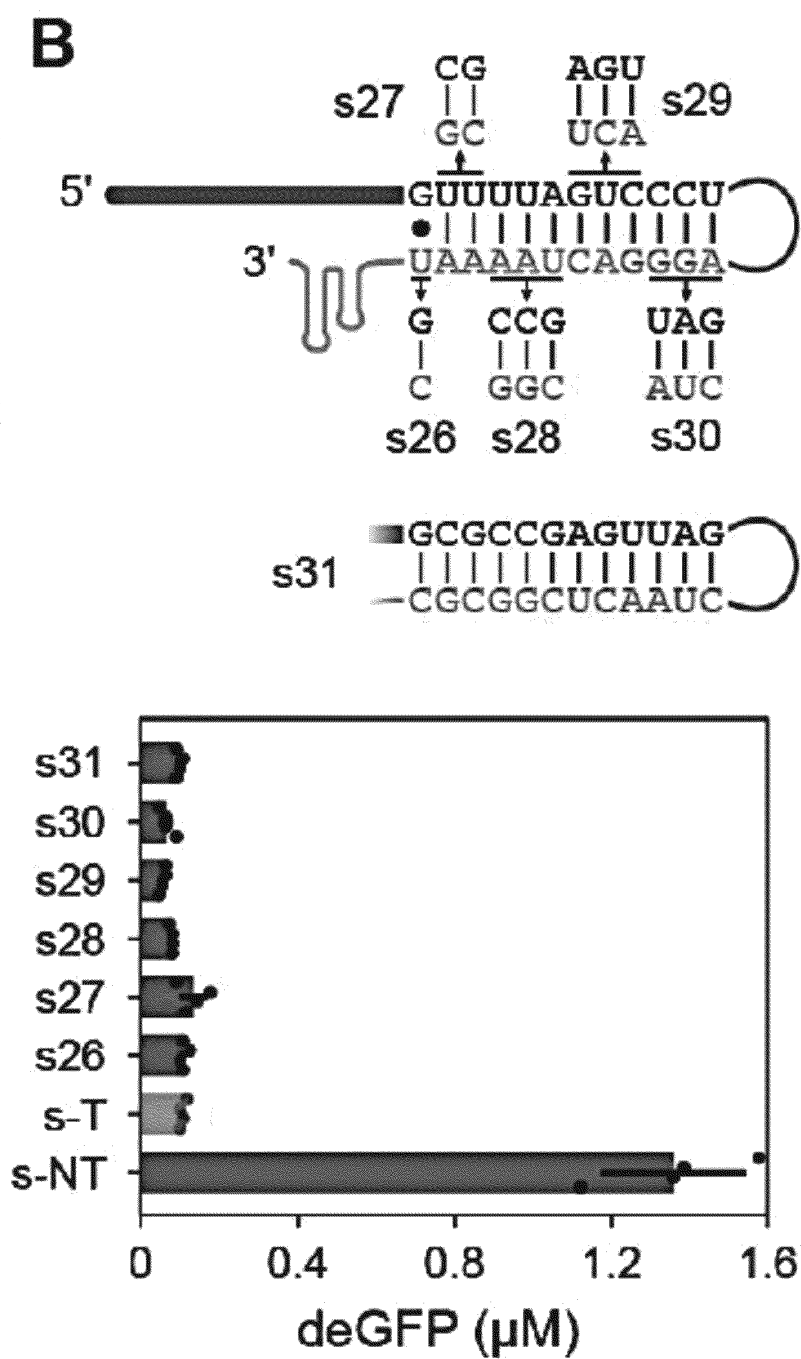


Figure 17 (continued)

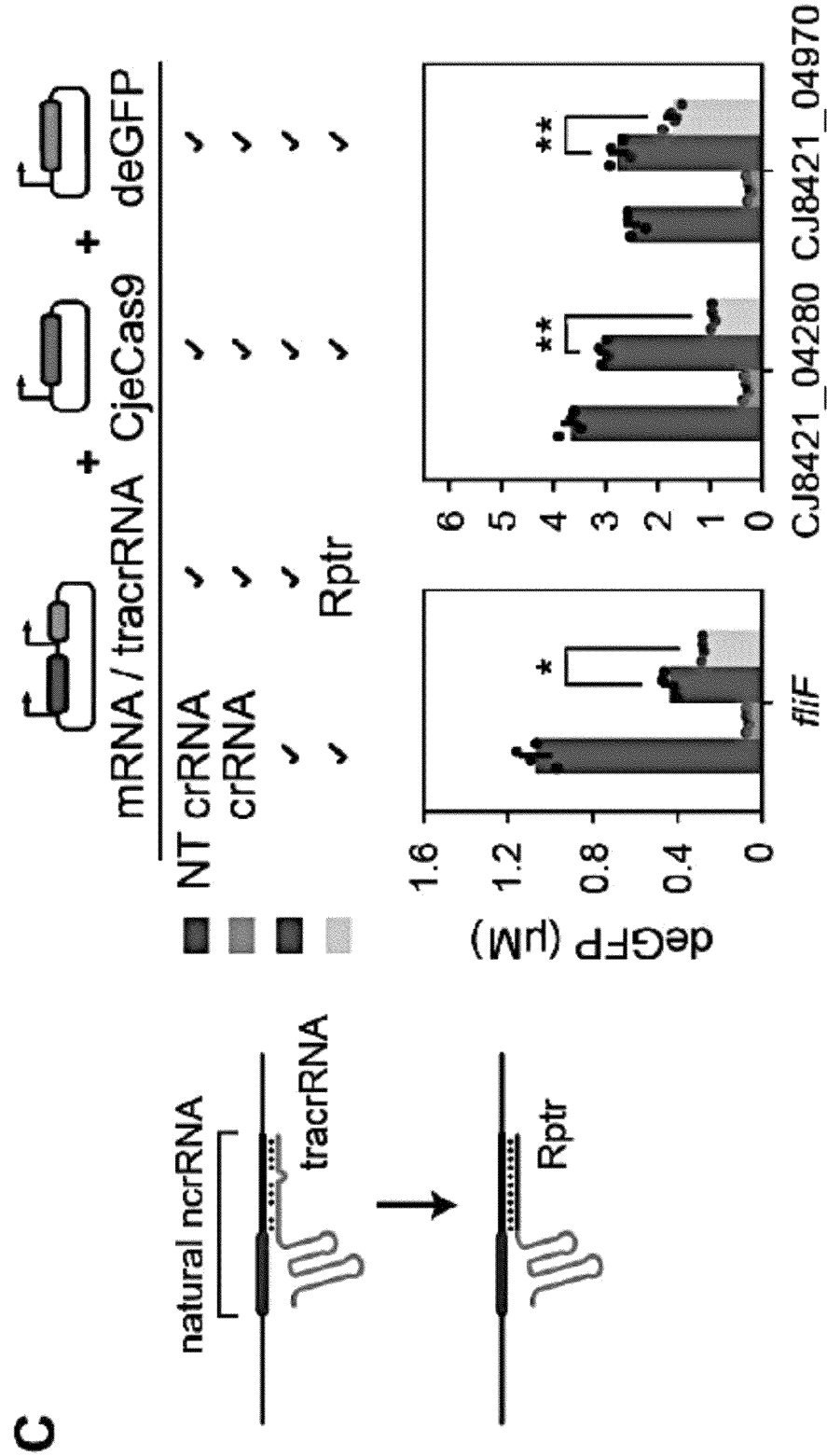


Figure 17 (continued)

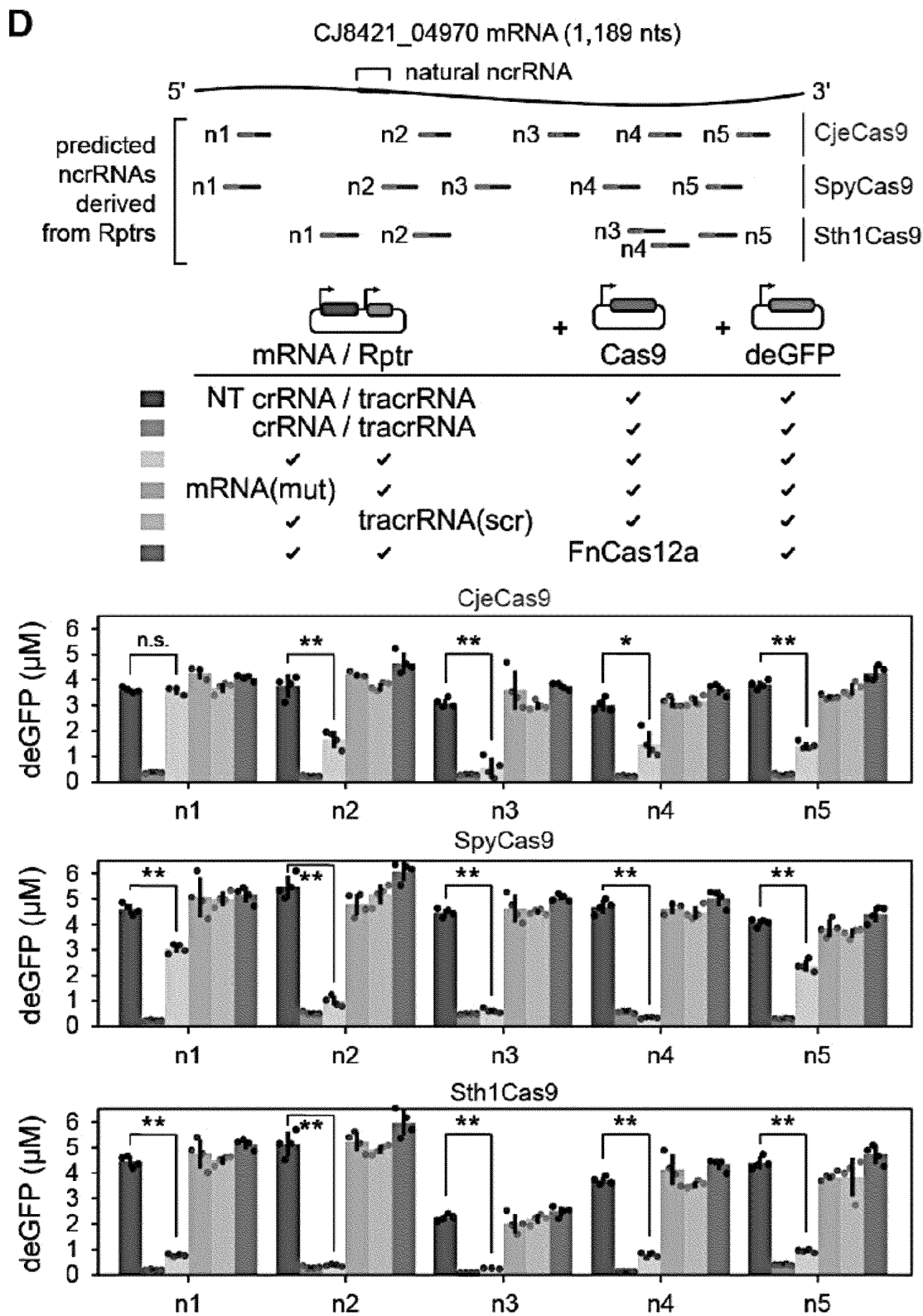


Figure 18

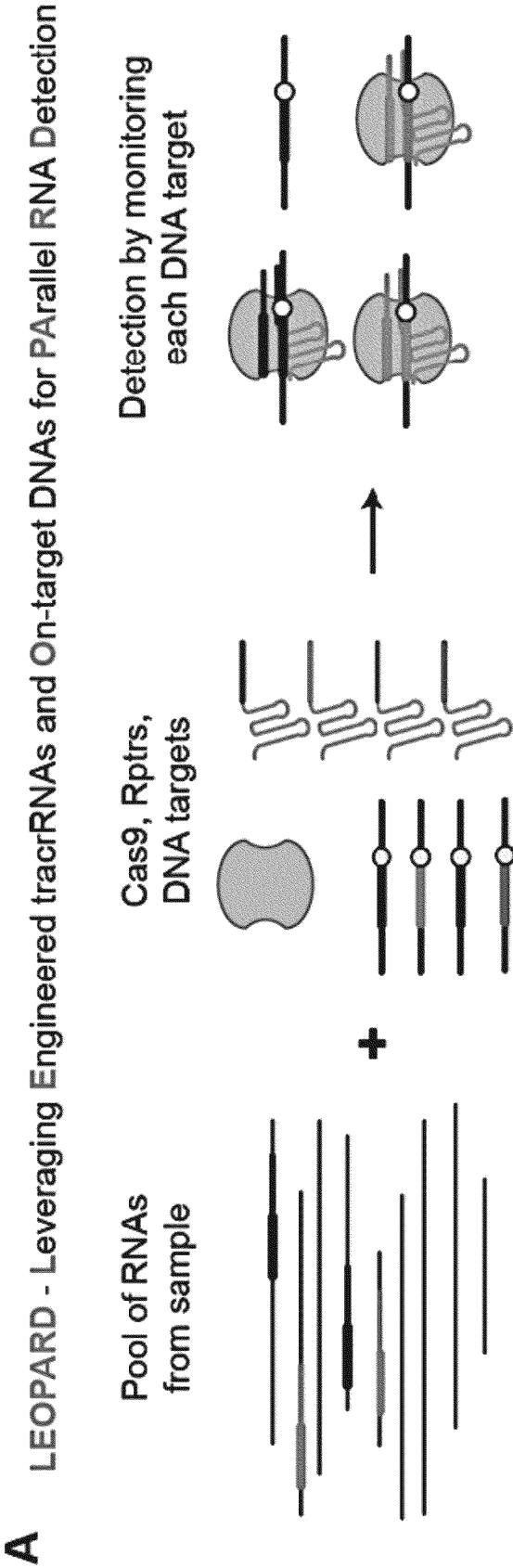


Figure 18 (continued)

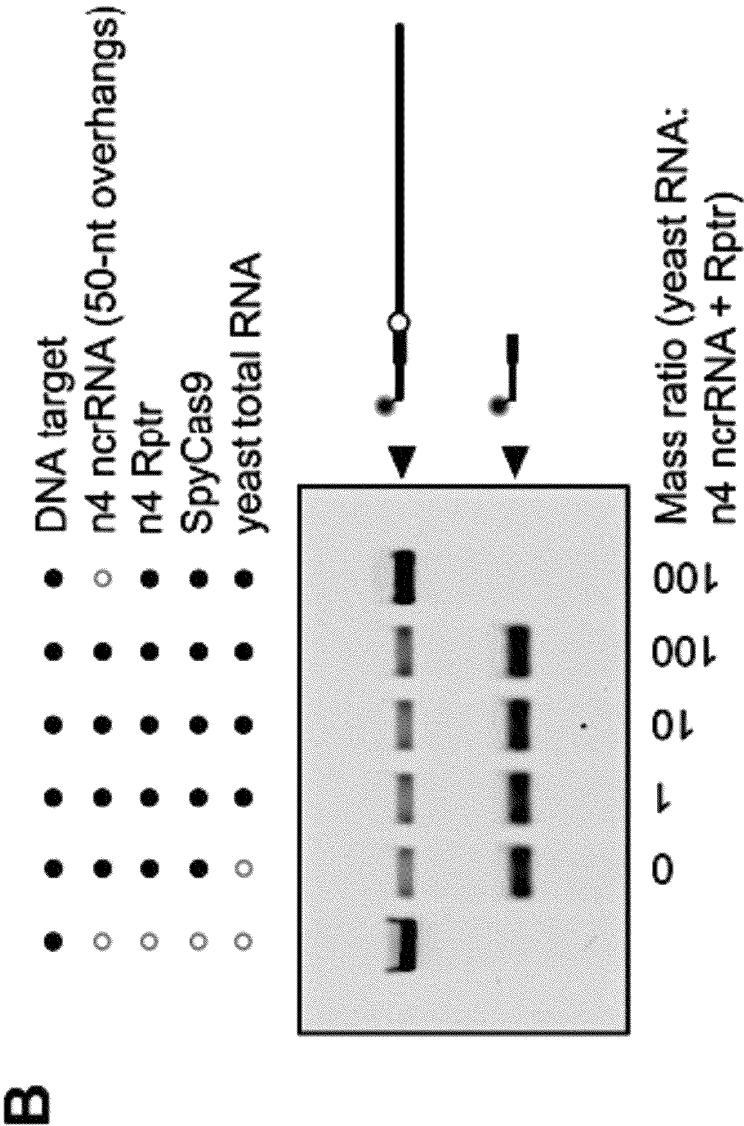


Figure 18 (continued)

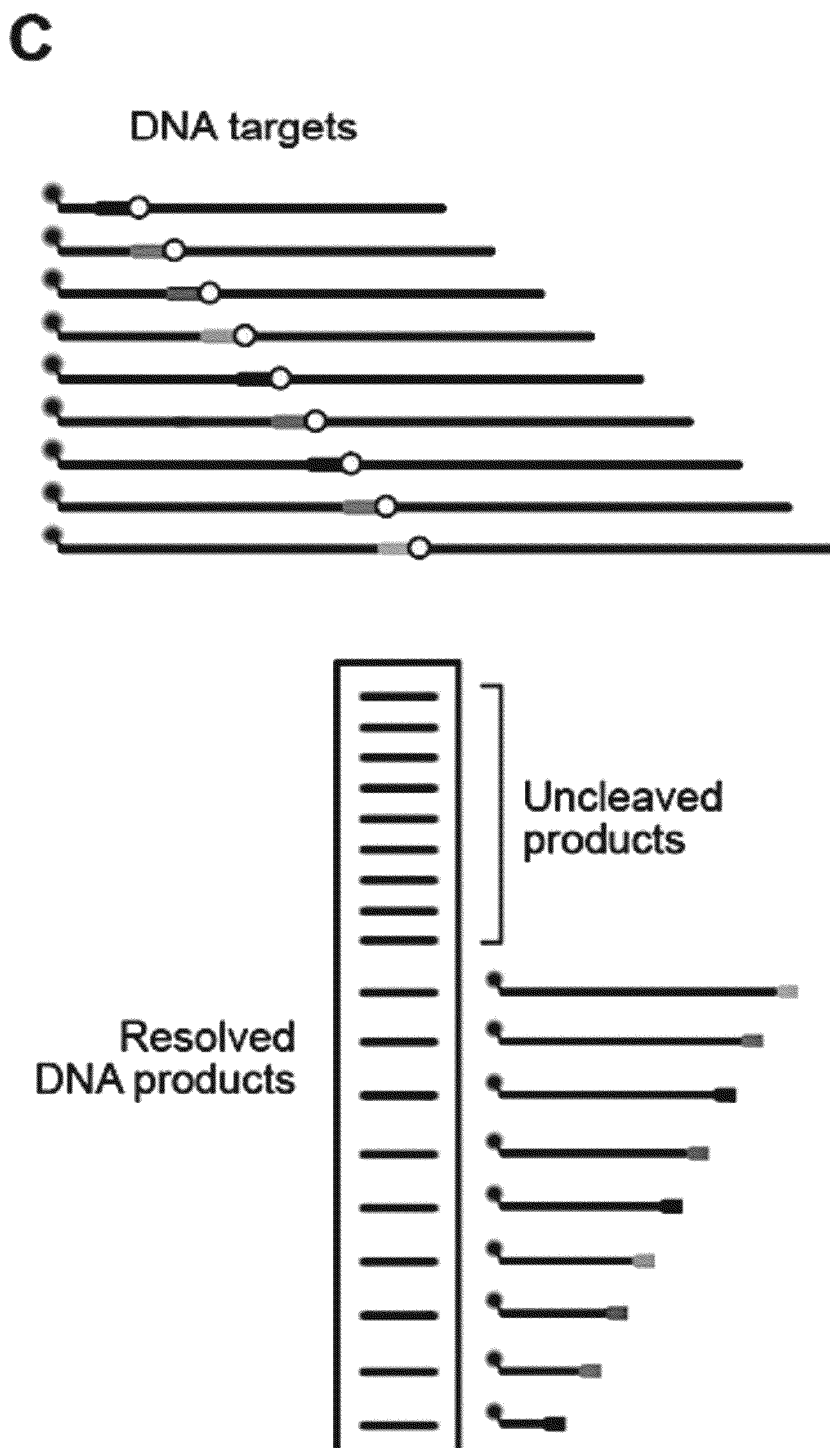


Figure 18 (continued)

Figure 18 (continued)

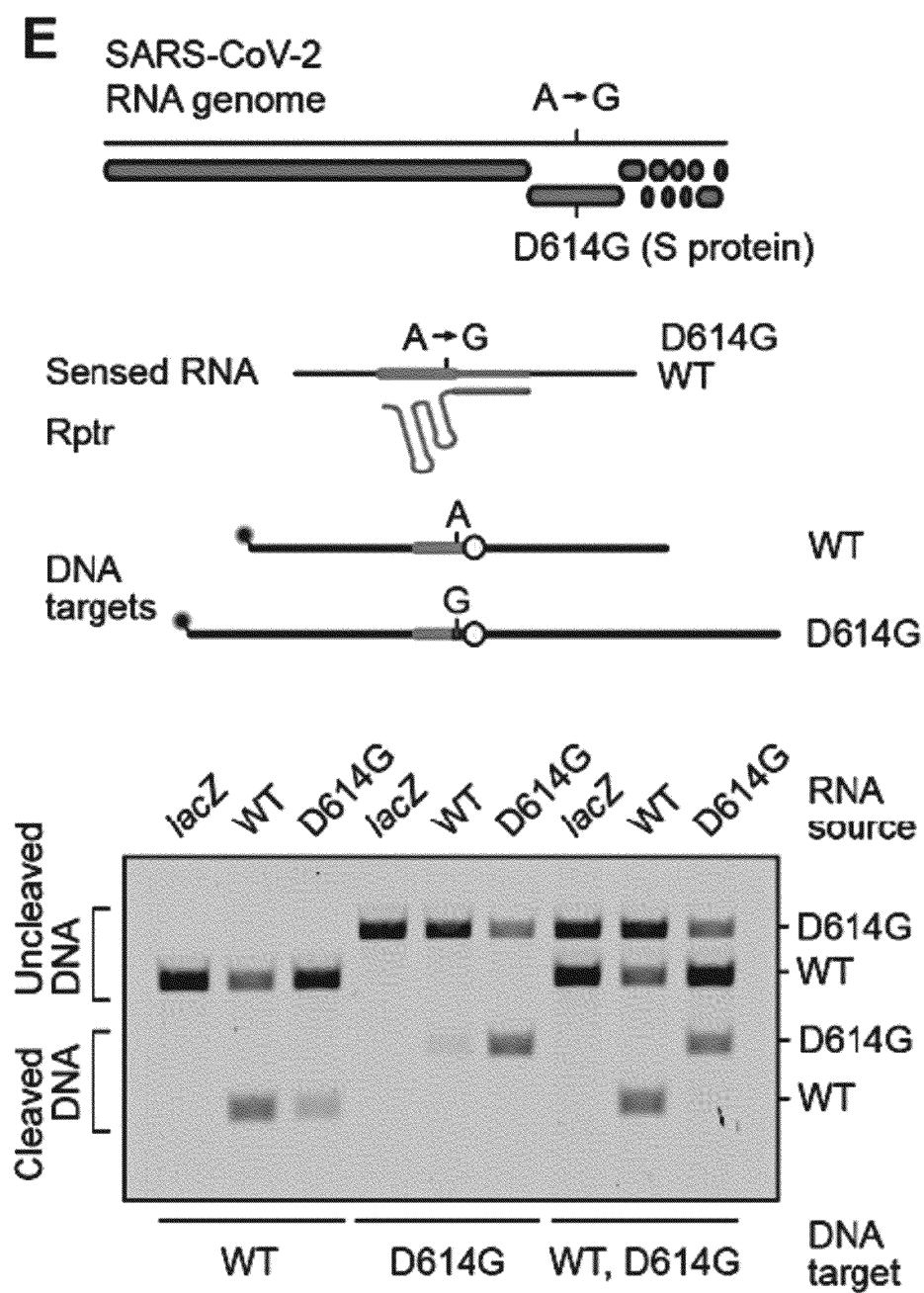


Figure 19



Figure 19 (continued)

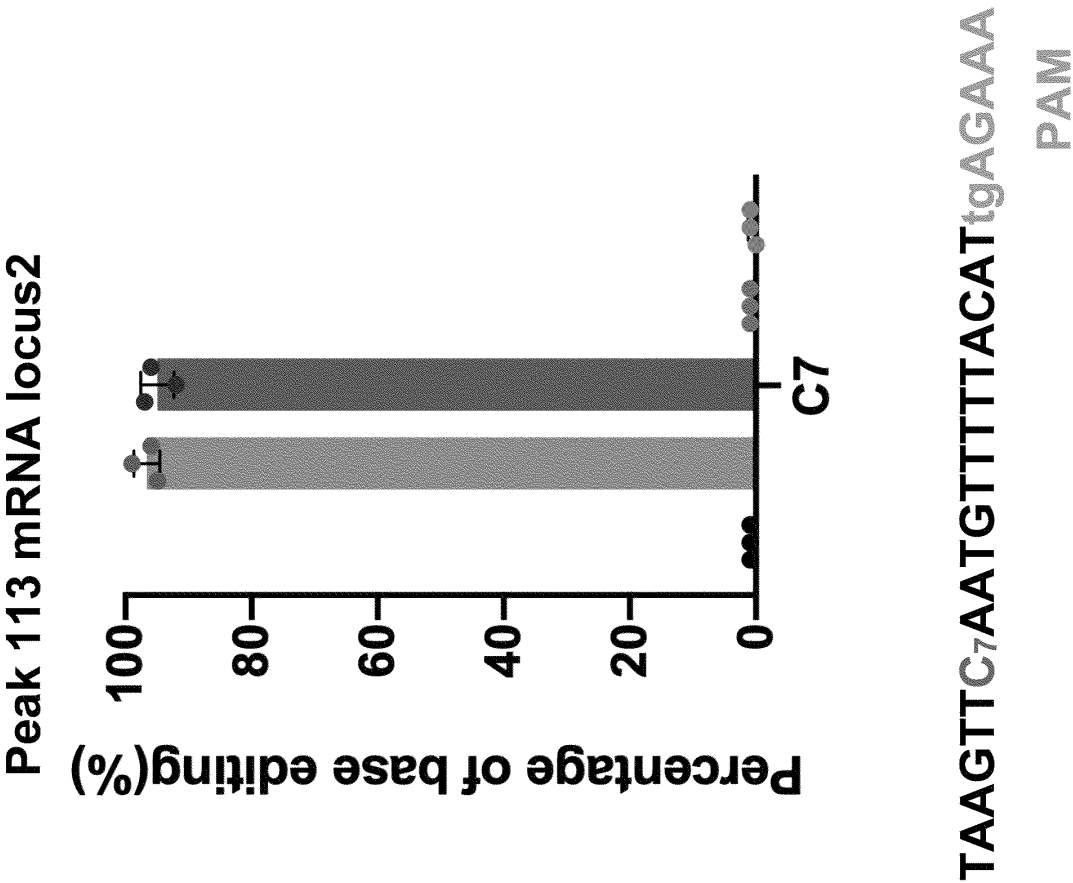
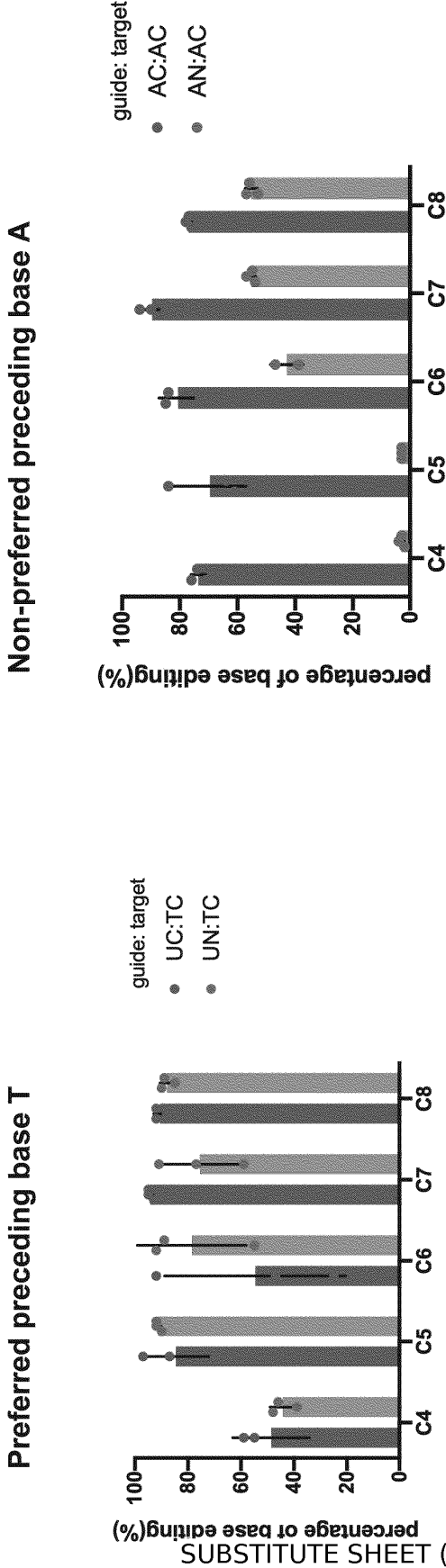


Figure 20



Guide AGA₃A₄U₅U₆U₇A₈UGUGAAUUUUUAUUG

Target AGA₃A₄T₅T₆T₇A₈TGTGAATTTTATTG_{tg}AGAAA

PAM

Figure 21

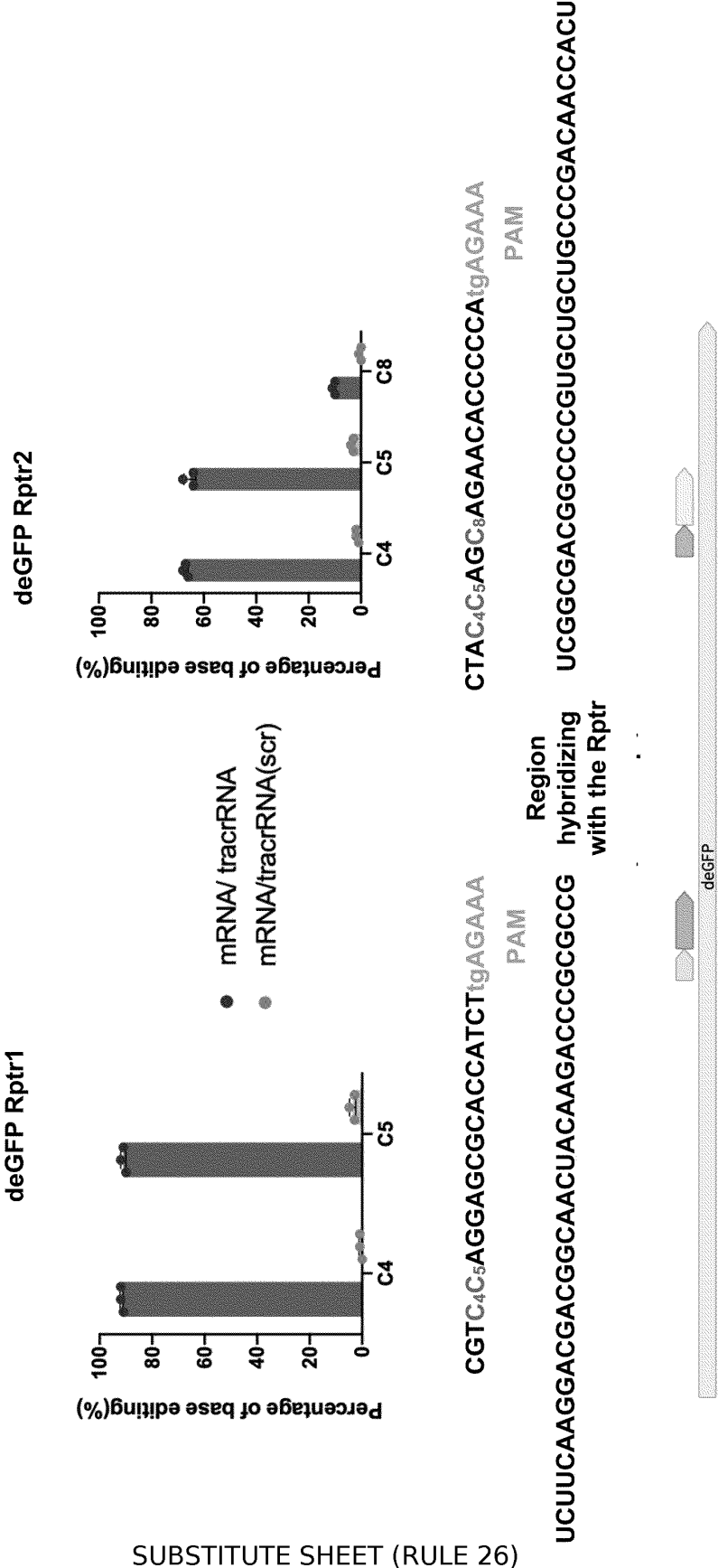
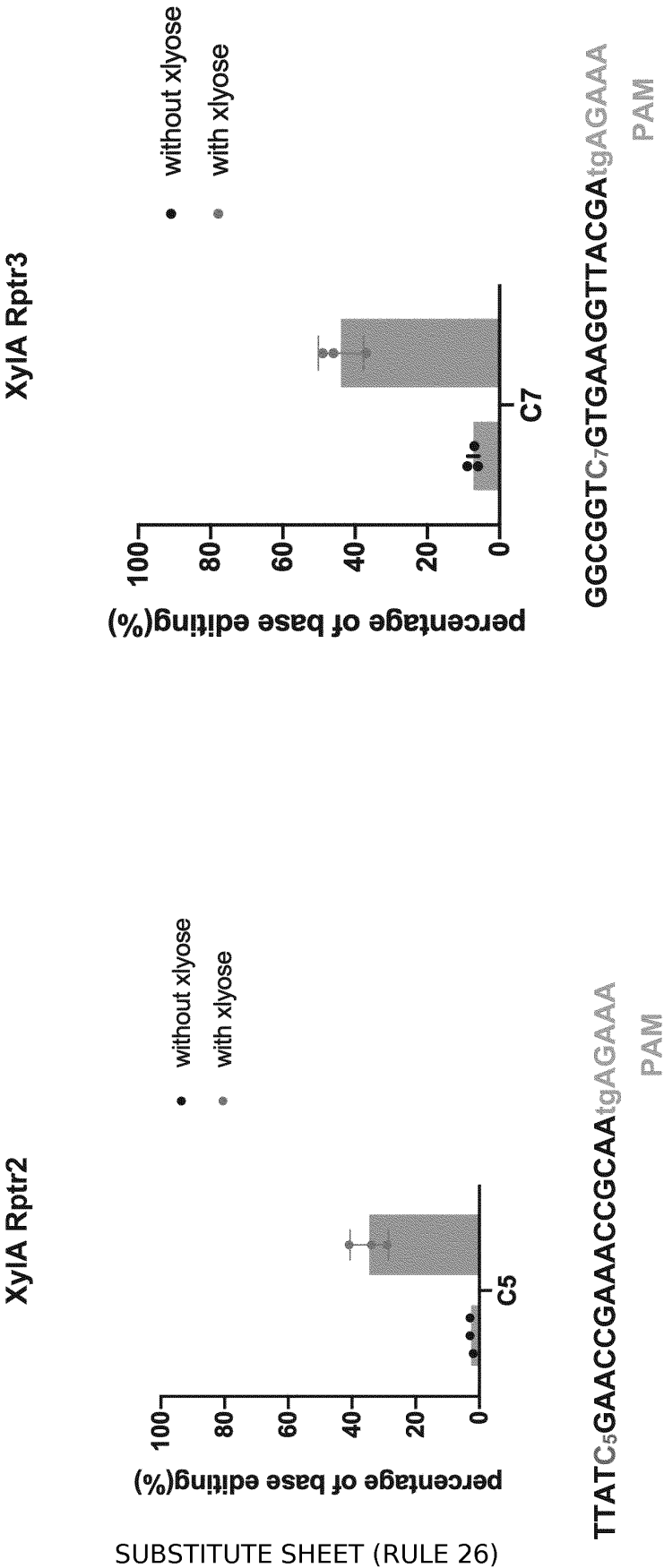


Figure 22



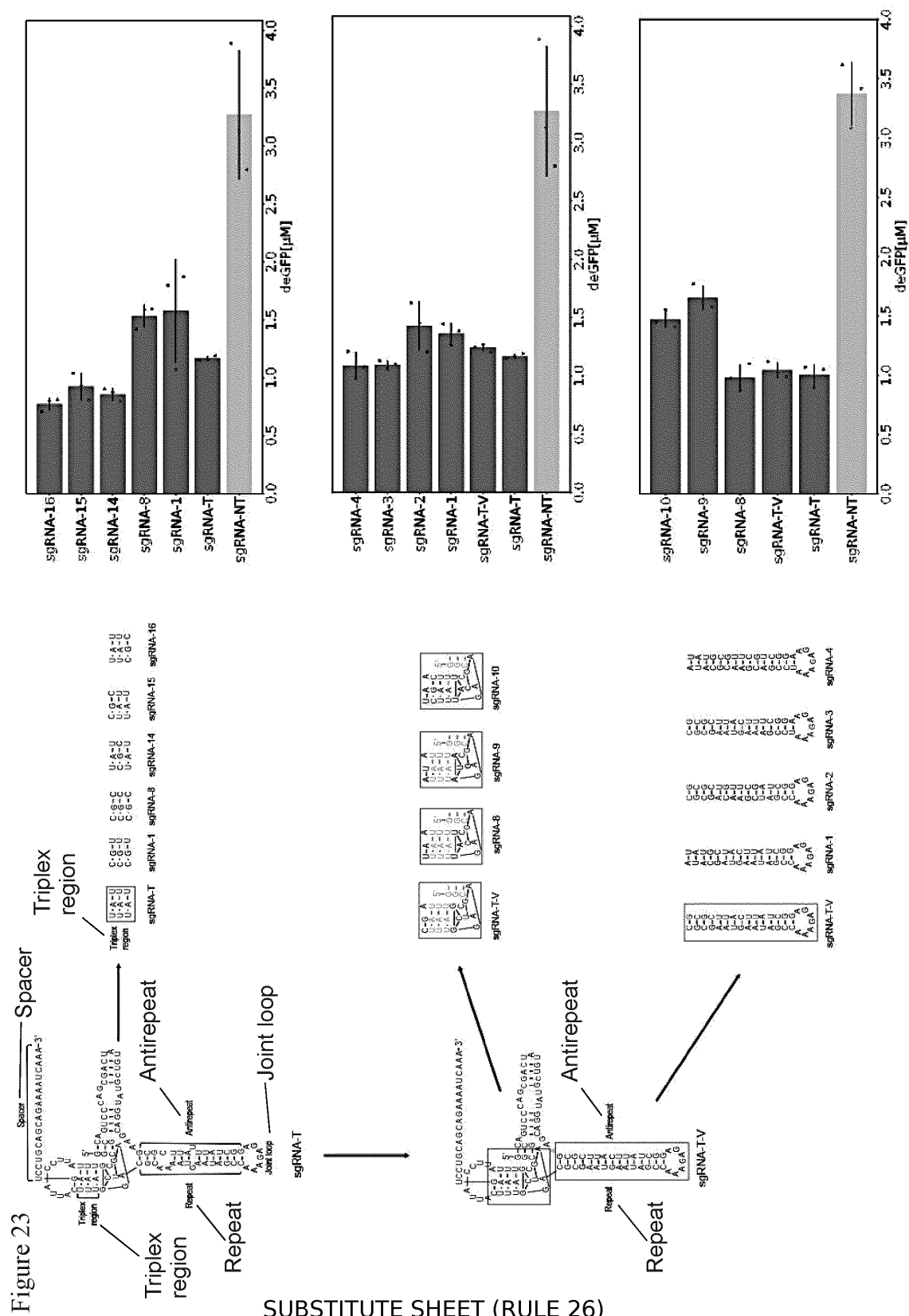


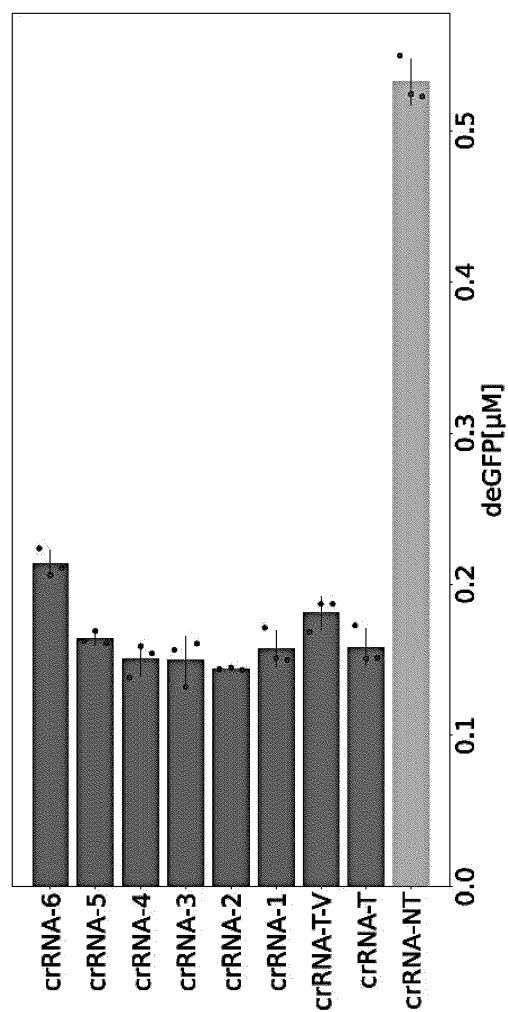
Diagram illustrating the formation of a repeat-antirepeat duplex from a single-stranded RNA sequence.

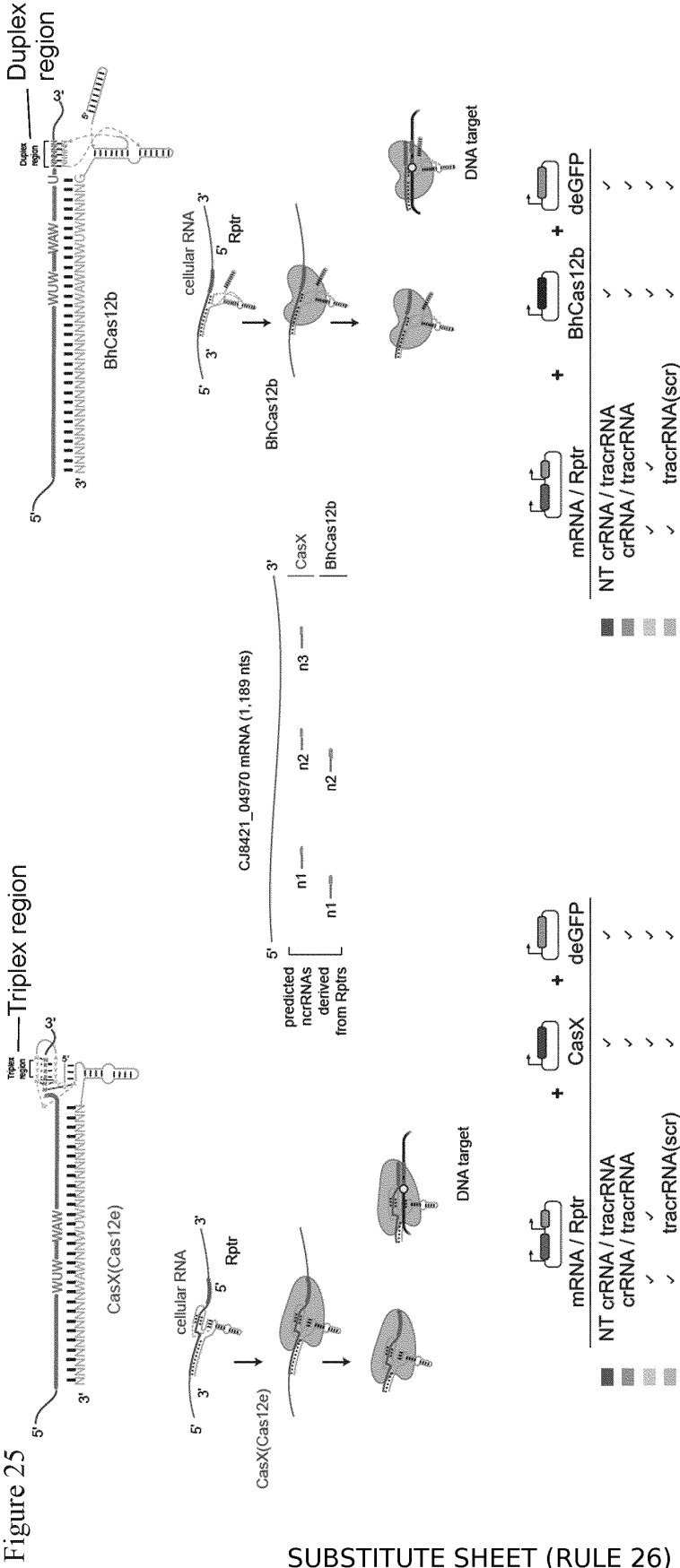
Single-stranded RNA (top):

- 5' end: 5'-quadruplet U U U U
- Sequence: G A A A U U U U A U A U C G C A U U U A A - 3'
- Regions: Duplex region (Lower stem, Upper stem), Bulge

Repeat-antirepeat duplex (bottom):

- Formed by the annealing of two single-stranded RNAs.
- Regions: Repeat-antirepeat duplex, Lower stem, Bulge, Upper stem.
- The Bulge is labeled "Bulge removed" and "Bulge".





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