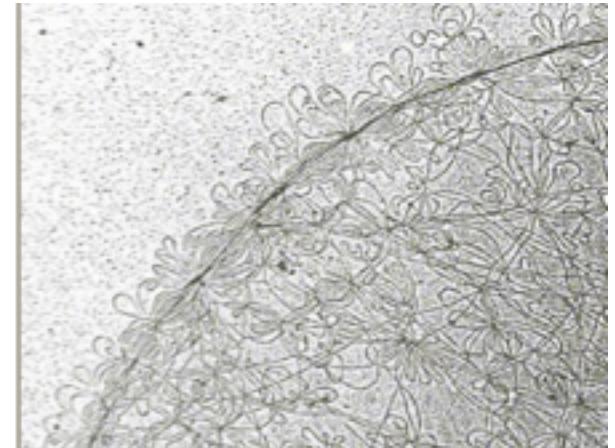


3' AAAUGAGuuuuuuuuuuuuuuCGAAA 5'

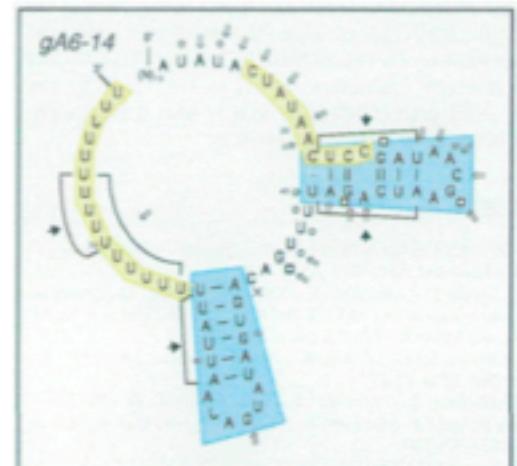


Guide RNA

Amy Heidersbach

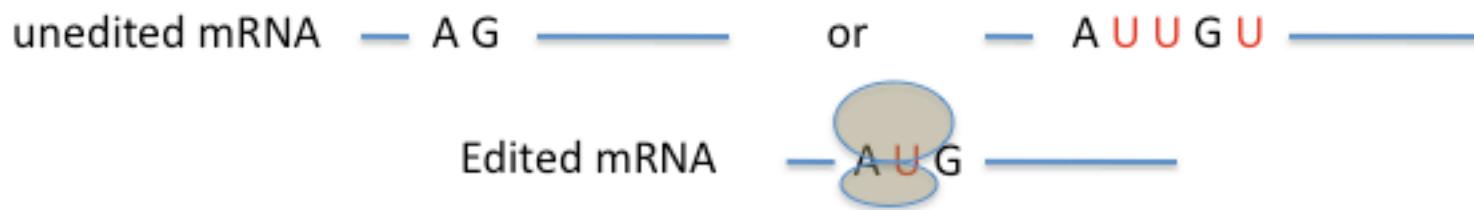
BMS 265

5/7/09



What is Insertion/Deletion RNA Editing?

- The addition or deletion of U residues from a pre mRNA transcript.



- Unique to the mitochondrial genome of Kinetoplastid Trypanosomes

- Usually* necessary for a functional open reading frame

Cell, Vol. 46, 819–826, September 12, 1986, Copyright © 1986 by Cell Press

Major Transcript of the Frameshifted *coxII* Gene from Trypanosome Mitochondria Contains Four Nucleotides That Are Not Encoded in the DNA

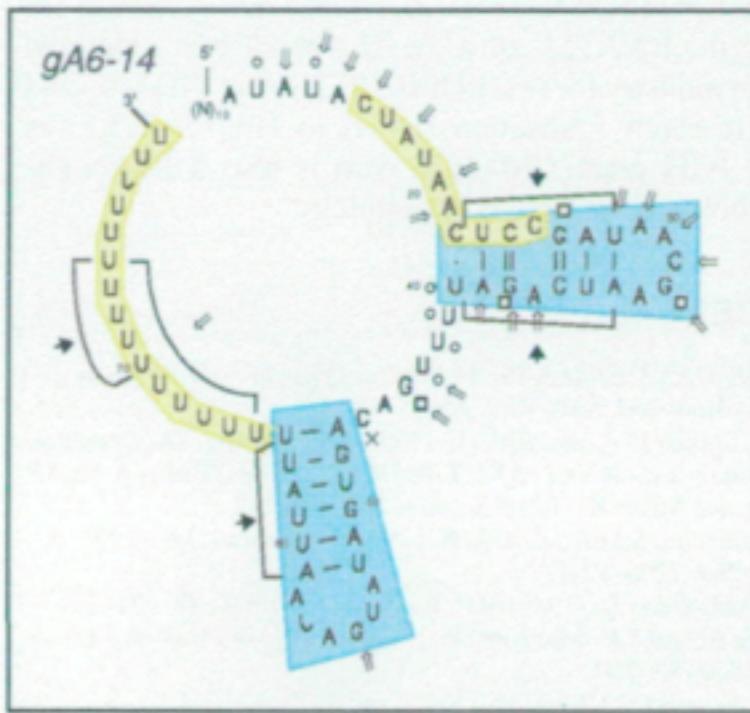
Benne et. al
1986

Blum et. al
1990

Cell, Vol. 60, 189–198, January 26, 1990, Copyright © 1990 by Cell Press

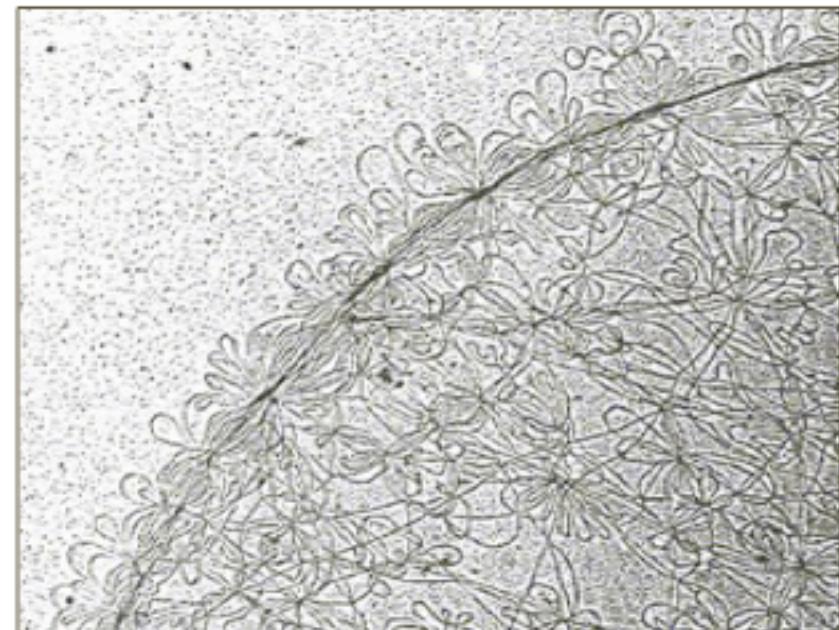
A Model for RNA Editing in Kinetoplastid Mitochondria: “Guide” RNA Molecules Transcribed from Maxicircle DNA Provide the Edited Information

What is a gRNA?

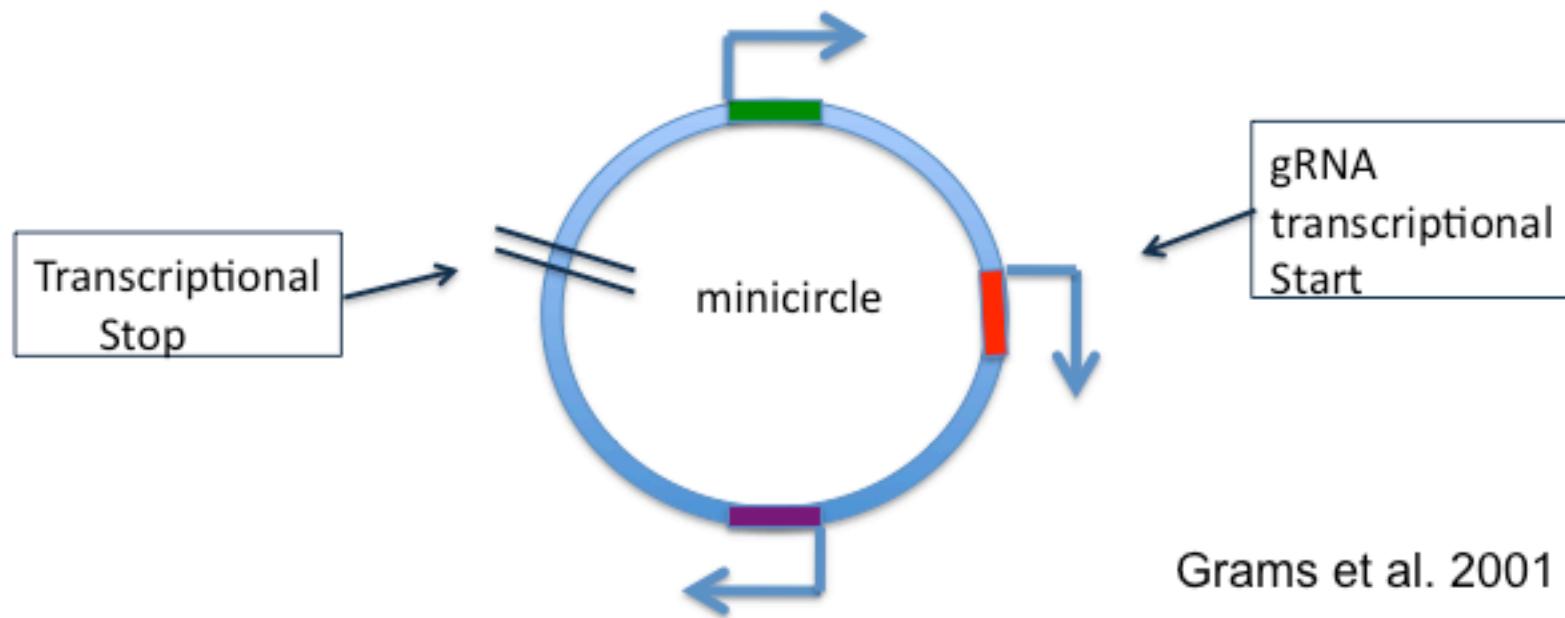


- 50-70 nt RNA species containing a 5' triphosphate and 3' poly U tail
- “Characteristic” double hairpin motif.
(Schmid et. Al. 1995)

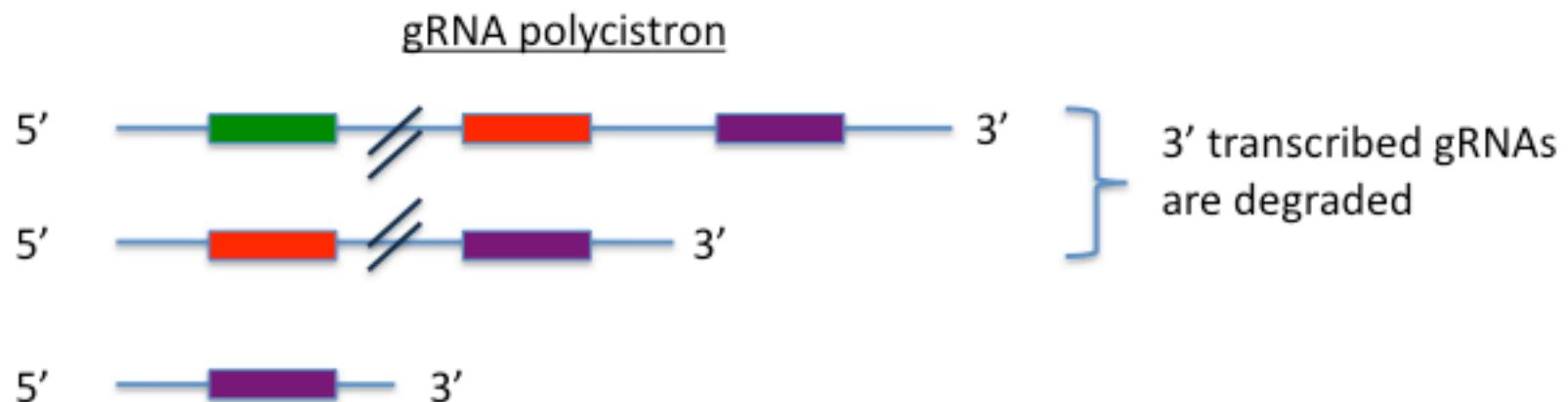
- Largely encoded by the mincircles of the Kinetoplastid mitochondrial genome.



gRNA Biogenesis transcription from minicircles



Grams et al. 2001



gRNA Biogenesis

Addition of a U Tail

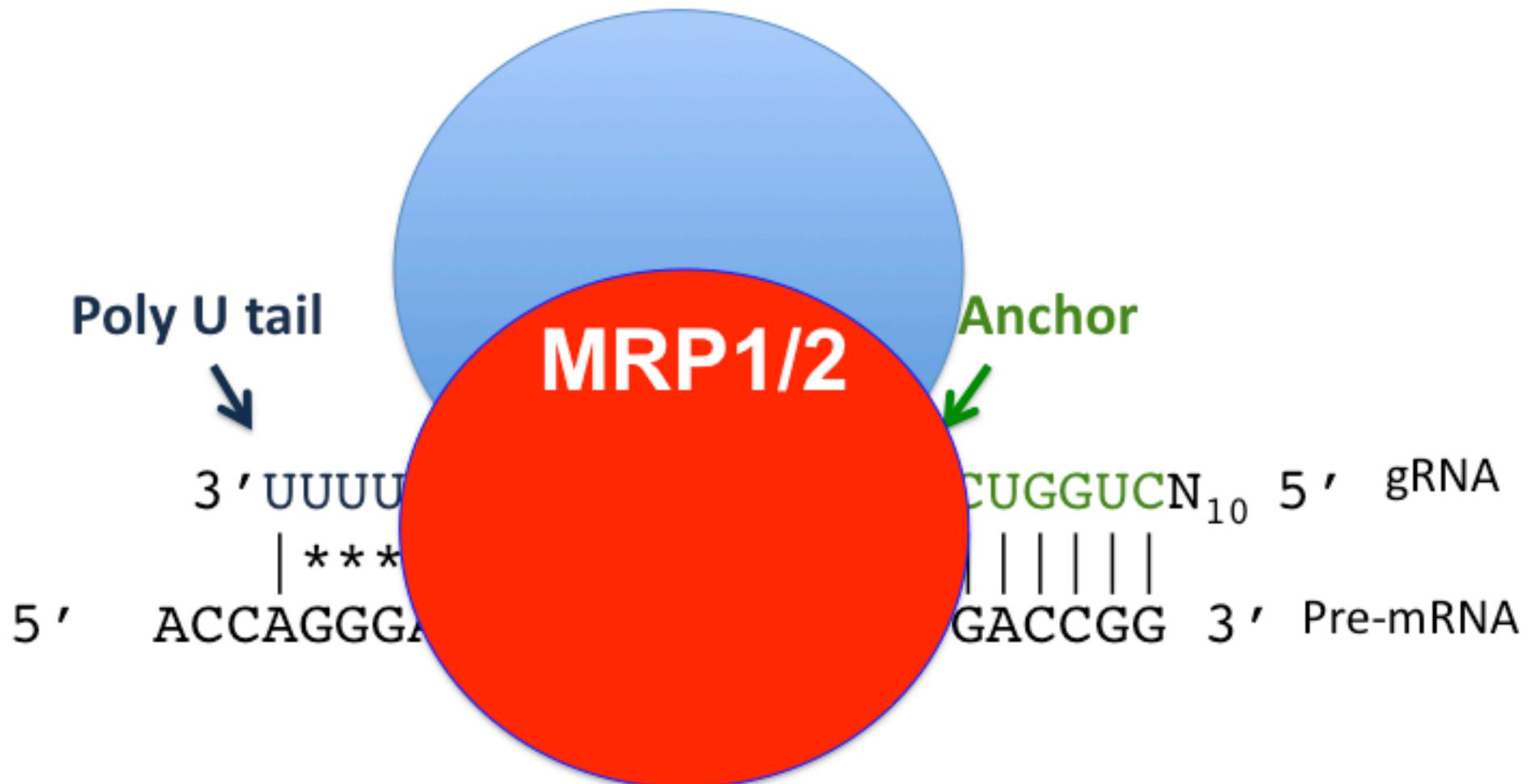


gRNA

Mechanism of Action

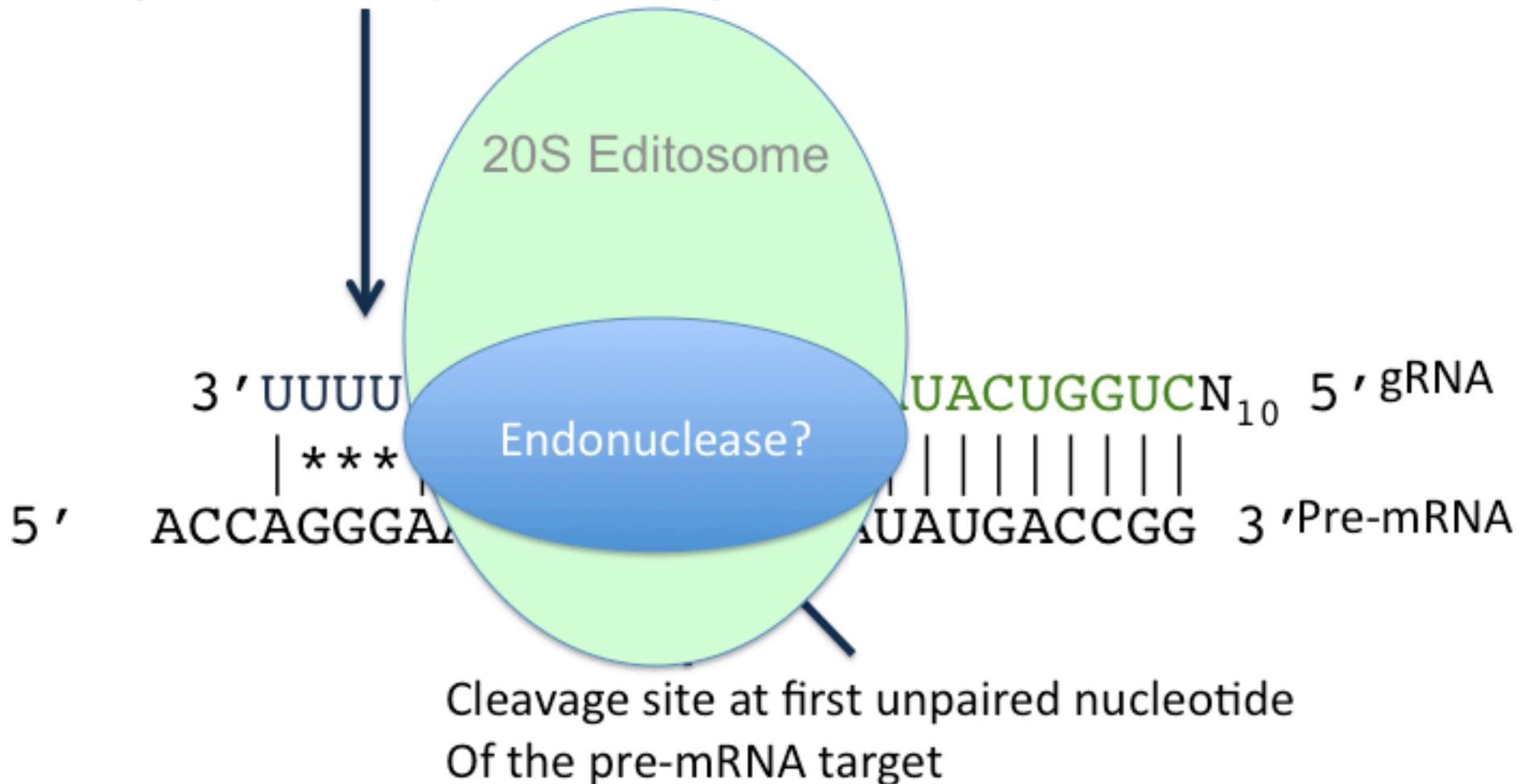
1. gRNA/pre-mRNA binding
2. pre-mRNA cleavage
- 3a. U insertion via TUTase action
- 3b. U deletion via ExoUase action
4. Re-ligation of mRNA fragments

1. gRNA/pre-mRNA binding



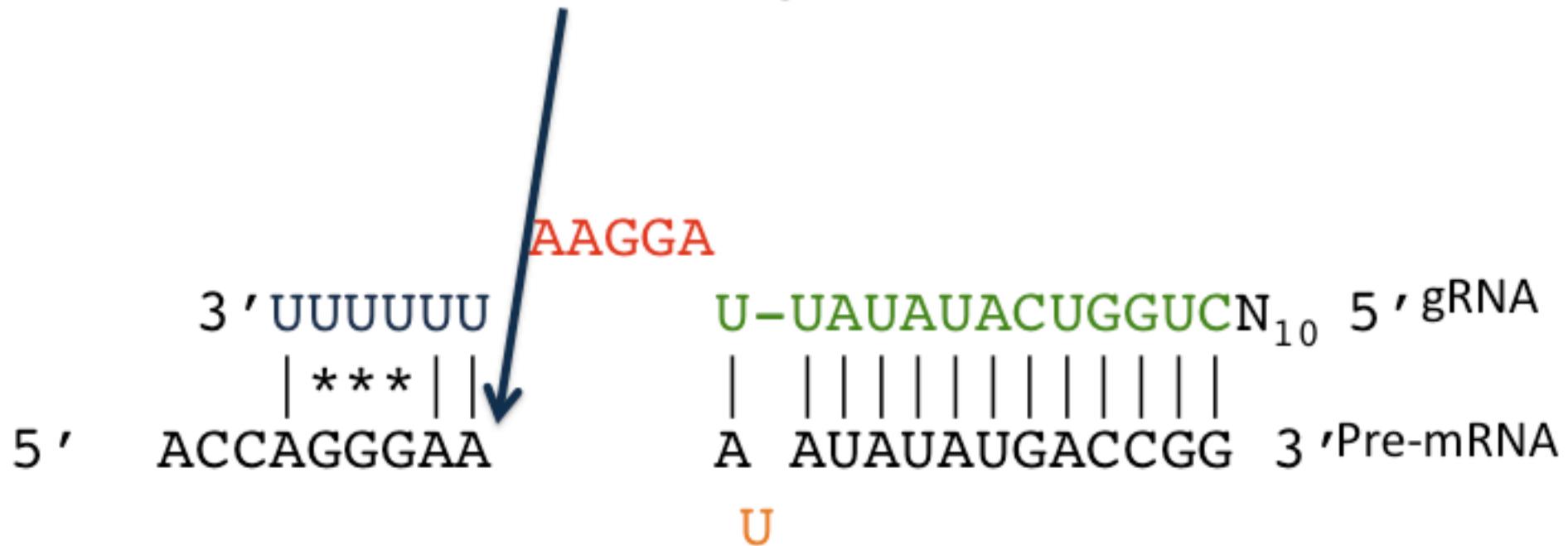
2. Pre-mRNA Cleavage

Poly U tail acts to tether the cleaved fragments of the pre-mRNA together



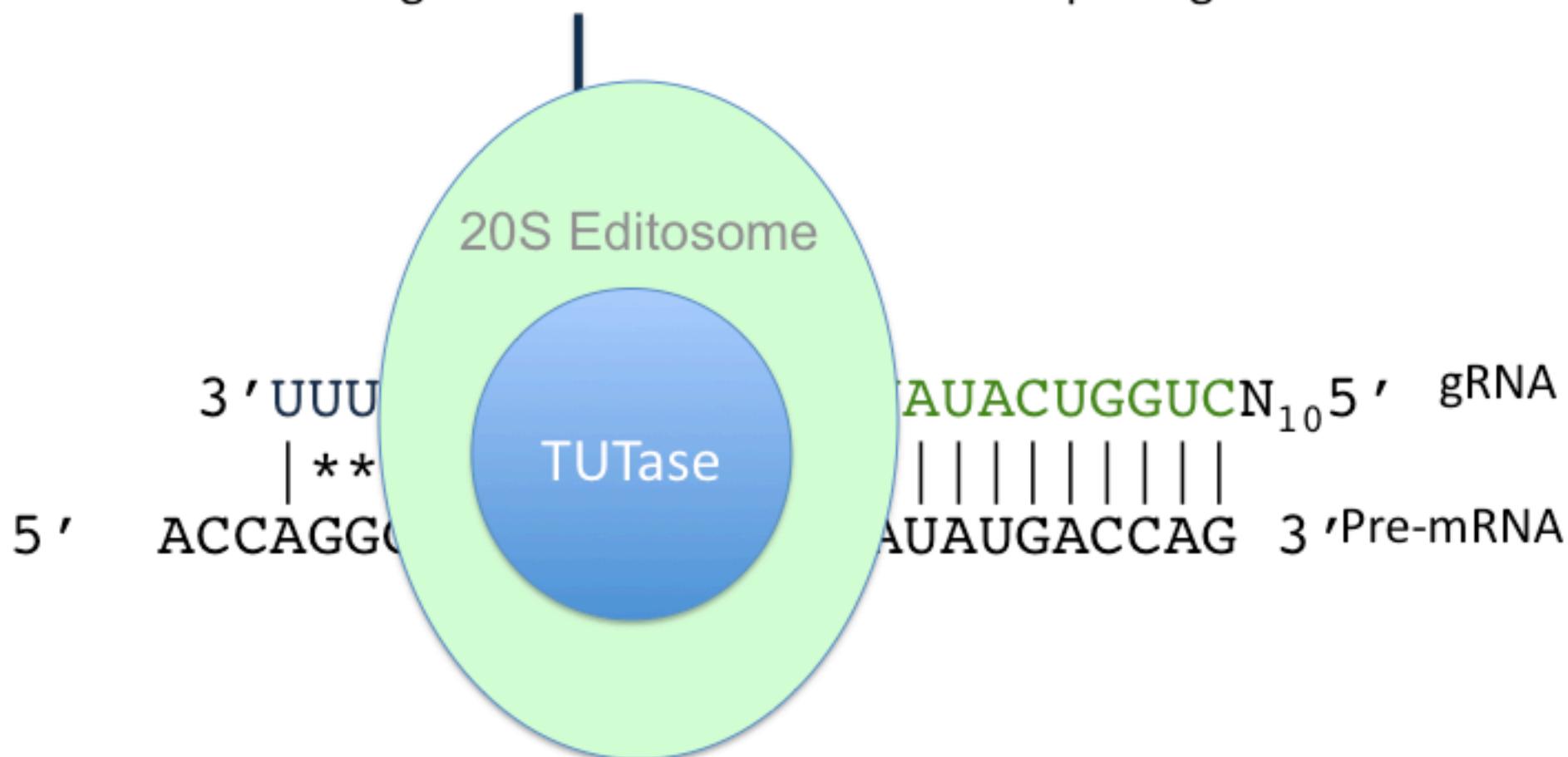
3a. U insertion

TUTase will add Uridylates to
the 3' end of the 5' fragment

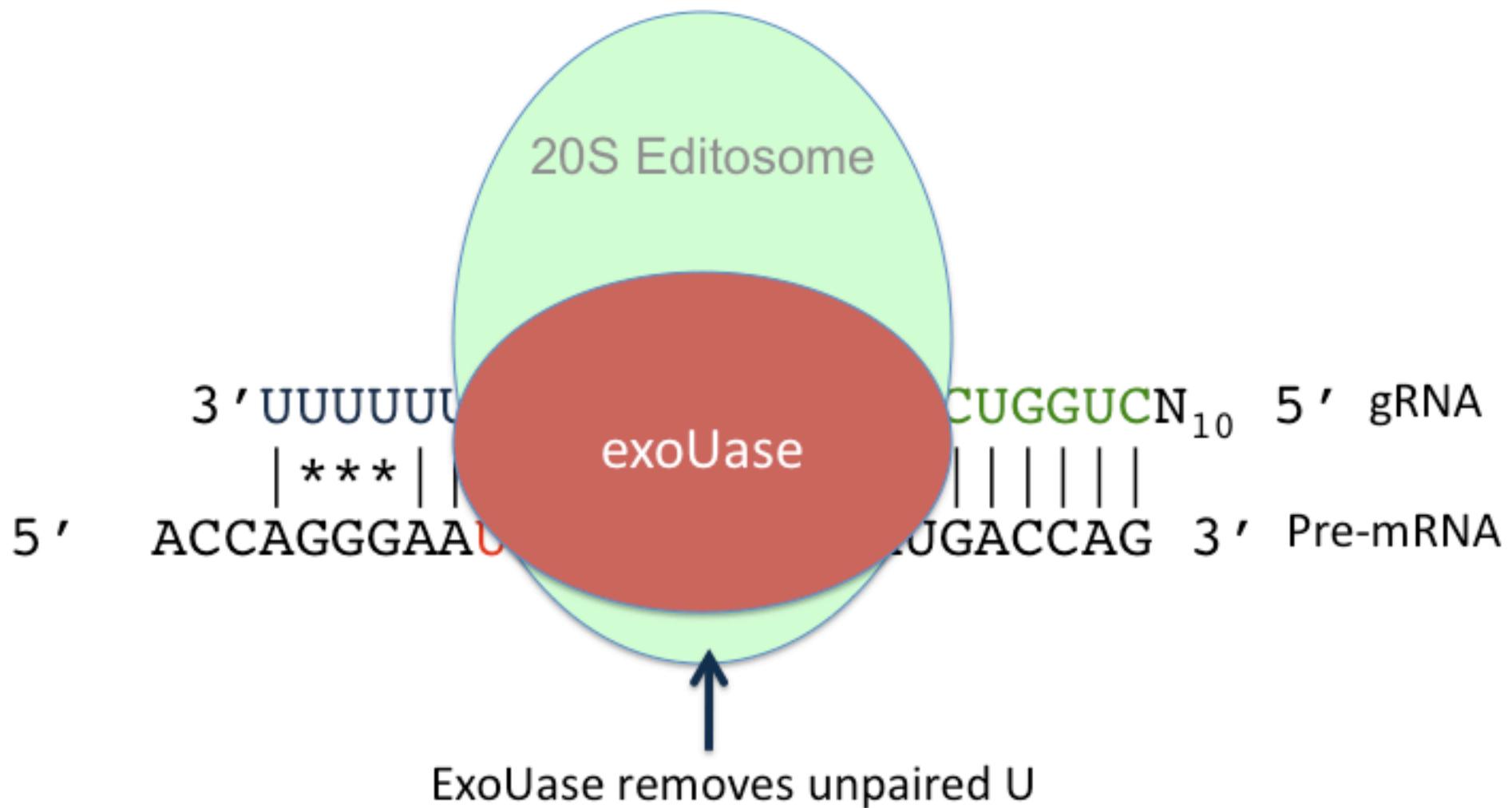


3a. U insertion

U addition/deletion results in pairing of gRNA template to mRNA through Watson-Crick and G:U base pairing



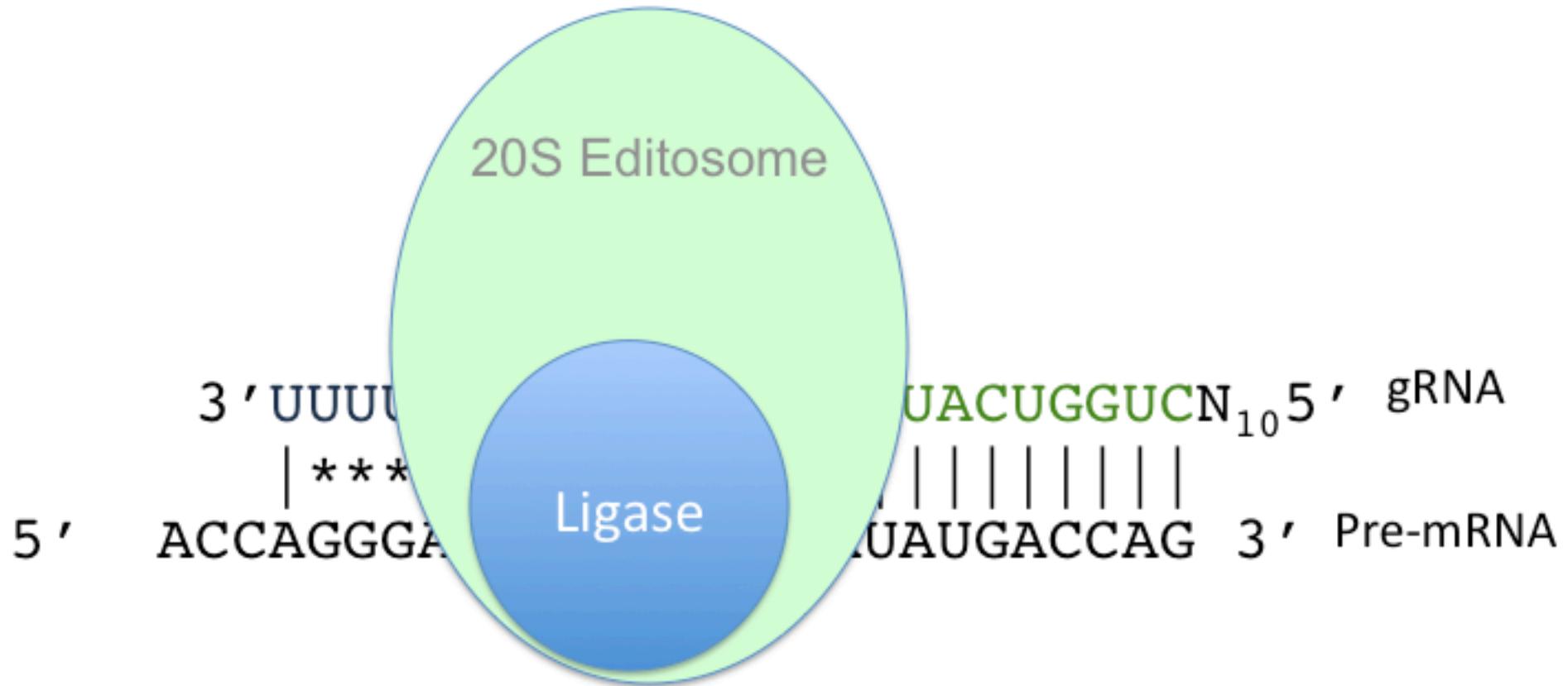
3b. U Deletion



4. Ligation



4. Ligation



1. gRNA/pre-mRNA binding

Editing proceeds 3' to 5' along the pre-mRNA



	New Nomenclature	Alternate Names	Function
20S Editosome	KREPA1	TbMP81/ LC-1/ Band II	Editing complex
	KREPA2	TbMP63/ LC-4/ Band III	
	KREPA3	TbMP42/ LC-7b/ Band VI	
	KREPA4	TbMP24/ LC-10/ Band VI	
	KREPA5	TbMP19	
	KREPA6	TbMP18/ LC-11/ Band VII	
	KREPB1	TbMP90	
	KREPB2	TbMP67	
	KREPB3	TbMP61/ LC-6a	
	KREPB4	TbMP46/ LC-5	
	KREPB5	TbMP44/ LC-8	
	KREPB6	TbMP49/ LC-7c	
	KREPB7	TbMP47	
	KREPB8	TbMP41	
	KREPC1	KREX1/ REX1/ TbMP100/ LC-2/	
	KREPC2	KREX2/ REX2/ TbMP99/ LC-3/ Band I	
	KREL1	REL1/TbMP52/ LC-7a/ Band IV	
	KREL2	REL2/TbMP48/ LC-9/ Band V	
	KRET2	RET2/TbMP57/ LC-6b	
	KREH1	mHel61p	
gRNA tutase	KRET1	RET1/ 3' TUTase	Adds polyU tail to gRNA
MRP1/2 Complex	MRP1	TbgBP21/ Ltp28/ CfgBP29	Assists gRNA/premRNA binding
	MRP2	TbgBP25/ Ltp26/ CfgBP27	
RBP16	RBP16		binds gRNA and regulates gRNA utilization

gRNA other stuff

Example members

<http://rna.bmb.uga.edu/kiss/>

<http://dna.kdna.ucla.edu/trypanosome/database.html>

Role in human Disease

gRNA's are non pathogenic but they are critical to the survival of the Trypanosome.



Potential as a Tool

Maybe, if you study Trypanosomes

Thanks!

