Supplementary Tables

Supplementary Table 1: Summary of substitutions overlapping with known SNPs, or predicted SNPs or RNA editing sites.

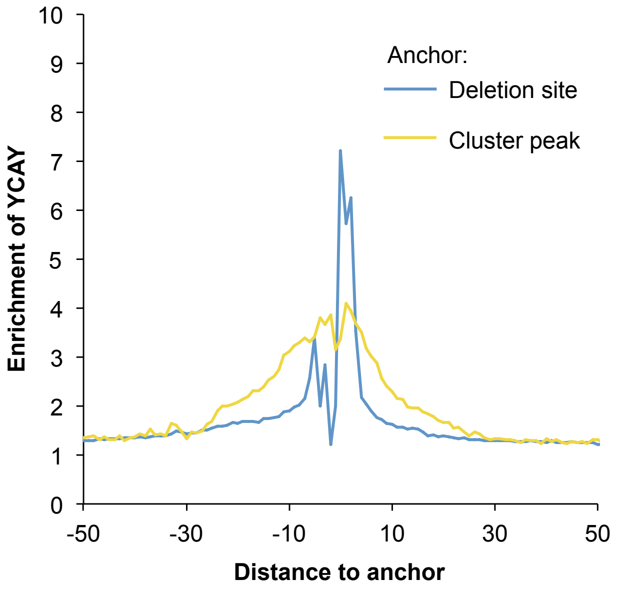
Datasets	Total	Overlapping with known SNPs	Overlapping with predicted SNPs/editing sites	Other
Nova CLIP	1,752,573	83,993 (4.8%)	40,171 (2.3%)	1,628,409 (92.9%)
Ago mRNA CLIP	917,585	39,494 (4.3%)	8,123 (0.9%)	869,968 (94.8%)

Supplementary Tables 2-4 are available in separate spread sheets.

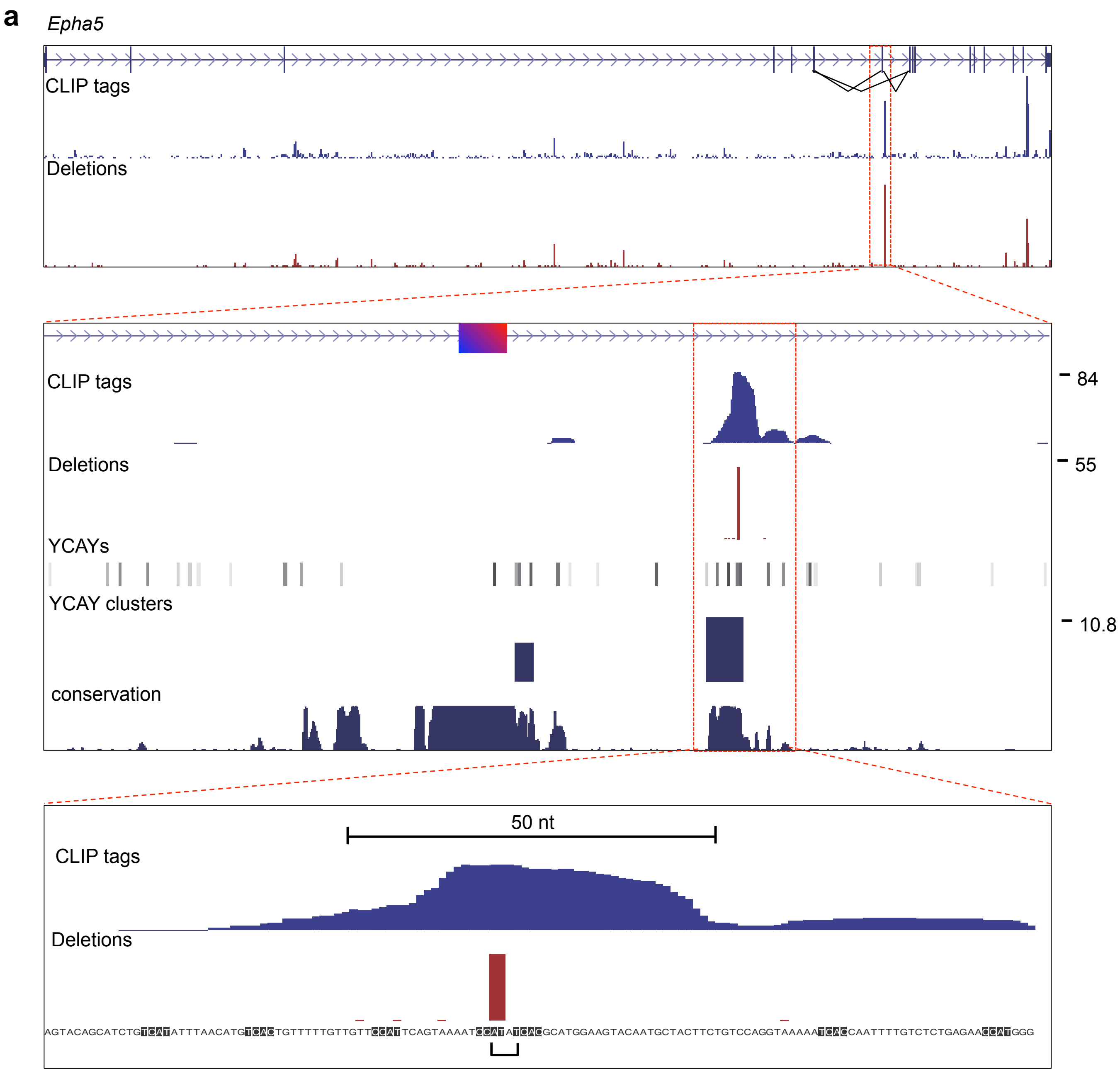
Supplementary Table 5: Summary of seed matches for the top 4 miRNAs identified from sequences around CIMS or cluster peaks.

mi-RNA (seed match)	CIMS [-10,+10]	Cluster peak [-10,+10]
miR-124 (UGCCUU)	100	50
miR-9 (CCAAAG)	60	21
let-7 (UACCUC)	26	19
miR-26 (ACUUGA)	28	5

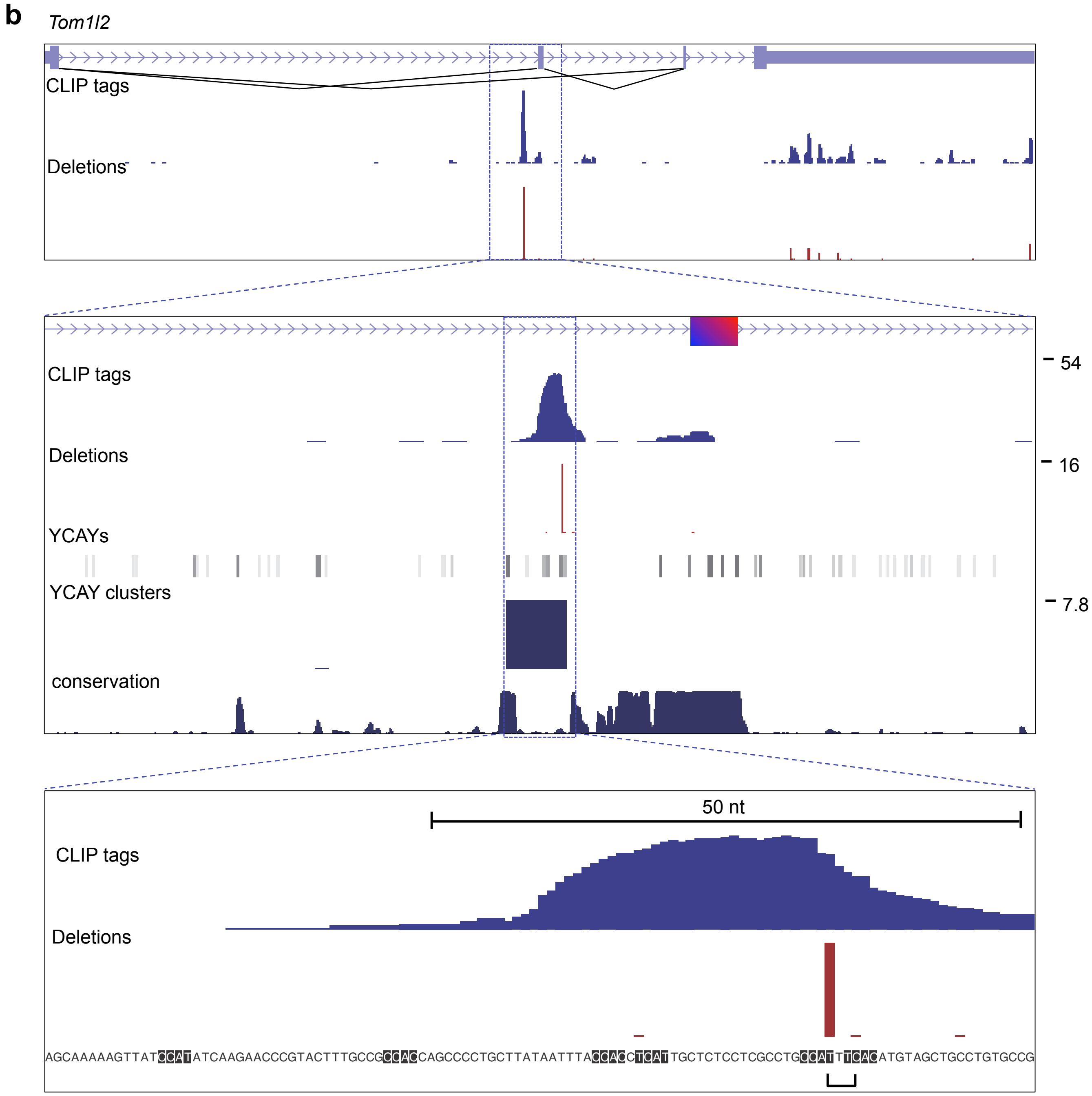
Supplementary Figures



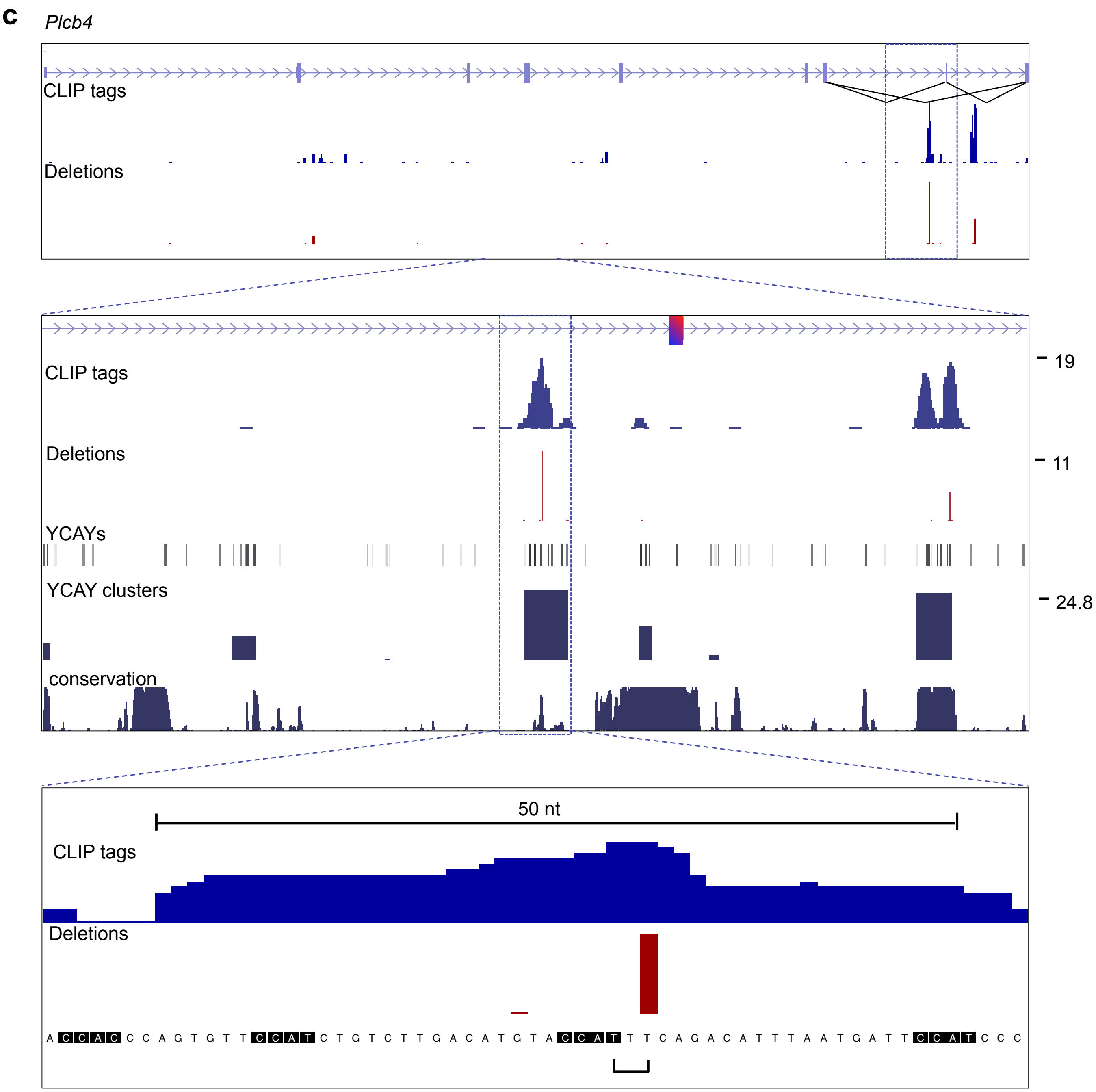
Supplementary Figure 1: CIMS analysis precisely maps Nova binding sites. Similar to Fig. 2c in the main text, but the enrichment of YCAY elements is shown for sequences around low-stringency CIMS with m=1 and those around the corresponding CLIP tag cluster peaks. Motif frequency is normalized using background sequences 500 nt away from CIMS.



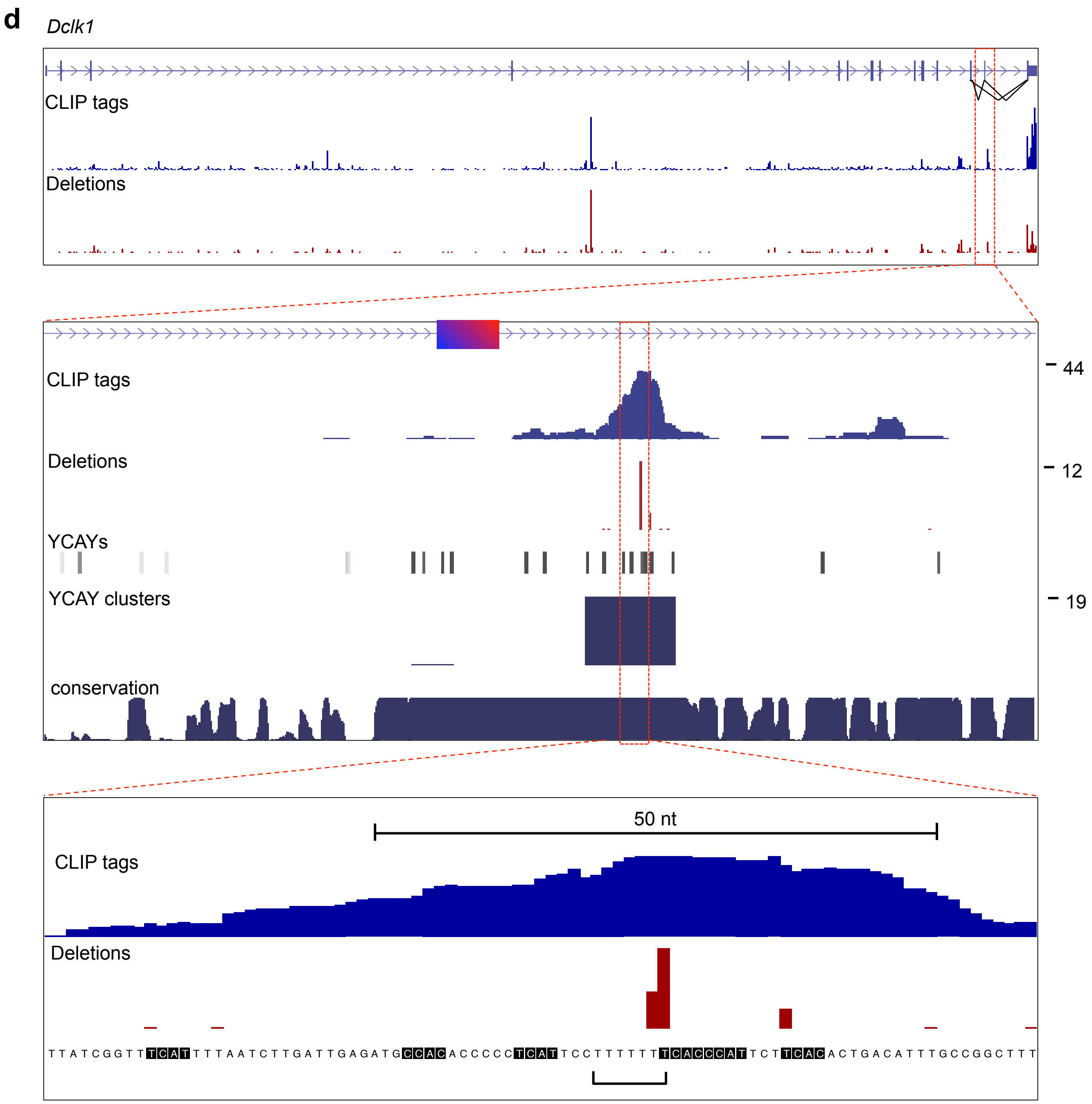
Supplementary Figure 2: Additional examples of Nova CIMS nearby validated Nova-regulated alternative exons.
See Fig. 3d legends in the main text for more details.



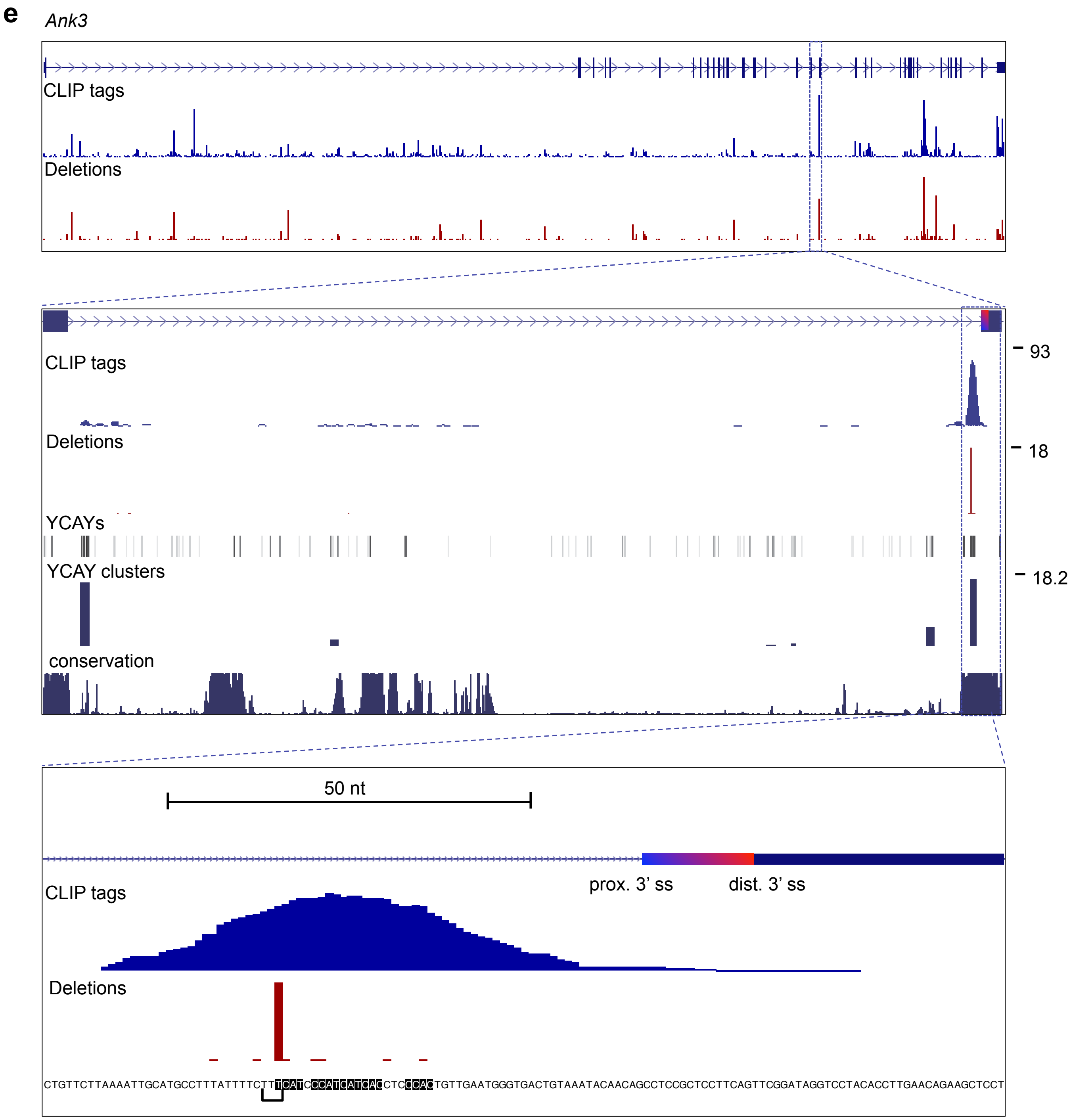
Supplementary Figure 2: Additional examples of Nova CIMS nearby validated Nova-regulated alternative exons (continued).
See Fig. 3d legends in the main text for more details.



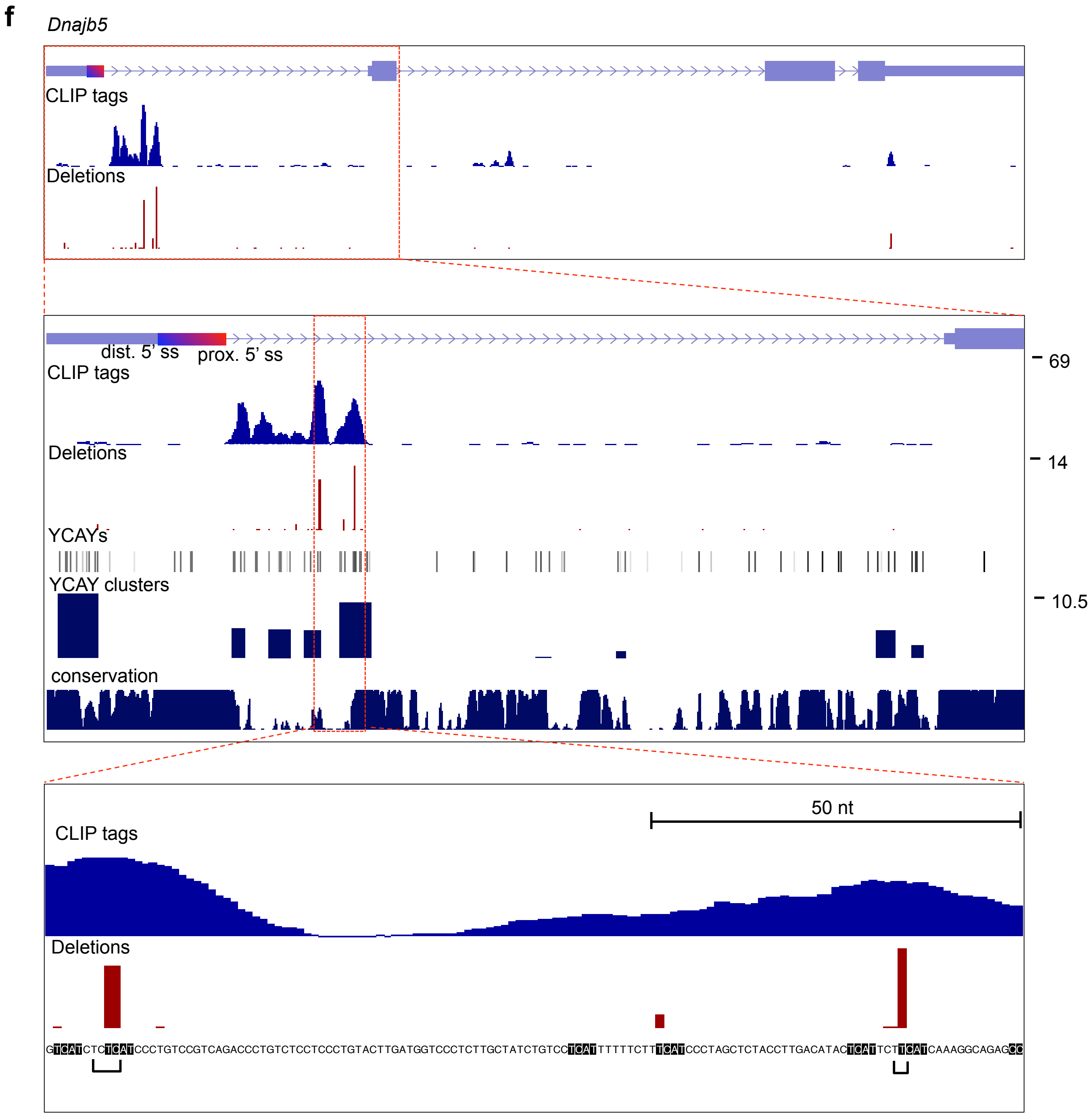
Supplementary Figure 2: Additional examples of Nova CIMS nearby validated Nova-regulated alternative exons (continued).
See Fig. 3d legends in the main text for more details.



Supplementary Figure 2: Additional examples of Nova CIMS nearby validated Nova-regulated alternative exons (continued).
See Fig. 3d legends in the main text for more details.

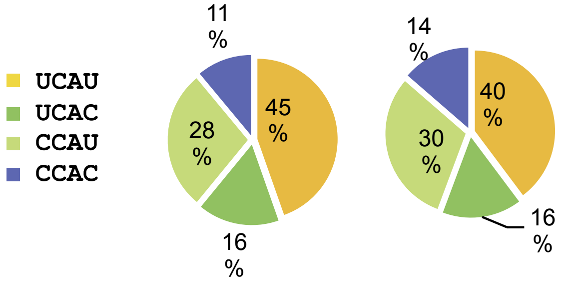


Supplementary Figure 2: Additional examples of Nova CIMS nearby validated Nova-regulated alternative exons (continued).
See Fig. 3d legends in the main text for more details.



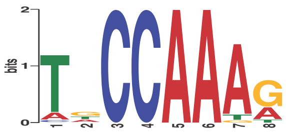
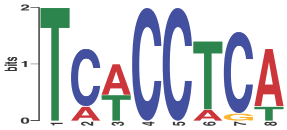
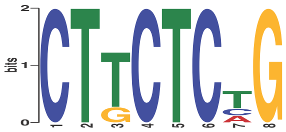
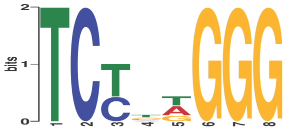
Supplementary Figure 2: Additional examples of Nova CIMS nearby validated Nova-regulated alternative exons (continued).
See Fig. 3d legends in the main text for more details.

Dataset:	CIMS [-16,-6]	CIMS [+6,+16]
YCAY/site	0.29	0.27

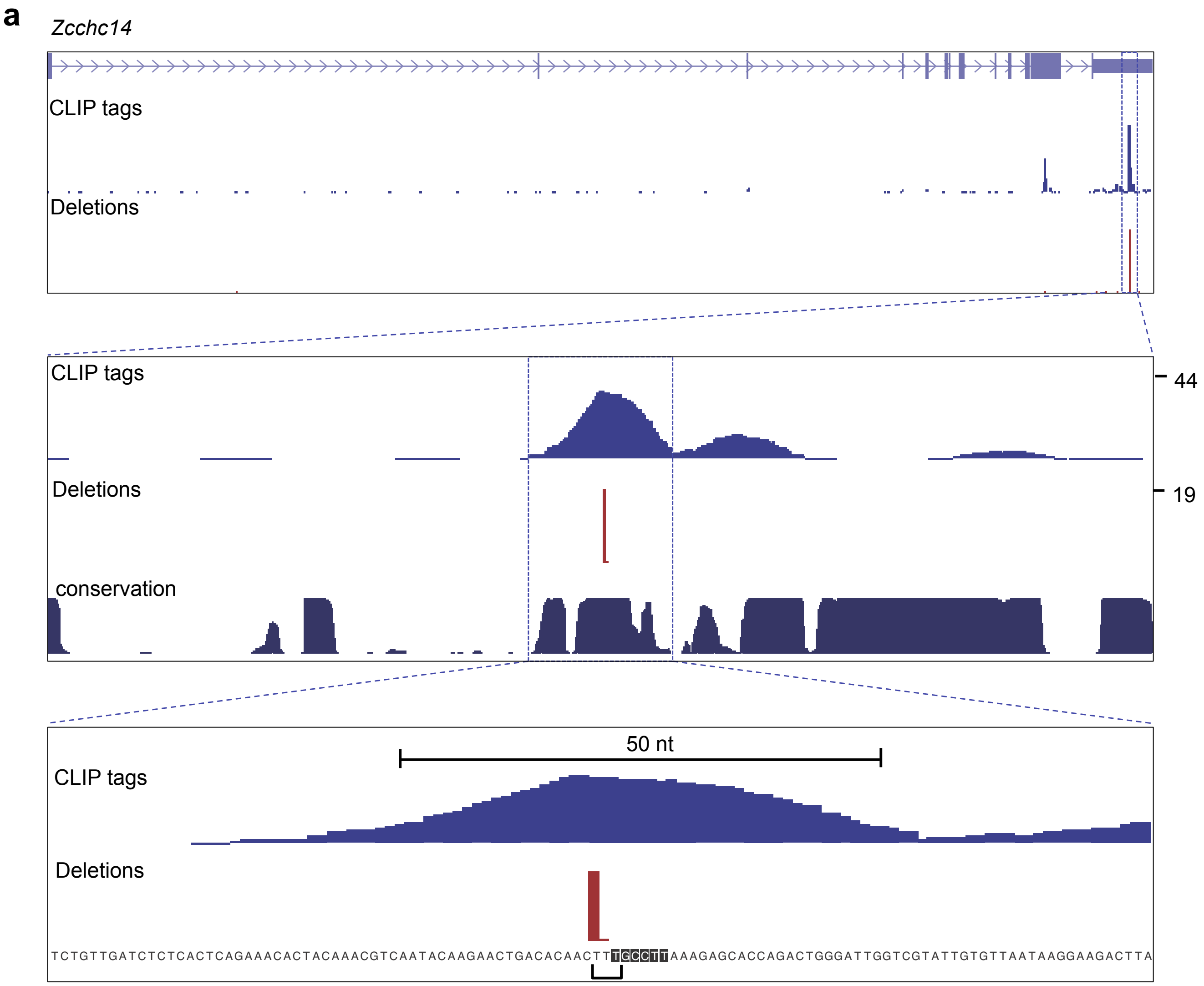


Supplementary Figure 3: Nova prefers U over C in the first or last position of the YCAY element.

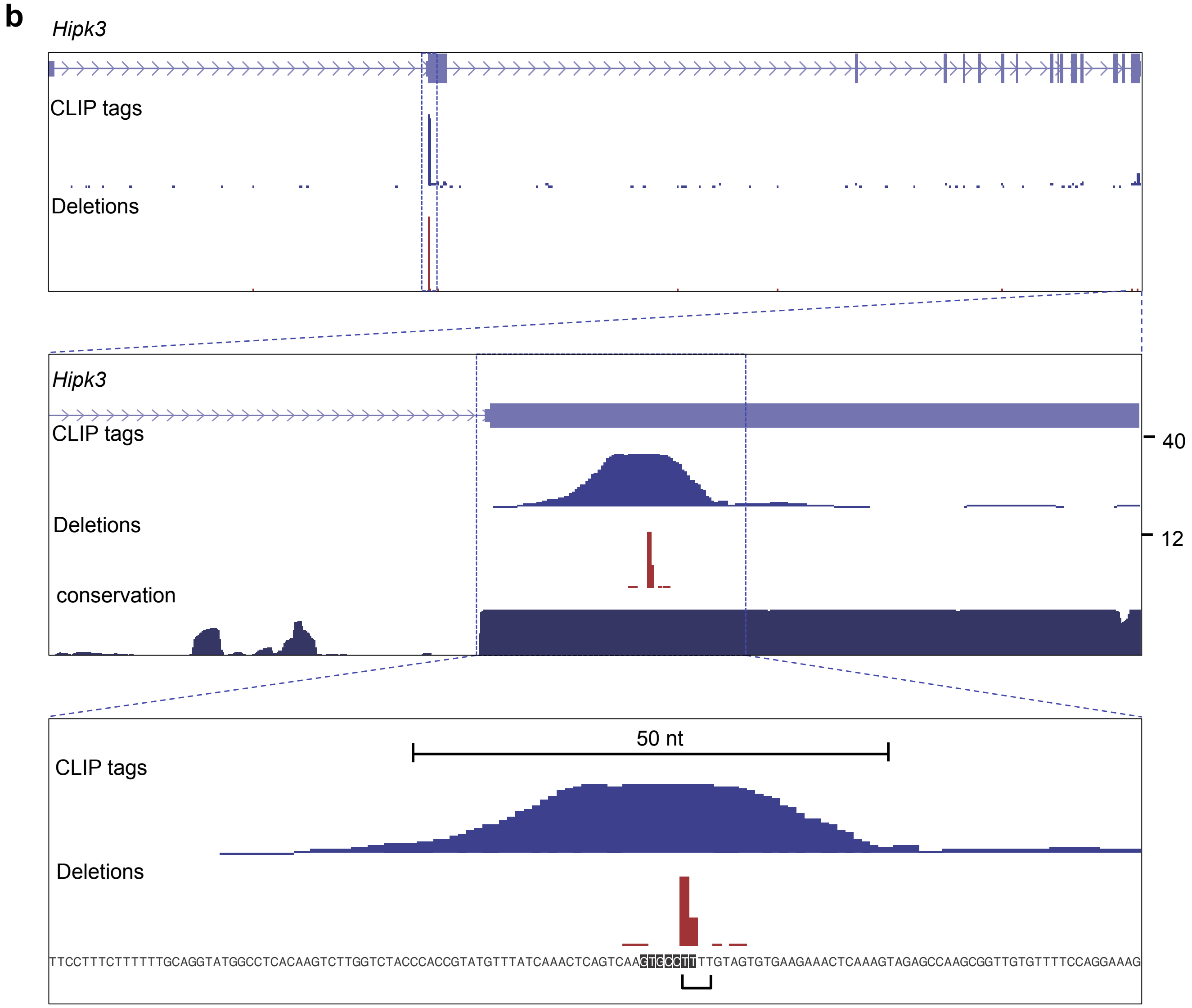
Supplementary to Fig. 4b in the main text. The overall frequency (top) and composition (bottom) of the four tetramers conforming to the YCAY consensus are shown for 11-nt sequences upstream (-16 to -6 nt) or downstream (6 to 16 nt) of CIMS.

	CIMS[-10,10]		Cluster peak[-10,10]	
Rank	**Motif logo**	**Annotation**	**Motif logo**	**Annotation**
1		**miR-124** E=7.0e-193 297 sites		**miR-124** E=1.7e-024 42 sites
2		**miR-9** E=3.3e-082 108 sites		**miR-9** E=5.1e-001 22 sites
3		**miR-27** E=1.5e-029 42 sites		
4		**miR-26** E=3.2e-010 23 sites		
5		E=2.2e-006 19 sites		
6		**let-7** E=4.4e-004 35 sites		
7		E=6.7e-003 18 sites		
8		E=1.4e-001 21 sites		

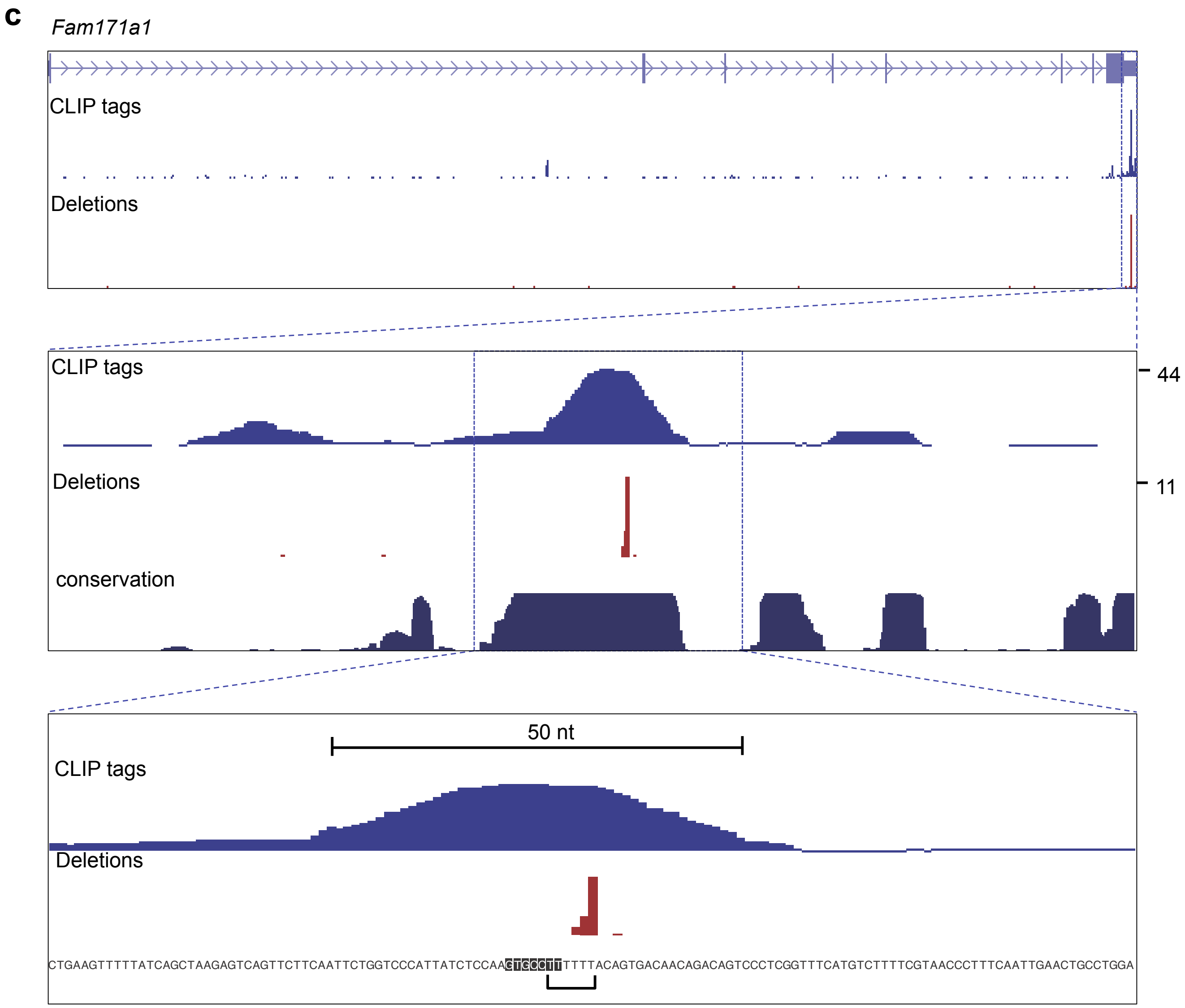
Supplementary Figure 4: *De novo* motif analysis of Ago mRNA CIMS data. Results obtained from sequences around CIMS (-10 to +10, 21 nt) or CLIP tag cluster peaks (-10 to +10, 21 nt) are compared. Only motifs with E-value < 1 are considered significant and shown here. The number of sites and E-value for each motif are indicated, together with the identity of miRNAs, when available.



Supplementary Figure 5: Examples of Ago CIMS with nearby miR-124 seed matches.
Top panel: the gene locus, with the number of CLIP tags and frequency of deletions shown in blue and red, respectively. Middle panel: a zoom-in view of sequences around the CIMS. In addition to CLIP tags and deletions, cross-species sequence conservation in mammals is shown. Bottom panel: A further zoom-in view of sequences around the CIMS. The miR-124 seed match (GUGCCUU or UGCCUU) is highlighted.



Supplementary Figure 5: Examples of Ago CIMS with nearby miR-124 seed matches (continued).
Top panel: the gene locus, with the number of CLIP tags and frequency of deletions shown in blue and red, respectively. Middle panel: a zoom-in view of sequences around the CIMS. In addition to CLIP tags and deletions, cross-species sequence conservation in mammals is shown. Bottom panel: A further zoom-in view of sequences around the CIMS. The miR-124 seed match (GUGCCUU or UGCCUU) is highlighted.



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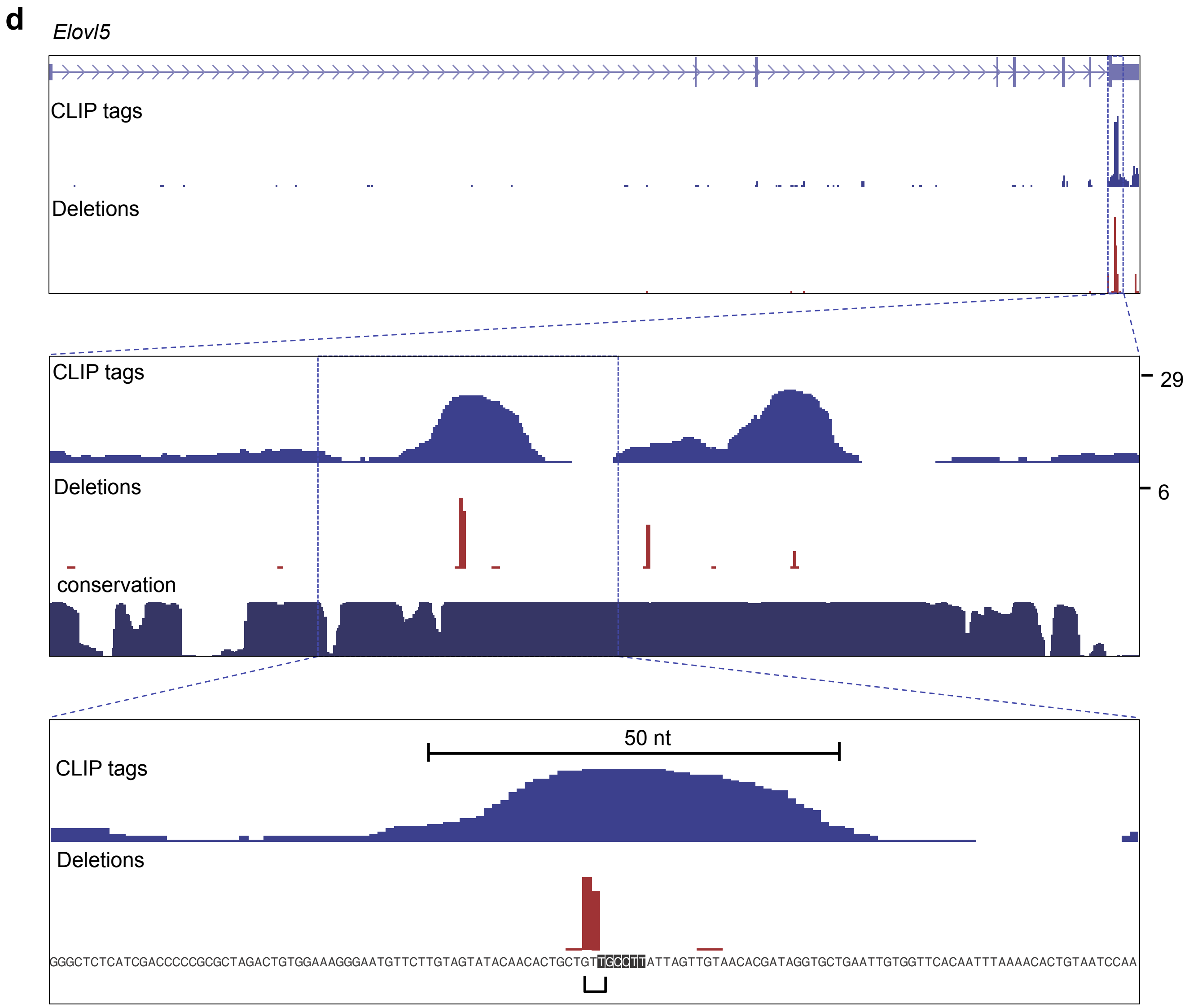

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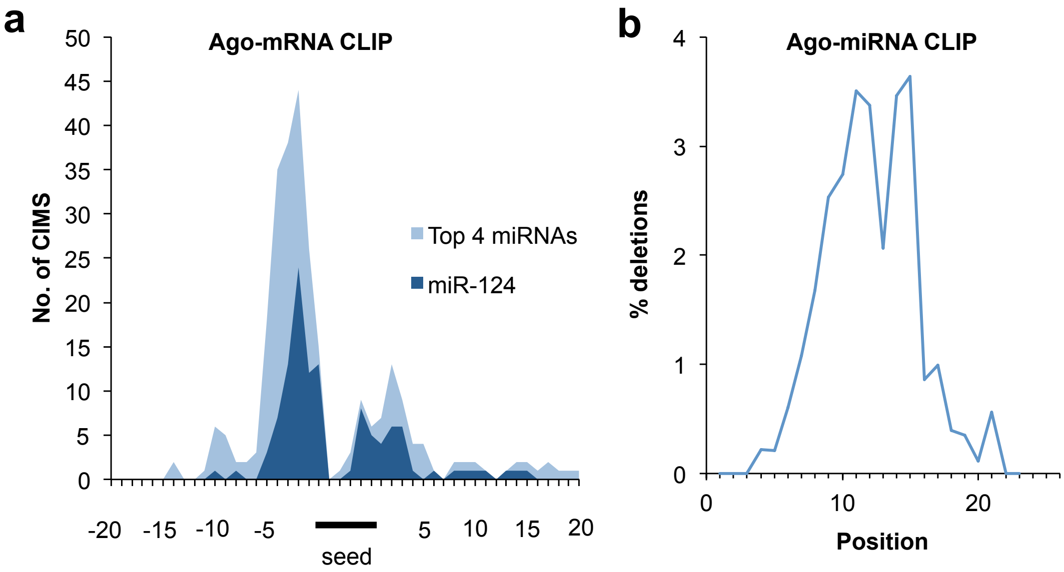

Supplementary Figure 6: Distribution of Ago cross-linking induced mutations on mRNAs relative to miRNA seed matches and miRNAs.

a. The frequency of CIMS in Ago-mRNA CLIP data is plotted relative to miRNA seed matches. The light and dark blue curves represent the top 4 miRNAs (miR-124, miR-9, let-7, and miR-26) pooled together or miR-124 alone.

b. The overall positional frequency of deletions in miRNAs with all miRNAs pooled together.