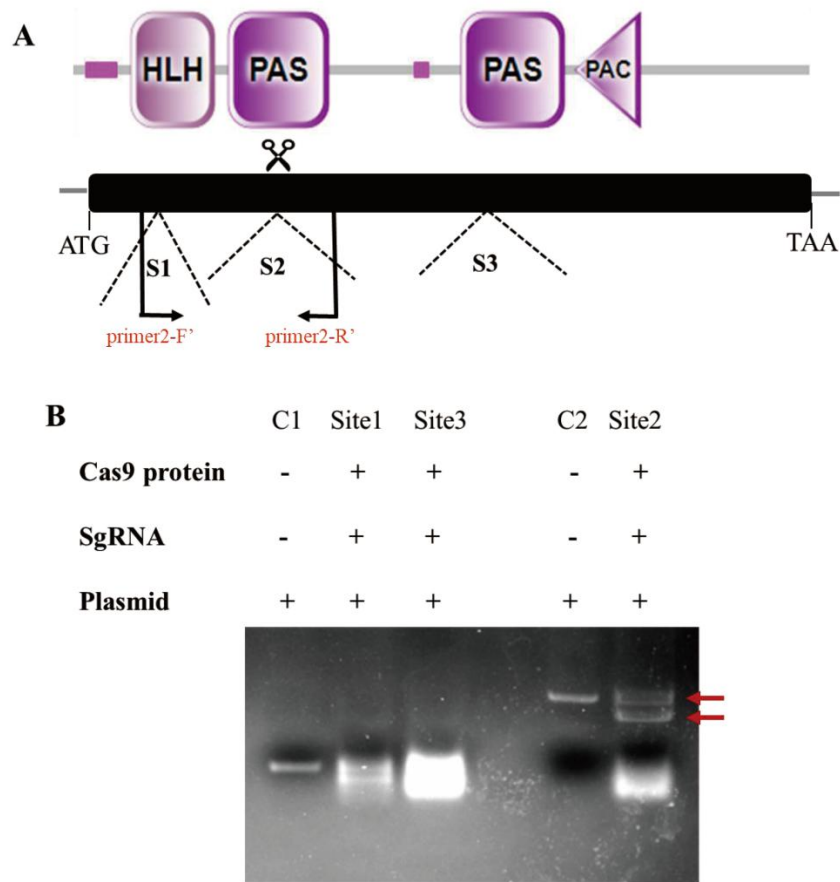
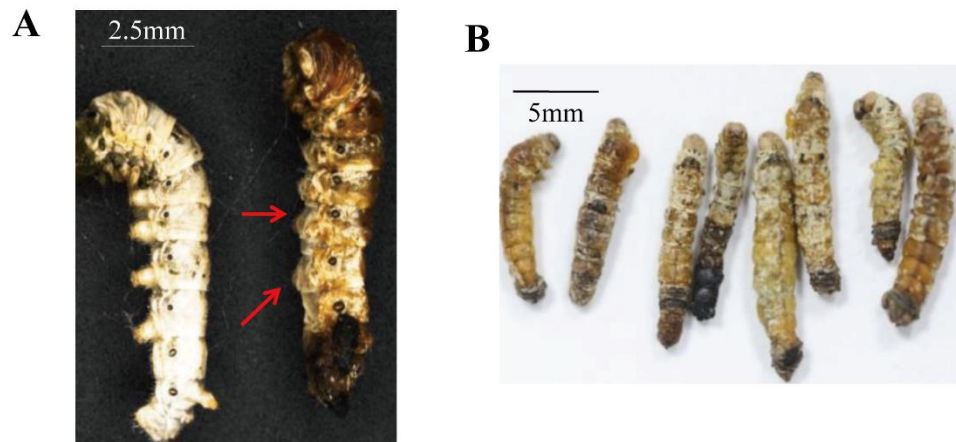


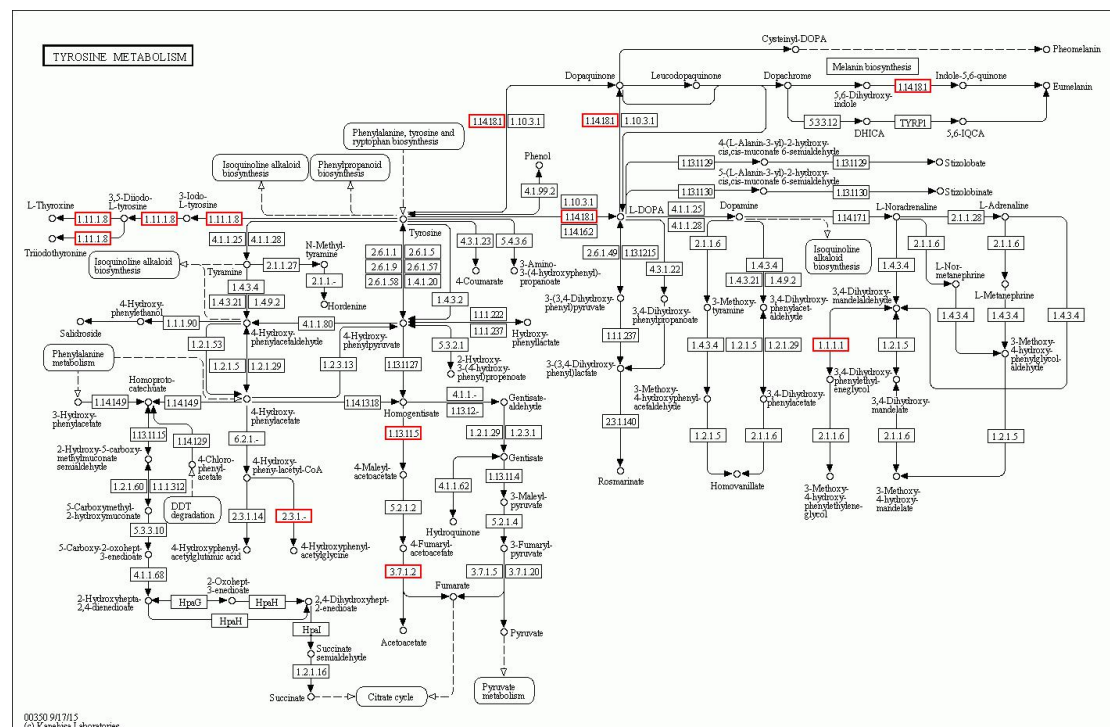
Supplementary Materials
Supplementary Figures



Supplementary Figure S1. Design of sgRNA target sites and *in vitro* verification of sgRNA activity in DNA editing. (A) Schematic of sgRNA-targeting sites. Black box indicates exon; S1, S2, and S3 indicate three sgRNA targeting sites. Primer2-F' and primer2-R' were used to anneal upstream and downstream regions of targeting site 2. Top of picture represents protein domains. (B) Detection of target site activity by *in vitro* DNA cleavage assay. C1 and C2 are two sets of controls. Red arrows indicate cleavage bands.



Supplementary Figure S2. Phenotypes of *Met1* mosaic mutants. (A) Mosaic larvae with degenerated abdominal legs (indicated by red arrows (scale bar: 2.5 mm). (B) Most mosaic larvae failed to shed their old L3 cuticles and pupal patches filled entire body (scale bar: 5 mm).



Supplementary Figure S5. Schematic of tyrosine metabolic pathway.

Supplementary Tables

Supplementary Table S1. Primers used in this study

Primer name	Primer sequence (5'–3')	Primer purpose
<i>Met1</i> -228-sgF1	TAATACGACTCACTATAGGATTAATGCATTGTACGTTTTAGA GCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC	Preparation of sgRNA templates
<i>Met1</i> -563-sgF2	TAATACGACTCACTATAGGGTAAATGTGACAACGTAGTTTTA GAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC	Preparation of sgRNA templates
<i>Met1</i> -899-sgF3	TAATACGACTCACTATAGGACGAGACATTTGATAGAGTTTTA GAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC	Preparation of sgRNA templates
sgRNA-R	AAAAGCACCGACTCGGTGCCACTTTTTCAAGTTGATAACGG ACTAGCCTTATTTTAACTTGCTATTTCTAGCTCTAAAA	Preparation of sgRNA templates
primer2-F	CCGTCAACAAACTGCGTAAC	Identification of somatic mutations
primer2-R	AACCGGAGCATCATCATAAG	Identification of somatic mutations
BmKr-h1-qRT-F	ACCCATACTGGCGAGCGACCAT	qRT-PCR
BmKr-h1-qRT-R	CCTCTCCTTTGTGTGAATACGACGG	qRT-PCR
BmUSP-qRT-F	AATGTCGGTAACTGCGTTGA	qRT-PCR
BmUSP-qRT-R	TCGAGTTCAACATTGGGTGT	qRT-PCR
BmRp49-qRT-F	CTCCCTCGAGAAGTCCTACGAACT	qRT-PCR
BmRp49-qRT-R	TGCTGGGCTCTTTCCACGA	qRT-PCR
Krh1-probe-biotin-F	GCGGTGGGCCTCCACGTGTCGAACG	EMSA
Krh1-probe-biotin-R	CGTTCGACACGTGGAGGCCACCGC	EMSA
Met-CDS-Sgfl-F'	GACCGCGATCGCCATGAACTCGTCTATTGGGACA	Preparation of <i>Met1</i> CDS
Met-CDS-PmeI-R'	GTGCGTTTAAACCAATCCACTGTGCCTTTTTAAAT	Preparation of <i>Met1</i> CDS

Supplementary Table S2. Summary of RNA-seq data.

Sample name	Total reads	Total mapped	Clean bases (Gb)
WT_pi_1	26,384,885	75.10%	7.92
WT_pi_2	23,800,305	75.30%	7.14
WT_pi_3	21,947,983	76.20%	6.58
MU_pi_1	30,877,089	75.70%	9.26
MU_pi_2	25,895,866	75.00%	7.77
MU_pi_3	20,127,450	76.00%	6.04
WT_nao_1	24,307,289	78.10%	7.29
WT_nao_2	19,944,469	73.30%	5.98
WT_nao_3	30,056,928	76.20%	9.02
MU_nao_1	38,577,544	73.80%	11.57
MU_nao_2	21,503,600	76.50%	6.45
MU_nao_3	20,181,953	76.90%	6.05
D-L5D3-nao-1	26,117,392	71.00%	7.83
D-L5D3-nao-2	20,514,005	75.60%	6.15
D-L5D3-nao-3	40,385,534	82.10%	12.12
D-L5D6-nao-1	23,959,344	78.60%	7.19
D-L5D6-nao-2	28,793,397	82.90%	8.64
D-L5D6-nao-3	26,844,531	82.40%	8.05
D-W-nao-1	26,127,440	81.40%	7.84
D-W-nao-2	28,294,379	82.00%	8.49
D-W-nao-3	26,469,482	82.20%	7.94
D-PP-nao-1	25,382,740	81.90%	7.62
D-PP-nao-2	23,045,512	81.30%	6.91
D-PP-nao-3	23,008,945	80.80%	6.90
D-P0-nao-1	28,704,179	79.60%	8.61
D-P0-nao-2	26,393,999	81.10%	7.92
D-P0-nao-3	22,502,410	81.20%	6.75
D-P4-nao-1	25,903,855	80.50%	7.77
D-P4-nao-2	22,714,798	81.40%	6.81
D-P4-nao-3	18,927,565	81.80%	5.86
Wild-4L2D-brain-1	29,172,011	57.60%	8.75
Wild-4L2D-brain-2	28,149,082	56.80%	8.44
Wild-4L2D-brain-3	25,948,446	57.70%	7.79
Wild-4L4D-brain-1	24,785,866	57.10%	7.44
Wild-4L4D-brain-2	24,994,197	57.40%	7.50
Wild-4L4D-brain-3	28,792,991	56.80%	8.64
Wild-W-brain-1	25,931,827	57.80%	7.78
Wild-W-brain-2	28,676,175	57.50%	8.60
Wild-W-brain-3	27,469,778	56.00%	8.24

WT_pi: wild type epidermis; MU_pi: mutant epidermis; WT_nao: wild type brain; MU_nao: mutant brain; D-L5D3-nao: *B. mori* brain at third day of fifth instar larval stage; D-L5D6-nao: *B. mori* brain at sixth day of fifth instar larval stage; D-W-nao: *B. mori* brain at wandering stage;

D-PP-nao: *B. mori* brain at prepupa stage; D-P0-nao: *B. mori* brain at day 0 of pupal stage; D-P4-nao: *B. mori* brain at fourth day of pupal stage; Wild-4L2D-brain: *B. mandarina* brain at second day of fourth instar larval stage; Wild-4L4D-brain: *B. mandarina* brain at fourth day of fourth instar larval stage; Wild-W-brain-1: *B. mandarina* brain at wandering stage; 1,2,3: Three sample repeats; Gb: Giga base.

Supplementary Table S3. Information on differentially expressed genes in wild-type and mutant (MU) epidermis.

Supplementary Table S4. Information on differentially expressed genes in wild-type and mutant (MU) brains.

Supplementary Table S5. Information on differentially expressed genes in *B. mori* and *B. mandarina* brains at mid-point of final larval stage (Mid_L).

Supplementary Table S6. Information on differentially expressed genes in *B. mori* and *B. mandarina* brains at final day of final larval stage (L_end).

Supplementary Table S7. Information on differentially expressed genes in *B. mori* and *B. mandarina* brains at wandering stage (W).

Supplementary Tables S3-S7 are listed as separate files due to their large size.

Supplementary Table S8. KEGG enrichment analysis of DEGs in *B. mori* and *B. mandarina* brains at three larval stages. Redundant and human disease items were removed.

	Rank	ID	Description	Corrected <i>p</i> -Value
<i>L_mid</i>				
	1	ko00350	Tyrosine metabolism	0.1295
	1	ko00052	Galactose metabolism	0.1295
	2	ko04512	ECM-receptor interaction	0.2036
	3	ko04360	Axon guidance	0.3100
	3	ko00430	Taurine and hypotaurine metabolism	0.3100
	3	ko04974	Protein digestion and absorption	0.3100
<i>L_end</i>				
	1	ko04360	Axon guidance	0.0215
	2	ko04520	Adherens junction	0.0670
	3	ko04919	Thyroid hormone signaling pathway	0.0837
<i>W</i>				
	1	ko04510	Focal adhesion	0.3502
	1	ko04151	PI3K-Akt signaling pathway	0.3502
	2	ko01210	2-Oxocarboxylic acid metabolism	0.4718
	2	ko04070	Phosphatidylinositol signaling system	0.4718
	2	ko04810	Regulation of actin cytoskeleton	0.4718
	2	ko02010	ABC transporters	0.4718
	3	ko04919	Thyroid hormone signaling pathway	0.5083