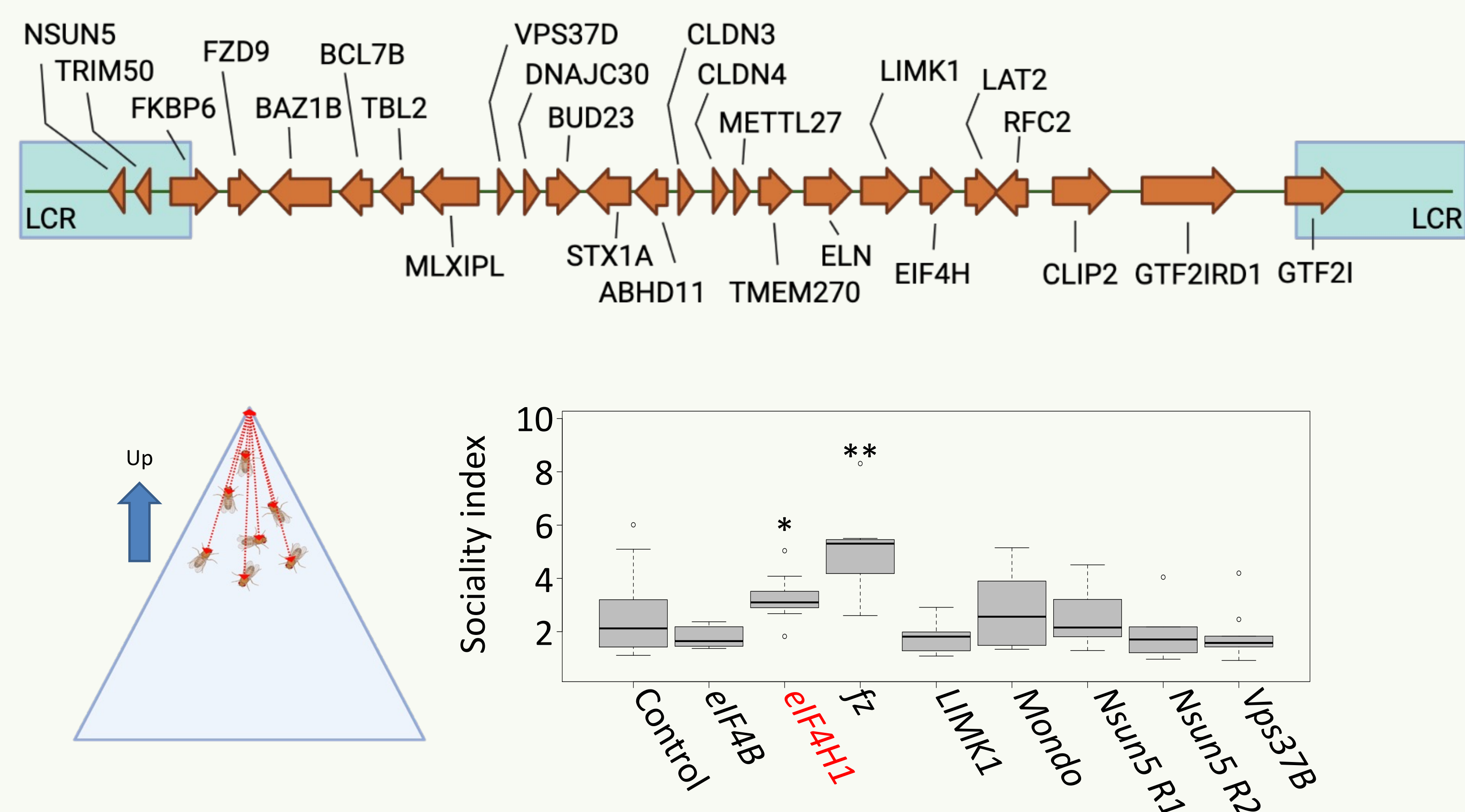


# A *Drosophila* model for the role of Williams Syndrome-related factor eIF4H in neural development and behavior

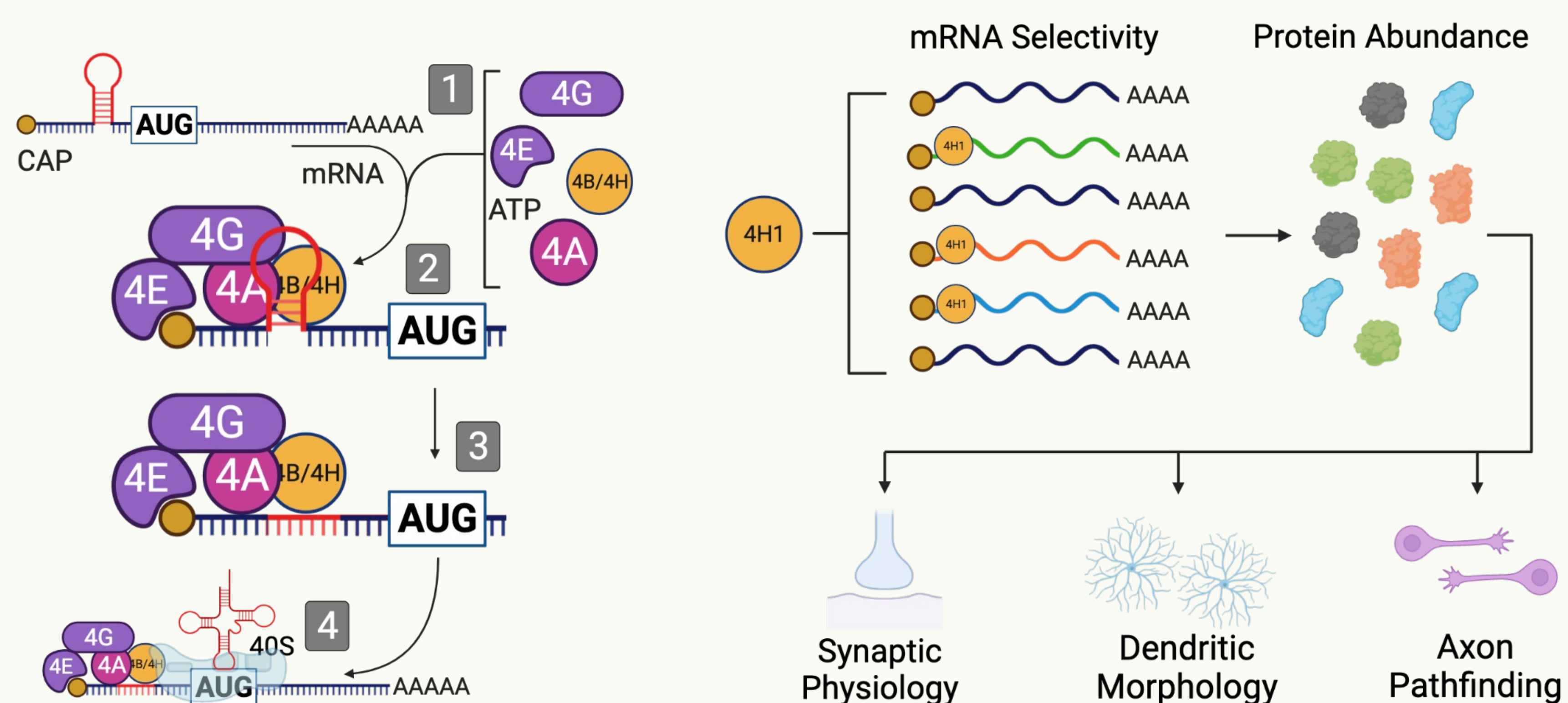
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## BACKGROUND



Top: Williams syndrome critical region (WSCR) deletion in humans results in haploinsufficiency of ~25 genes and a characteristic cognitive profile<sup>1</sup>. Bottom: Knockdown of *Drosophila* WSCR orthologs reveals *eIF4H1* as a regulator of fly social behavior.

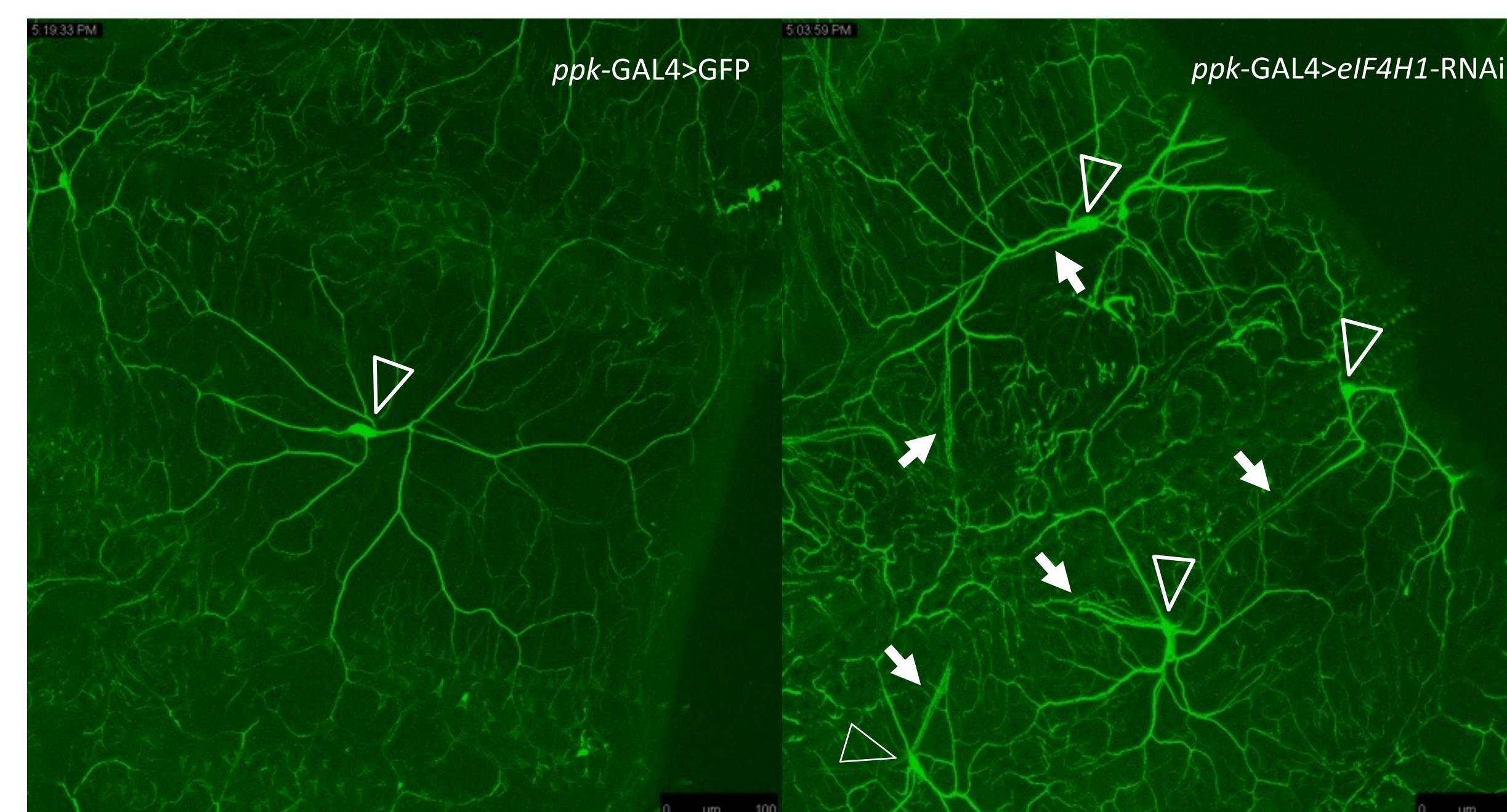
## WORKING MODEL



Left: Fly eIF4H1 functions to resolve RNA secondary structure in the 5' UTR and promote translation initiation<sup>2</sup>. Right: We hypothesize that eIF4H1 binds specific mRNA species, thus regulating protein abundance and diversity in the translome.

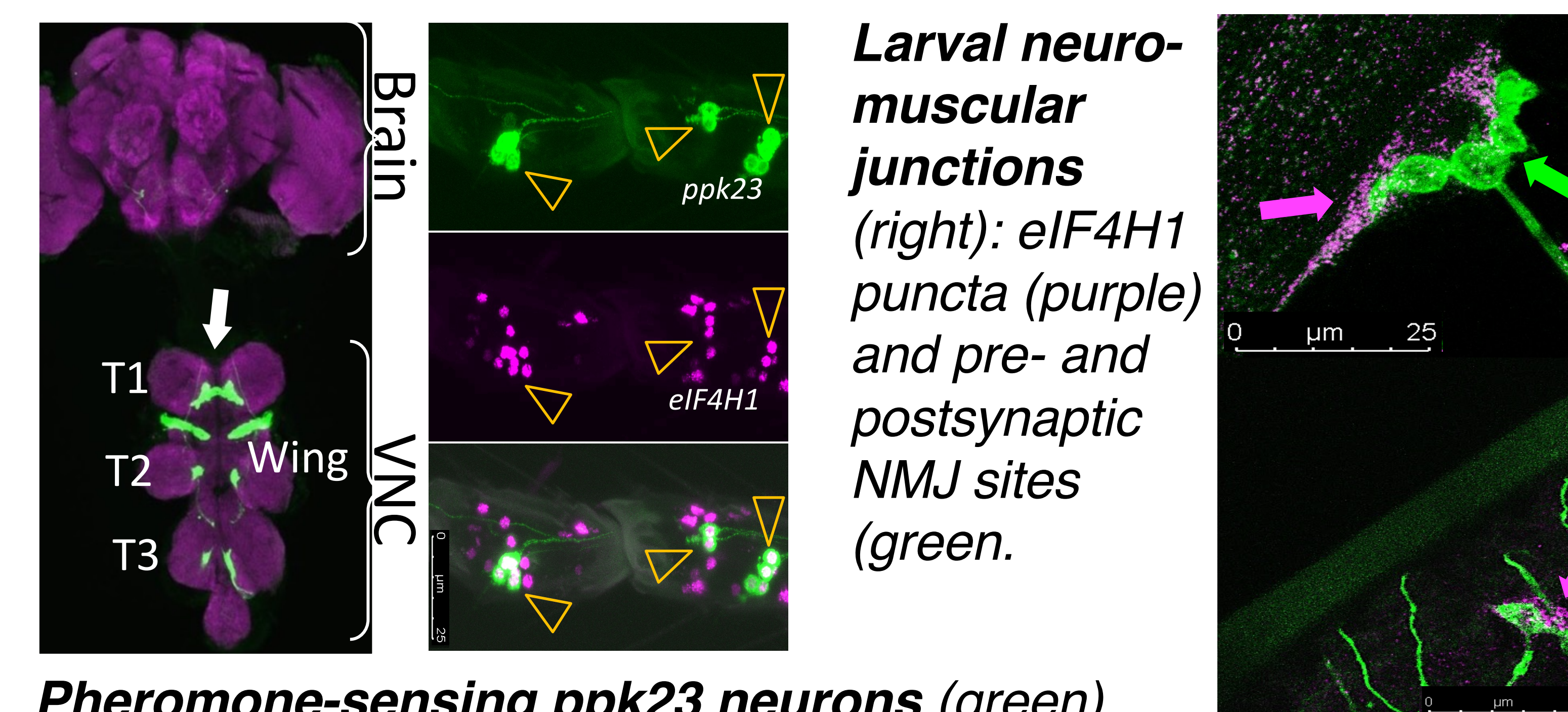
## PRELIMINARY RESULTS

### (1) eIF4H1 knockdown yields abnormal dendritic field morphology



Larval multidendritic neurons: soma (arrowheads) and dendrite branches, collapsed in RNAi condition (solid arrows).

### (2) GFP-tagged allele of eIF4H1 is present in specific neuron subpopulations



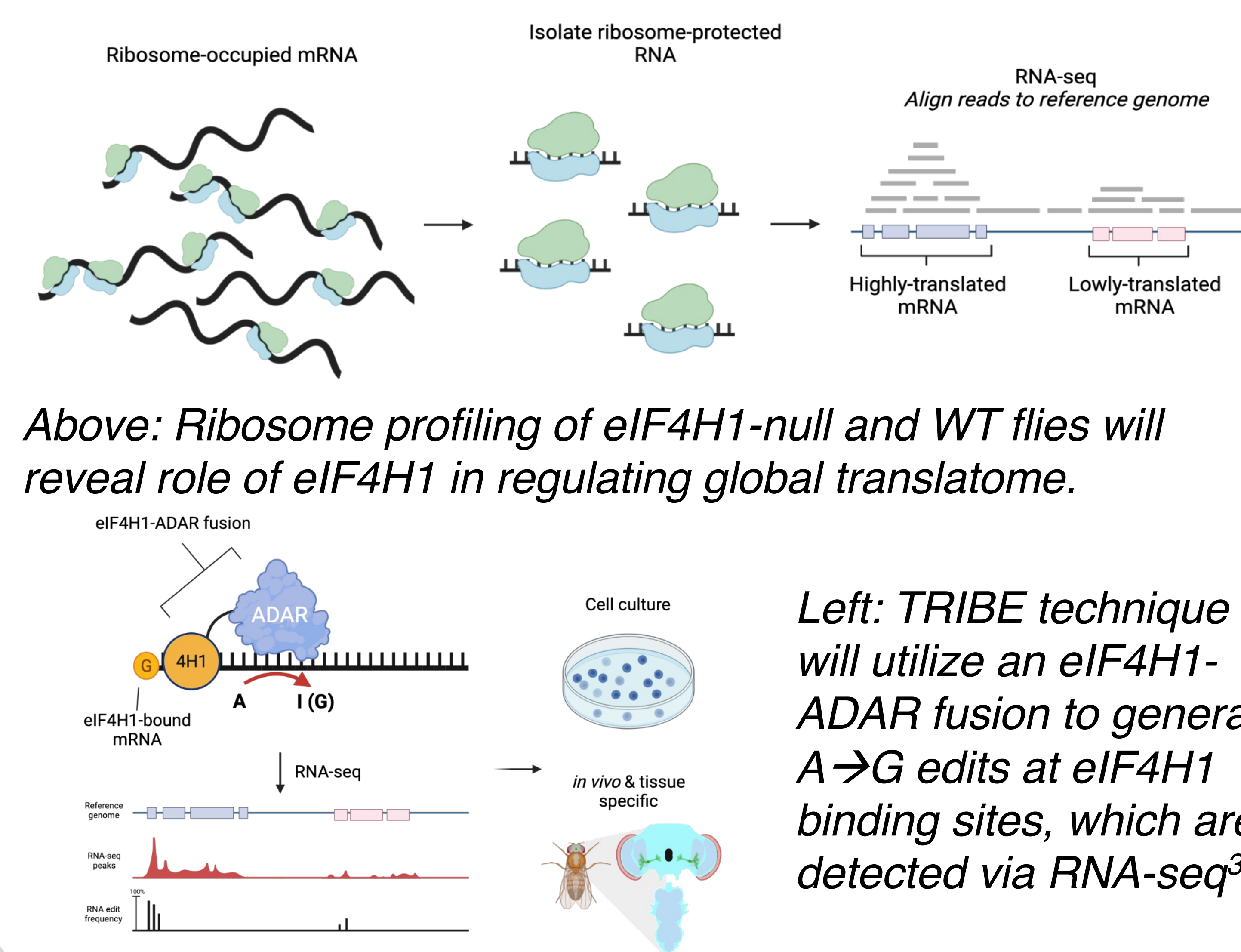
Pheromone-sensing *ppk23* neurons (green) and eIF4H1 puncta (purple); midline crossing (arrow)

## APPROACHES

### Characterize neuronal outcomes of *eIF4H1* knockdown via RNAi

- Larval multidendritic neurons:
  - Sensory neurons that tile the larval body wall
  - Quantify and describe effect of *eIF4H1* RNAi on dendrite branching (right)
- ppk23*-expressing sensory neurons:
  - Only cross body midline in male T1 segment of the ventral nerve cord (see (2) in prelim. results)
  - Determine effect of RNAi on midline crossing
- Larval neuromuscular junction:
  - Determine effect of *eIF4H1* RNAi on NMJ presynaptic neuron quantity and morphology

### Identify mRNA targets of eIF4H1



Above: Ribosome profiling of *eIF4H1*-null and WT flies will reveal role of *eIF4H1* in regulating global translome.

Left: TRIBE technique will utilize an *eIF4H1*-ADAR fusion to generate A→G edits at *eIF4H1* binding sites, which are detected via RNA-seq<sup>3</sup>.

## REFERENCES

- Kozel et al. 2021 *Nat. Genet.* (source for WSCR figure)
- Parsyan et al. 2011 *Nat. Rev. Genet.*
- McMahon et al. 2016 *Cell* (source for TRIBE figure)
- Figures created with BioRender.com

