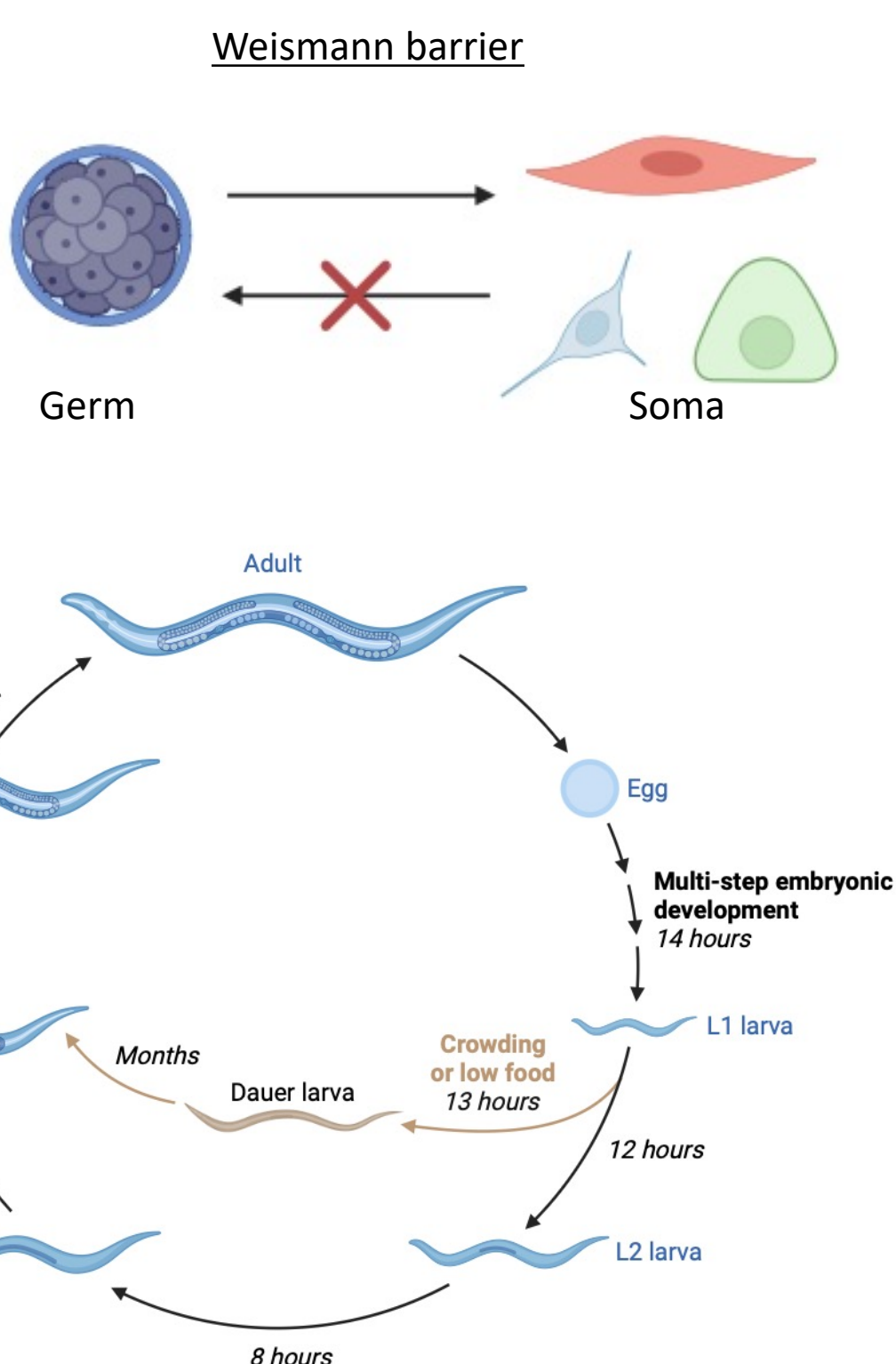


# Neuronal miRNAs regulate the expression of histone writers to maintain germline stem cell quiescence

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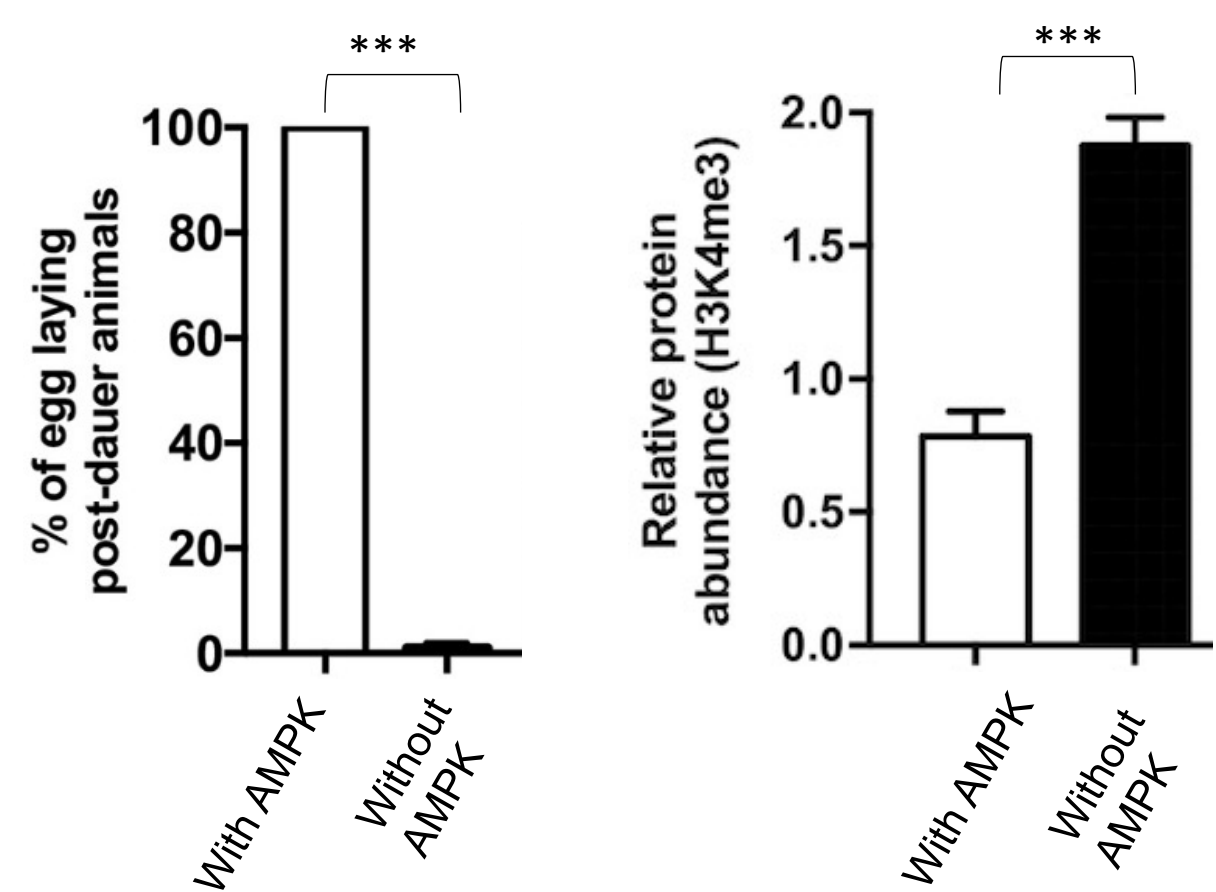
## Background

Weismann barrier stipulates that information only travels from the germline to the soma

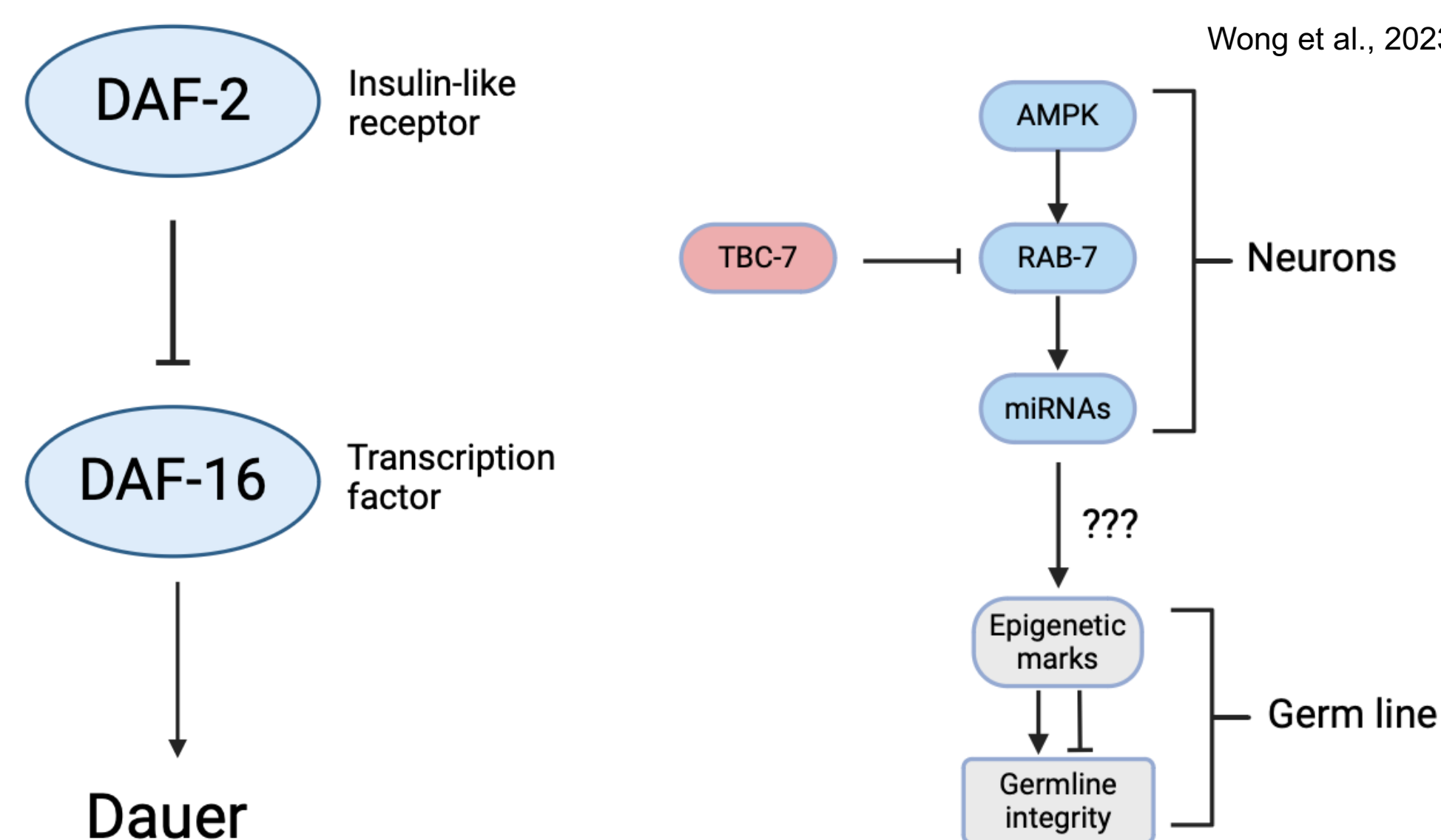


*C. elegans* can enter a quiescent stage under environmentally stressful conditions

- AMPK mutants lose their germline integrity due to inappropriate germ cell divisions
- AMPK mutants have altered epigenetic marks in their germline



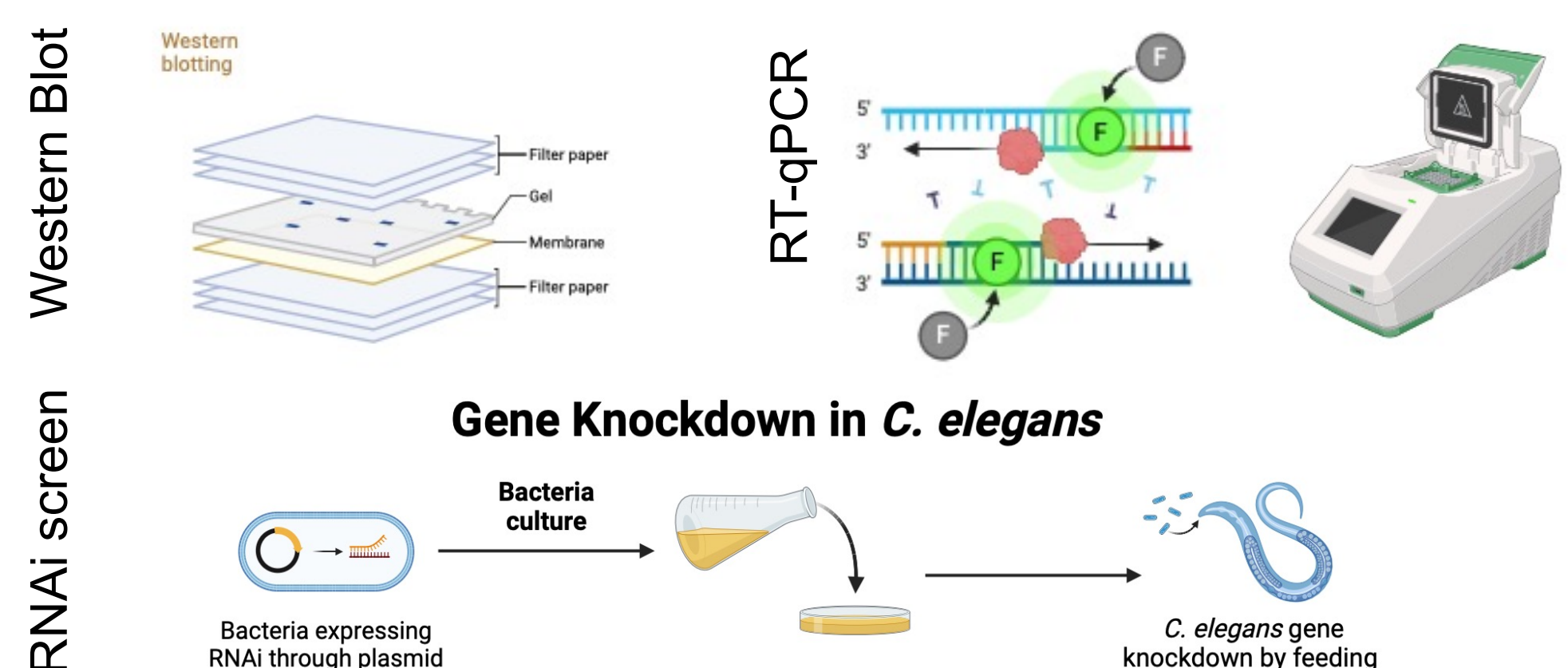
Wong et al., 2023



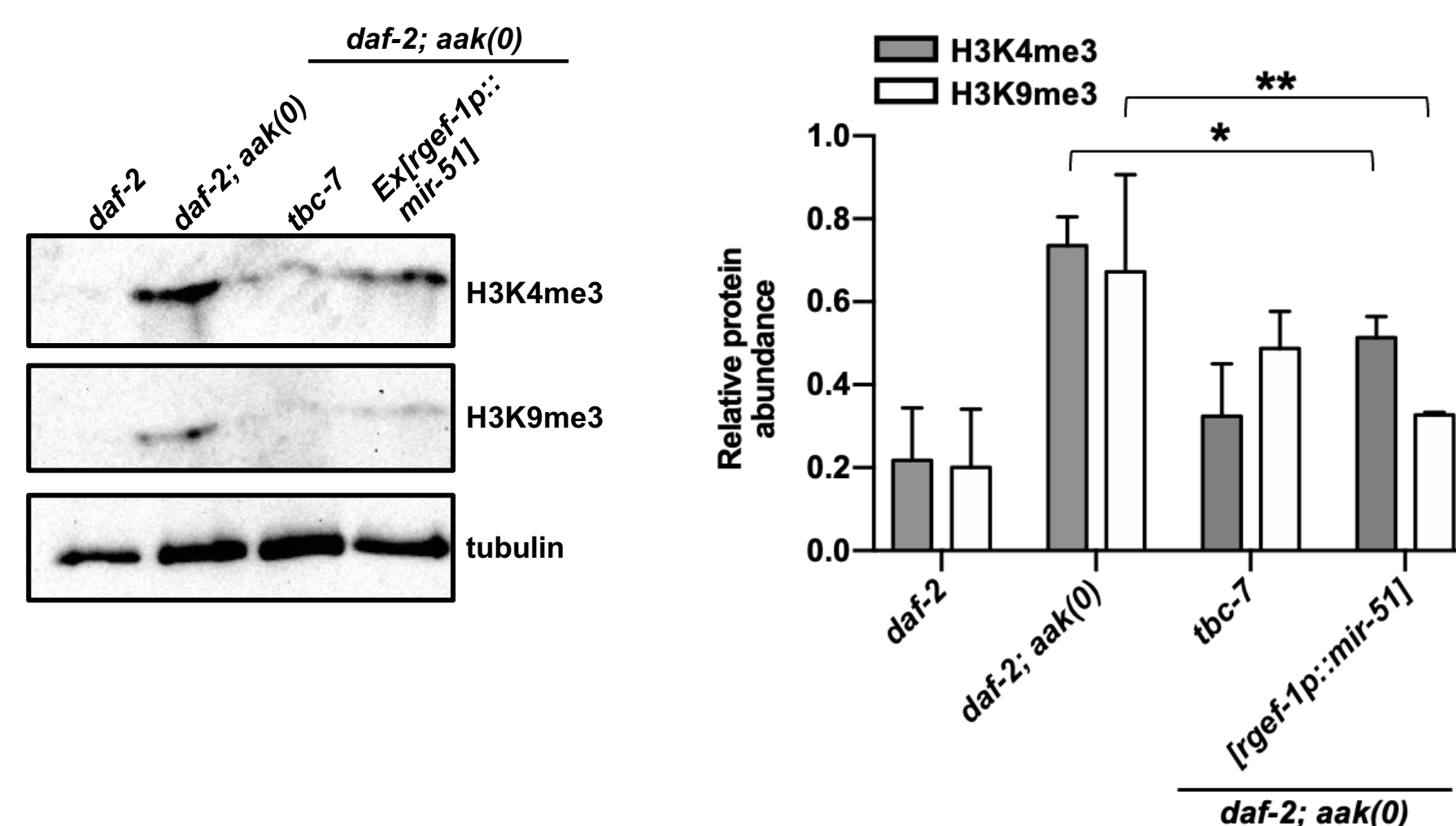
- A temperature-sensitive allele of *daf-2* induces dauer formation at restrictive temperatures
- AMPK signaling releases miRNAs from neurons packaged inside exosomes
- Lack of AMPK signal results in altered epigenetic marks in the germ line

How do neuronal miRNAs regulate germ line gene expression?

## Methods



## Results



Loss of AMPK signaling results in altered epigenetic marks while expression of neuronal miRNAs partially restores epigenetic marks

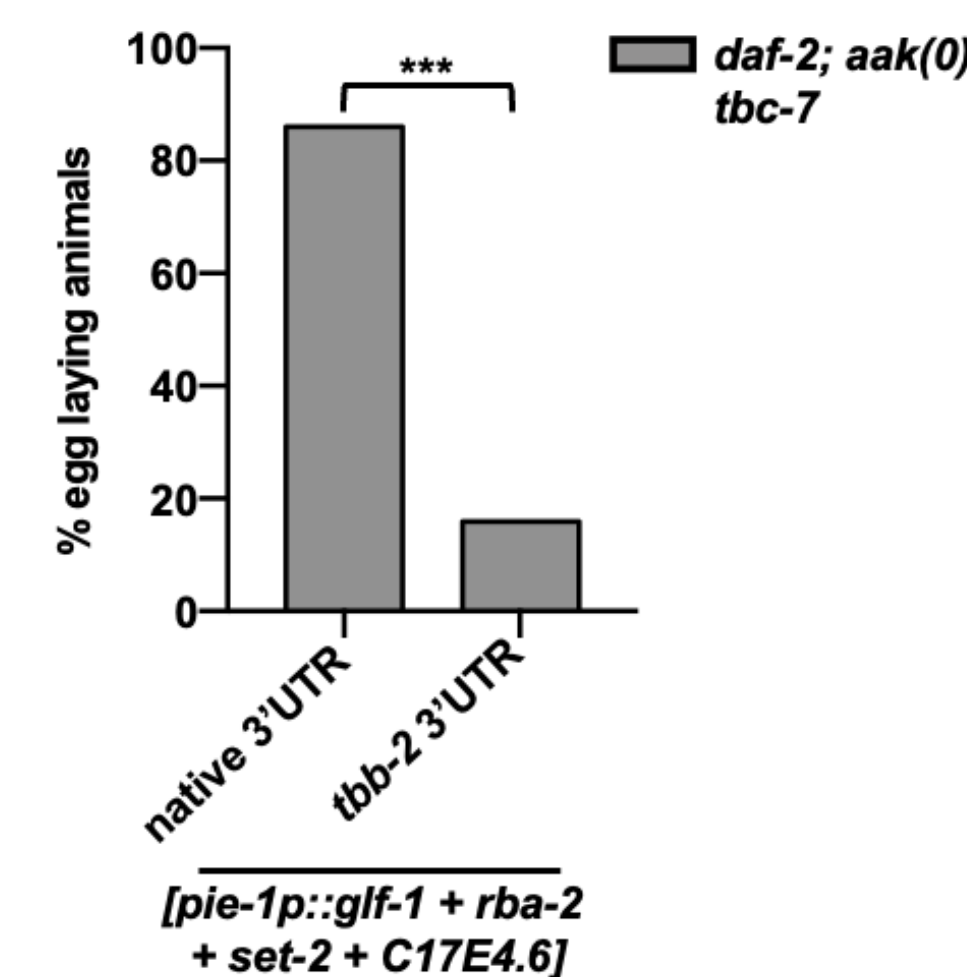
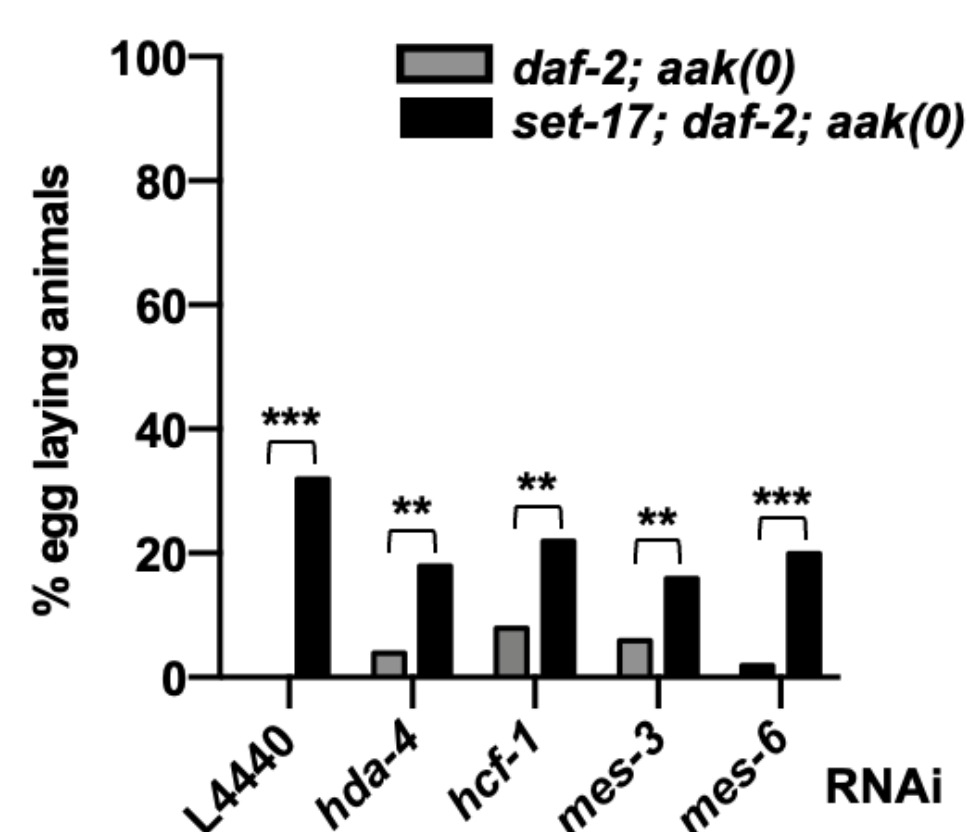
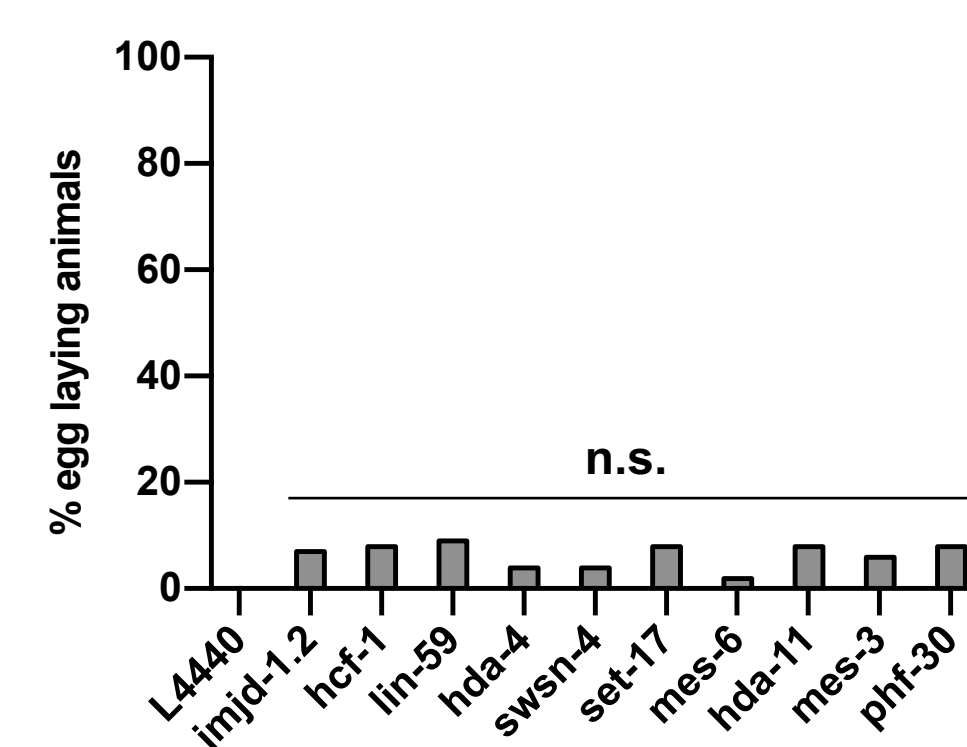


Germline HMEs are upregulated in the absence of AMPK

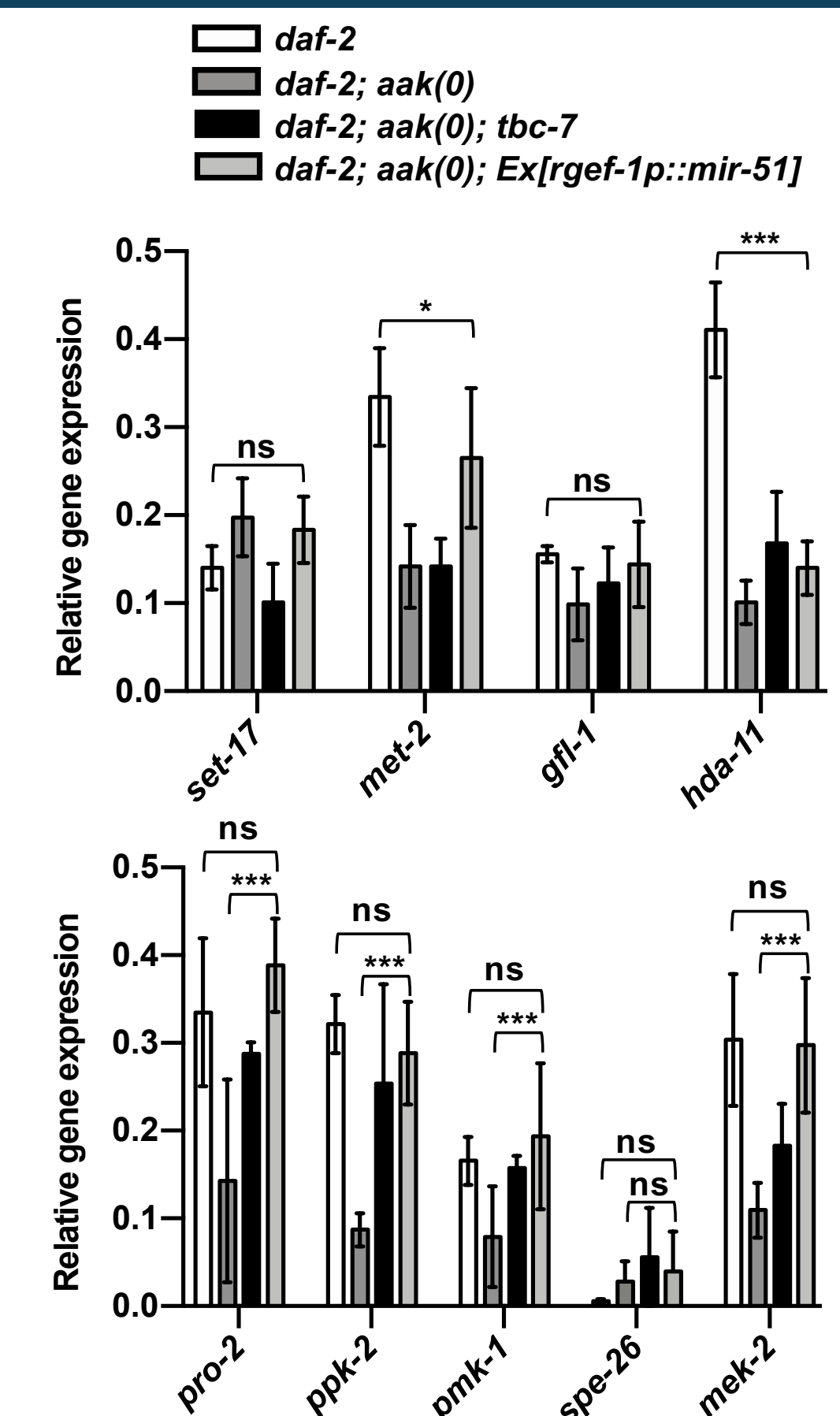
The knockdown of any individual HME cannot correct the germline defects

Knockdown of multiple HMEs suppresses the germline defects, suggesting that HMEs act collectively to regulate germline quiescence

Germline integrity is only maintained under miRNA regulation of HMEs



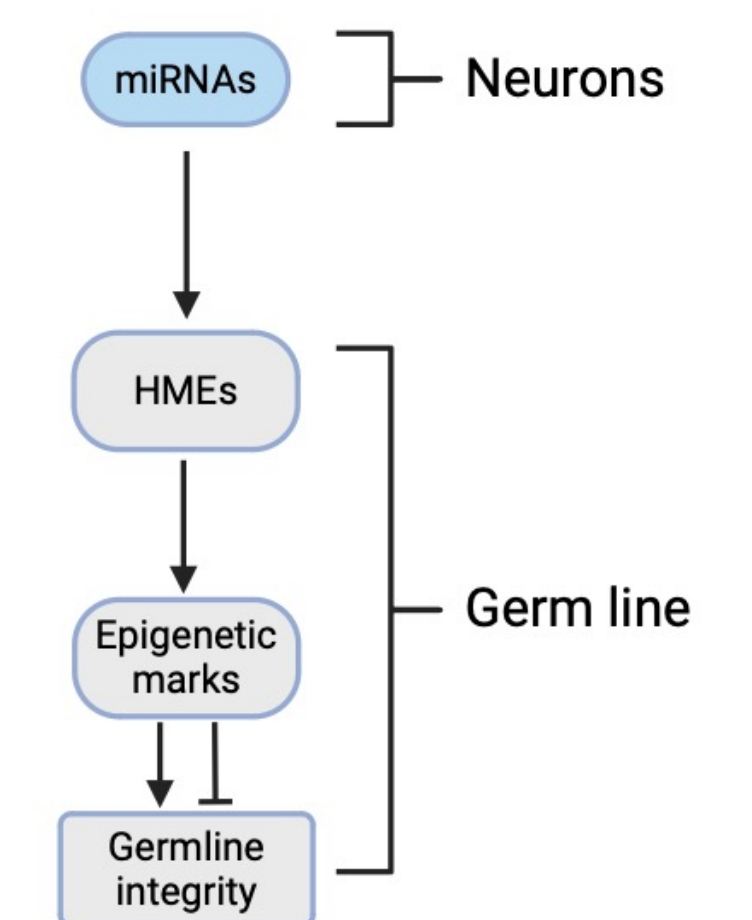
Neuronal miRNAs can restore some of the germline's HMEs expression levels



Neuronal miRNAs restore germline gene expression to wild-type levels

## Conclusion

- Neuronal miRNAs target histone-modifying enzymes in the germline that modify gene expression
- HMEs modify germline gene expression collectively to maintain germline quiescence
- Overexpression of neuronal miRNAs can rescue germline defects
- Understanding which genes are targeted by the HMEs to induce dauer could help us understand how cell division is regulated and could provide some potential insight on how to treat cancer
- Understanding how the neuronal miRNAs can target the germline could help us design new therapeutics able to target the germline



## Future Directions

- Identify which HMEs are targeted by these essential miRNAs
- Identify which genes are regulated by these HMEs and how these genes regulate germline integrity and quiescence
- Determine if these HMEs directly regulate the expression of known germline cell cycle regulators

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