How "Jumping Genes" are kept in check

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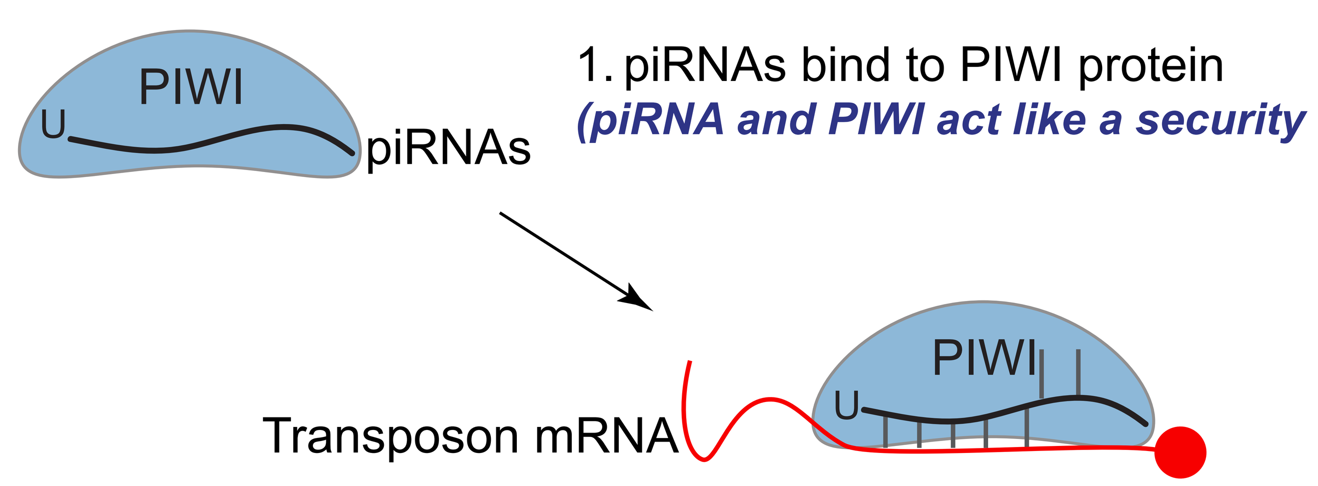
Introduction

PIWI-interacting RNAs, or piRNAs, are tiny RNA molecules that do not code for proteins but help protect the genetic material in reproductive cells. They work with PIWI proteins to silence jumping genes—also known as transposons—which are pieces of DNA that can move around and cause mutations. By keeping these transposons in check, piRNAs help maintain genome stability in sperm and egg cells.

piRNA function in transposon suppression



1. piRNAs bind to PIWI protein *(piRNA and PIWI act like a security team)*

2. piRNA and PIWI work together to find transposons mRNA *(like guards tracking intruders in the genome)*

3. Silence transposons and protecting germline integrity *(like shutting down intruders to keep the genome safe)*

How do we study the piRNA pathway?

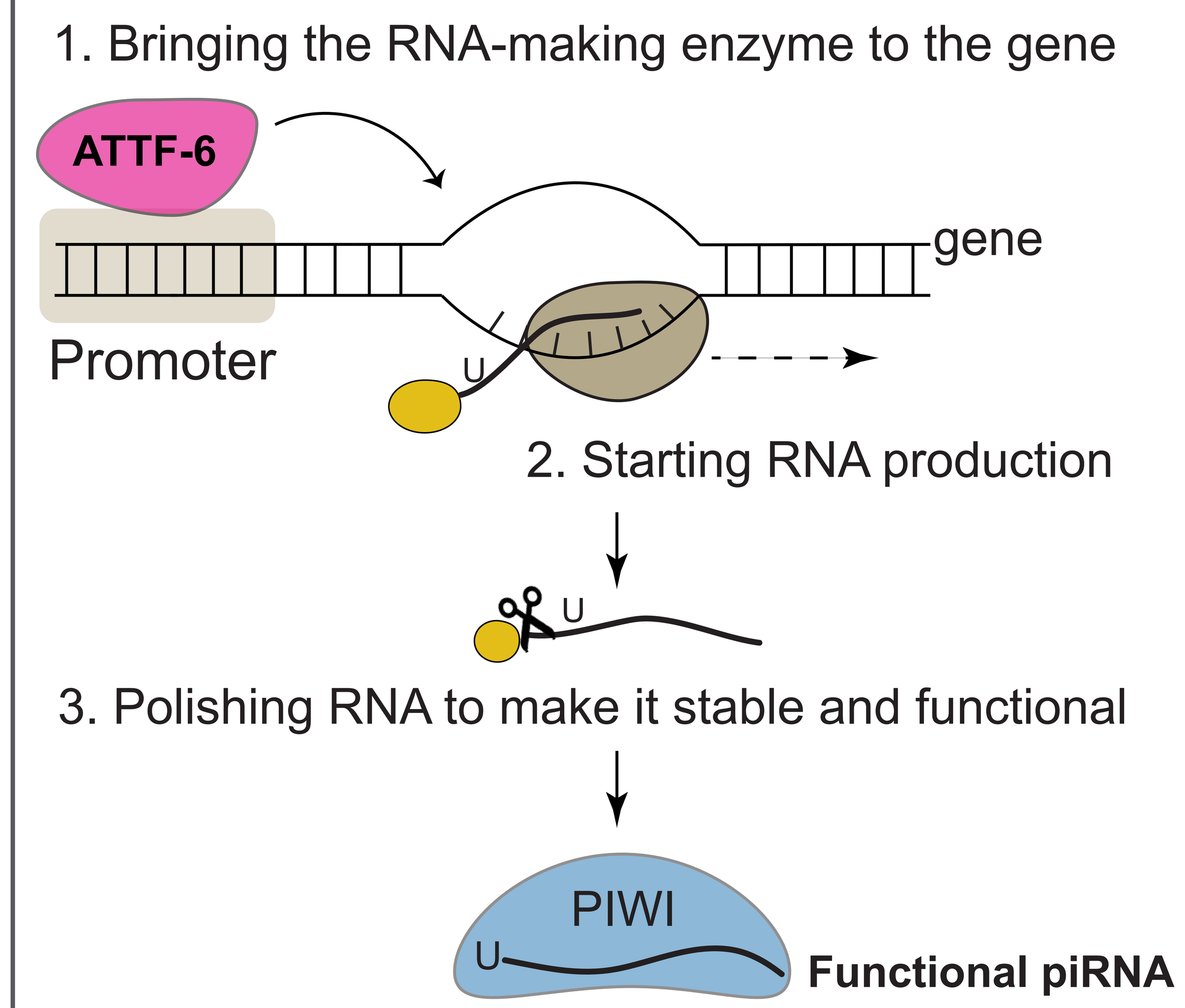
C. elegans worm as a genetic model organism

Reverse Genetics: Start with a gene and study its function

Forward Genetics: Start with a phenotype and figure out which genes are required for the trait

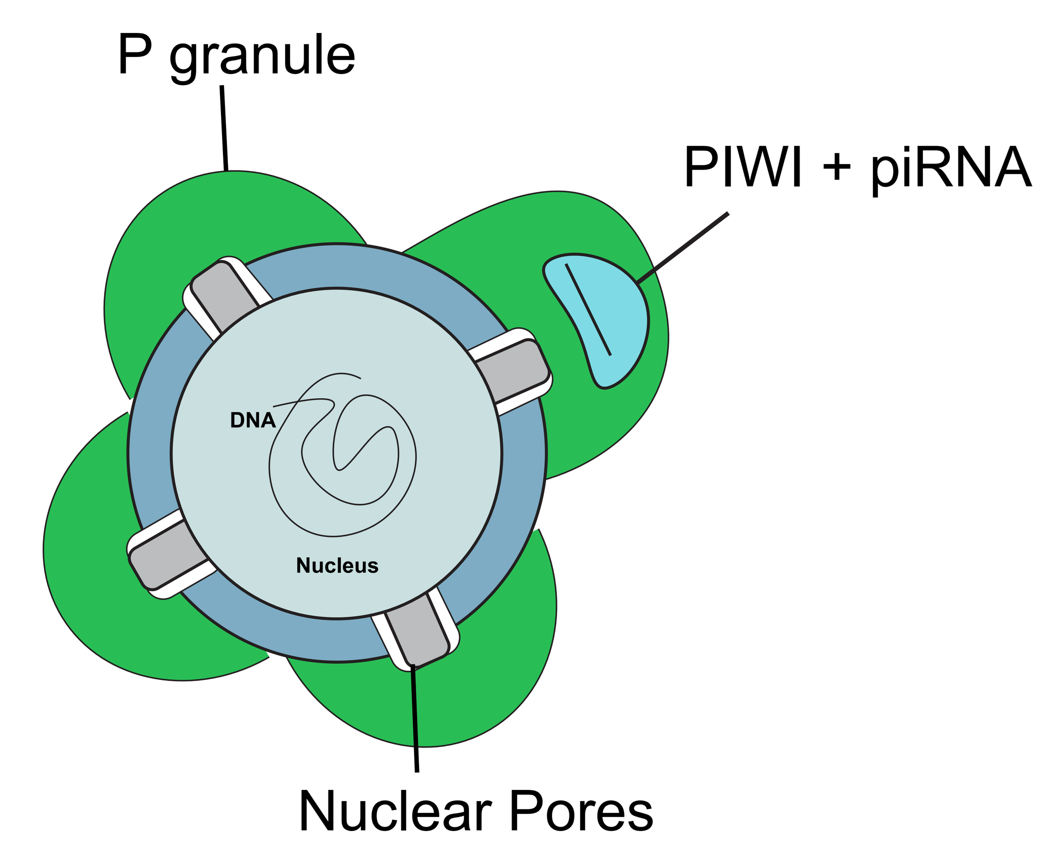
Common Techniques:
- Biochemistry (study proteins in vitro)
- Confocal Microscopy
- RNA-sequencing
- Computational Biology
- RNAi Knockdown
- CRISPR/Cas9 mutagenesis

How are piRNAs made?



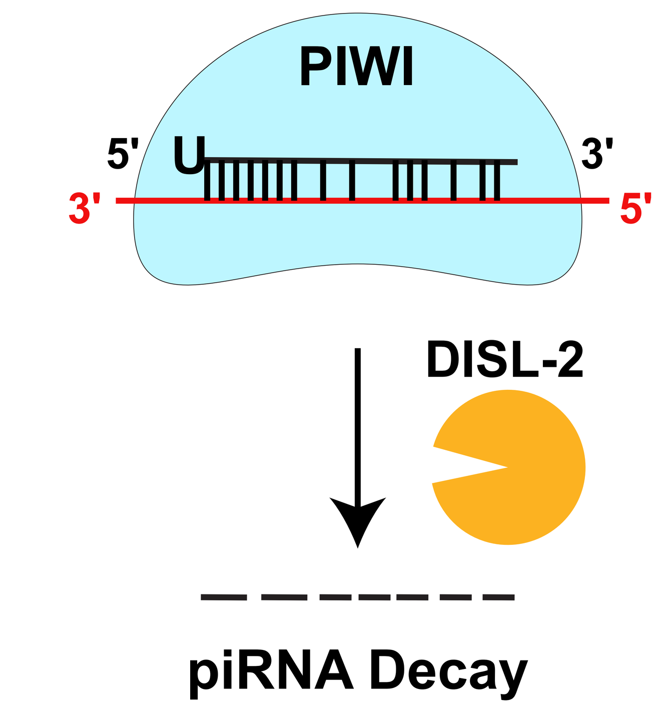
Where do piRNAs funciton?

piRNAs are localize to "germ granule" in the germline



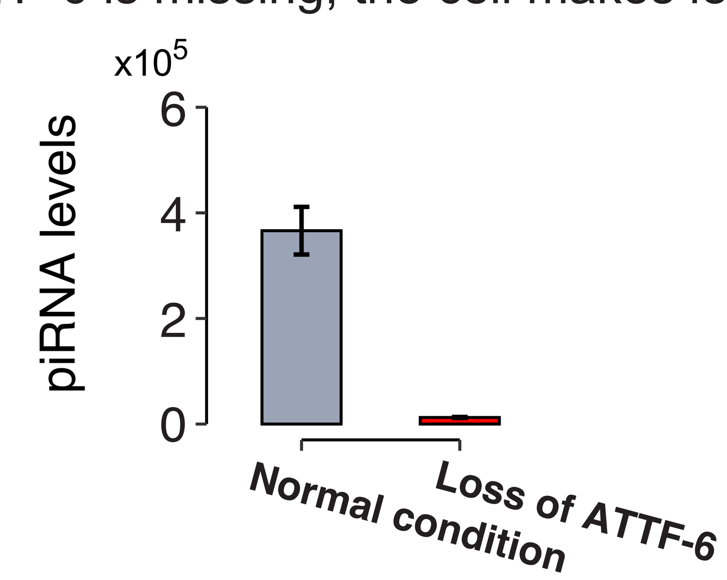
How are piRNAs degraded?

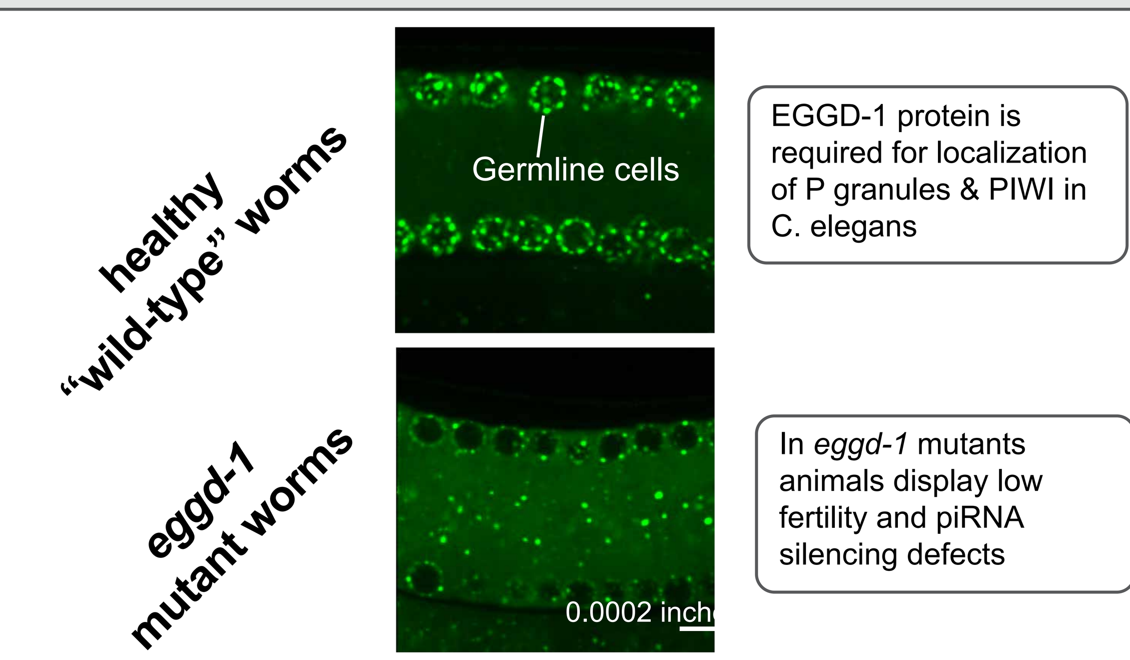
piRNAs are degraded by the exonuclease DISL-2 in *C. elegans*

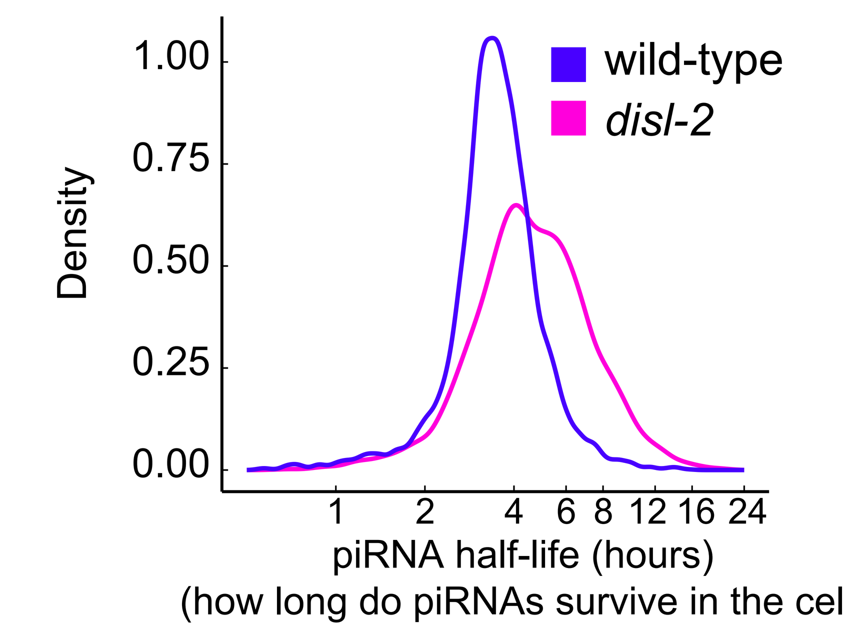


Research Findings

When ATTF-6 is missing, the cell makes less piRNA



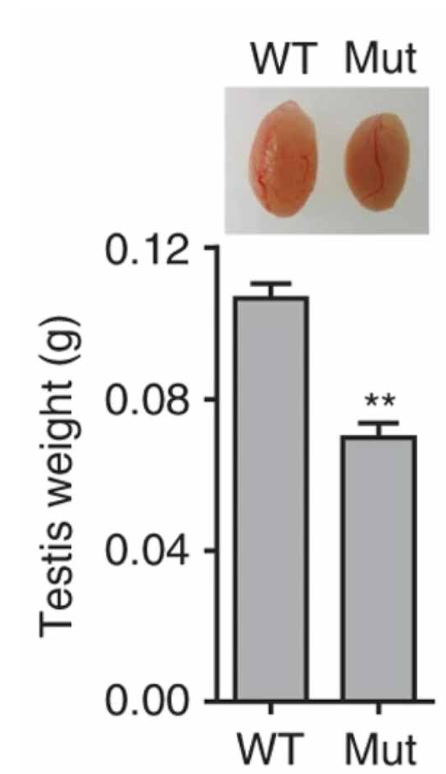




Relevance to human disease

Processing defect:

PNLDC1 plays a key role in trimming the 3′ end of pre-piRNAs, which is a crucial step in their maturation. When the Pnldc1 gene is mutated in mice, it causes a buildup of unprocessed piRNAs, leading to fewer mature piRNAs in the testes. This results in a failure to silence transposons and disrupts the process of sperm development.



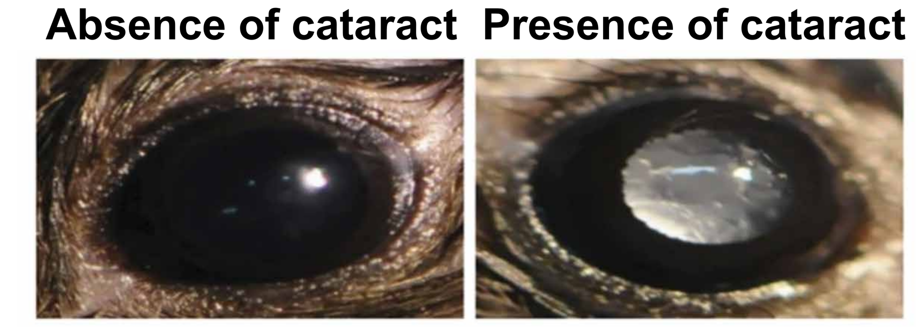
- *Nat Commun 8, 819 (2017)*

Mislocalization:

C. elegans eggd-1 is similar to the human genes *tdrd5* and *tdrd7*. Mutations in *tdrd5* and *tdrd7* in patients have been identified to cause male infertilty. Additionally *tdrd7* mutations can cause pediatric cataracts and glaucoma.

Normal TDRD7 — **Absence of cataract**

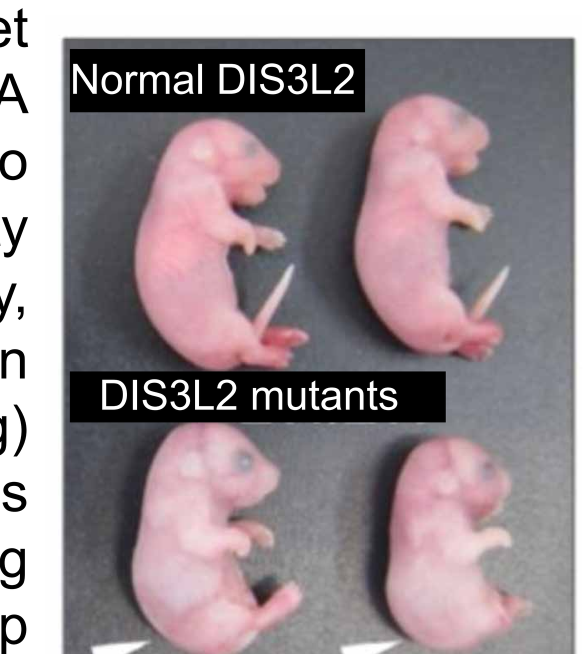
Loss of TDRD7 — **Presence of cataract**



- *Genet Med 21, 1209–1217 (2019)*

piRNA decay and DISL-2 in humans :

The function of piRNA decay in animals is not yet known. Yet, studying piRNA decay in worms may lead to insights into human fertility diseases. Additionally, humans with mutations in DIS3L2 (DISL-2 ortholog) experience Perlmans syndrome. Thus, studying DISL-2 in worms can help yeild insight into the pathogenesis of this disease.



Abnormal curvature of the spine

- *Genes & Dev. 32, 903-908 (2018)*