Genetic Regulation of Cell Migration

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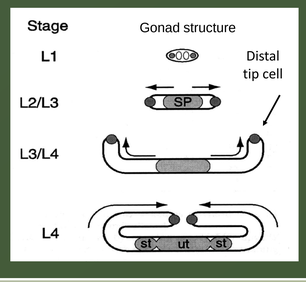
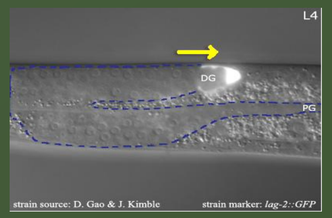
Abstract

During animal development, genes provide instructions for the movement and function of individual cells. In *C. elegans* the two gonad arms follow a U-shape pattern directed by the migration of the distal tip cells. Our goal is to determine how distal tip cell migration would be disrupted using RNAi of the genes *mel-11, nmy-1, rho-1,* and *let-502*. Humans have genes similar to those in *C. elegans*. By understanding gene functions in a model organism, our knowledge may be applicable to cellular functions in humans, such as tissue development and cancer metastasis.



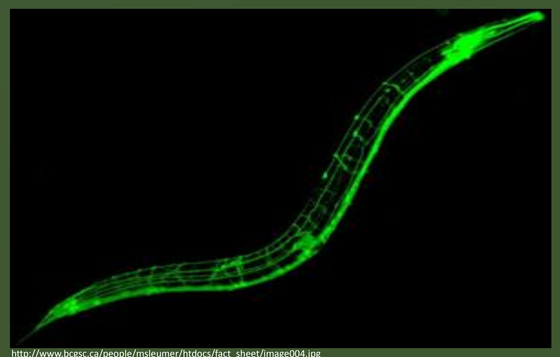


From Blelloch
Dev. Bio. 216, 382-393 (1999)

Why *C. elegans*?

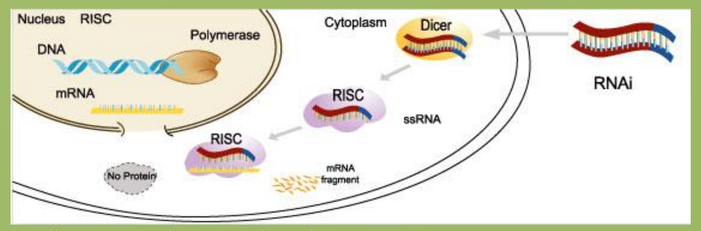
C. elegans is a useful model organism in genetics experiments for many reasons:

- It is a simple species with few cells, so it is small, cheap, and easy to move and handle, but it is complex enough to have all the major body systems of a developed animal (muscular, nervous, digestive, reproductive)
- Its entire genome has been sequenced
- It reproduces quickly (egg to adult in three days) with 300-1000 offspring; most are self-fertile hermaphrodites.
- It is transparent and is ideal for use with fluorescent reporters.
- It takes in dsRNA, making RNAi experiments easier.



http://www.bcgsc.ca/people/msleumer/htdocs/fact_sheet/image004.jpg

How RNAi works

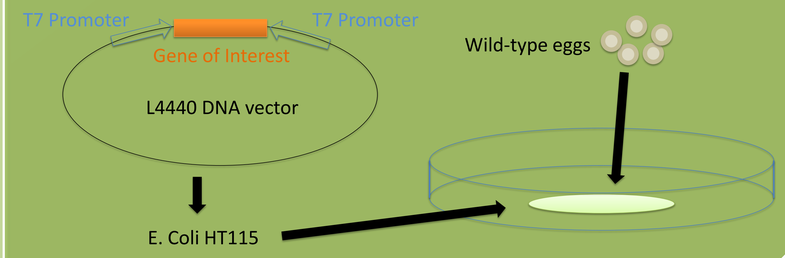


http://www.abnova.com/new_products/images/Chimera_RNAi_3.jpg

RNAi prevents genes from being made into proteins. dsRNA (double stranded RNA) is introduced, processed by the cell, and then marks mRNA for destruction.

RNAi Procedure

A target gene is inserted into a plasmid, which is inserted into bacteria that replicates our gene, producing dsRNA. The eggs are then extracted from the worm, and placed on plates with the bacteria. The eggs will hatch and the newly hatched worms will eat the bacteria. Because the young worms have few cells, all their cells will quickly uptake the dsRNA. When the worms have fully matured, they are observed for unusual distal tip cell migration patterns.



Acknowledgements

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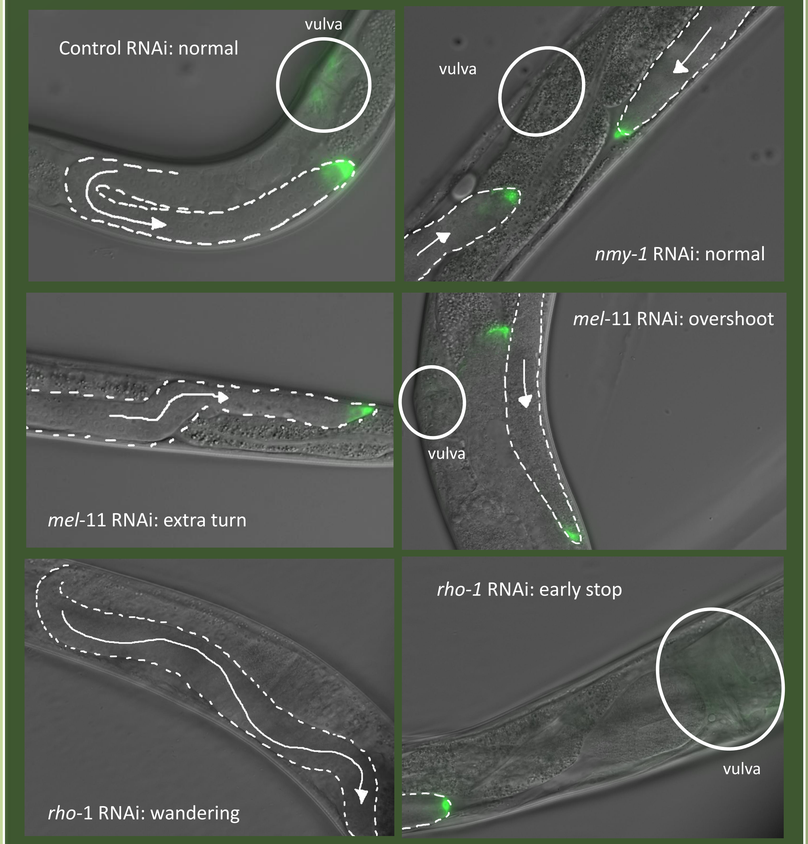
Results and Analysis

We looked at young adult worms for the following phenotypes:



RNAi	Normal (%)	Overshoot (%)	Extra Turns (%)	Wandering (%)	No Arms (%)	Early Stop (%)
Control	100	-	-	-	-	-
rho-1	**33**	**-**	**51**	**8**	**-**	**8**
let-502	75	-	25	-	-	-
par-4	79	-	7	-	14	-
mel-11	70	5	15	-	-	10
nmy-1	100	-	-	-	-	-

Future Goals

- Understand the regulatory pathway by which these genes work
- Check for other phenotypes of these genes, such as fertility
- Understanding abnormal cell migration in *C. elegans* can help understand cancer metastasis in humans

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Claire Duggan, Program Director

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