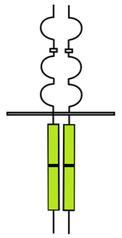
Classification of Novel Components of the Fibroblast Growth Factor Receptor

Fardin Ahmed[1], Jason E. Webb[1], Mariya Stefinko[2], Carolina Gaudenzi[1], Yanely Alonso[1], Michael J. Stern[2], Cindy Voisine[2], and Te-Wen Lo[1]

[1]Ithaca College, [2]Northeastern Illinois University

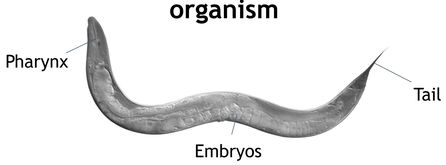
Background

FGFR in Humans



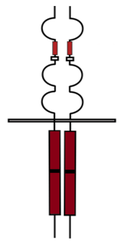
- Cell Migration
- Cell Differentiation
- Cell Proliferation

C. elegans as a model organism



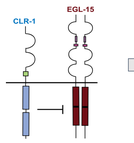
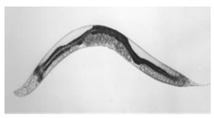
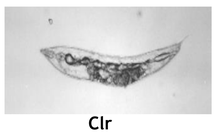
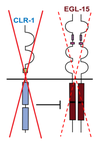
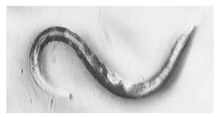
- Small nematode
- Cheap and easy to maintain
- Short life cycle
- Many progeny/generations
- 35% of genes are similar to genes in humans
- Contains only one FGFR: EGL-15

FGFR in *C. elegans* EGL-15



- Fluid Homeostasis
- Cell Migration

Dramatic Phenotypes Reflect EGL-15 Activity

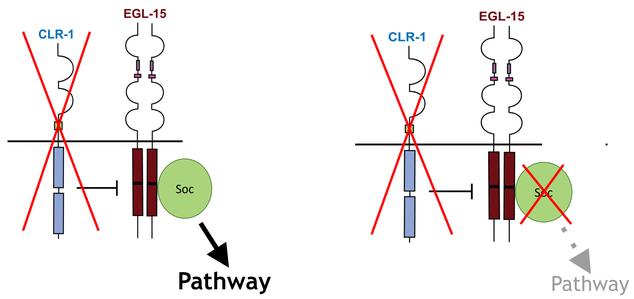
Genotype	Phenotype
	 Wild-type (non-Clr)
Hyperactivation	 Clr
	 Soc (non-Clr)

EGL-15 is negatively regulated by CLR-1, resulting in wild type phenotype.

Mutations in *clr-1* cause hyperactivation of EGL-15, resulting in a Clr phenotype.

Compromised activity of EGL-15 can reduce EGL-15 hyperactivity, causing the Clr phenotype to be suppressed. (Suppressor of Clr = Soc)

Basic Screen

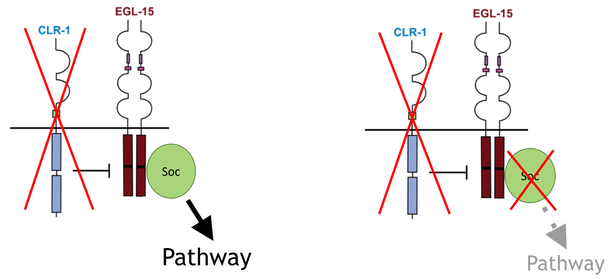


Phenotype: **Clr** **Soc**

Signaling pathway status: **Functional** **Compromised**

soc mutations can identify signaling pathway components by reducing pathway hyperactivity.

Enhancer Screen



Phenotype: **Clr** **Soc**

Signaling pathway status: **Functional** **Compromised**

An enhanced Soc screen was designed to identify components of this semi-redundant pathway.

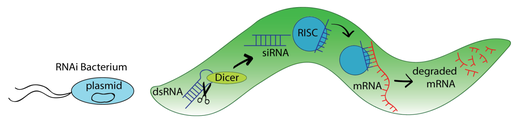
Characterization of Putative Novel *soc* Genes

	Gene	Basic Screen Isolates	Enhancer Screen Isolates
Autosomal Mutations	*soc-1*	many	*ay151*
	soc-2	many	
	unmapped		*ay169, ay157, ay172*
X-Linked Mutations	unmapped		*ay167, ay171, ay173, ay176*
	"soc-3"	*n2200, n2208*	*ay156*
	sem-5	many	
	?		*ay154*
	egl-15	many	many

Whole-genome sequencing identified *cca-1* as a potential *"soc-3"* gene

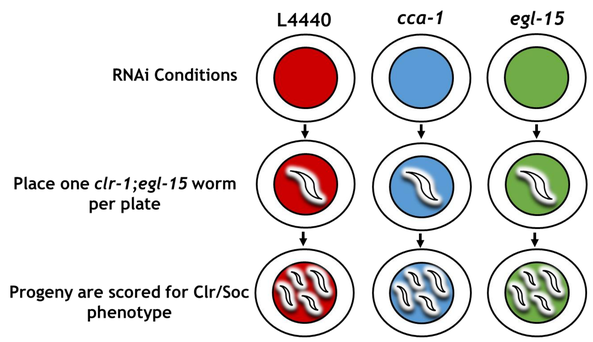
Is *cca-1* a *soc* Gene?

RNAi Mechanism



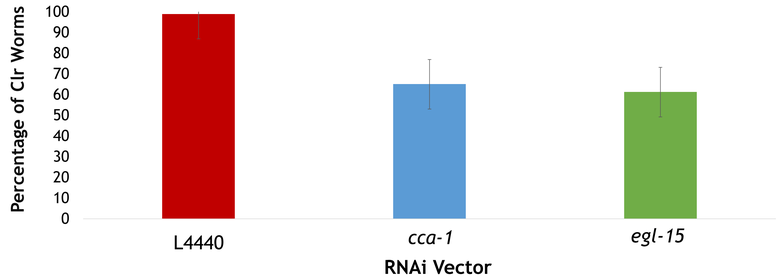
mRNA is degraded preventing translation from occurring. Thus, the protein is not synthesized.

RNAi Protocol



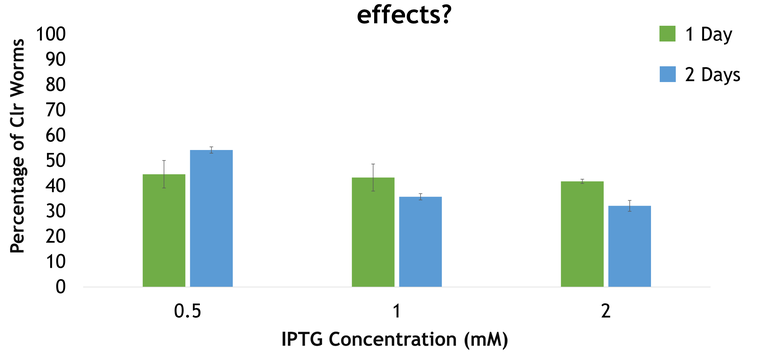
Results

Is *cca-1* a *soc* gene?

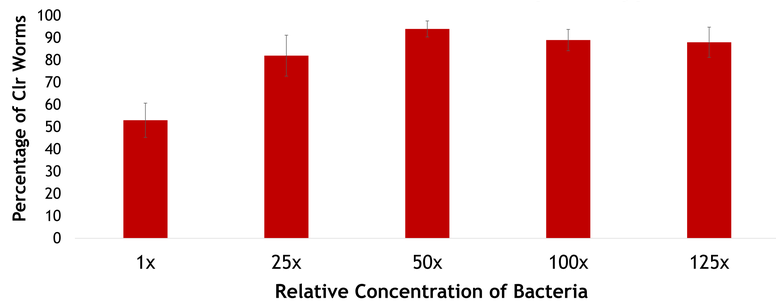


- No true Soc worms were observed, which indicates the RNAi was not working optimally.
- To optimize the protocol, different conditions were tested (IPTG concentration, induction length and concentration of bacteria).

Do IPTG concentration and induction length have phenotypic effects?



Does the concentration of bacteria have phenotypic effects?



Discussion and Conclusions

- In addition to improving RNAi methods, we will use a *cca-1* mutant worm to test if *cca-1* is a bona fide *soc* gene.
- Identification of novel components, such as CCA-1, will further our understanding of FGFR signaling in *C. elegans* and potentially in humans.

Acknowledgements

Ithaca College Biology Department
Nancy Pierce, Ian Woods, Jun (Kelly) Liu