Regulation and function of the *odd-skipped 2* transcription factor in *C. elegans*

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Introduction

***Odd-skipped* genes:**

- Evolutionarily conserved transcription factors[1]
- Roles in mammalian tissue development including the colon[2], intestine[2], prostate[2], lung[2], kidney[3,4] and heart[4]
- In mammals, can help prevent lung, gastric and renal cell cancer[5,6,7]
- Known to regulate genes of the WNT pathway[4,5]
- Expressed in the *C. elegans* gut[1]
  - ODD-1 and ODD-2 expressed in the intestine[1]
  - ODD-2 also expressed in the rectal gland cells[8]

Methods

Screen for transcription factors that regulate *odd* genes

- Transcription factors knocked down using RNA interference (RNAi)
- Prioritized transcription factors that:
  - Were conserved in humans
  - Bound *odd-skipped* promoters[9] or were expressed in intestine/rectal gland
- Fluorescent reporter strains *odd-1::GFP* (JR2004) and *odd-2::GFP* (JR2005) used to visualize *odd-skipped* expression
- L4 worms or bleached L1 worms were subjected to feeding RNAi

***Odd-2* RNAi in *egl-20* reporter (CF1045)[10]**

- Created *Pegl-20::egl-20::GFP; rrf-3(pk1426)* strain (AG21)
- L4 worms subjected to *odd-2* feeding RNAi for two and three days
  - 2 days = experimental (microscopy of L1s)
  - 3 days = demonstrate functional *odd-2* RNAi by lethality

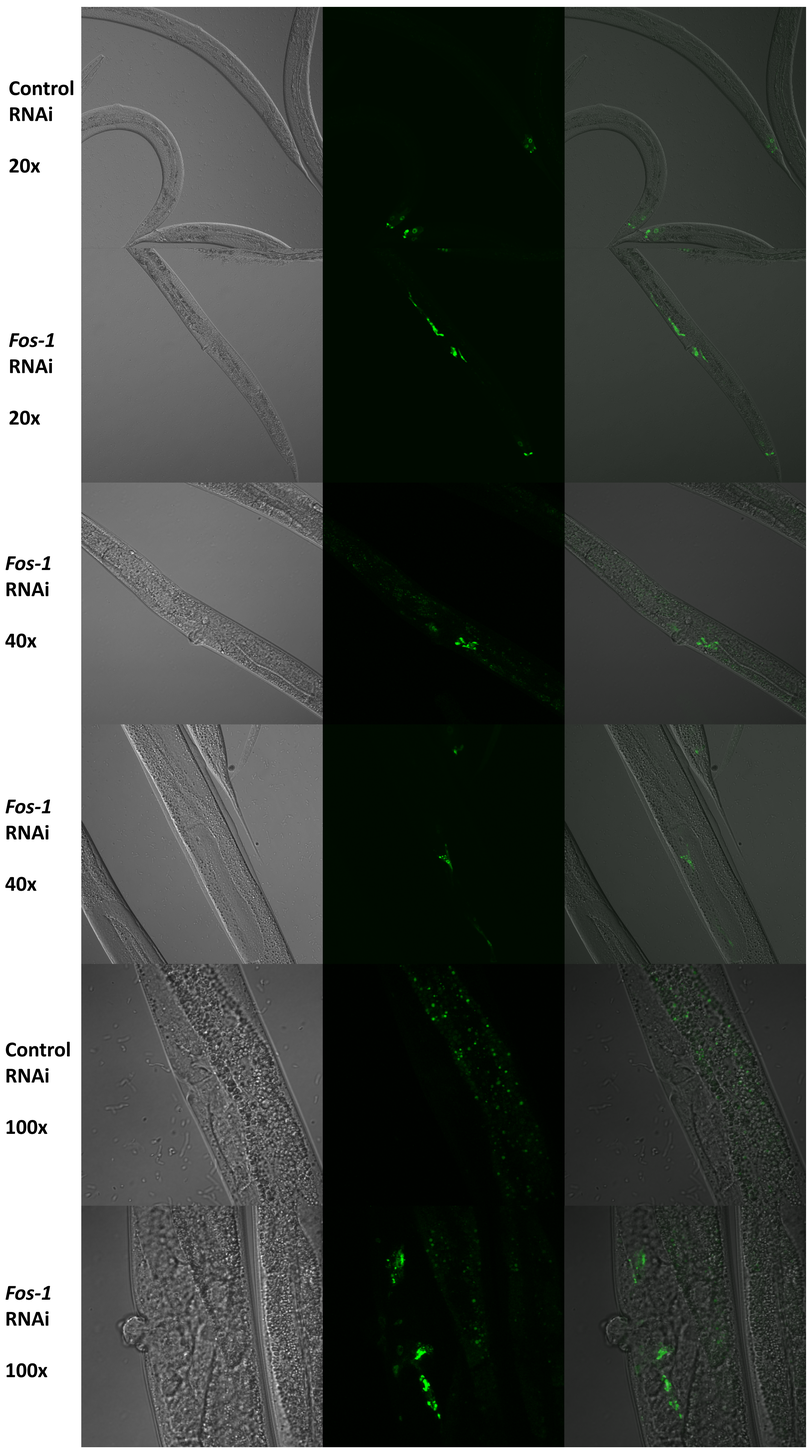
Results

Effect of transcription factor knockdown on *odd-2* expression

Gene	*Odd-1* (Number of replicates)	*Odd-2* (Number of replicates)
blmp-1	No effect (3)	Reduced intestinal (2)
ceh-14	No effect (1)	No effect (2)
ces-1	No effect (1)	No effect (2)
ces-2	No effect (1)	No effect (2)
daf-16	No effect (1)	Not yet tested (0)
dpl-1	No effect (1)	No effect (1)
dve-1	No effect (2)	Reduced intestinal (1)
egl-5	No effect (3)	No effect (2)
fos-1	Increased intestinal (4)	Reproductive tissue expression (3)
ham-1	No effect (1)	No effect (1)
jun-1	Increased intestinal (1)	No effect (1)
lim-7	No effect (1)	No effect (2)
lin-35	No effect (1)	No effect (2)
lin-48	No effect (1)	Reduced intestinal (1)
nfya-1	No effect (3)	No effect (2)
nhr-17	Reduced intestinal (5)	No effect (3)
nhr-35	No effect (1)	Not yet tested (0)
nhr-49	No effect (1)	No effect (1)
pha-4	No effect (2)	No effect (1)
pqm-1	Reduced intestinal* (3)	Increased intestinal* (2)
unc-120	No effect (1)	No effect (1)
unc-62	No effect (3)	Increased intestinal (2)
zag-1	No effect (1)	No effect (1)

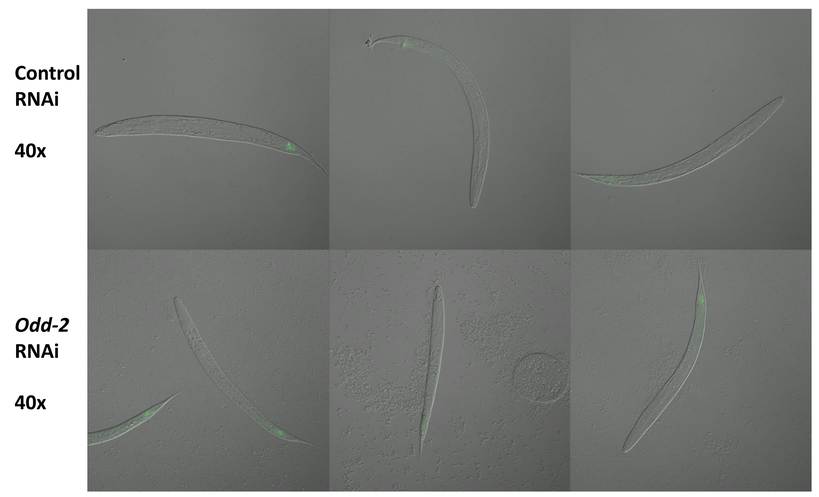
*Slower development

ODD-2::GFP expression after RNAi treatment



Max intensity GFP Z projections and a representative brightfield slice.

EGL-20::GFP expression after RNAi treatment



Conclusions

- *Fos-1* knockdown caused ectopic expression of ODD-2 in/around the germline/vulva
- FOS-1, JUN-1, UNC-62 and PQM-1 knockdown increased *odd* expression while NHR-17, PQM-1, DVE-1, BLMP-1 and LIN-48 knockdown decreased *odd* expression
- No obvious effect of *odd-2* RNAi on *egl-20* expression

Future Directions

- Verify RNAi results in a *fos-1* mutant strain
- Examine ectopic ODD-2 expression at different developmental stages
- Identify specific cells ectopically expressing *odd-2*
- Test effect of *odd-2* on other Wnt pathway genes

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