

Identification of ESRE Regulatory Molecules

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The ESRE Pathway in *C. elegans*



- ▶ Activated by heat shock, osmotic stress, redox stress, ethanol, & bacterial pathogen exposure
- ▶ Slr-2 and jmjc-1 are upstream participants
- ▶ Acts through a promoter motif termed ESRE (for ethanol and stress response element)

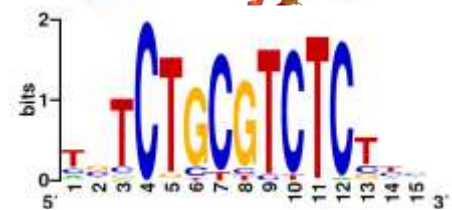
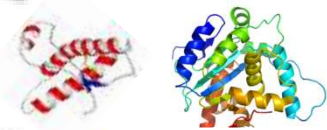
Stress

SLR-2

JMJC-1

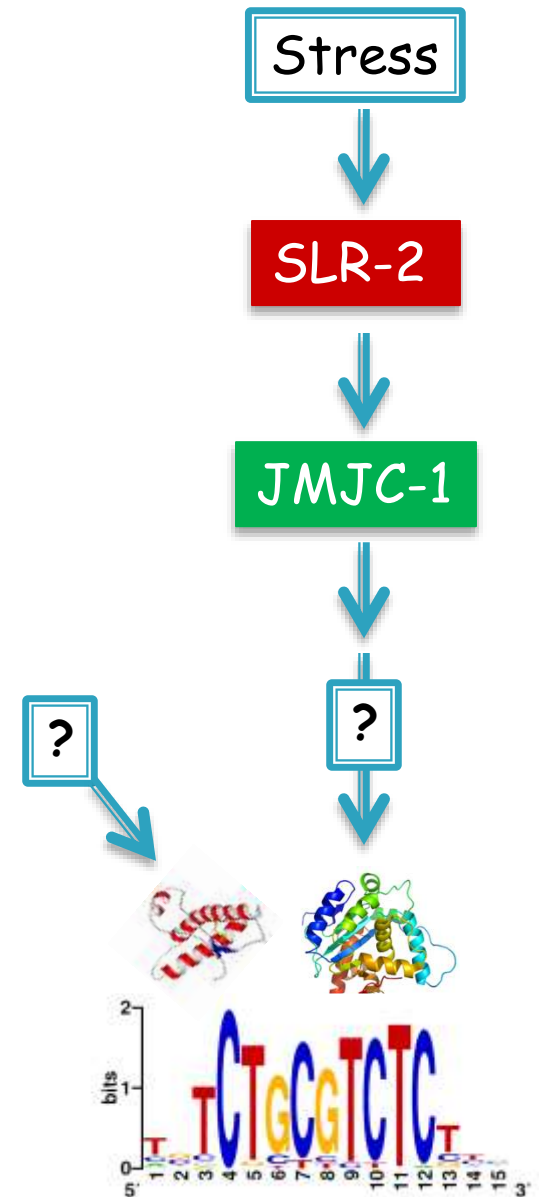
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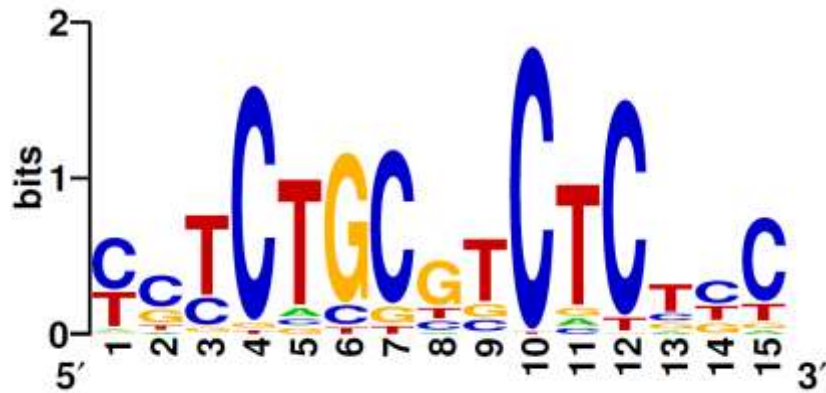
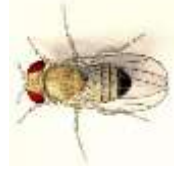
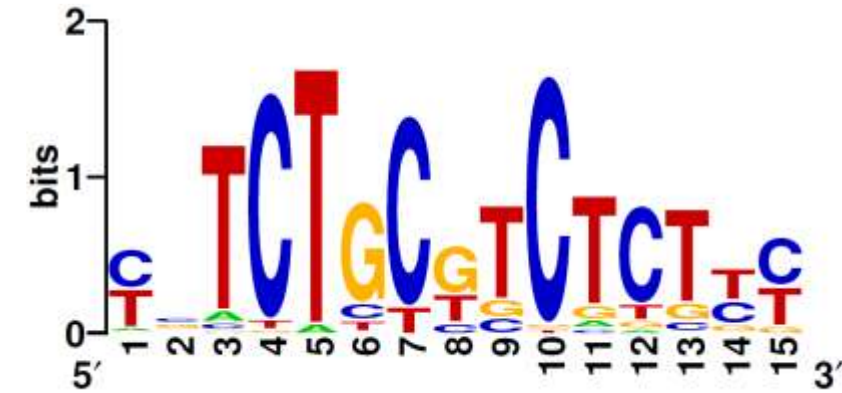


Research Questions

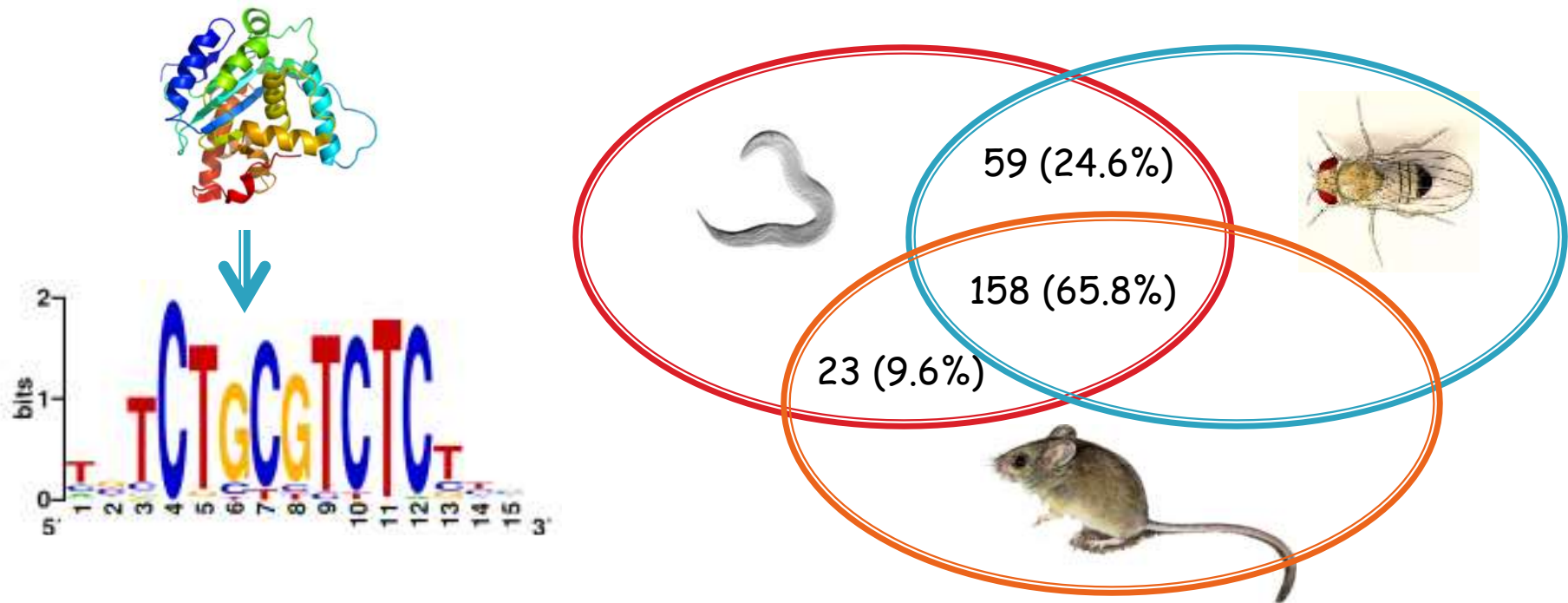
- ▶ How does the ESRE pathway work?
- ▶ Who are the players?
 - Identify the EBP (ESRE-binding protein)
 - Identify other participants in the ESRE pathway



- ▶ The ESRE motif sequence, *slr-2*, and *jmjc-1* are highly conserved among worms, flies, and mammals



ESRE pathway participants are likely also conserved



RNAi Screen

- ▶ Double-stranded RNA used to knock down one gene at a time
- ▶ 3xESRE::GFP, *rol-6* reporter to visualize ESRE driven gene expression

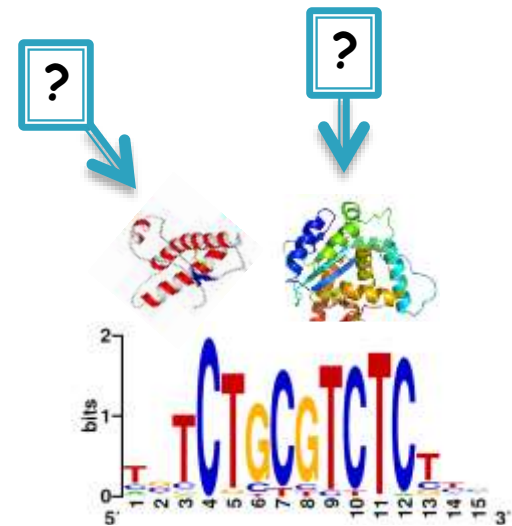


Roller

Non-Roller

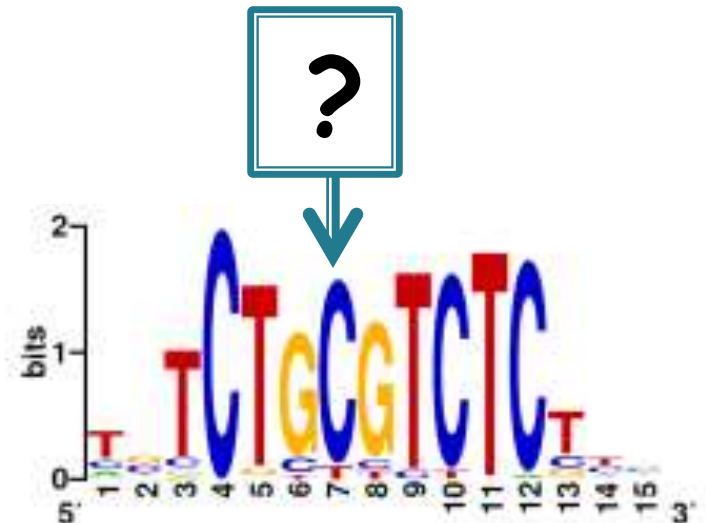
RNAi Screen

- ▶ Tested 217 clones of evolutionarily conserved **transcription factors** in worms
- ▶ Tested 173 clones of known **signaling molecules**



RNAi Screen Results

- ▶ C08B1 1.3 RNAi knocks down 3xESRE::GFP expression by 2-fold
 - SWI/SNF nucleosome remodeling complex component
- ▶ No other genes identified from screen
 - ESRE pathway components are essential
 - Functional redundancy
 - Complex that binds ESRE



Strain Construction: Microinjection

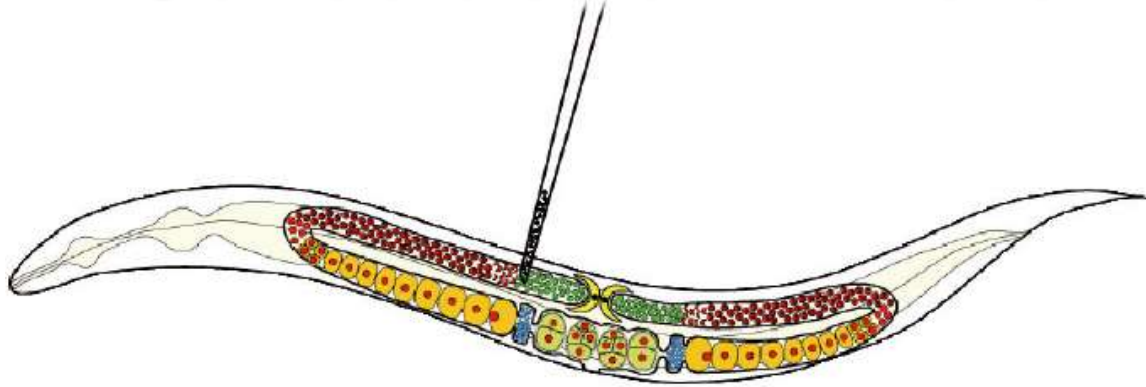
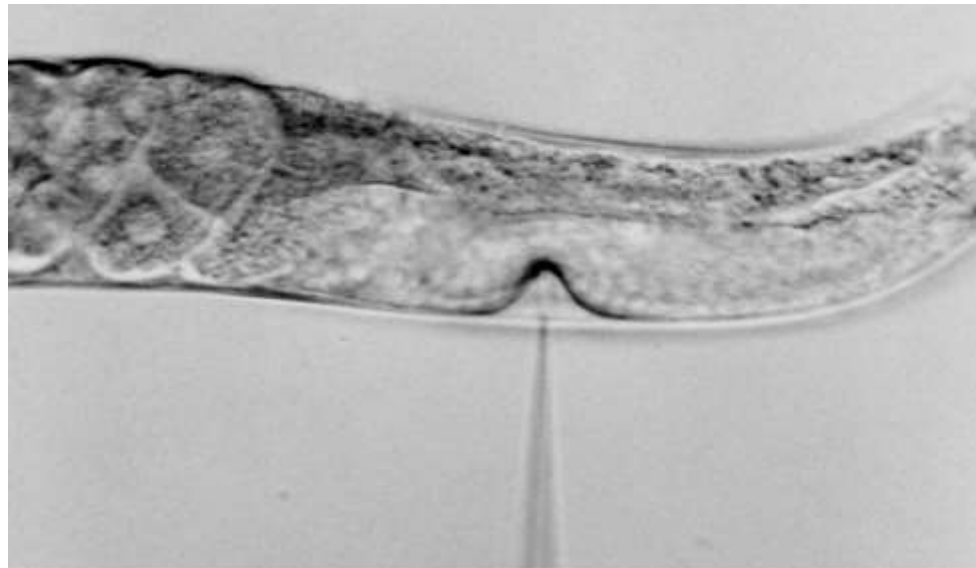


FIG. 1: Intra-*gonadal* injection in *C. elegans*



Strains

- ▶ 3xESRE::GFP, *myo-2*
 - Muscles of the pharynx
- ▶ 3xESRE::GFP, *myo-3*
 - Body wall muscles



Acknowledgements

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Aleksandra Kuzmanov

Questions?