C. Elegans Aging on Stress Response Gene Expression

Anirudh Seshadri & Michael Yao

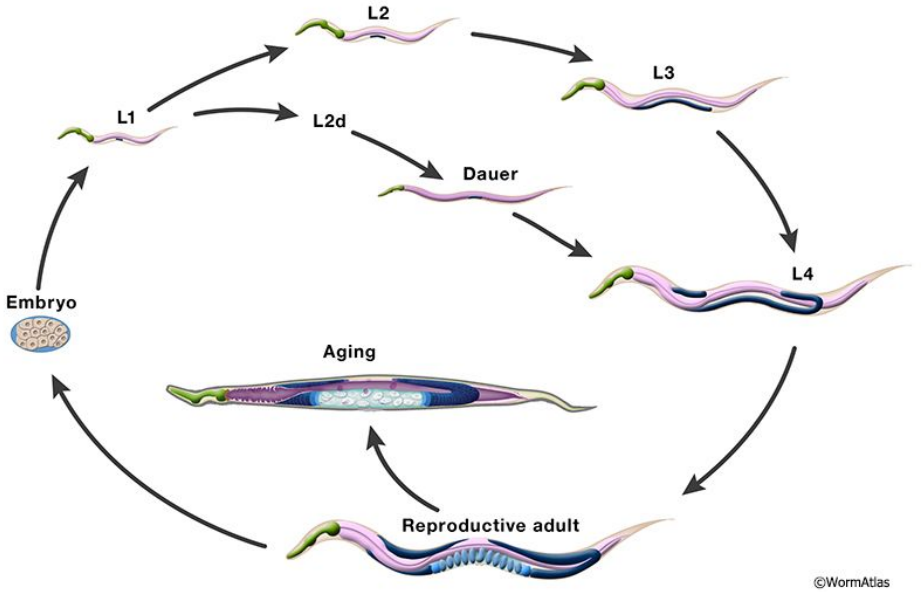
CARNEGIE SCIENCE

JOHNS HOPKINS UNIVERSITY

Doctoral Program in
Cell, Molecular, Developmental Biology, and Biophysics

Aging and Stress Response

- Stress Genes (e.g. heat shock proteins)
- Tissue Specific Responses
- Aging has shown a general decline in their function



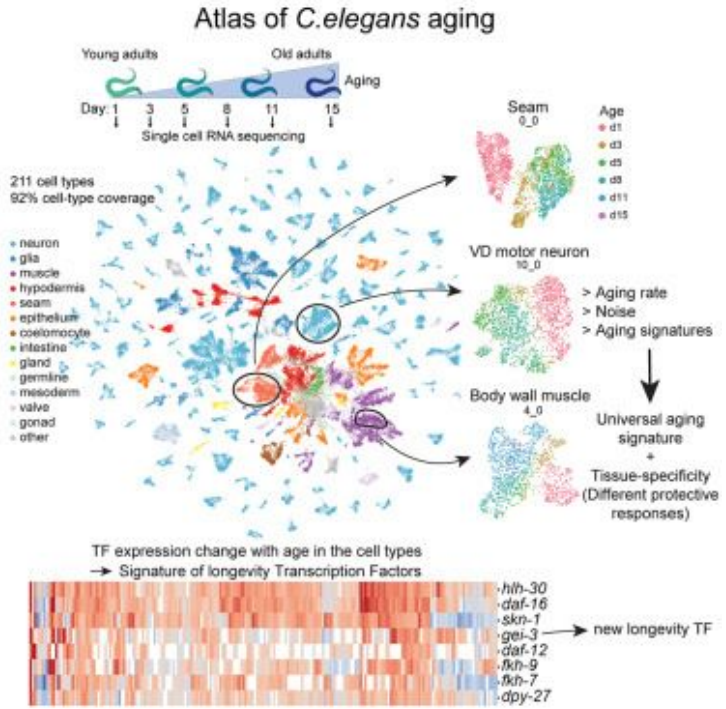
https://www.wormatlas.org/aging/introduction/AIntroframeset.html

C. Elegans Single Cell Aging Database

- Single Cell RNA-Seq data across lifespan in C. Elegans
- Timepoints: 1, 3, 5, 8, 11, 15 days
- .h5ad file
- Enables celltype specific & global analyses (what we want)

Individual cell types in *C.elegans* age differently and activate distinct cell-protective responses

Antoine Emile Roux [1,2], Han Yuan [1,2], Katie Podshivalova [1], David Hendrickson [1], Rex Kerr [1], Cynthia Kenyon [1], David Kelley [1,3]



How does expression of select stress hallmark genes in neurons change as worms age?

Project Goals

1. **Parse both global and neuron specific stress gene expression at distinct timepoints (Python)**
2. **Stat analysis + Visualization (R)**
3. **Identifying differentially expressed genes**

ScanPy

- Single cell RNA-seq toolkit for preprocessing, clustering, filtering, scaling, dimensionality reduction etc.

- Built-in visualization: gene expression, clusters, embeddings

Python Analysis/Parsing Summary

- Loaded .h5ad dataset
- Provided list of stress response genes
- Identified neuron clusters (PCA + Clustering)
- Average stress gene expression per time point
- DE Analysis

.csv file

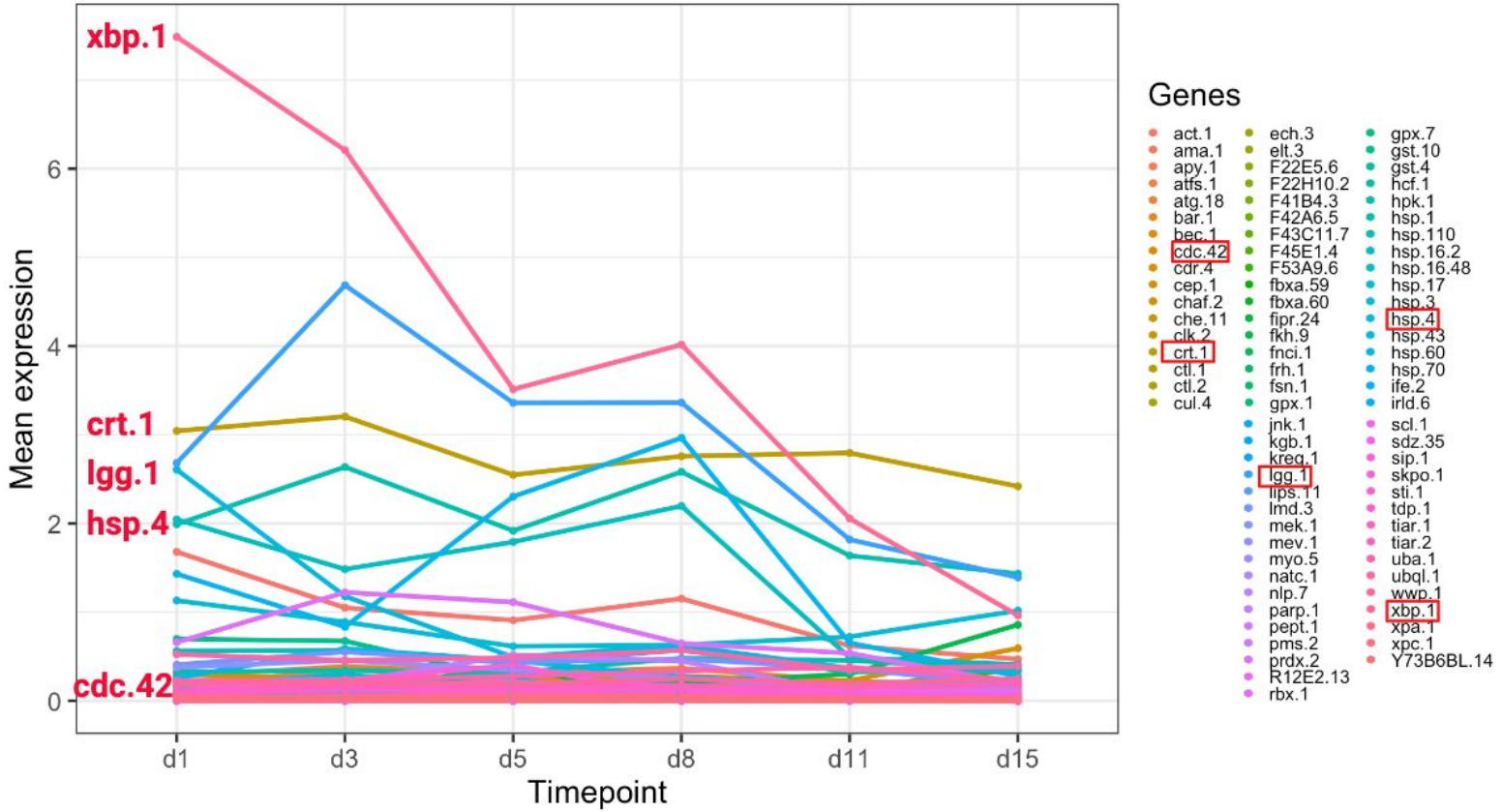
timepoint	hsp-4	hsp-6	hsp-16.1	hsp-16.2	hsp-16.41	hsp-16.48	hsp-17
d1	2.607166	0.06128405	0.00016213	2.0463684	1.5556906	0.00072957	0.14802206
d3	1.180211	0.09232448	0.00029101	1.4846853	1.186977	0.00087304	0.30571118
d5	0.49409643	0.08461791	0.00049196	1.792555	1.4511315	0.00016399	0.0874057
d8	0.62468874	0.1408734	0.00019153	2.1980464	1.9591074	0.00124497	0.0750814
d11	0.36919048	0.2559459	0.0002182	0.488981	0.4634519	0.00109099	0.16364826
d15	0.20547946	0.5936073	0	0.41095892	0.37899545	0.00456621	0.20091324

names	logfoldchang	pvals	pvals_adj	scores
hpk-1	3.148331	1.05193483	2.73840216	8.829448
lmd-3	1.6273521	4.29408590	0.0002564	4.596616
act-1	2.1133246	0.0016797	0.057514	3.1417043
cdc-42	1.7176492	0.0017156	0.0585477	3.135497
uba-1	1.8448367	0.00255	0.0823189	3.0173395
ama-1	3.5398037	0.0035134	0.10727718	2.918838
fsn-1	2.2747693	0.0314064	0.66648320	2.1518855

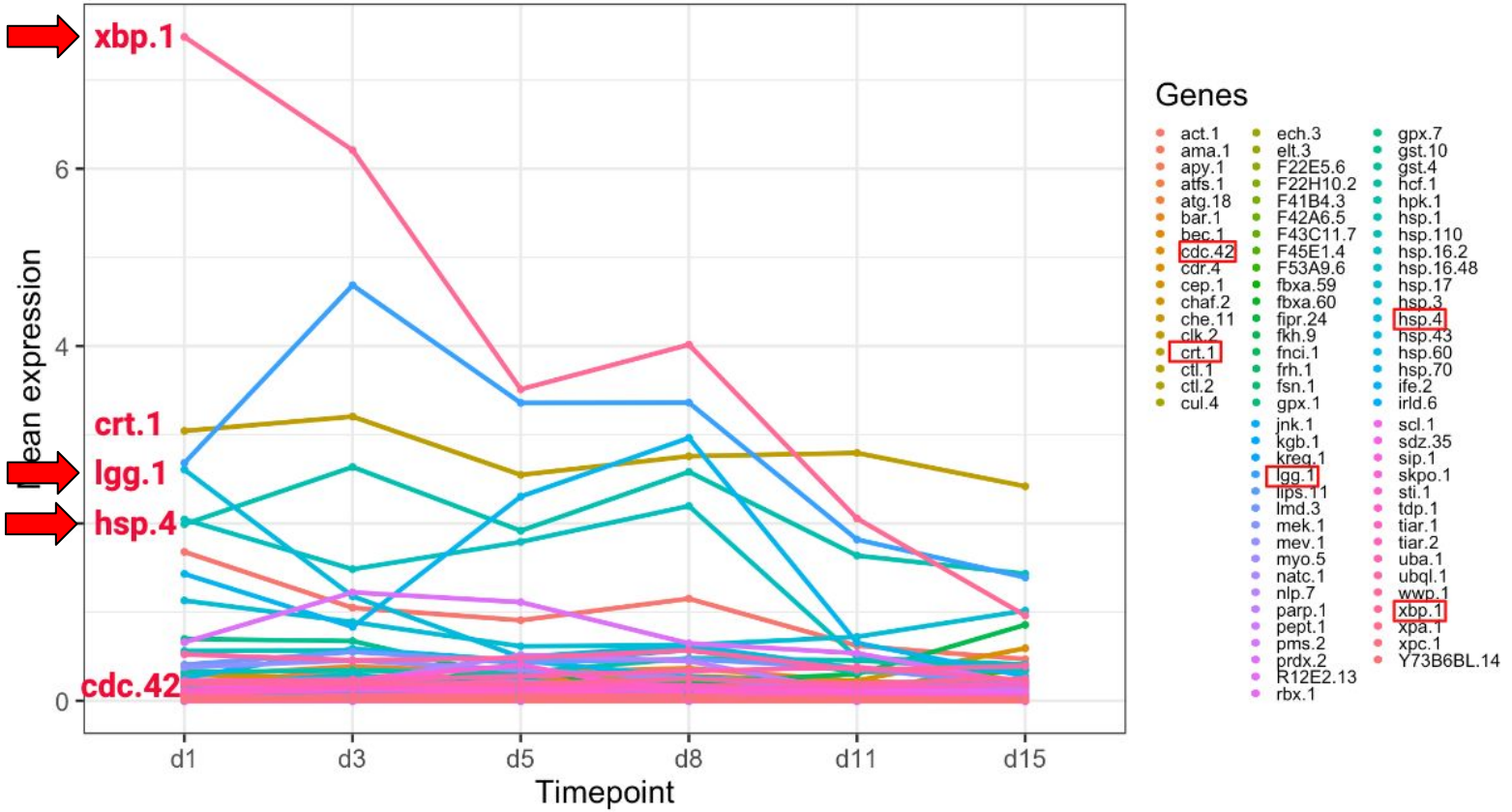
Data Visualization (R)

1. Loaded CSV files with stress gene expression across worm aging and tissues.
2. Creating the global and neuron-specific line plots
3. Performing statistical comparison using volcano plot

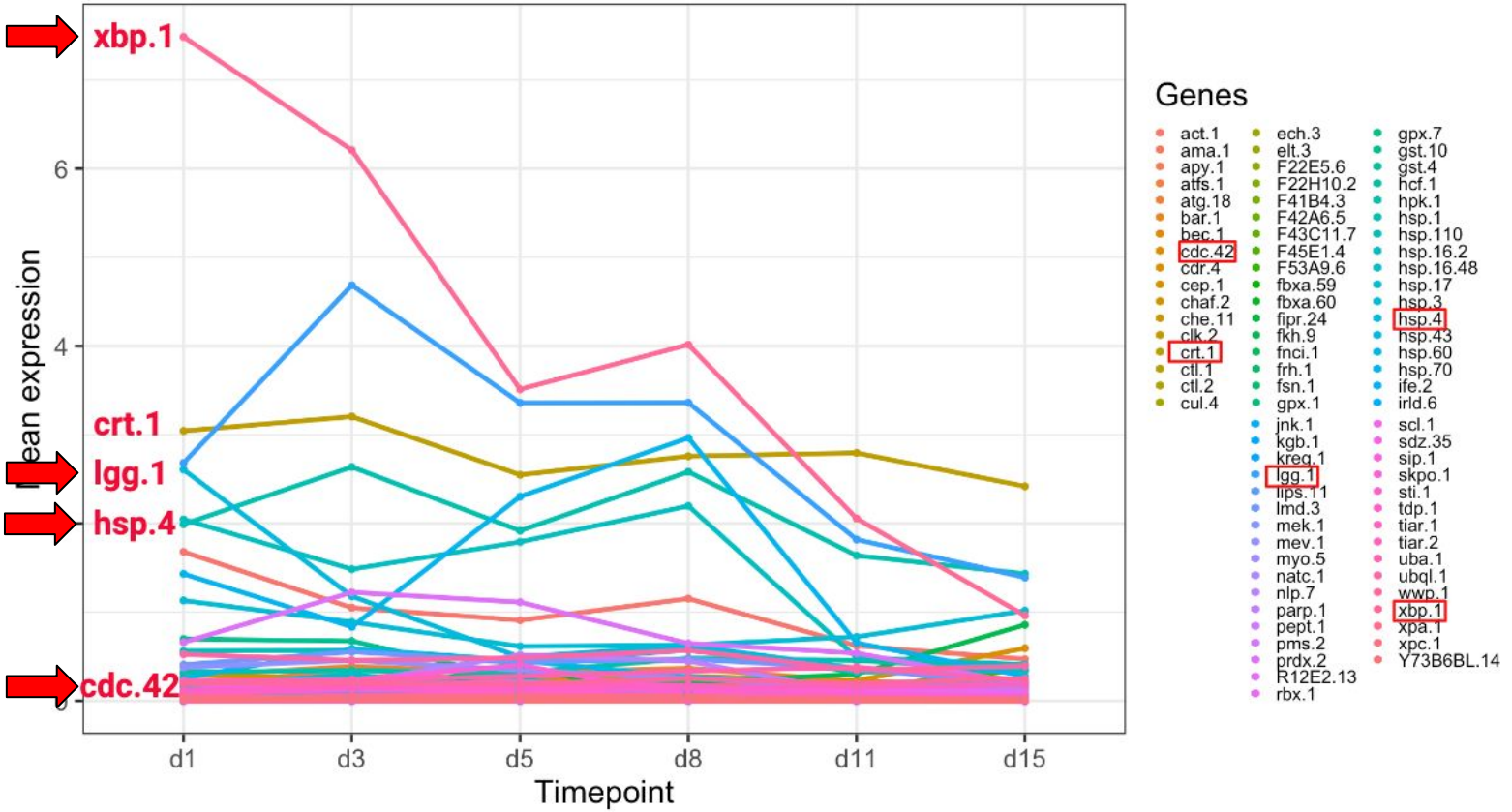
Global Stress Gene Expression Over Time (Line graph)



Global Stress Gene Expression Over Time (Line graph)



Global Stress Gene Expression Over Time (Line graph)



XBP-1
(Transcription Factor)

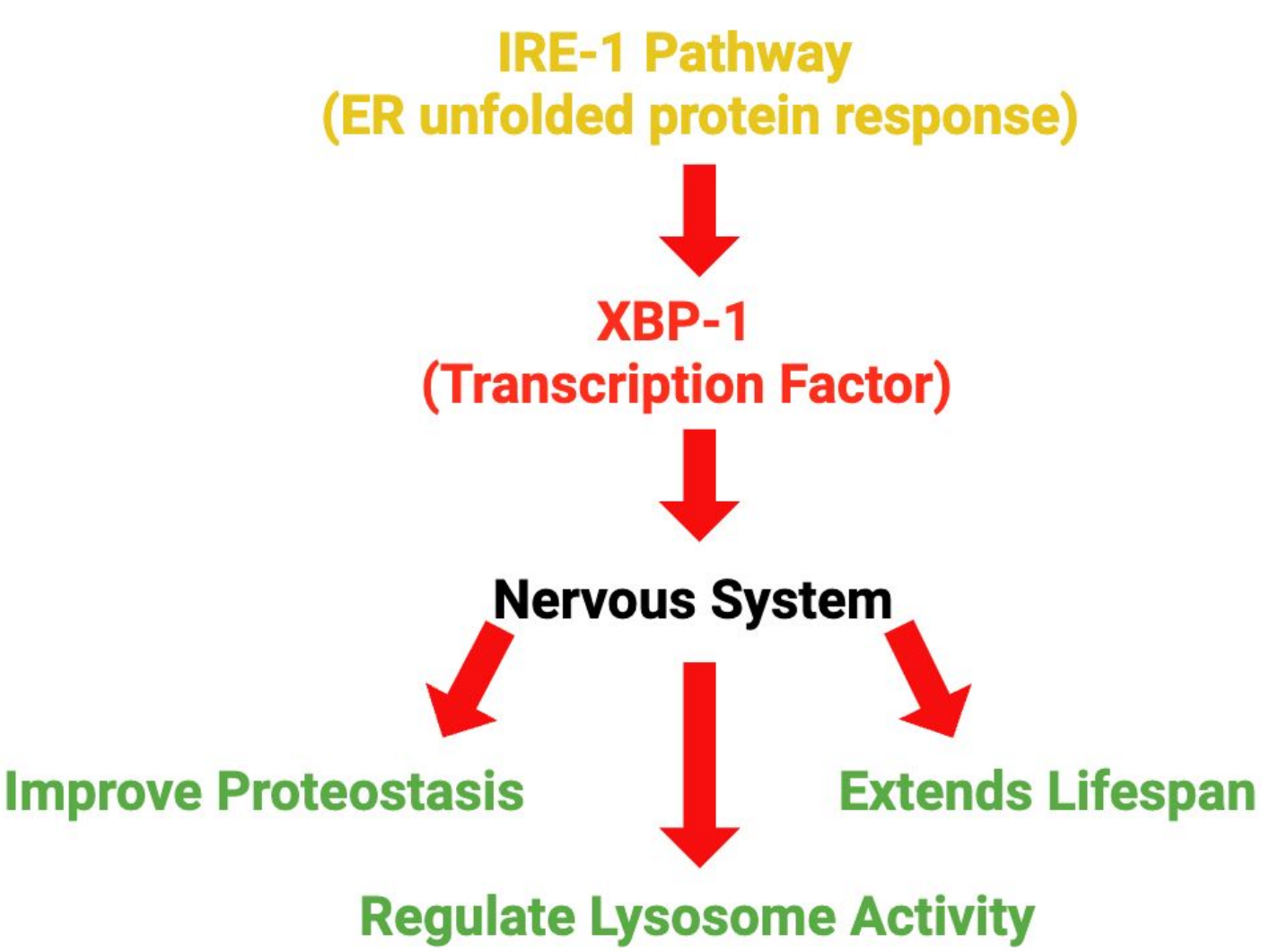
IRE-1 Pathway
(ER unfolded protein response)

XBP-1
(Transcription Factor)

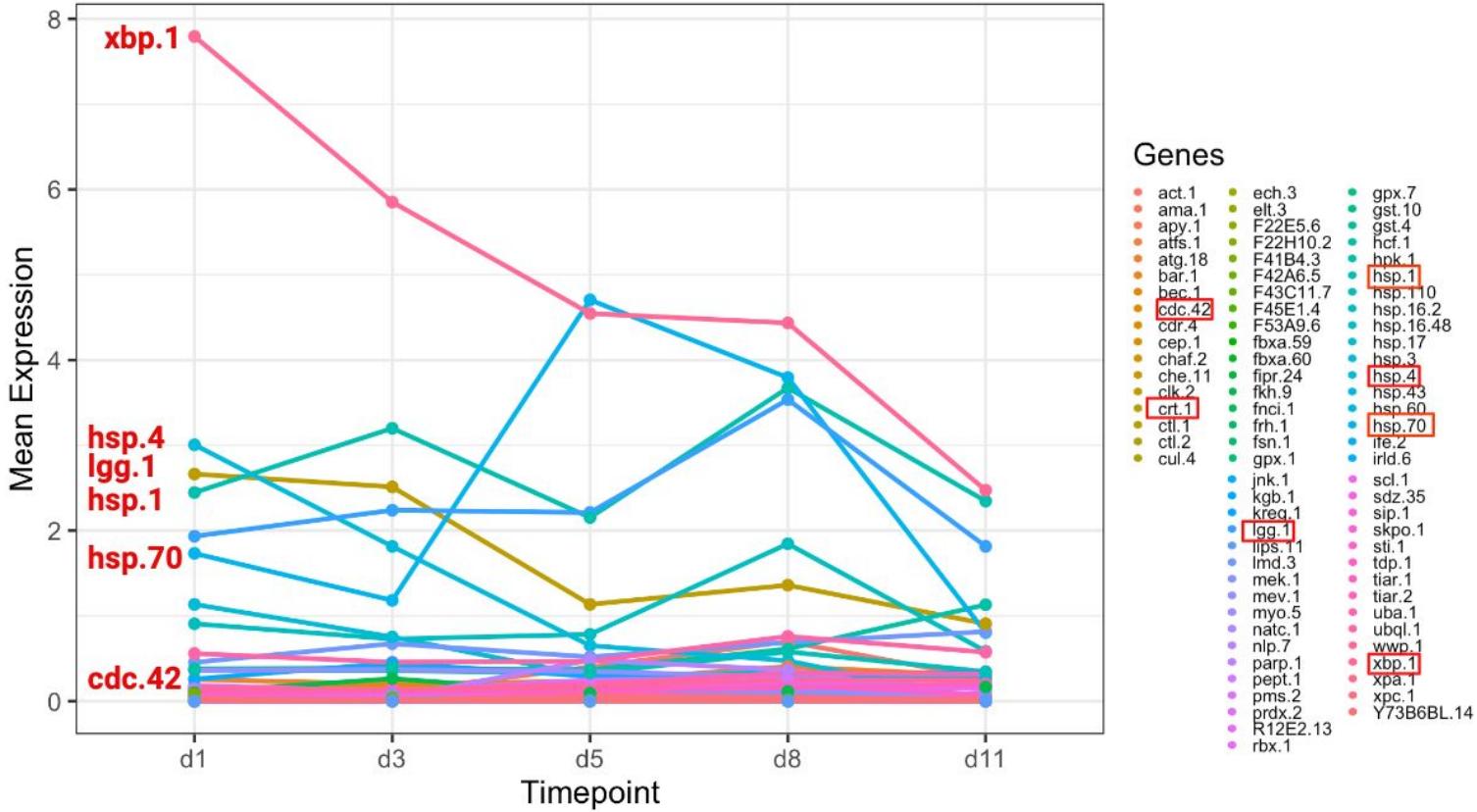
IRE-1 Pathway
(ER unfolded protein response)

XBP-1
(Transcription Factor)

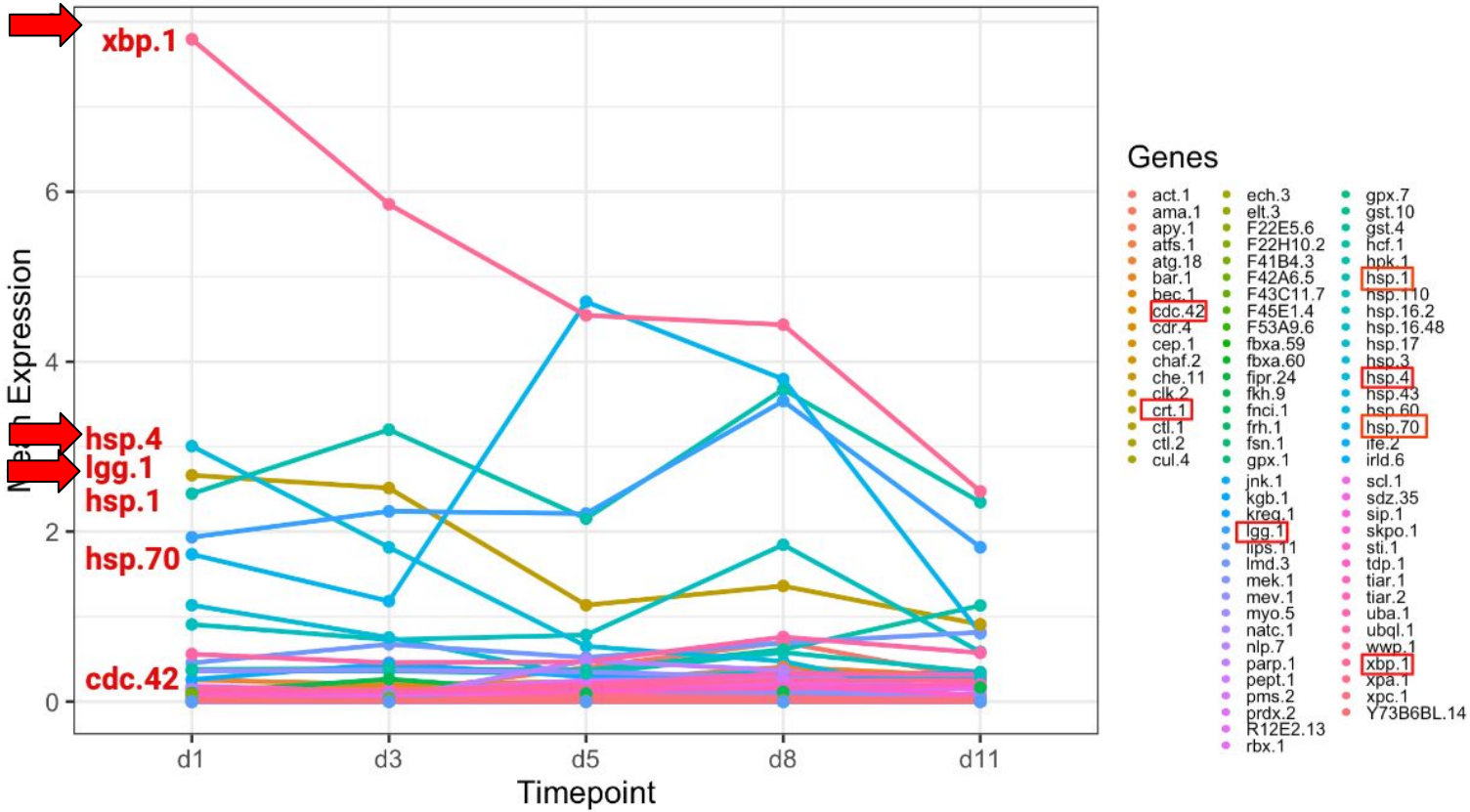
Nervous System


IRE-1 Pathway
(ER unfolded protein response)
XBP-1
(Transcription Factor)
Nervous System
Improve Proteostasis
Extends Lifespan
Regulate Lysosome Activity

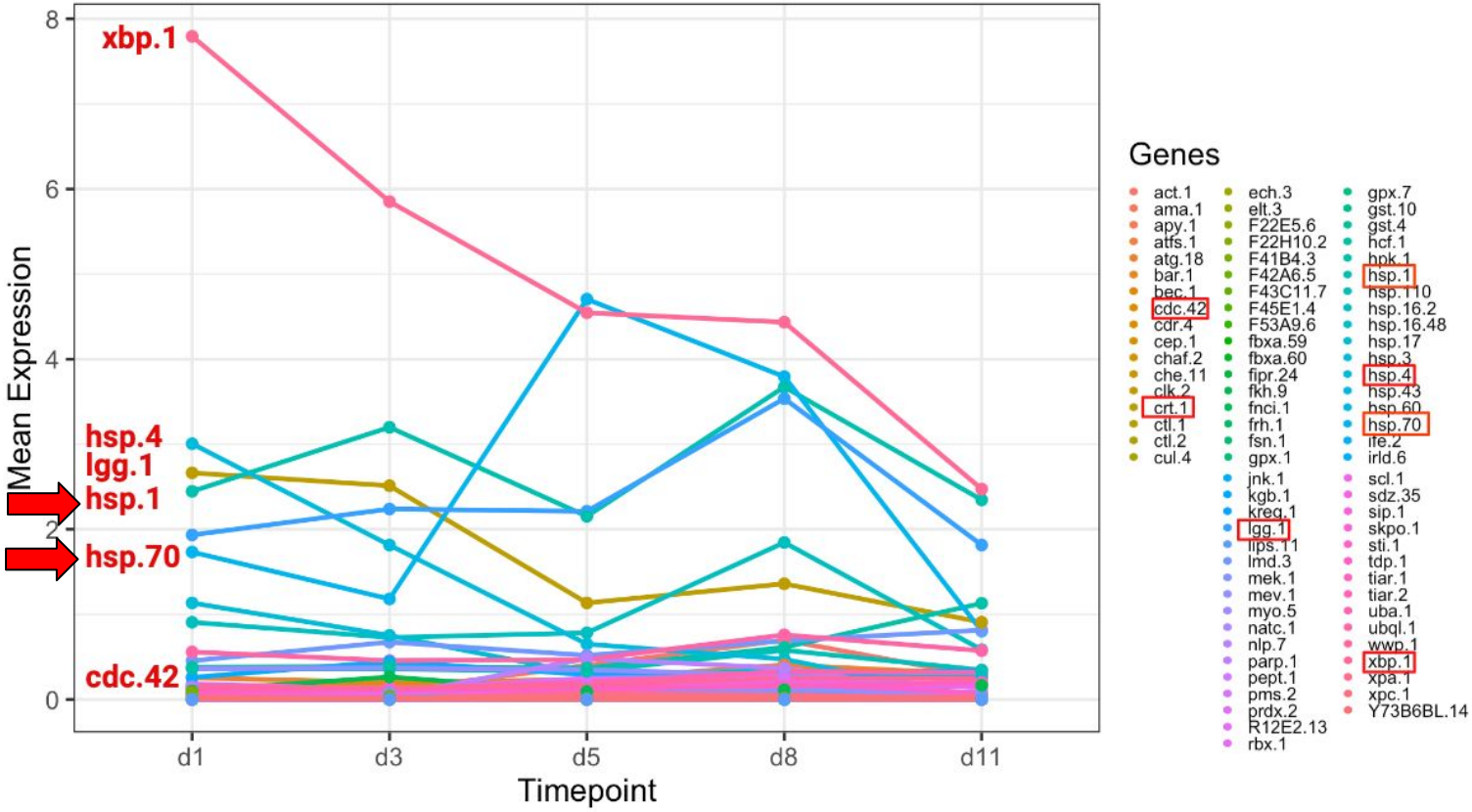
Neuron-specific Stress Gene Expression Over Time (Line graph)



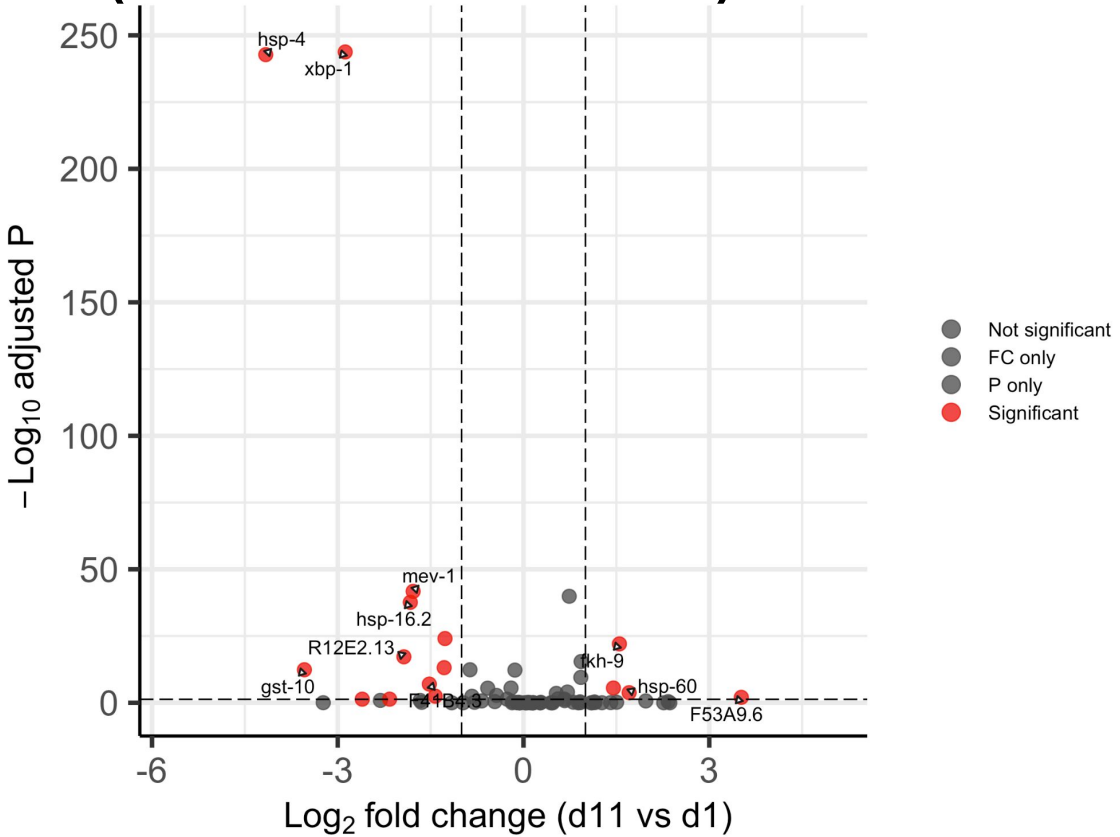
Neuron-specific Stress Gene Expression Over Time (Line graph)



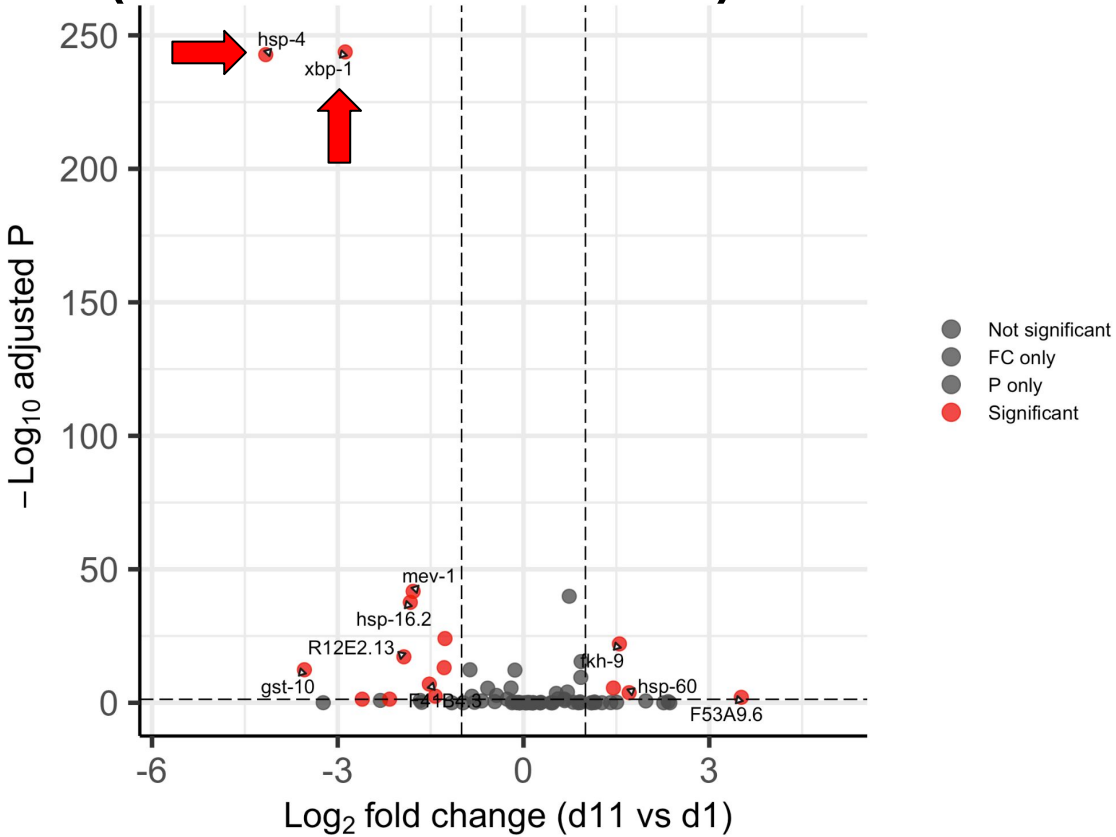
Neuron-specific Stress Gene Expression Over Time (Line graph)



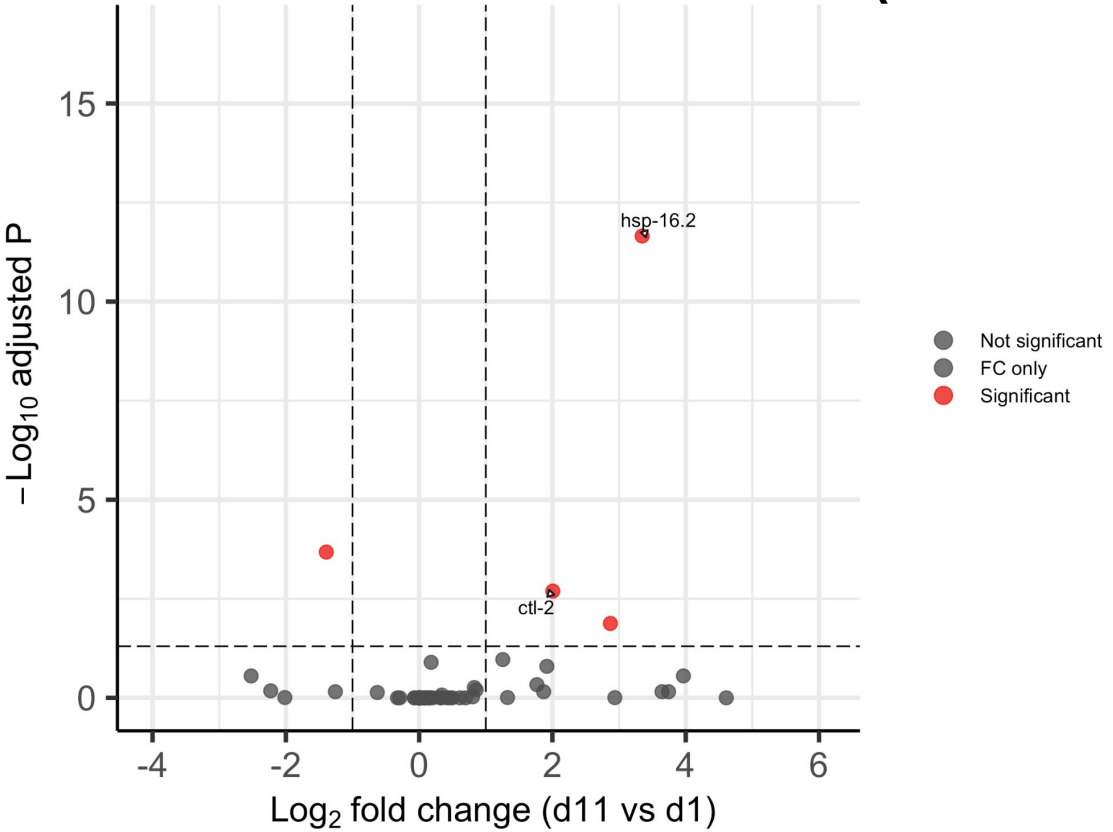
Global Stress Gene Expression Over Time (Volcano Plot)



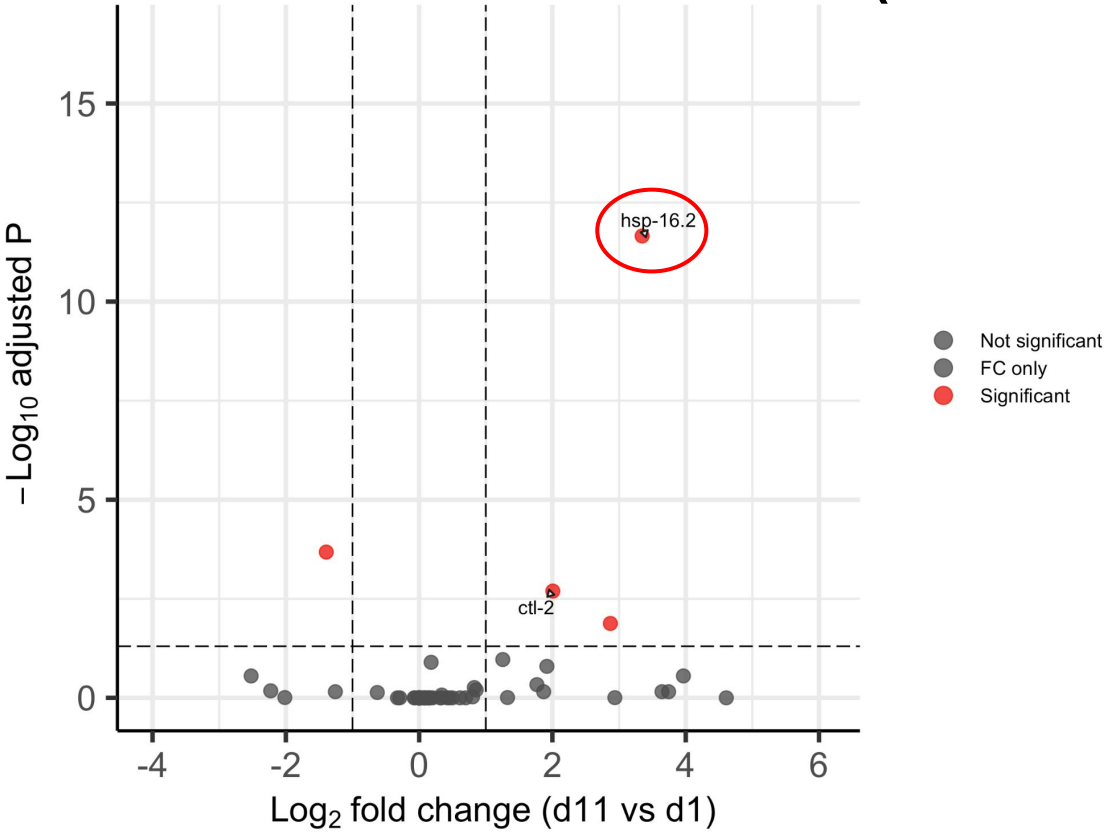
Global Stress Gene Expression Over Time (Volcano Plot)



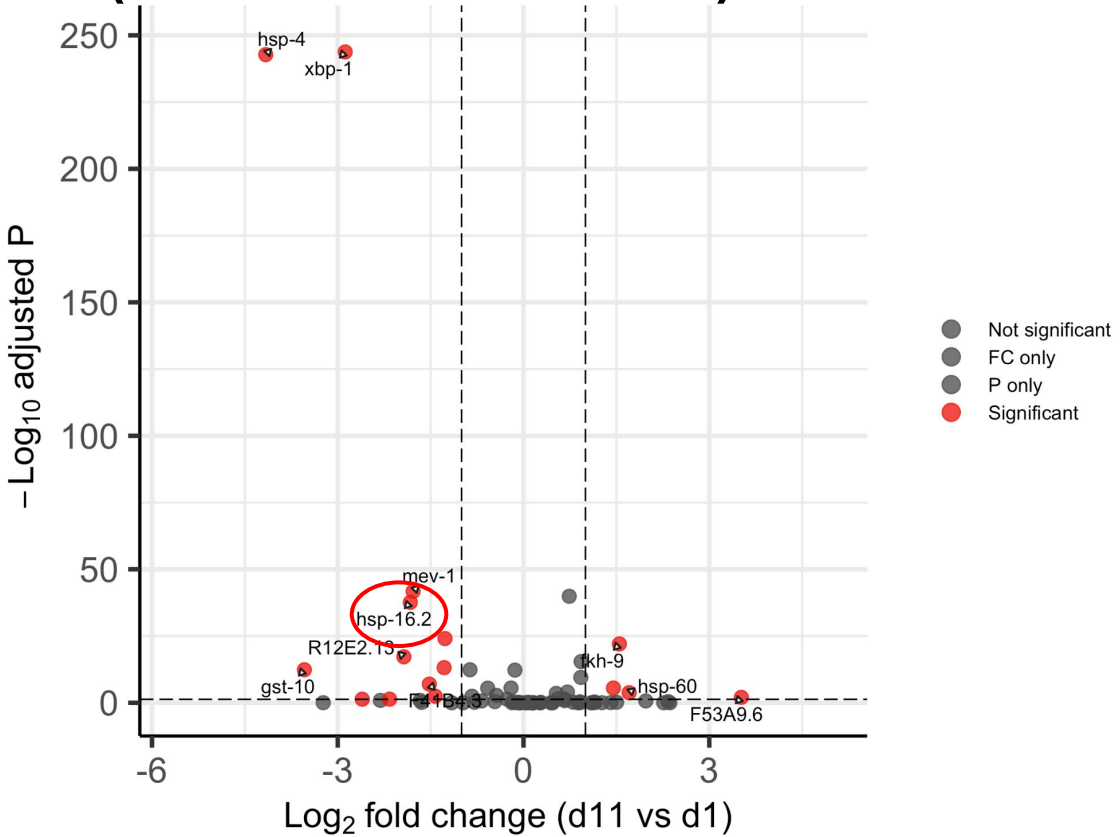
Neuron-specific Stress Gene Expression Over Time (Volcano)



Neuron-specific Stress Gene Expression Over Time (Volcano)



Global Stress Gene Expression Over Time (Volcano Plot)



Summary

- **Extract the single cell RNA sequencing dataset**
  -scanpy and python

- **Identified neuron clusters**
  -PCA + Clustering

- **Visualization using line graph and volcano plots**
  -Rstudio

Conclusions

- **Identified changes in stress gene expression**

-xbp-1, hsp-4, lgg-1,

- **Certain genes show changes in neuronal cells, while others do not.**

-hsp-1, hsp-70

- **Found the global decline and neuronal compensation of hsp-16.2**

Thank You!

Limitations

Conclusions

- Globally, hsp-16.2 drops by day 11, showing loss of systemic heat shock responsiveness.
- This matches the known collapse of HSF-1 driven chaperone induction with age.
- In neurons, hsp-16.2 instead rises, one of the few stress genes that increases.
- Neurons therefore retain a unique compensatory chaperone response.
- hsp-16.2 becomes a neuron-specific marker of late-life proteostasis decline.