WEIZMANN INSTITUTE OF SCIENCE

Department of Molecular Cell biology
Department of Molecular Neuroscience

Effects of zygotic and maternally contributed RE-1 silencing transcription factor on stress coping in Zebrafish larvae

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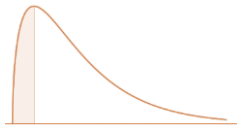
Stress Coping and Resilience

Stress – a state in which an external or internal stimulus forces the system away from its physiological homeostatic steady state (Kyrou & Tsigos, 2009).

Stress response – physiological and behavioral changes towards regaining homeostatic stability, determined by **genetics** and **environment** (Kyrou & Tsigos, 2009).



Variability in stress response – difference in the rate and efficiency to rebound defines resilience or susceptibility to stress (Swaminathan et al., 2023).

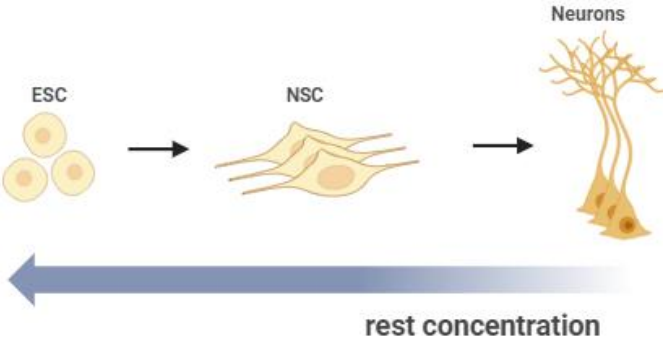
Stress coping and stress-related disorders – coping patterns play a role in the development of disorders such as major depression, anxiety and post-trauma (Franklin et al., 2012).

RE-1 Silencing Transcription Factor (Rest)

Transcriptional repressor – modifies chromatin structure, silencing transcription of over 2,000 neuron-specific target genes (Mampay & Sheridan, 2019).

Expression patterns :

Highly expressed in embryonic stem cells and non-neuronal tissues (Mampay & Sheridan, 2019).

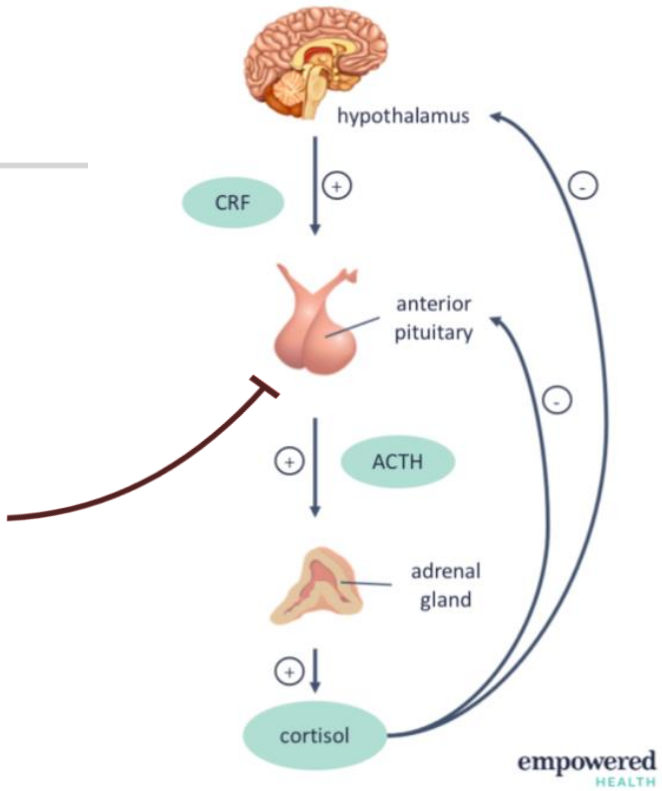


Highly expressed in neuronal stem cells and gradually downregulated during development to allow neuronal differentiation (Mampay & Sheridan, 2019).

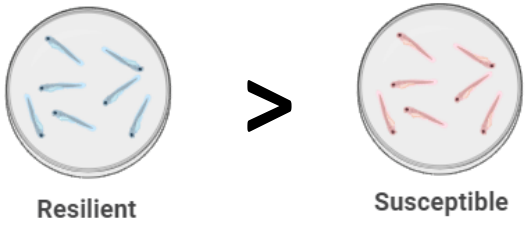
Rest-mediated Stress Response

Upregulated following stress (Mampay & Sheridan, 2019)

Attenuates the neuroendocrine stress response via repression of the Corticotropin releasing hormone (CRH) that plays a key role in the hypothalamic-pituitary-adrenal axis (Seth & Majzoub, 2001).



Promotes Neuronal equilibrium

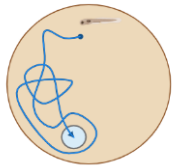


High rest concentrations in resilient individuals (Swaminathan et al., 2023)

Maternal Rest mRNA deposition to the oocyte

Transcription regulation during early development – Until the mid-blastula stage the embryonic genome is transcriptionally silent, and development is driven mainly by maternally deposited mRNA in the cytoplasm (Winata & Korzh, 2018).

Depletion of maternal Rest mRNA results in :



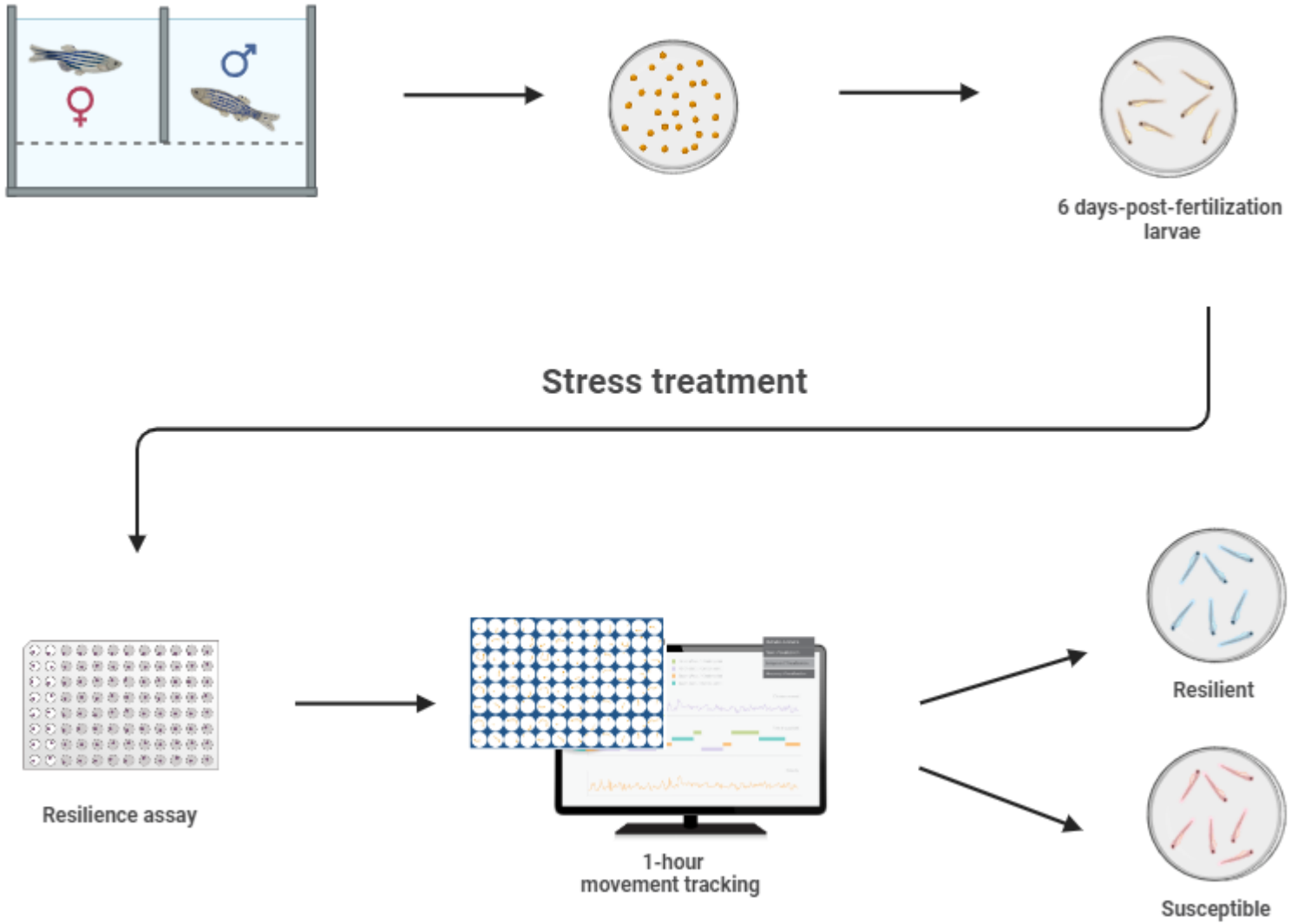
Behavioral locomotor changes in larvae, that persist into adulthood (Moravec et al., 2016).

Altered primary motor neuron architecture (Moravec et al., 2016).

Research Question :

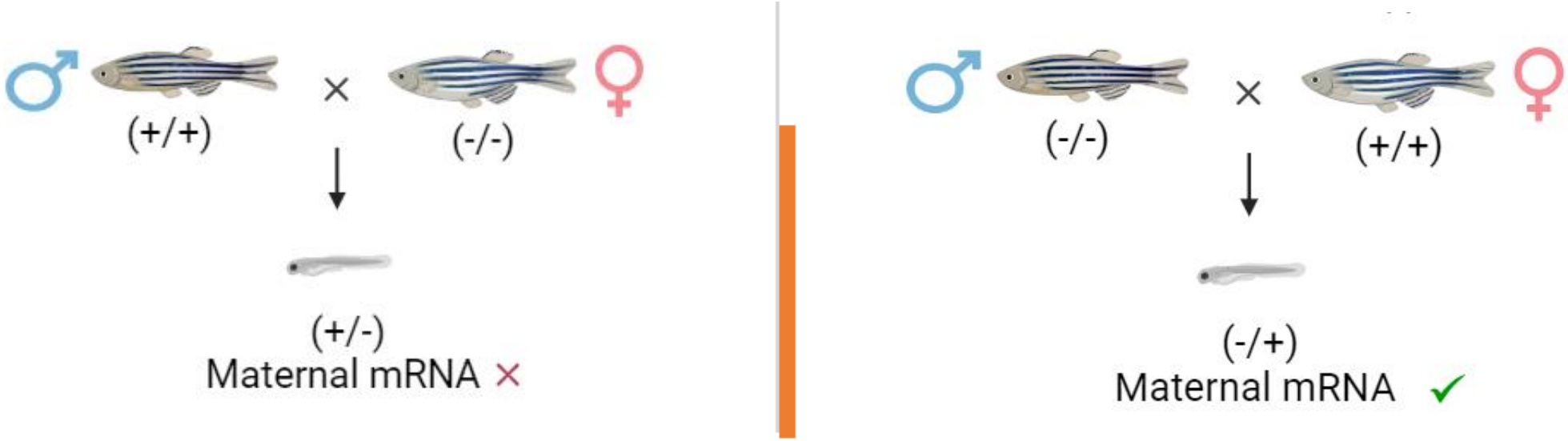
What is the effect of zygotic and maternally contributed Rest on stress coping in Zebrafish larvae?

The Stress-inducing Behavioral Paradigm



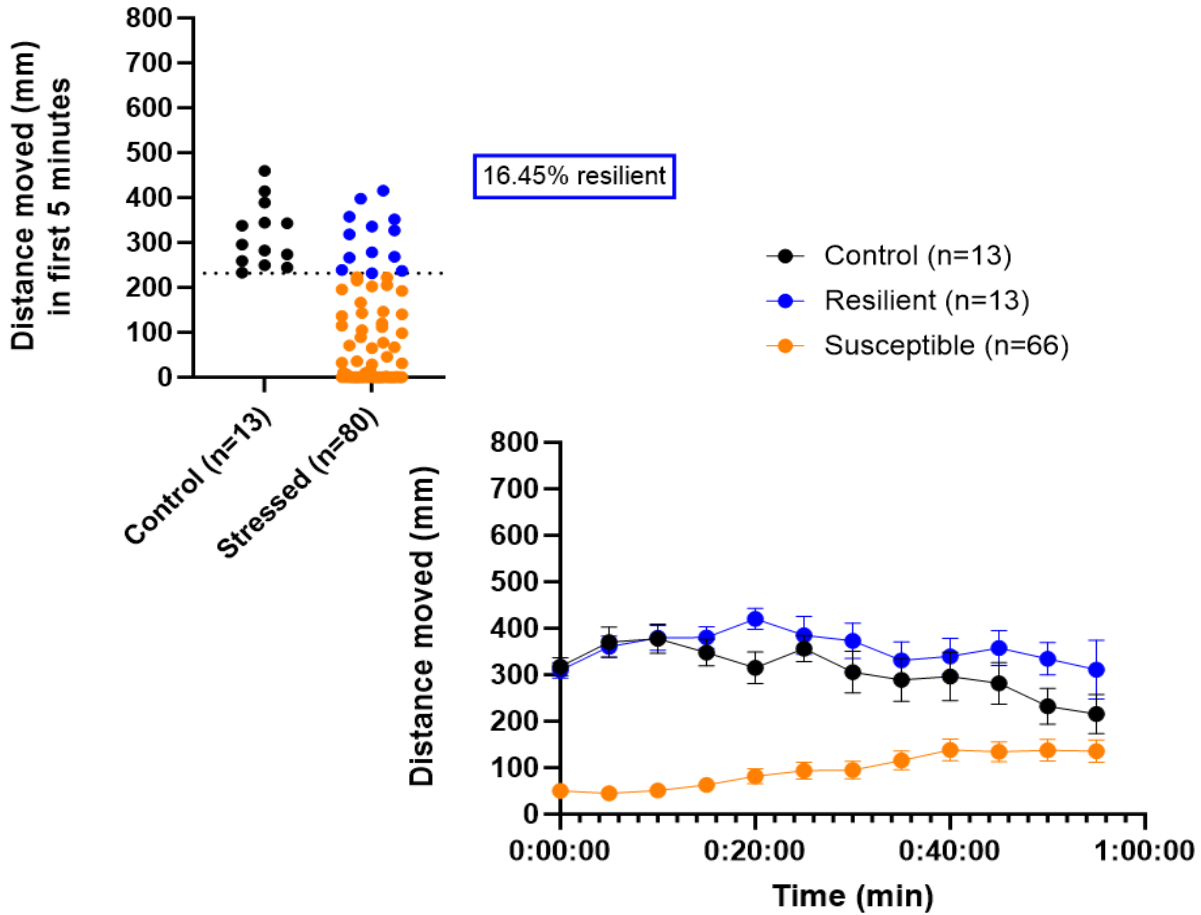
Investigating the Effect of Maternally Contributed Rest

Created two different mutants :

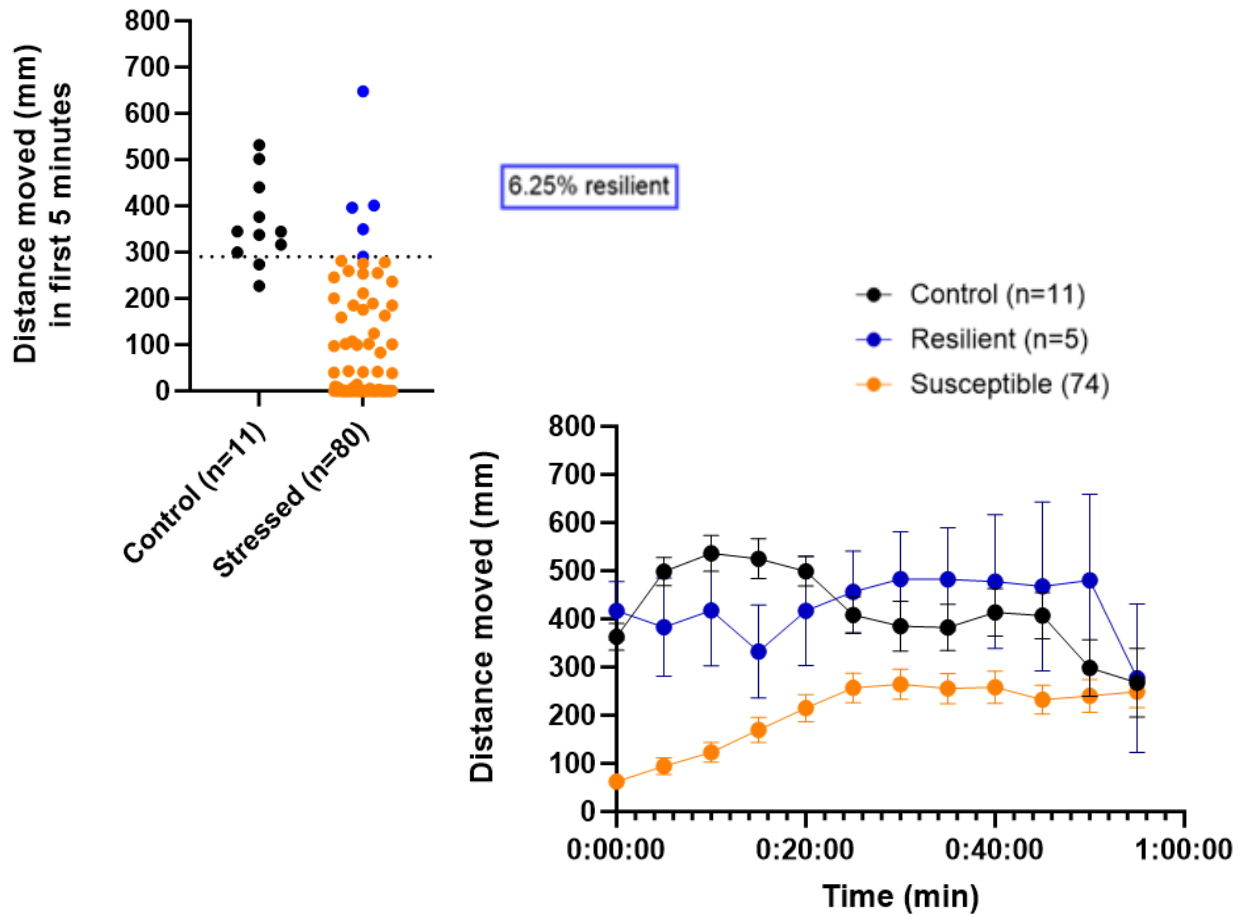


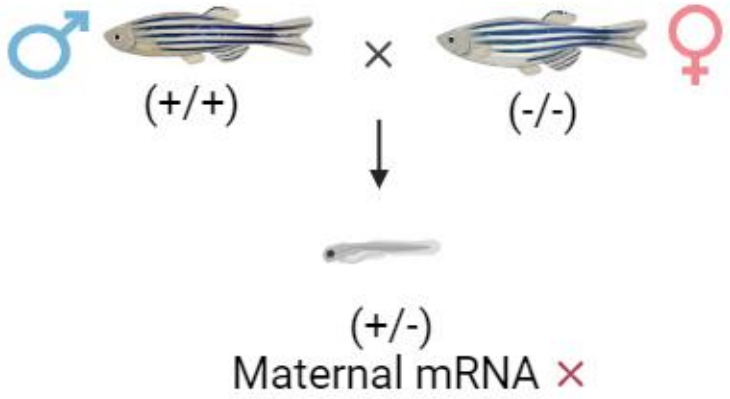
One genotype per plate ⟶ compare between plates

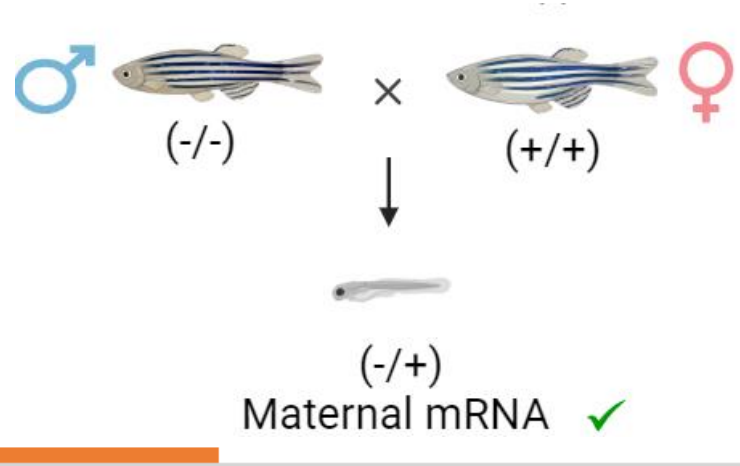
(+/-)
Maternal mRNA ×



(-/+)
Maternal mRNA ✓



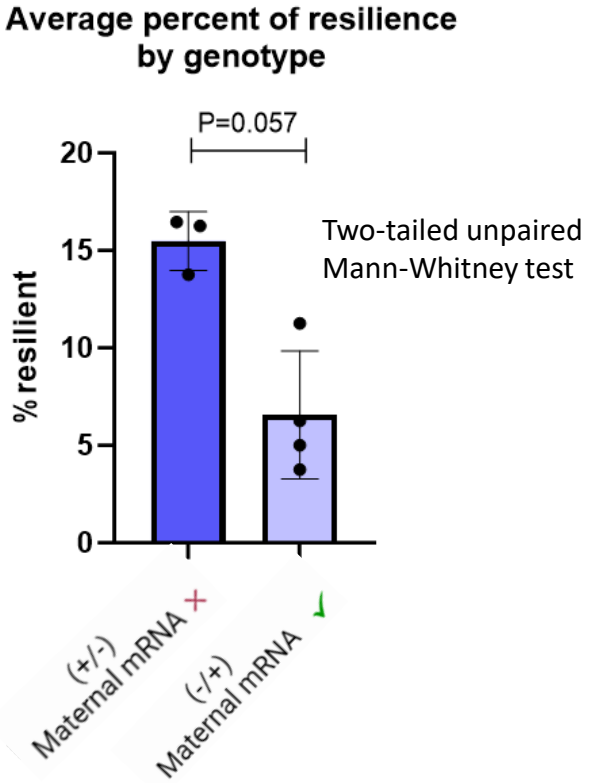




13.75% resilient

16.25% resilient

16.45% resilient



5% resilient

3.75% resilient

11.25% resilient

6.25% resilient

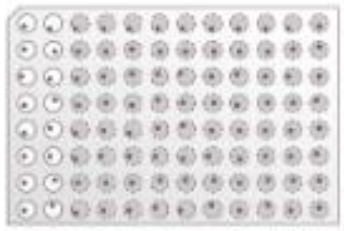
Depletion of maternal Rest mRNA promotes resilience

Effect of Maternally Contributed Rest

(+/-)
Maternal mRNA ×

→ **Resilience**

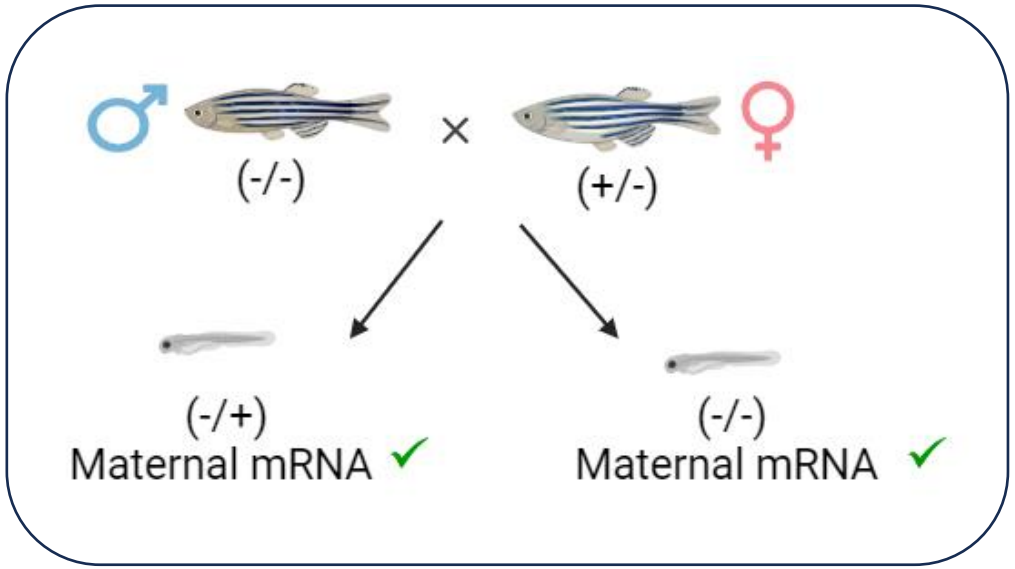
- Additional neurophysiological stress factors regulated by Rest
  - Rest splice variants

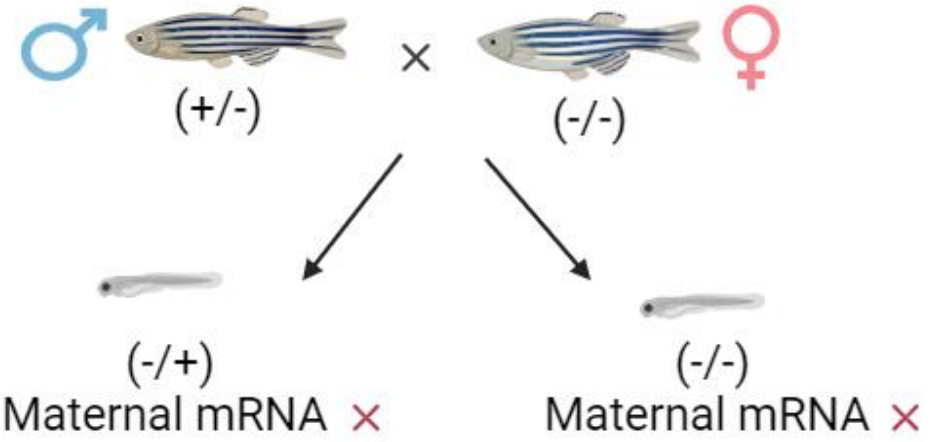


More repetitions are needed to elucidate the results

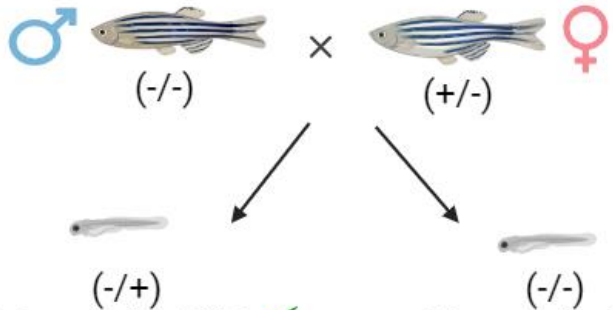
Investigating the Effect of Zygotic contributed Rest

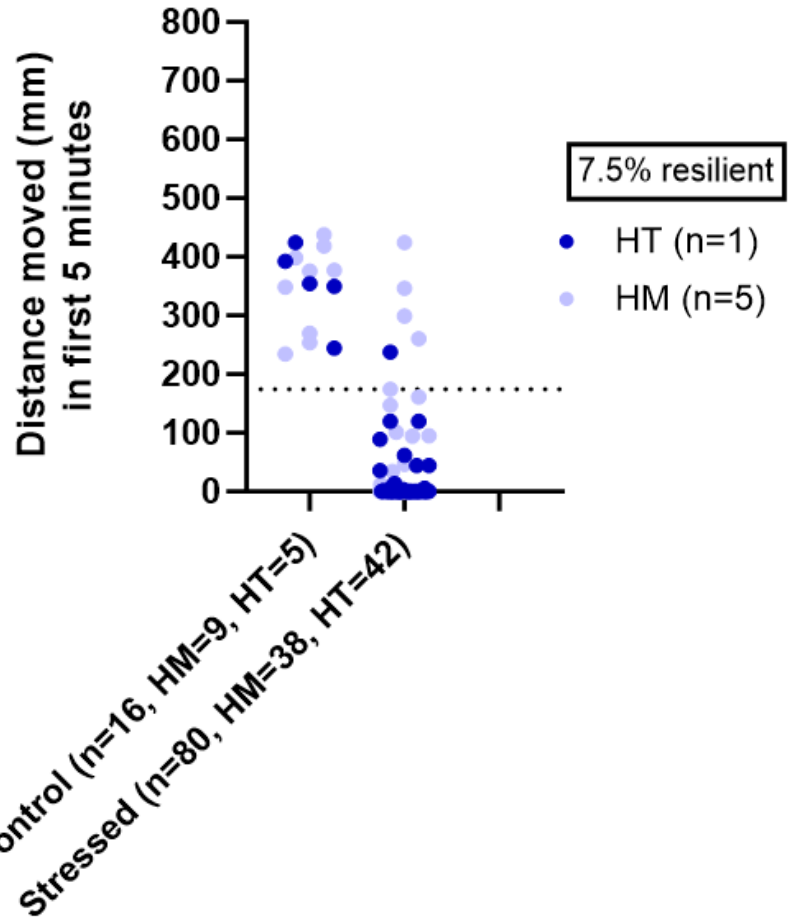
Created two different crosses :

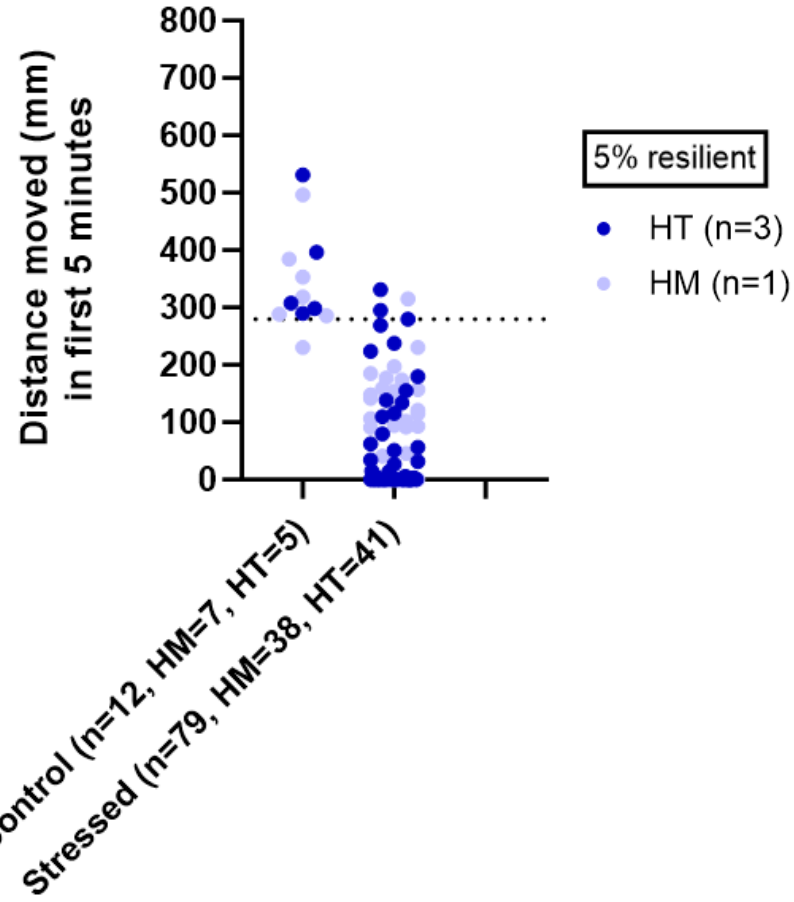




Two genotypes per plate ⟶ compare inside plates

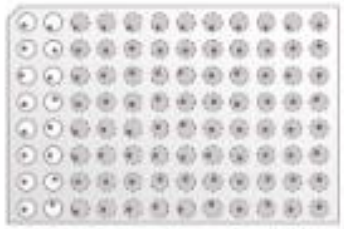

(-/-)
×
(+/-)
(-/+)
(-/-)


Distance moved (mm) in first 5 minutes
800
700
600
500
400
300
200
100
0
7.5% resilient
HT (n=1)
HM (n=5)
Control (n=16, HM=9, HT=5)
Stressed (n=80, HM=38, HT=42)

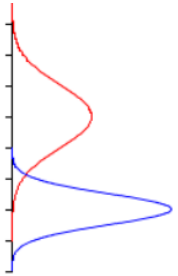

Distance moved (mm) in first 5 minutes
800
700
600
500
400
300
200
100
0
5% resilient
HT (n=3)
HM (n=1)
Control (n=12, HM=7, HT=5)
Stressed (n=79, HM=38, HT=41)

Discussion - Effect of Zygotic Contributed Rest

From the results collected we can not conclude about the effect of zygotic Rest



More repetitions are needed to elucidate the results



Bigger resilient population to investigate genotype distribution

Reducing stress intensity

- Lower salt concentrations
- Shorter stress periods

Discussion – Additional Steps and Future Directions

Investigate the **combined effect** of both Maternal mRNA depletion and Zygotic

Maternal mRNA inheritance pattern - Check maternal mRNA levels in fertilized wild-type eggs compared to fertilized heterozygous.

Additional factors - Look for different maternally inherited factors that play a role in stress coping mechanisms during development.

Questions ?

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Thank You !