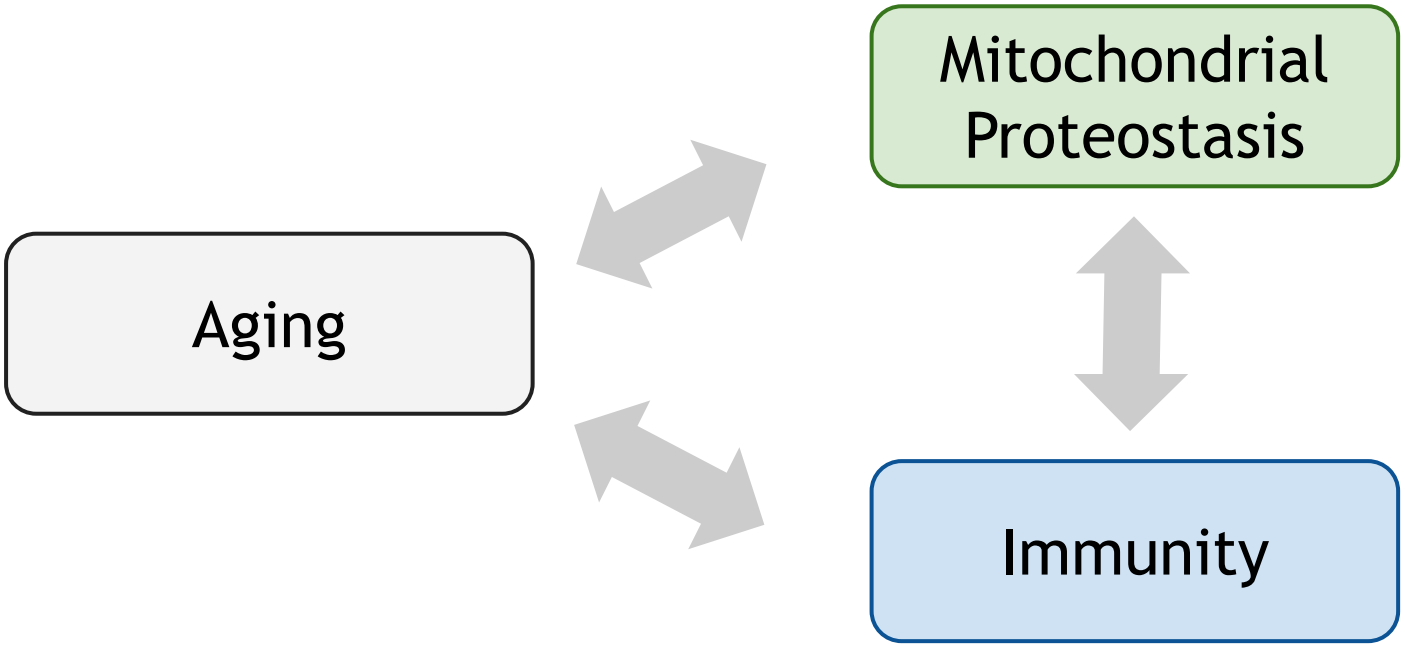
Mitochondrial Protein Degradation and Immune Response in *Drosophila melanogaster*

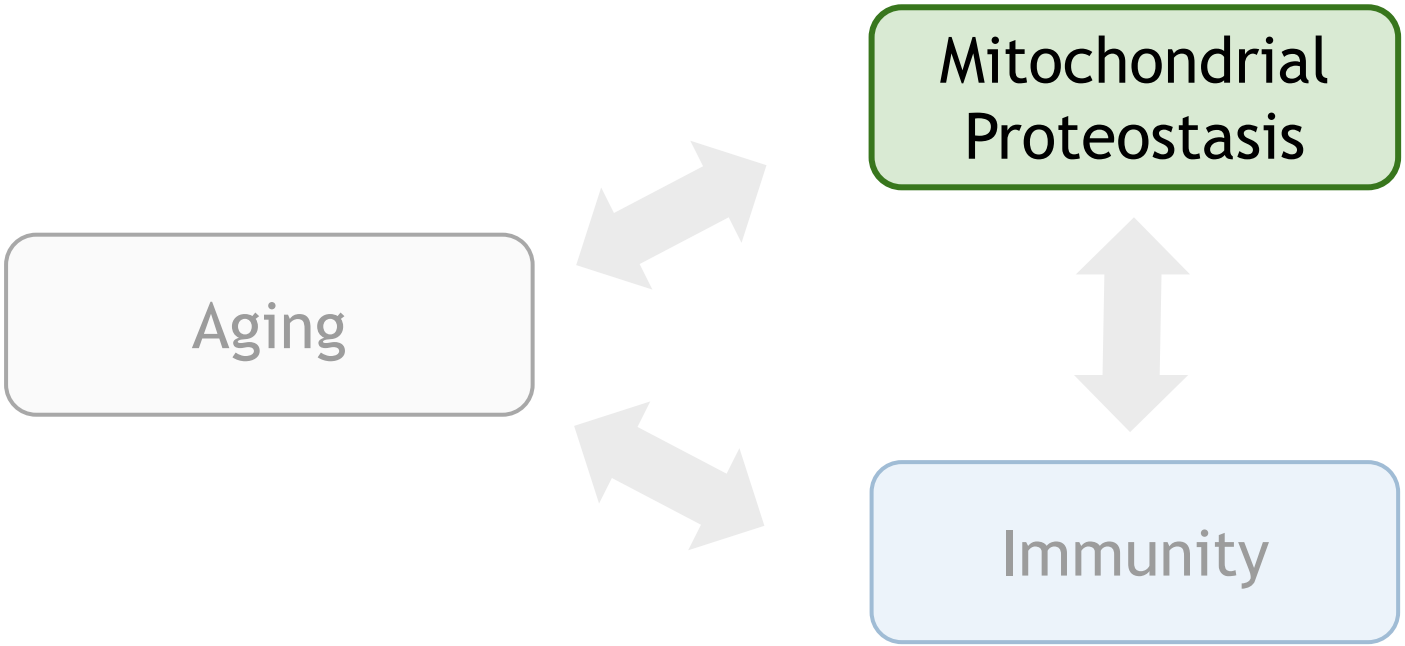
Fuminori Tanizawa
Hur Lab

May 5, 2025

Mitochondrial Proteostasis and Immunity



Mitochondrial Proteostasis and Immunity



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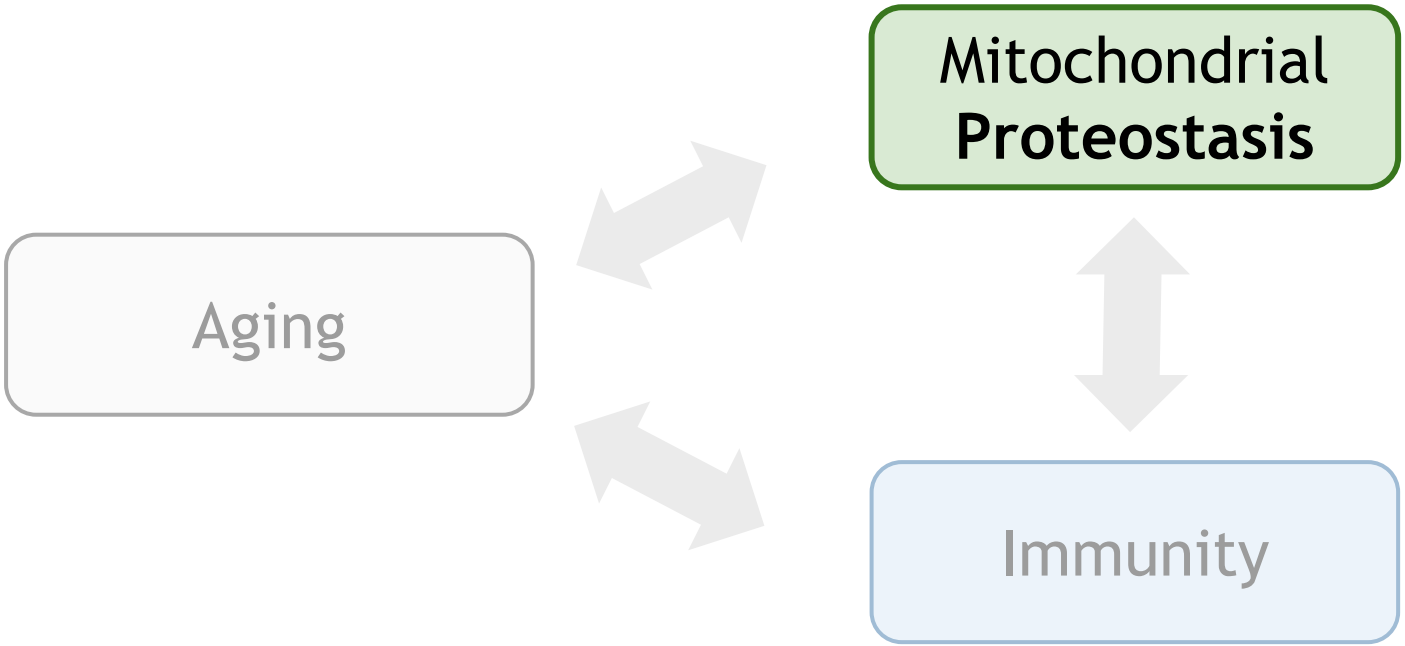
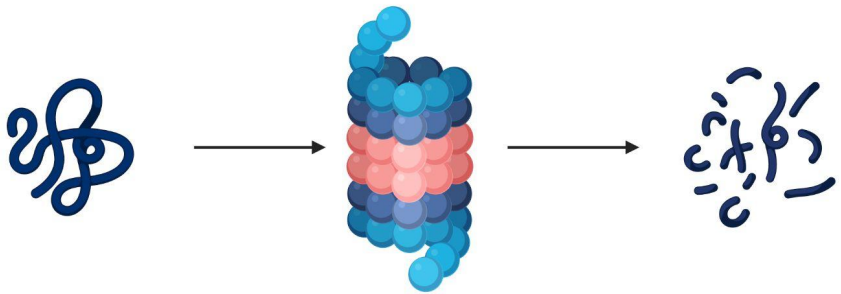


Proteostasis

- Protein Homeostasis (**Proteostasis**)
  - Protease: enzyme degrading misfolded or damaged proteins

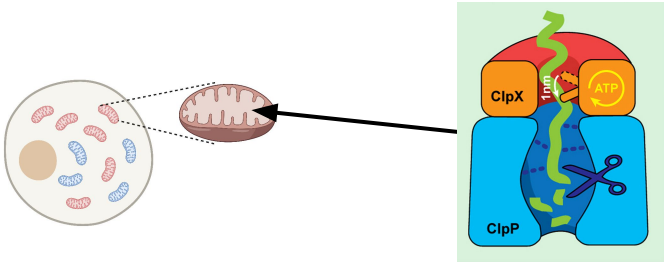


Protease

(Nouri, Feng, & Schimmer, 2020)

Mitochondrial Proteostasis

- Maintaining function of mitochondria
- Mitochondrial proteases (eg. ClpXP)



(Nouri, Feng, & Schimmer, 2020)

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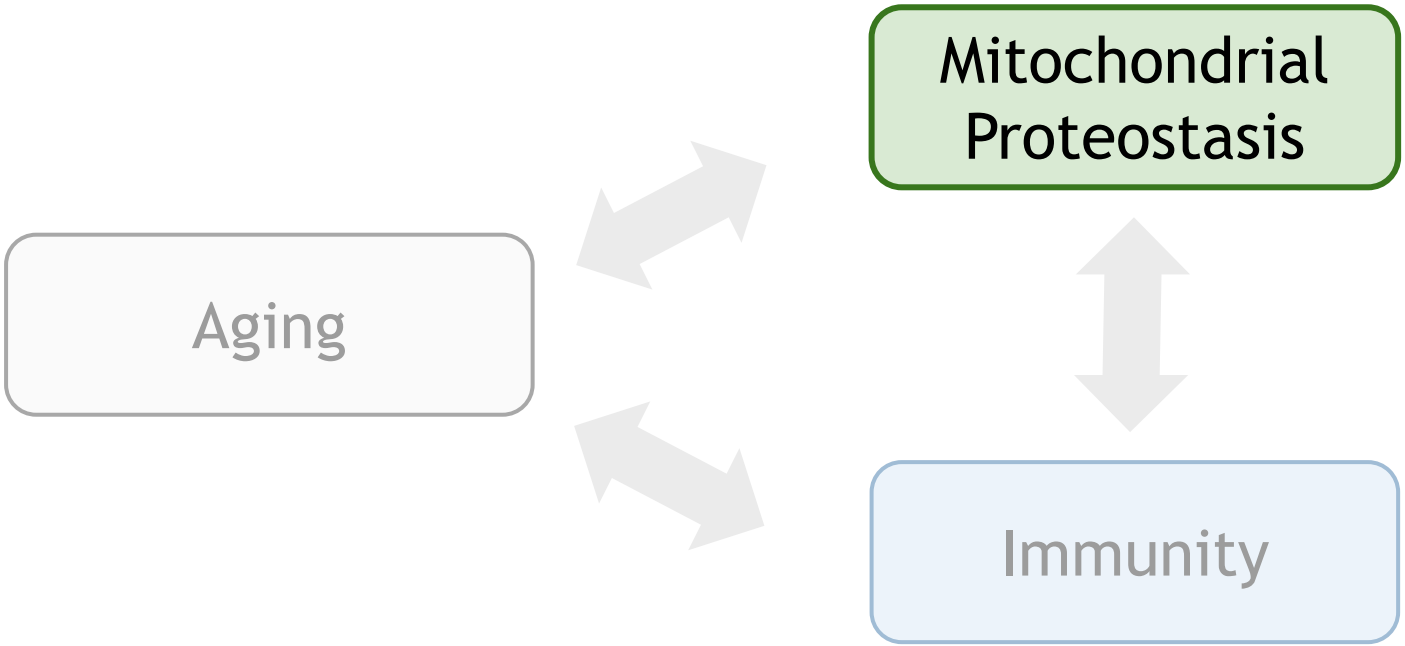

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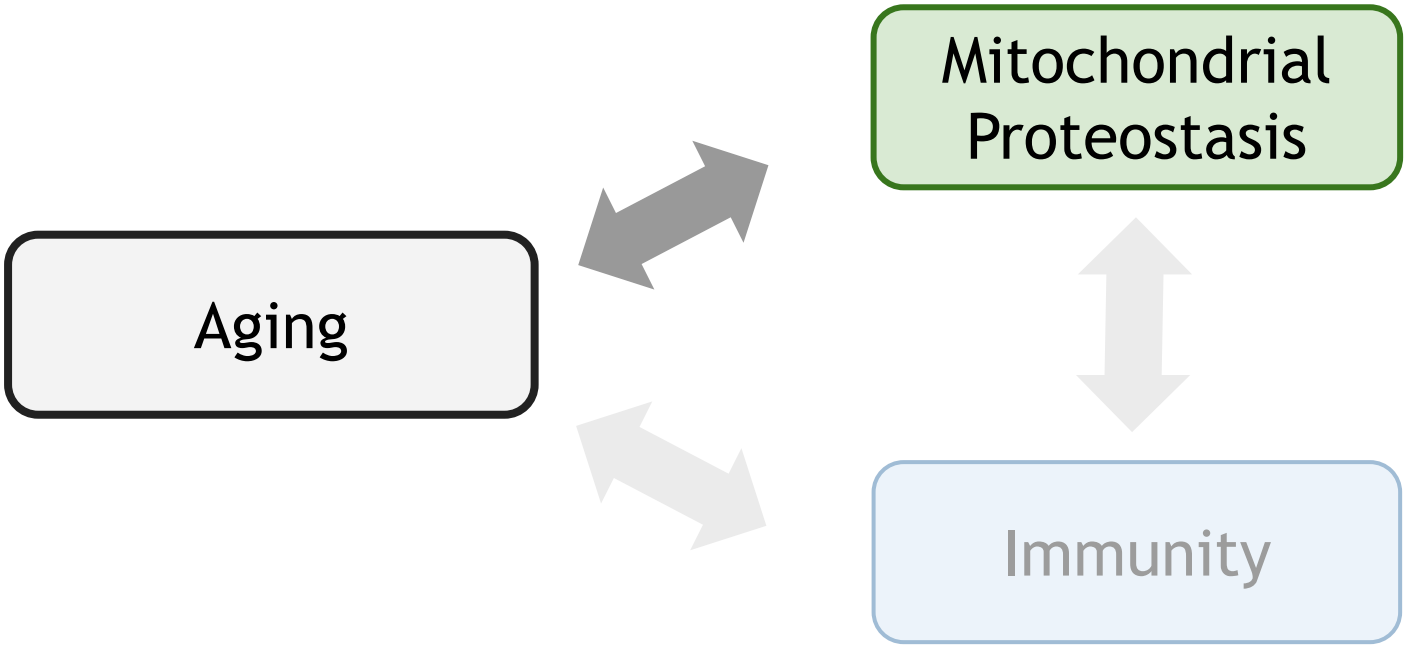
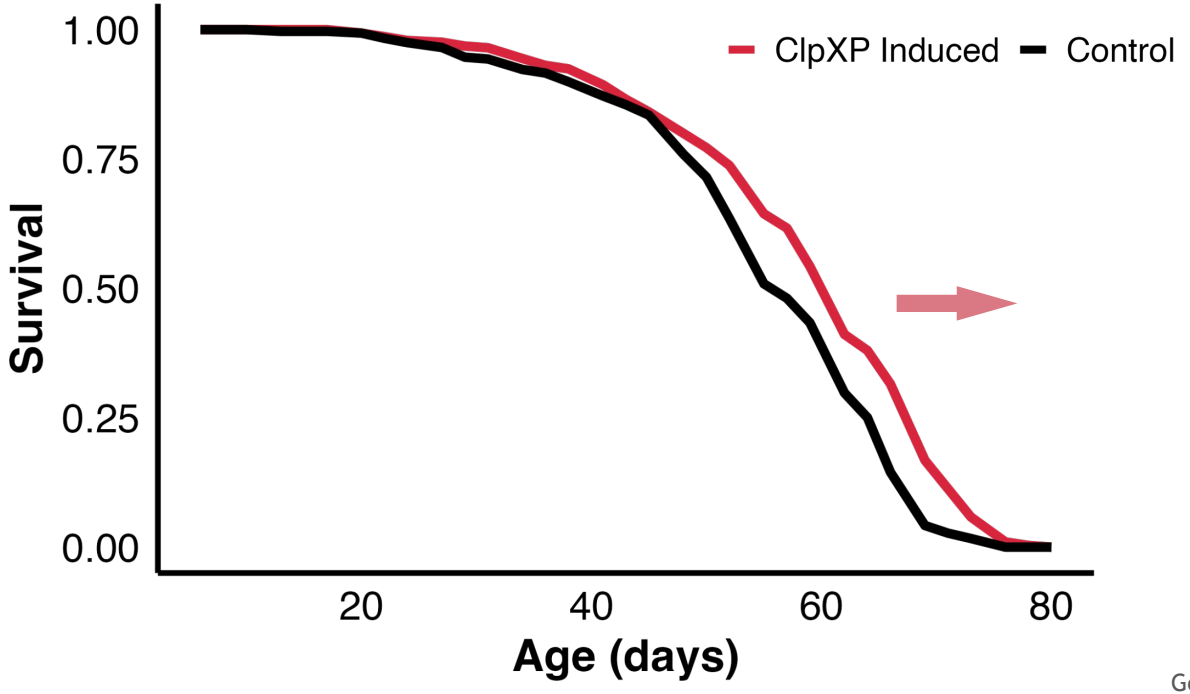
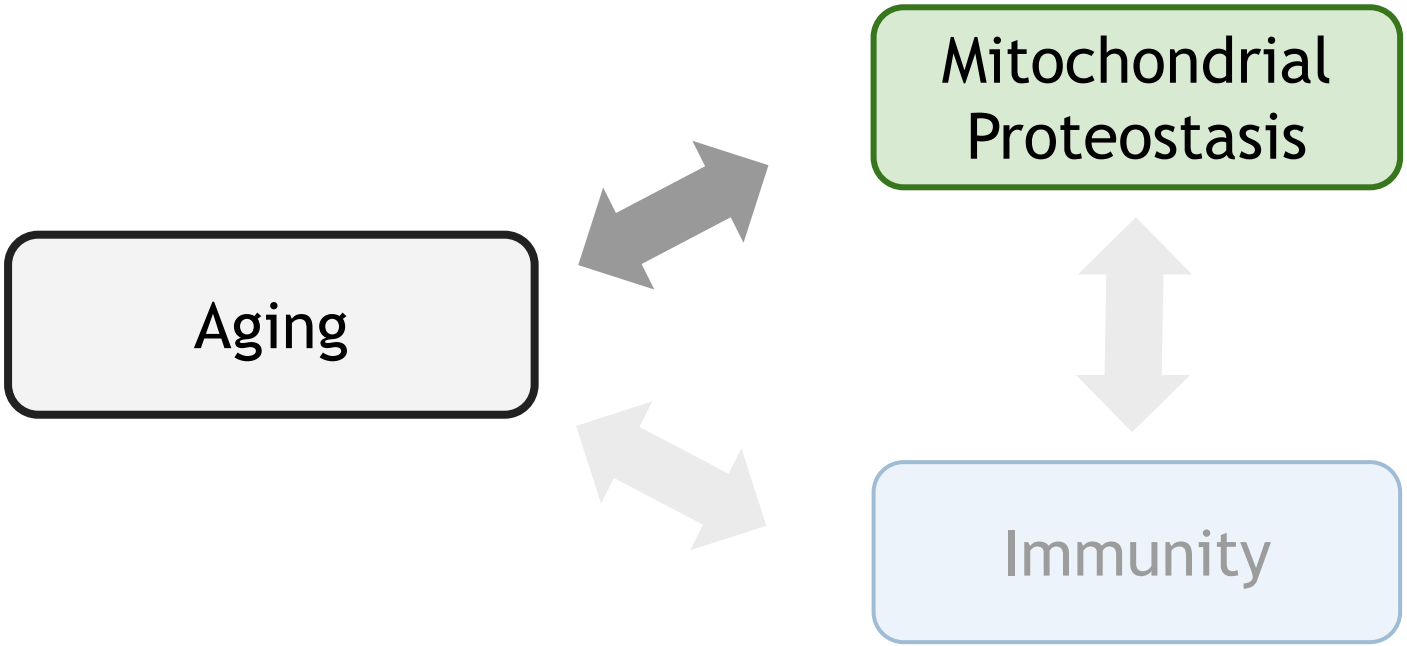
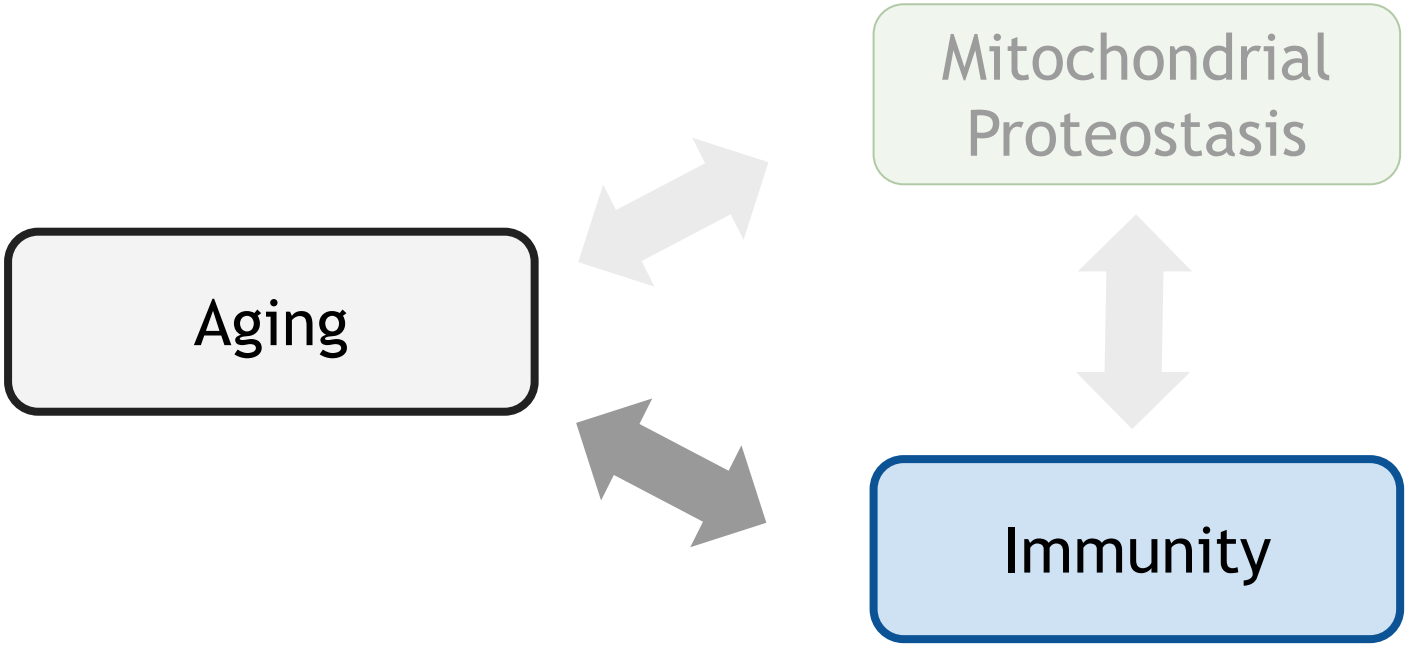


Mild overexpression of mitochondrial protease ClpXP **increases** longevity



Goldman C. & Hur J. (2019)


Mitochondrial Proteostasis
Aging
Immunity


Mitochondrial
Proteostasis
Aging
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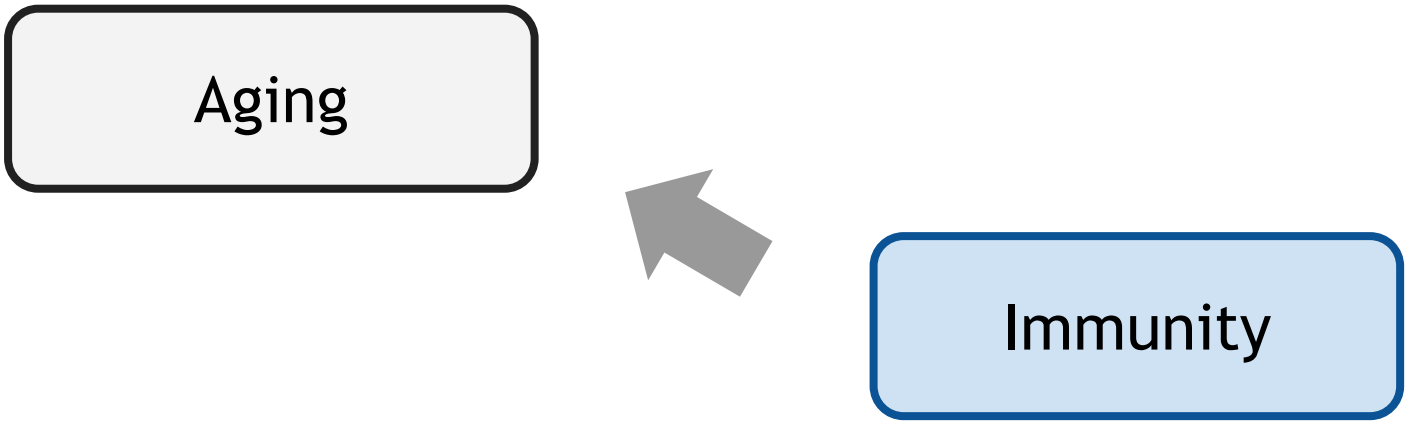
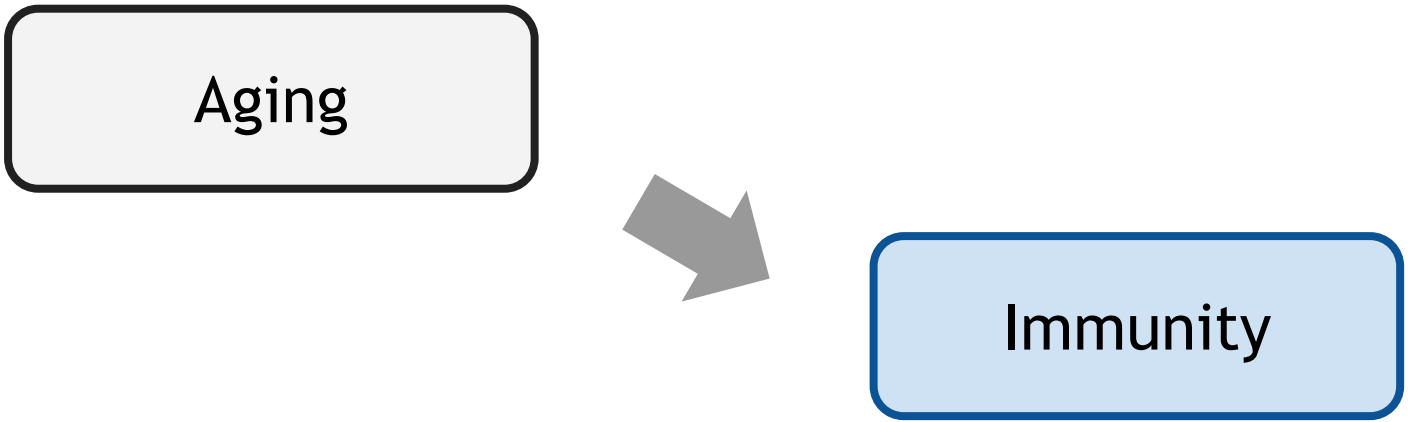
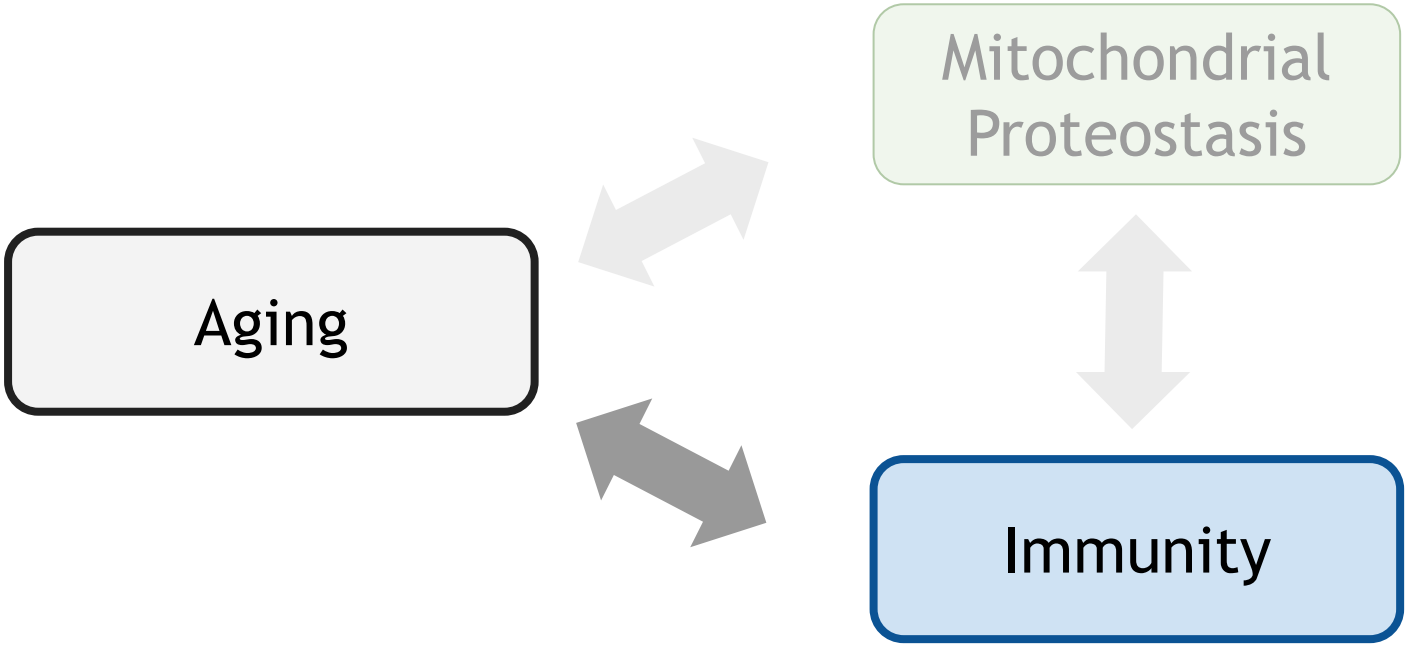
- Tissue damage and metabolic disruption



- Decline in immune function (**Immunosenescence**)
- Chronic inflammation (**Inflammaging**)

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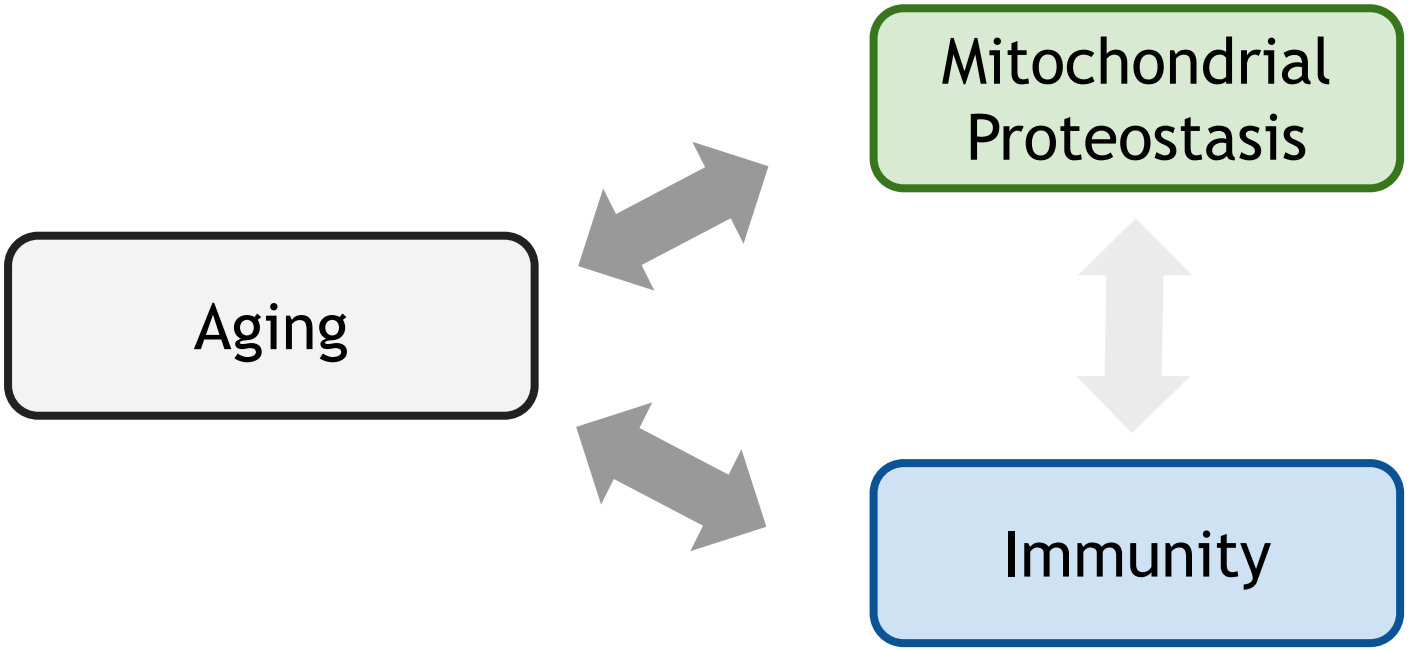
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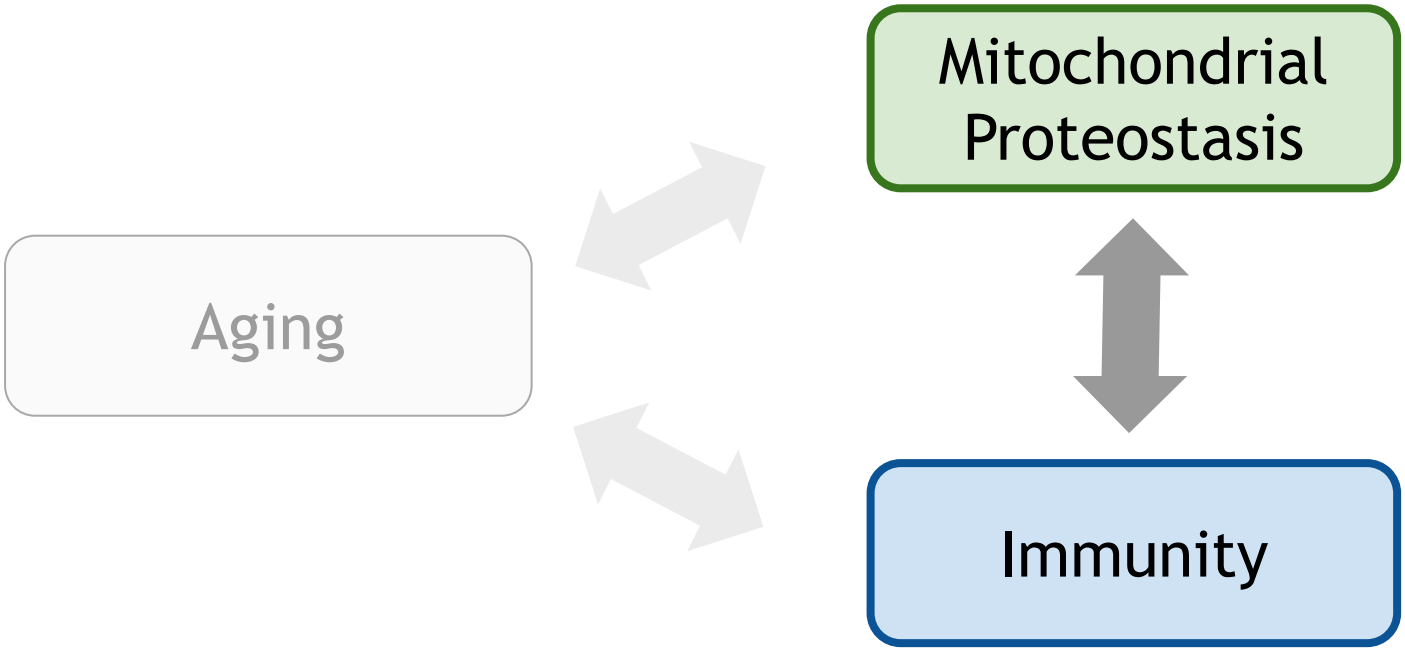
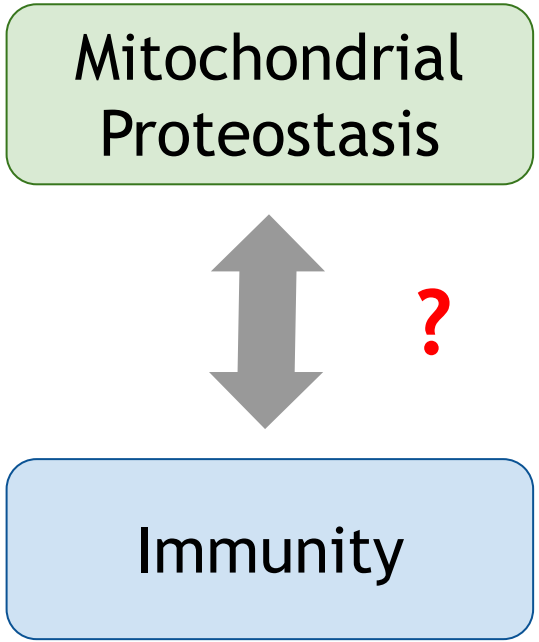


Disruptions in

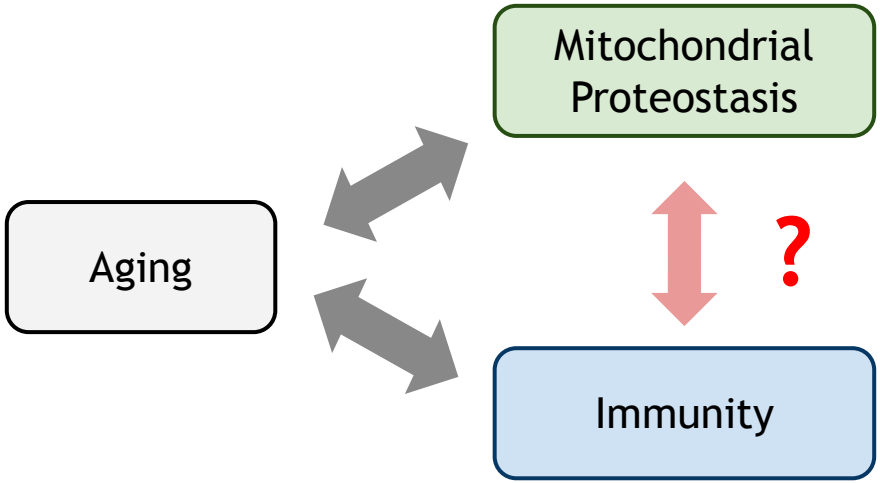
mitochondrial quality control

invoke innate immune response



(Moehlman & Youle, 2020)

How does increasing mitochondrial protein degradation affect the immune response in *Drosophila melanogaster*?



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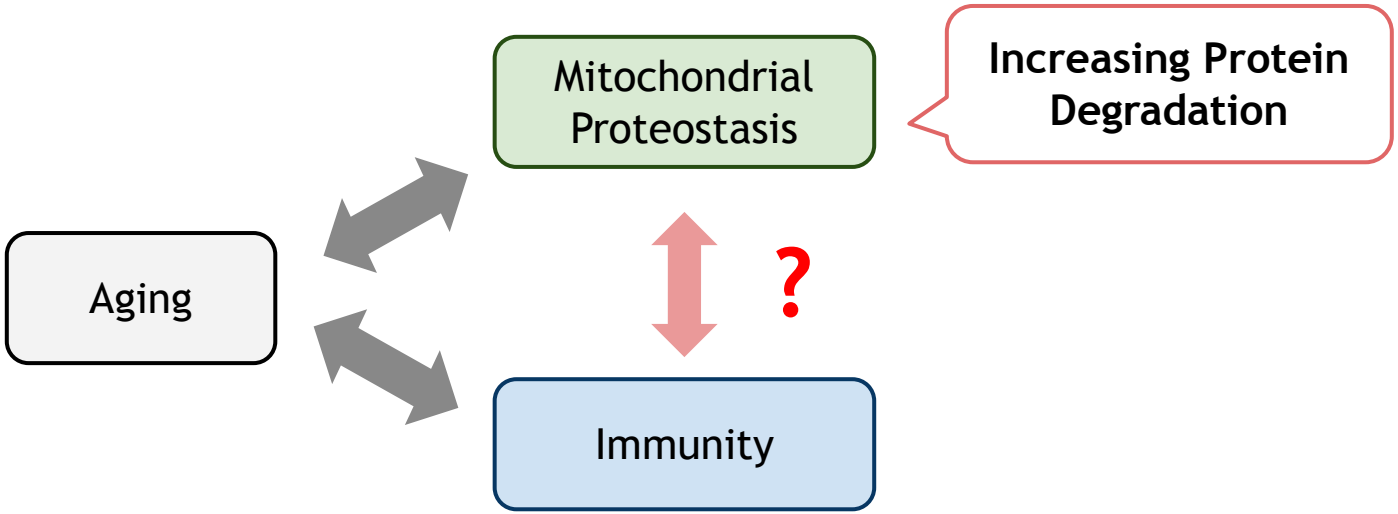

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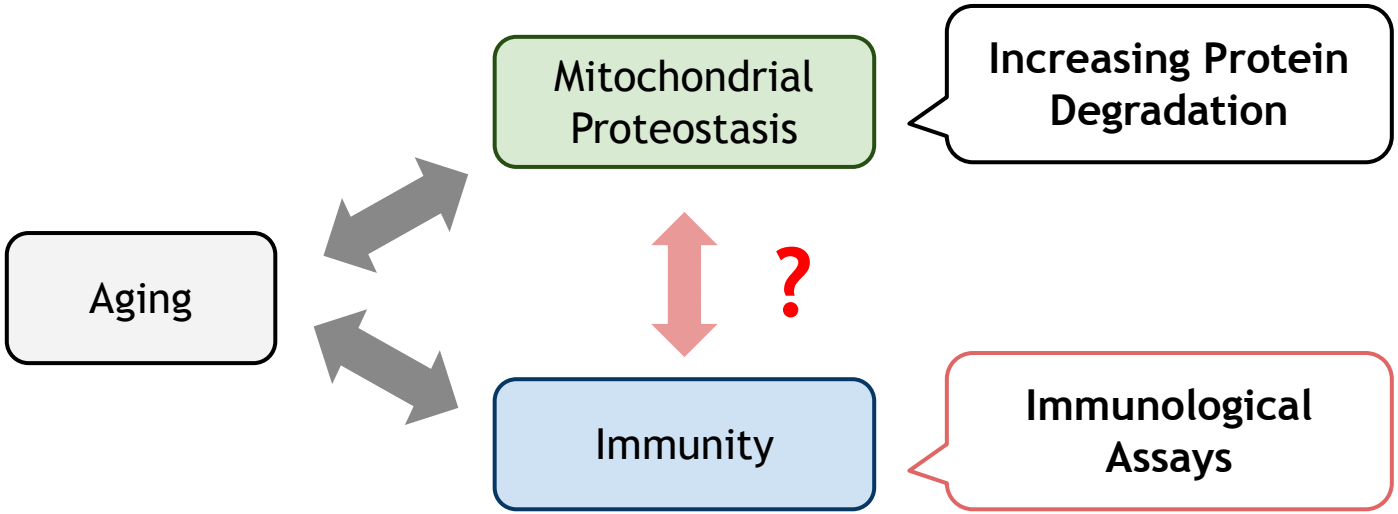
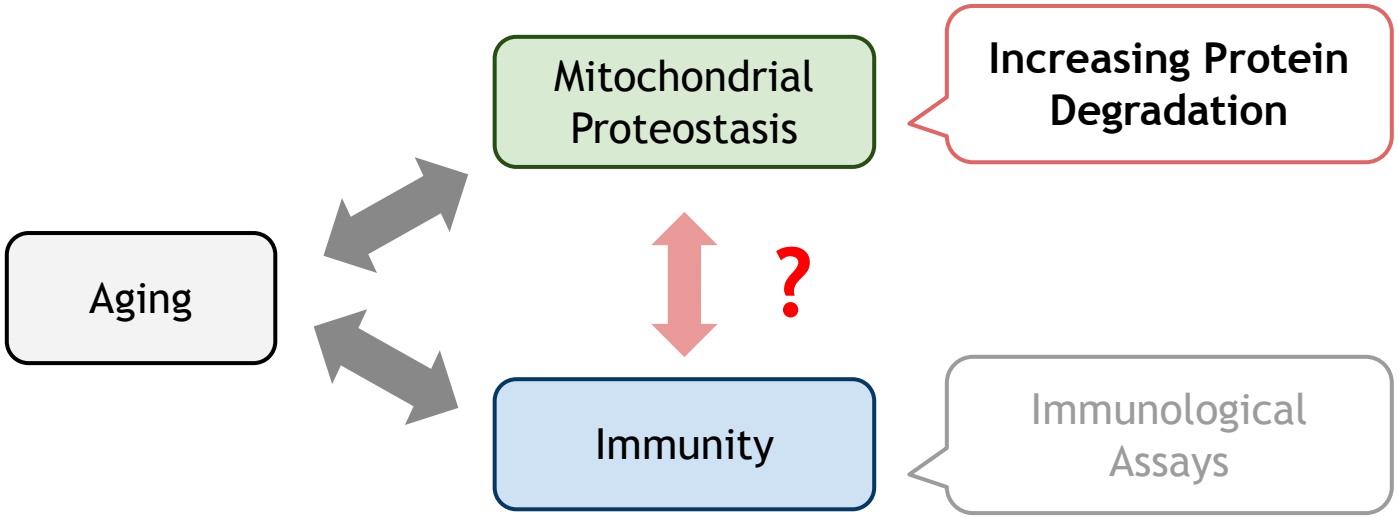
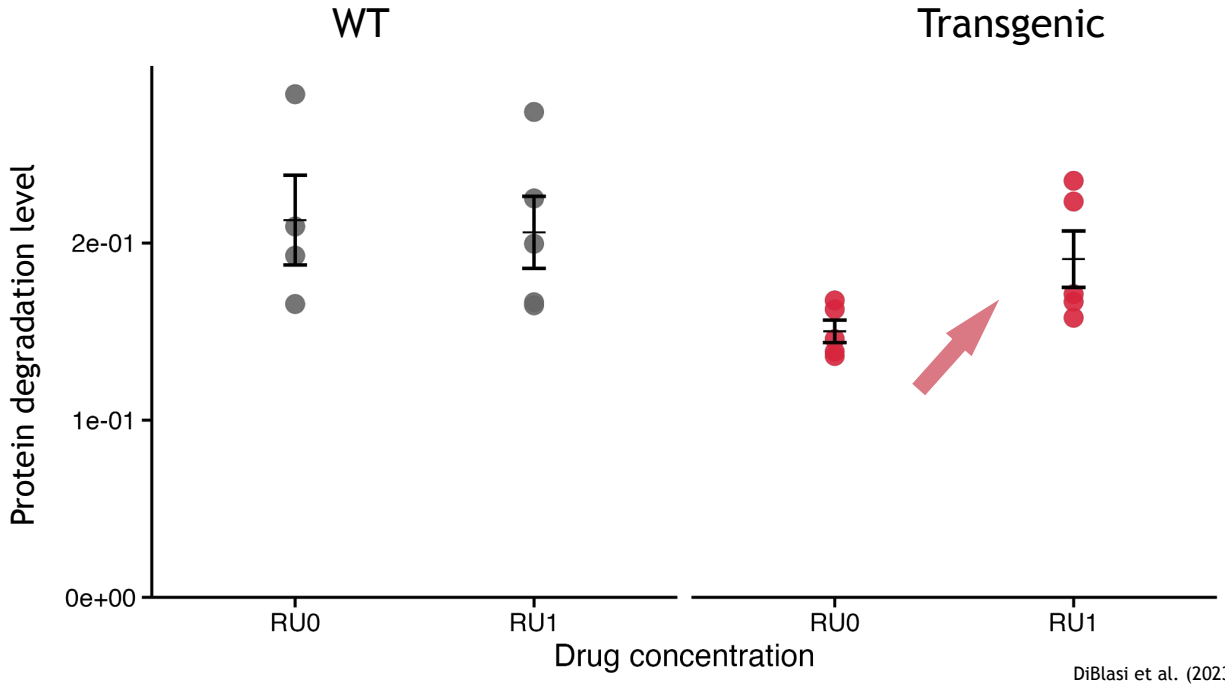


Methods


Mitochondrial Proteostasis
Increasing Protein Degradation
Aging
?
Immunity
Immunological Assays

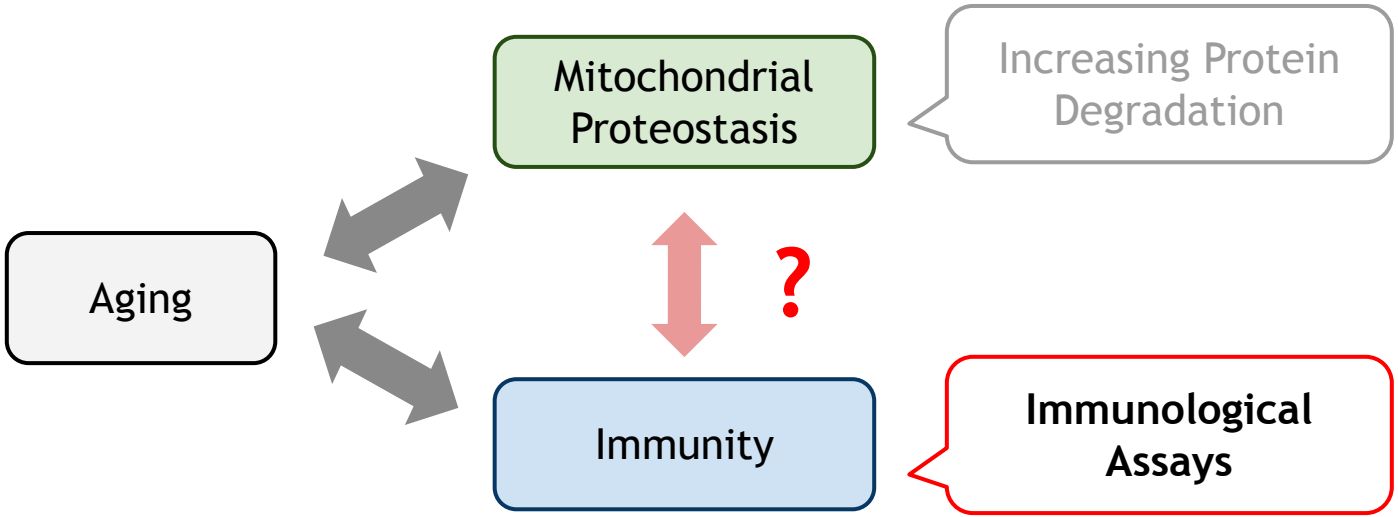
Increasing Protein Degradation

- Overexpressing mitochondrial protease ClpXP
  - *daGS/UAS-clpXP*



DiBlasi et al. (2023), Harvey Mudd Biology Summer Report.

Methods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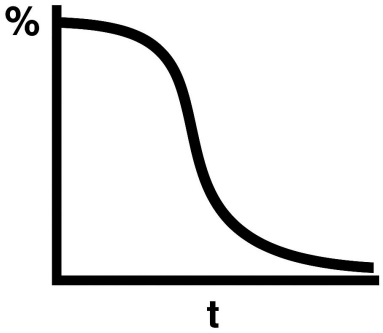
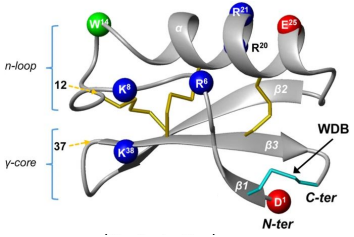
Bacterial Infection Assay

Serratia marcescens

Survivorship Assay



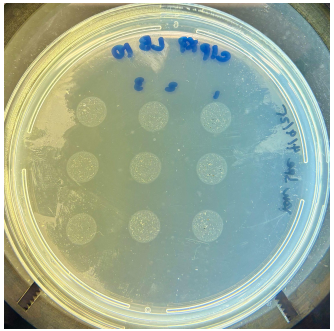
Antimicrobial Peptide Expression Level



Diptericin

(Gao & Zhu, 2016)

Bacterial Load Assay



Bacterial Infection Assay

Serratia marcescens

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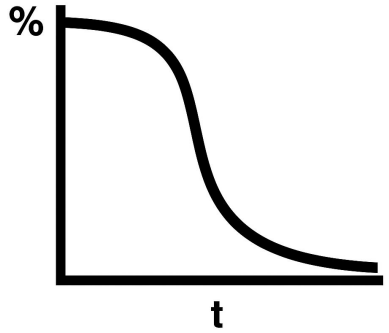

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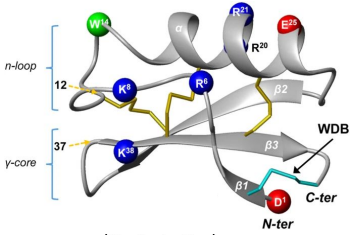

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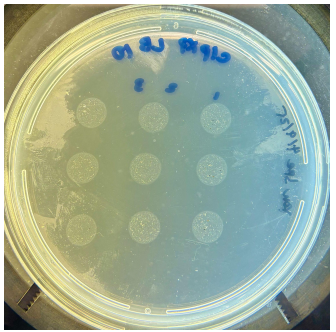
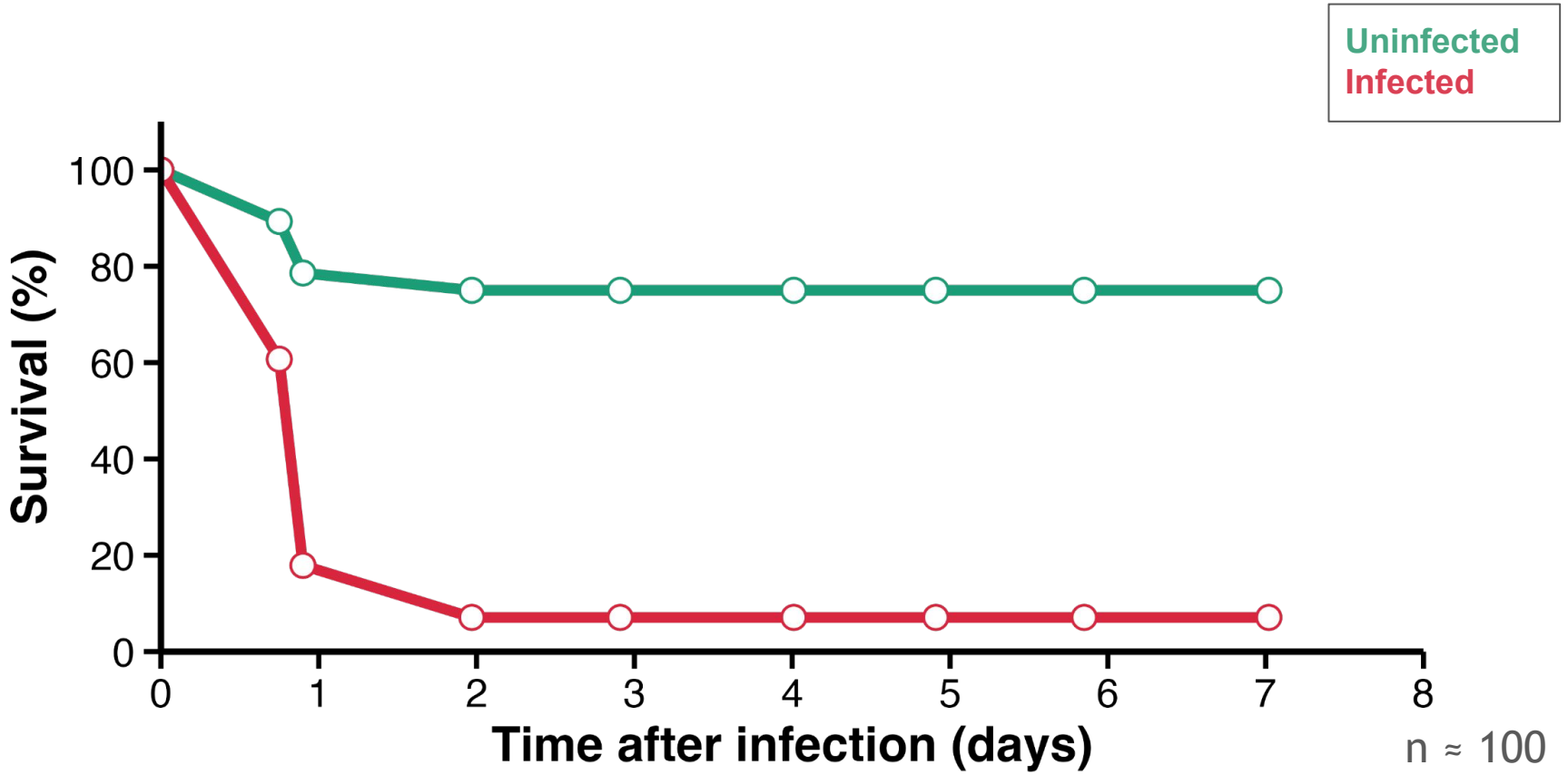
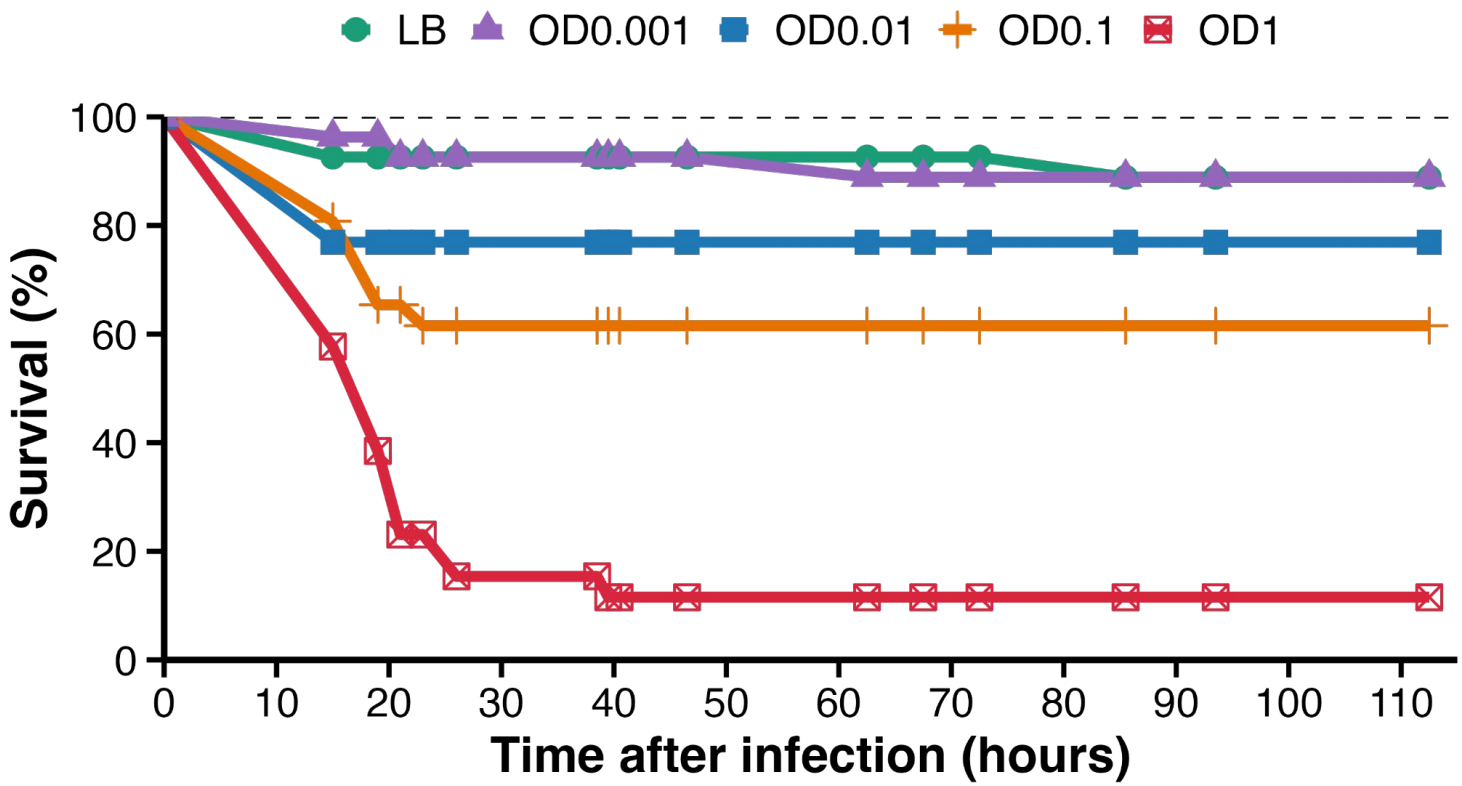


Infection Assay Validation

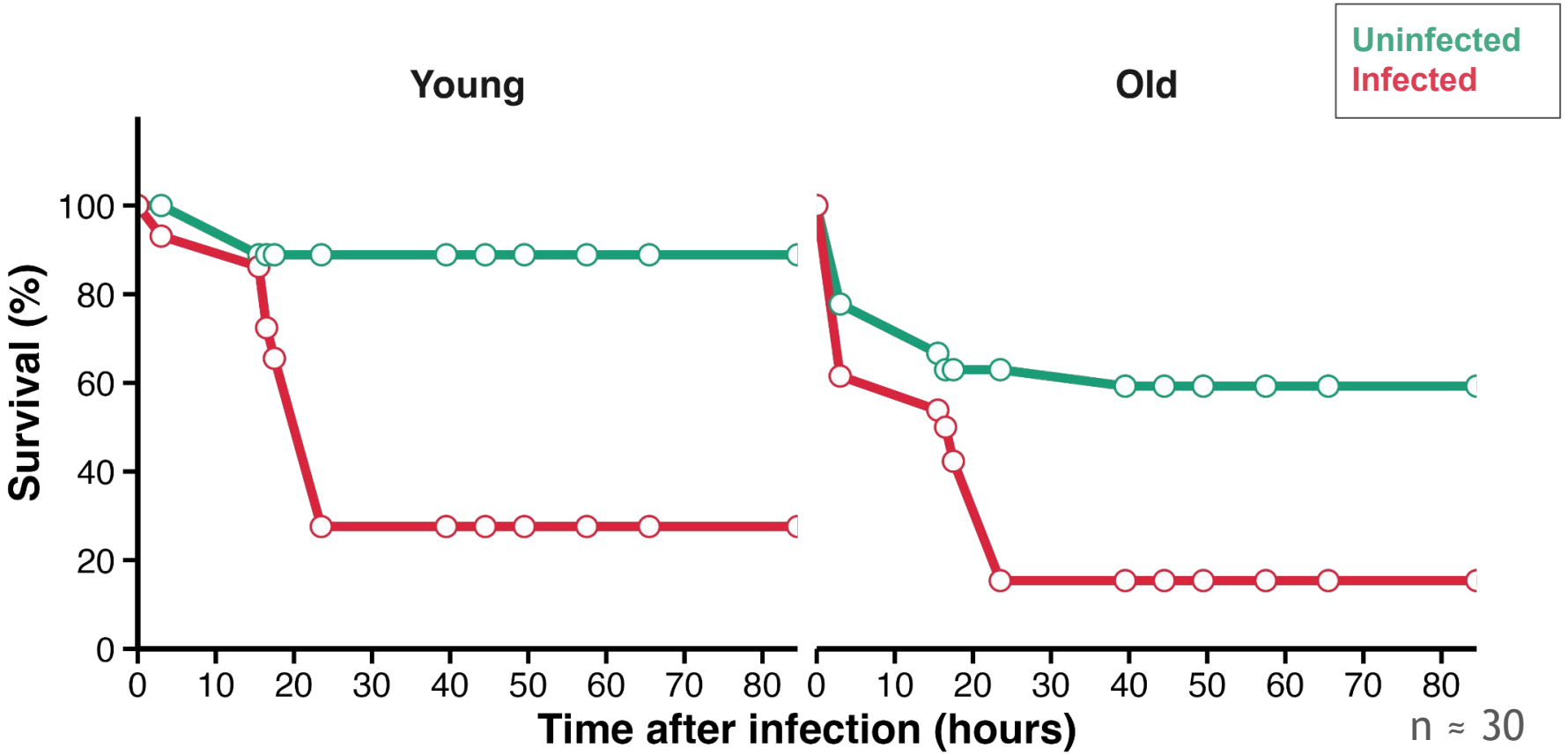


Infection Assay Validation - Infectious Dose



n ≈ 30

Infection Assay Validation - Age Difference



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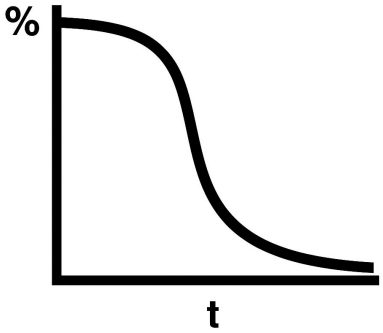
Bacterial Infection Assay

Serratia marcescens

Survivorship Assay



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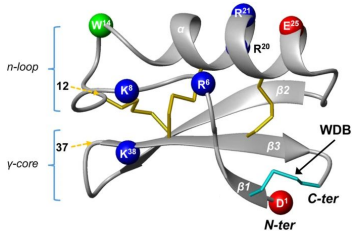

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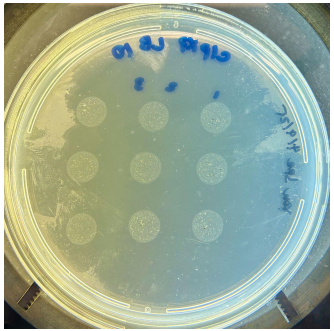
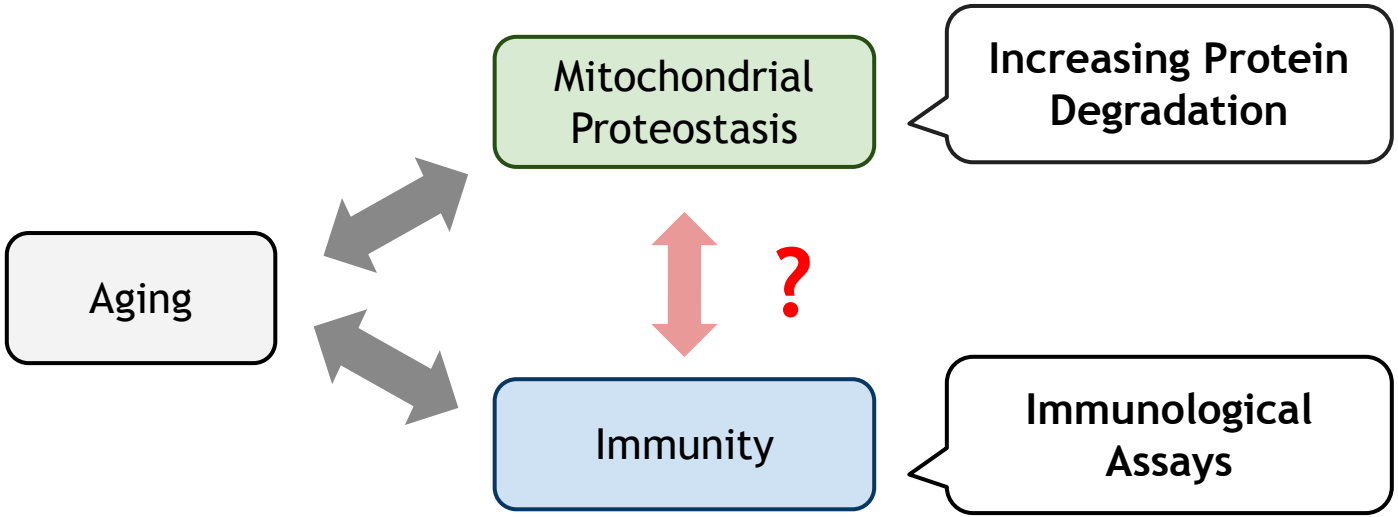


Results

- **Developed Immunological Assays**
  - Sensitive to infectious doses
  - Sensitive to age-difference

Results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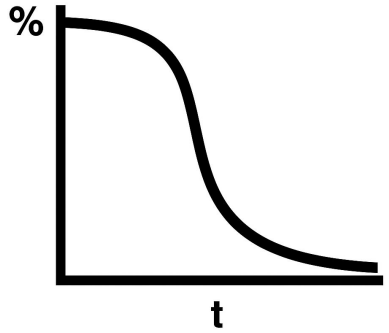

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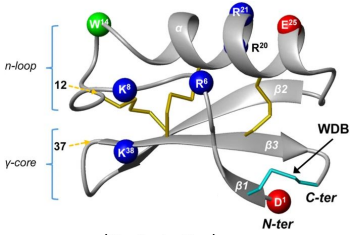

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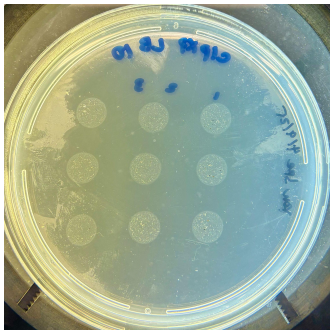
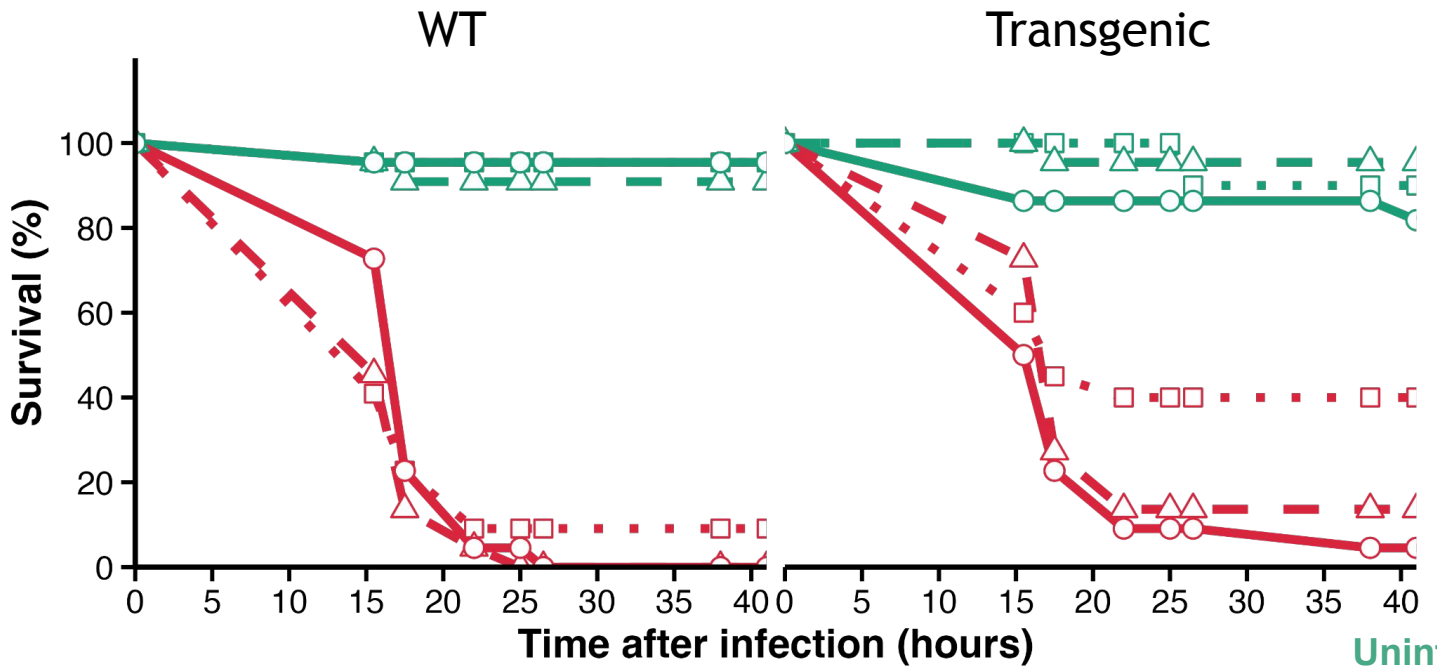


ClpXP overexpression did not change Survival rate after infection

Drug	ClpXP Overexpression
□ 0 µg/mL	No
△ 1 µg/mL	Mild
○ 10 µg/mL	High

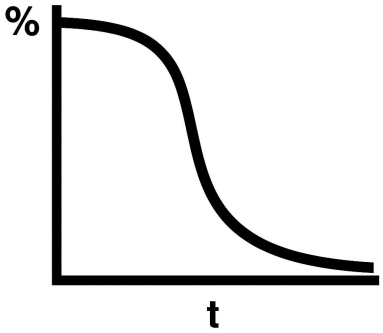


n ≈ 25

Bacterial Infection Assay

Serratia marcescens

Survivorship Assay



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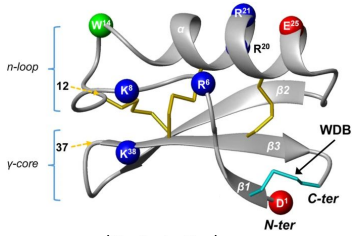
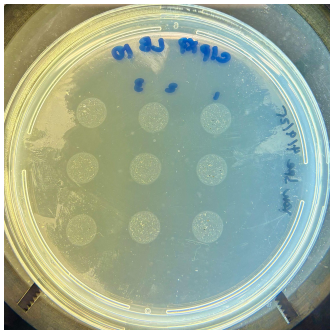


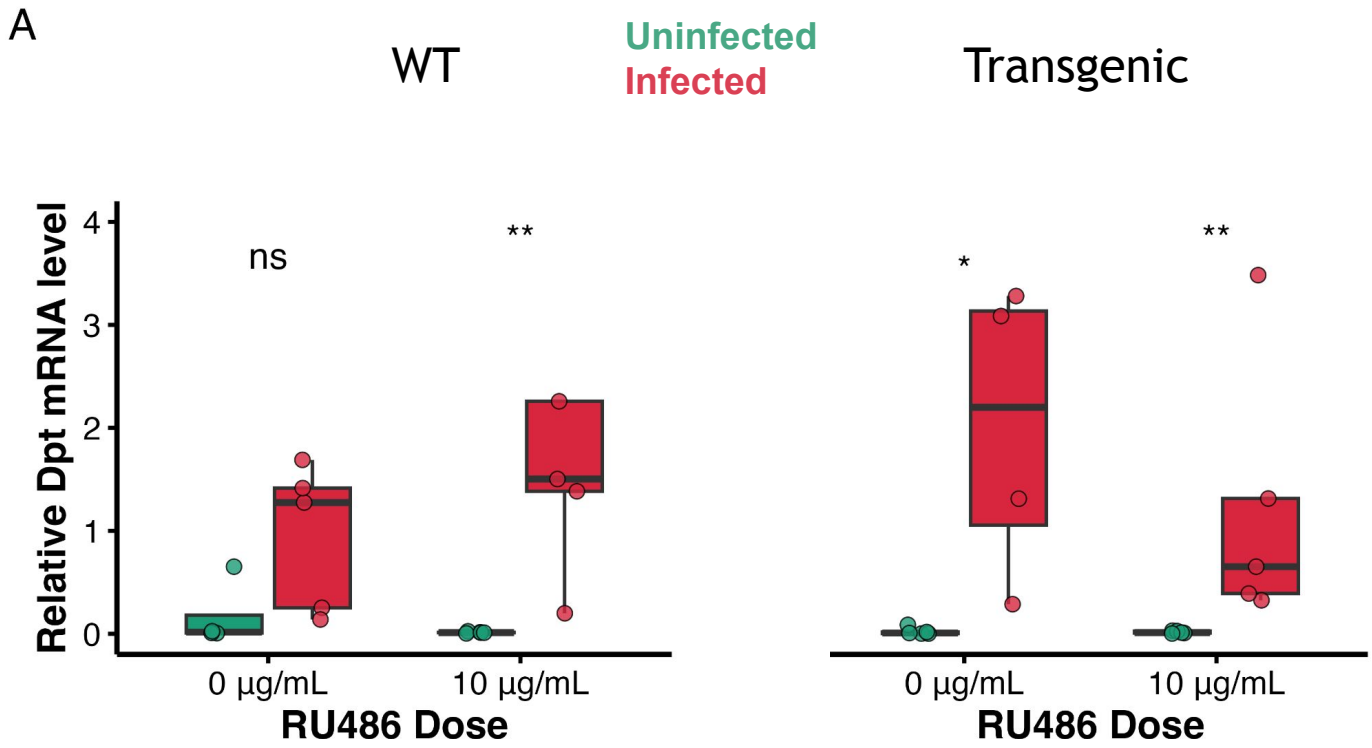
Diptericin

(Gao & Zhu, 2016)

Bacterial Load Assay



ClpXP overexpression did not change *Diptericin* level after infection

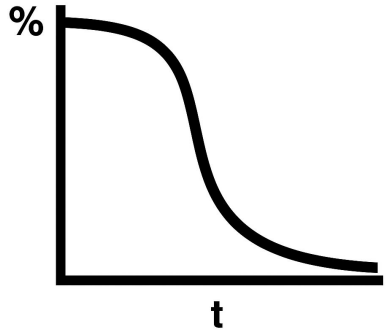


n ≈ 5

Bacterial Infection Assay

Serratia marcescens

Survivorship Assay



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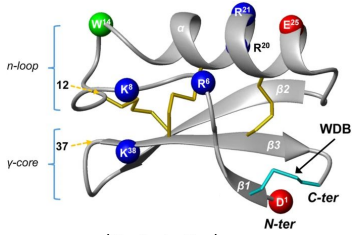

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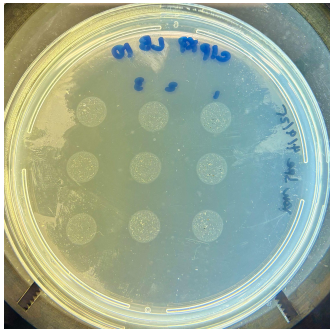
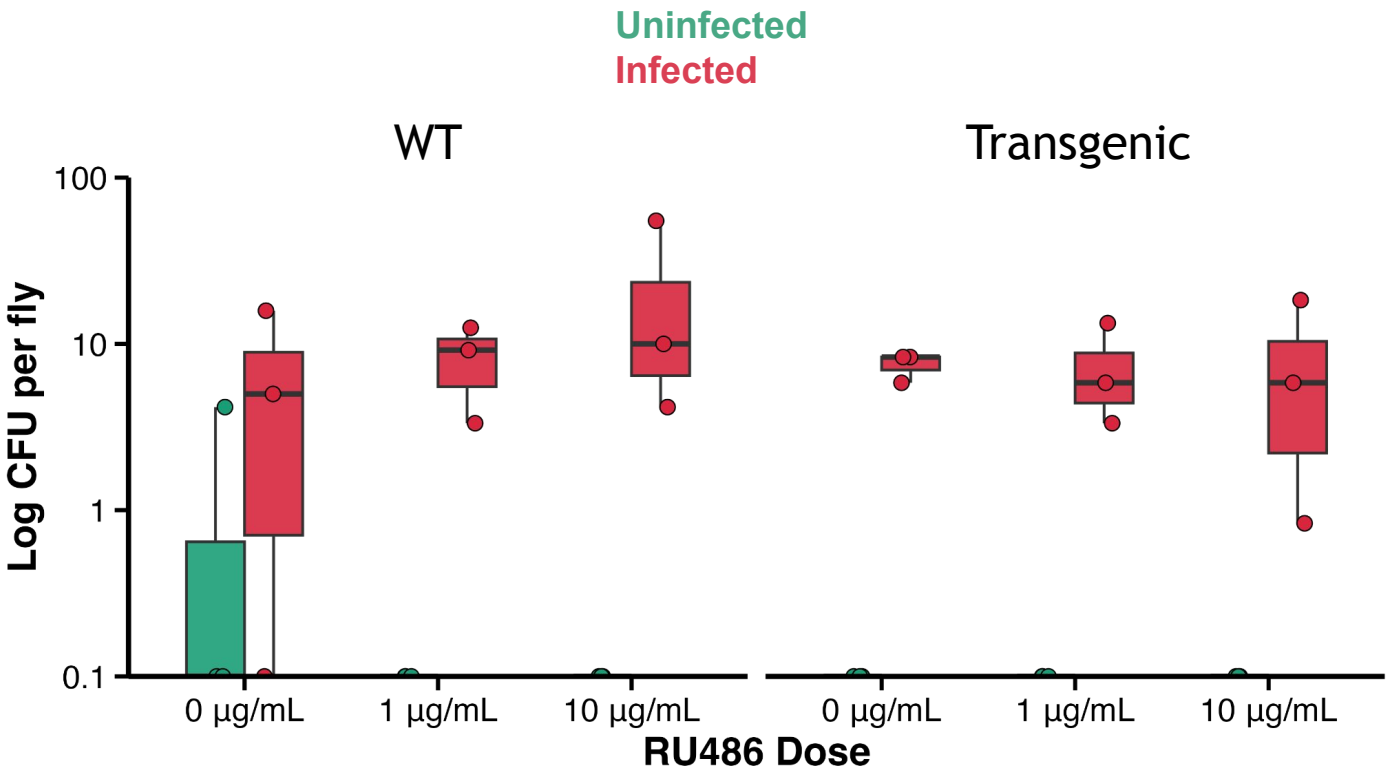


ClpXP overexpression did not change bacterial load after infection



n ≈ 3 of 5 flies

Results

- **Developed Immunological Assays**
  - Sensitive to infectious doses
  - Sensitive to age-difference

- ClpXP overexpression had **no significant effect** on:

  - **Survival** after pricking infection
  - ***Diptericin* expression** after pricking infection
  - **Bacterial load** after oral infection

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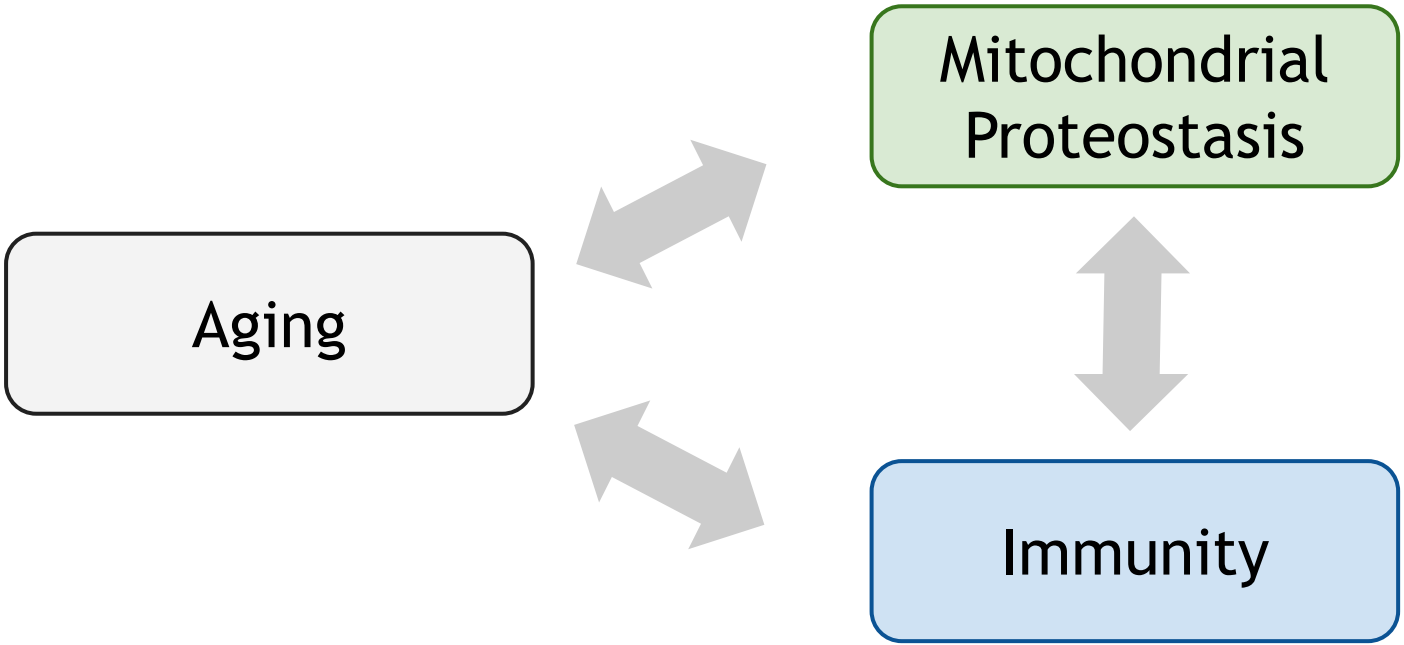
Overexpressing ClpXP did **not** impact immune response


Mitochondrial Proteostasis
Aging
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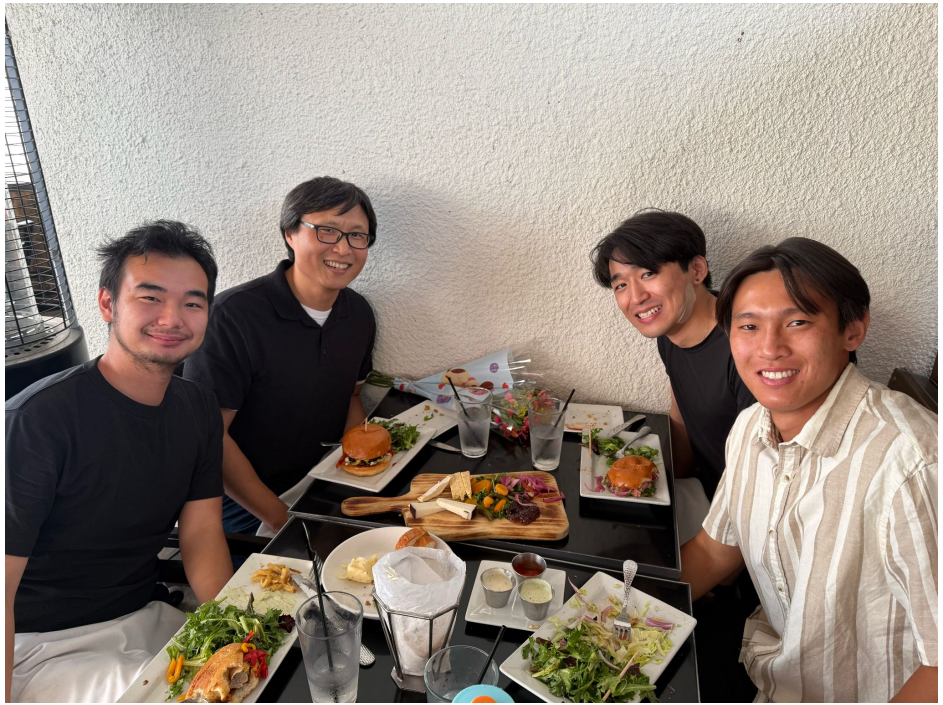
Acknowledgement

- Professor Jae Hur
- Professor Daniel Stoebel
- Professor Stephen Adolph
- Kris Chang & Ethan Lee
- Members of the Hur Lab
- Biology Department, Harvey Mudd College



Thank You!

References