Spring 4-21-2020

Cancer: The Role of Bax Inhibitor in C. elegans

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ER Stress in *C. elegans*

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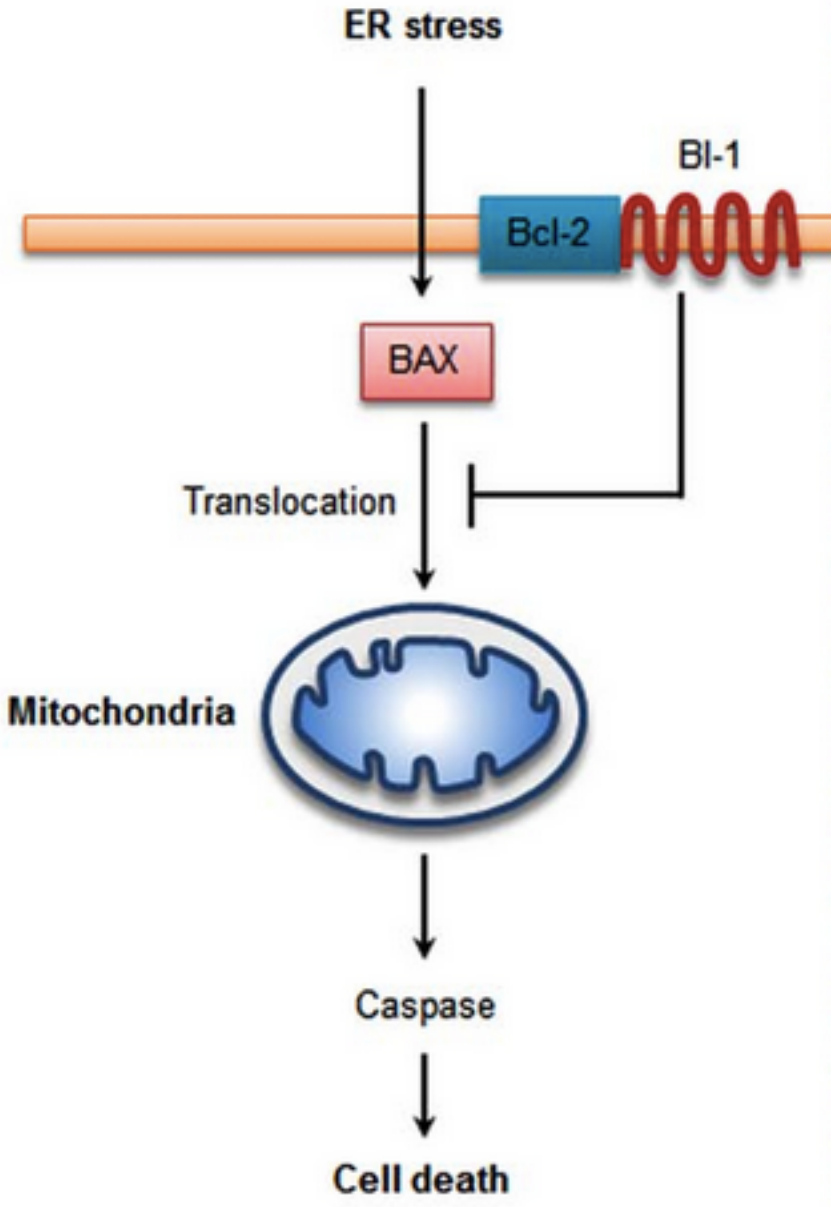
ER Stress and Protein Homeostasis

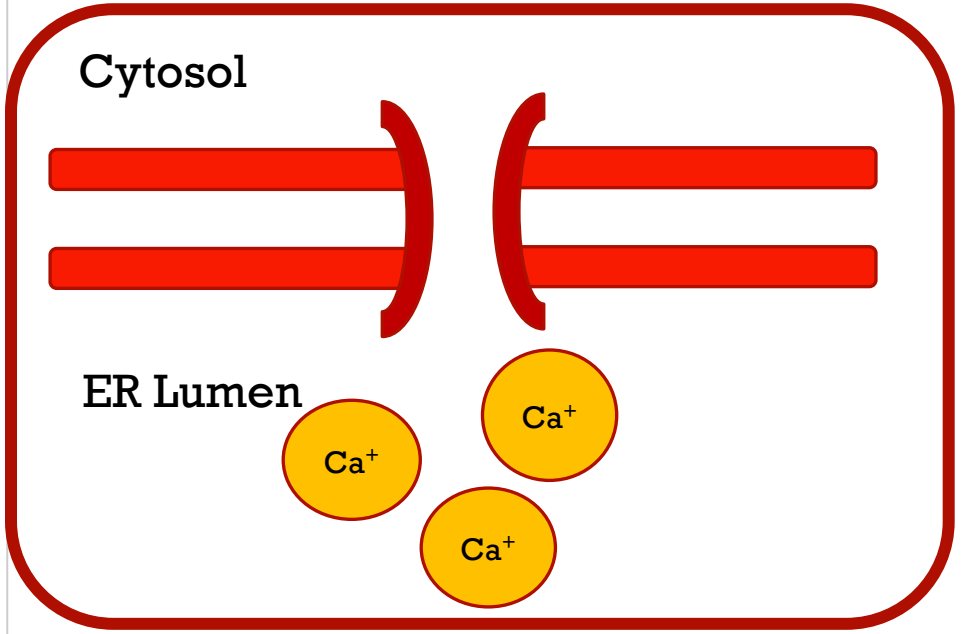
- Occurs when the ER is impaired which leads to misfolded proteins
- Misfolded proteins may cause the cell to function improperly, causing cell death.
- Bax Inhibitor protein (BI-1) responds to ER stress by inhibiting Bax-induced cell death.

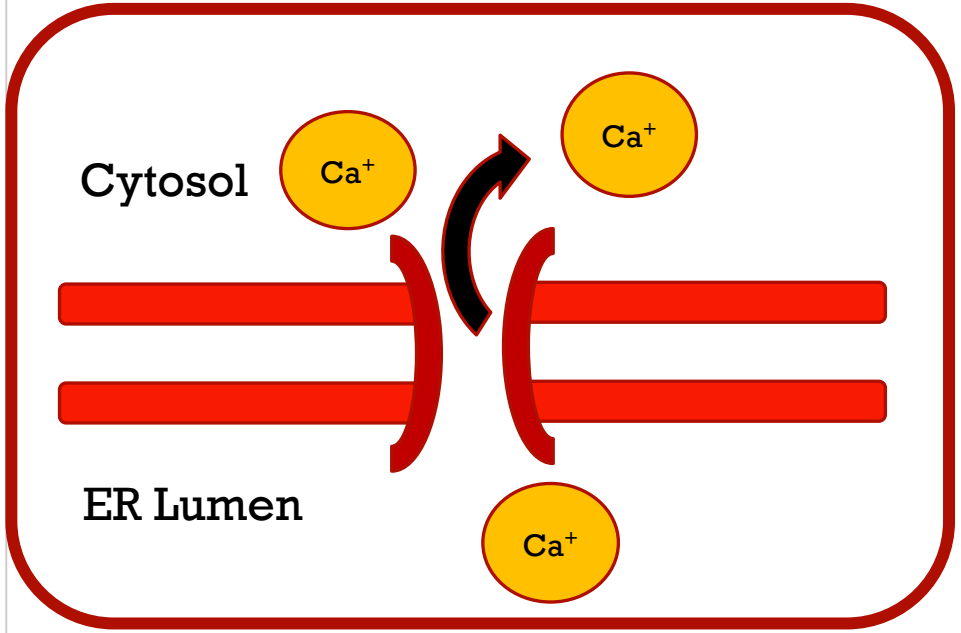


Yadav et al, *Current Molecular Medicine* 2014

Bax Inhibitor

- Is a Ca^+ channel that regulates calcium levels in the ER and cytosol.
- Increased calcium in the cytosol inhibits Bax protein, which prevents the cell from Bax-induced apoptosis.

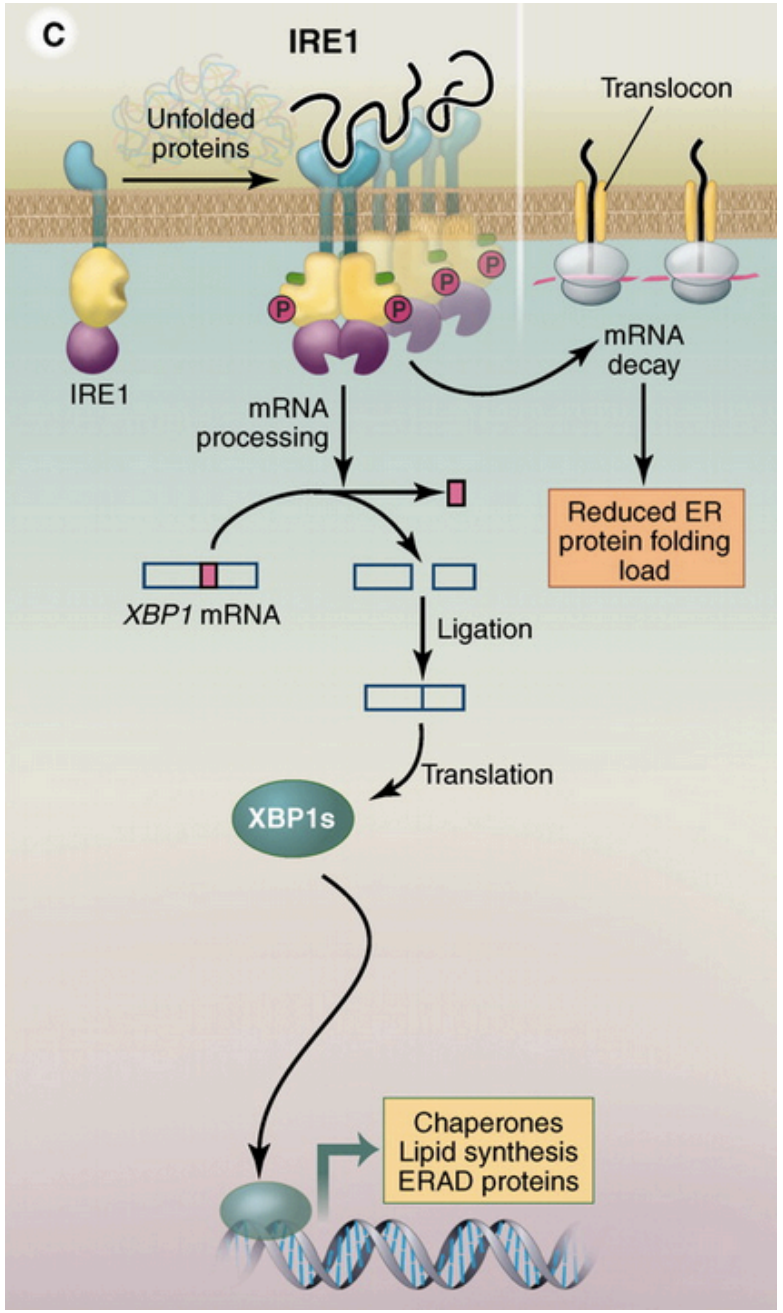




IRE-1 is required for ER Stress

- The Unfolded Protein Reponse occurs when there is an accumulation of misfolded proteins in the ER, which may result in cell death.

- Inositol-requiring enzyme 1 (ire-1) is a protein in the ER that detects ER stress. It responds to this stress by activating downstream targets that upregulate genes necessary for maintaining homeostasis in the cell.



Walter P, Ron D. *Science* 2011

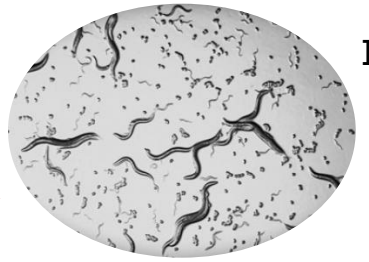
Our Goal

- Our project: to determine if tmbi-4 is involved in the ER stress pathway.
  - What factor(s) are regulating tmbi-4 expression?

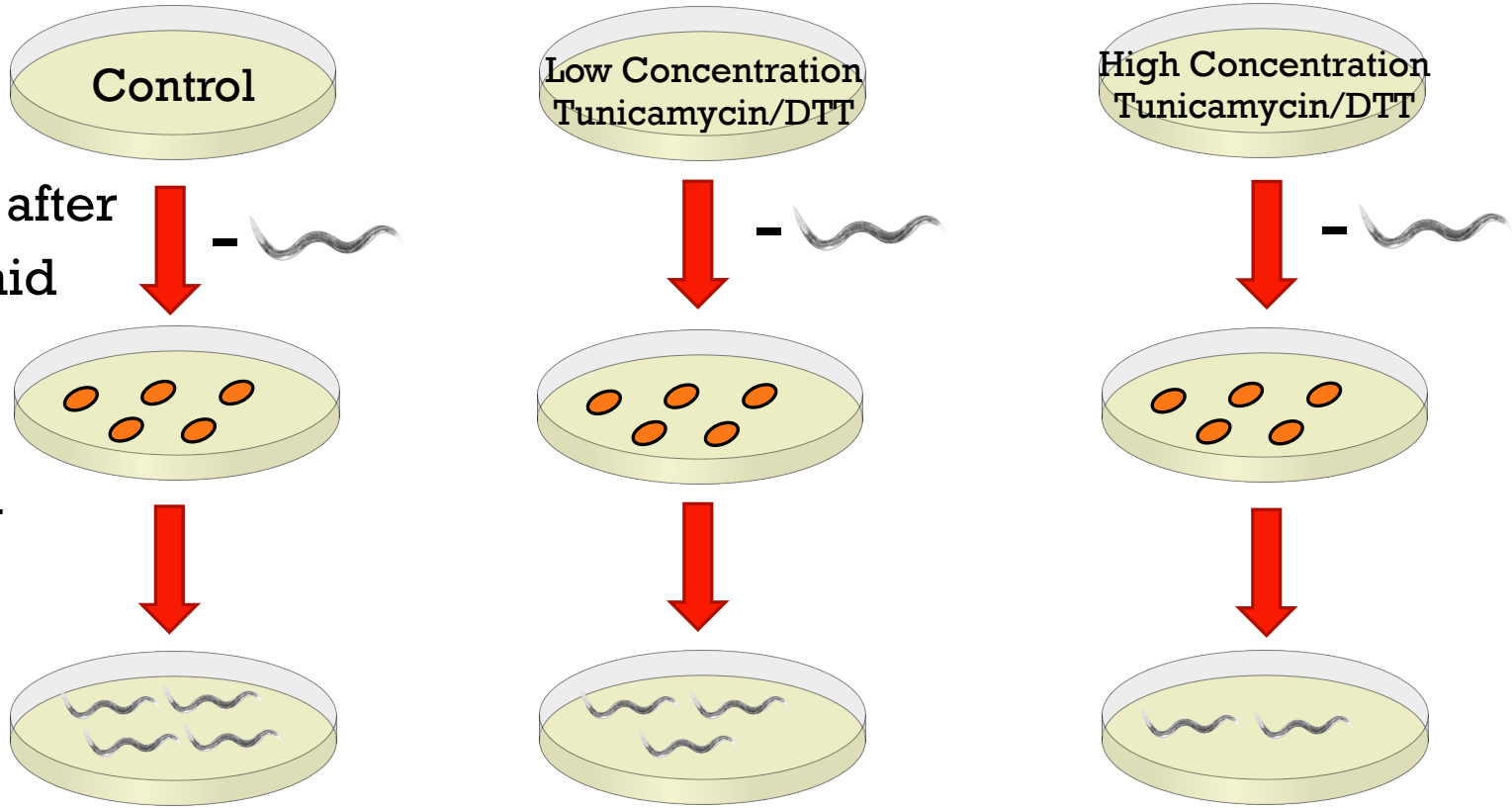
- Further research of these questions will provide insights to how BI-1 is regulated in cancer.

Methods

1. Isolate egg-laying adults on conditioned plates



N2 (wt), tmbi-4*, and ire-1* worms



2. Remove adults after enough eggs laid

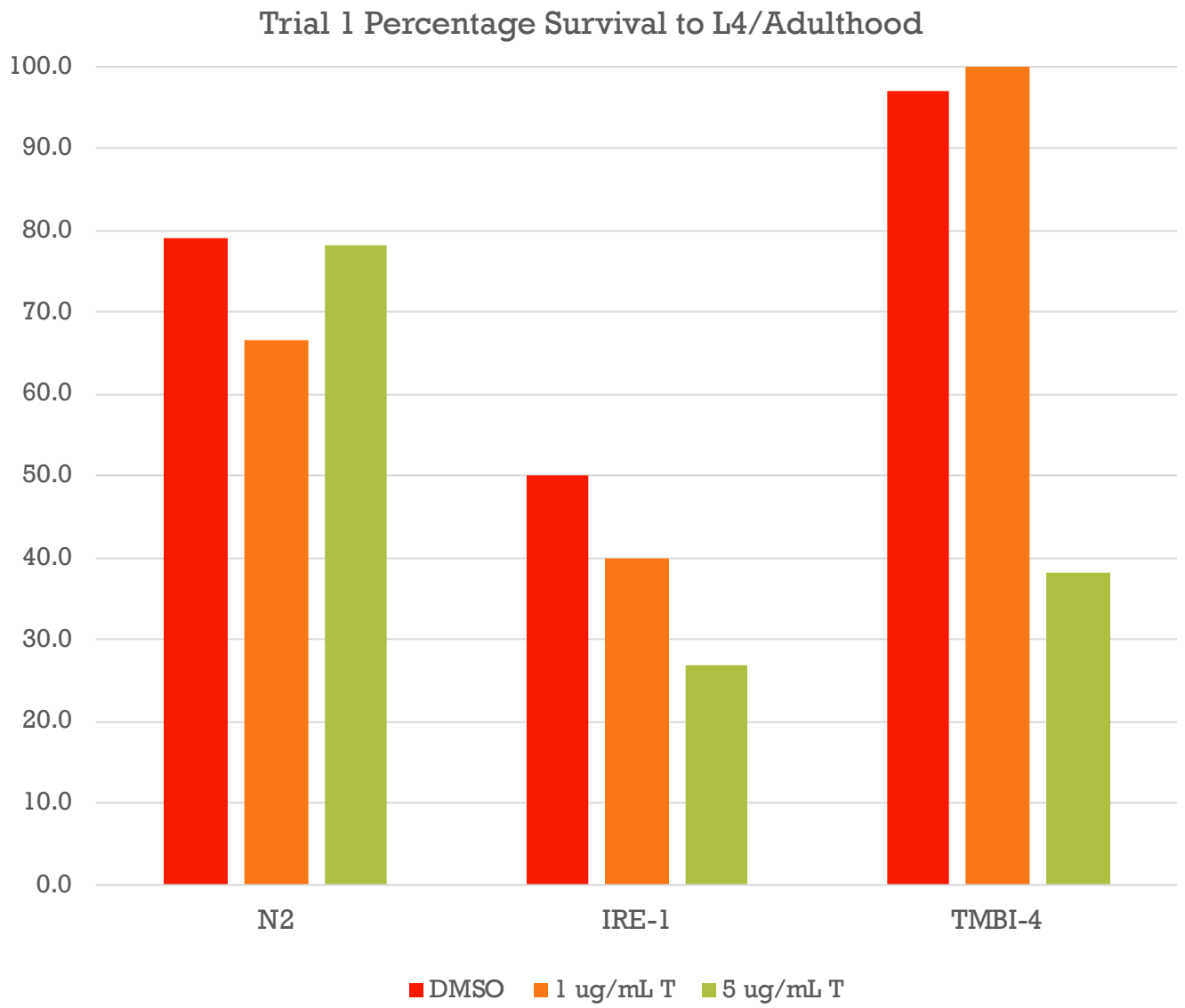
3. Assess number of L4/adults

4. Determine percentage survival (eggs laid/worms hatched)

* loss of function mutants

Data + Results

- With increasing concentration of ER stress-inducing drug, there is a decrease in survival in tmbi-4, similar to ire-1 mutants.
- Our few trials suggest that Bax Inhibitor may act in the same pathway as ire-1, the ER stress pathway.



Future Directions

- Further research must be done in order to replicate and confirm these results.

- Other projects:
  1. Lifespan assay on mutants to discover possible phenotypes
  2. Crossing worms to make a double (tmbi-4 and ire-1) mutant for experimenting (ER stress assay)
  3. Tagging GFP to Bax inhibitor in order to visualize its location in the cell using confocal microscopy

Acknowledgements

- We would like to thank:
  - our advisors Dr. Melissa Silvestrini and Fr. Nicanor Austriaco
  - Providence College Biology Department
  - Amy Goggin
  - The Center for Engaged Learning

- All provided this wonderful learning experience to us and gave us the opportunity to present our work, making it a blessing to be part of.