

The SARS-CoV-2 E Protein is a Potential Target for Antiviral Drug Development

Liana Owen & Dr. Brandon Johnson



**THE QUEEN'S
MEDICAL CENTER**

SARS-CoV-2 is an ongoing public health crisis

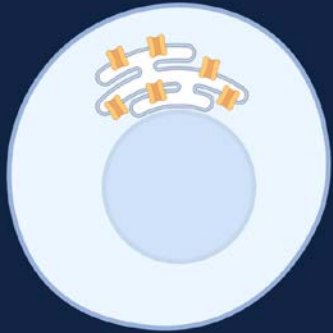
203,295,170

Confirmed case

4,303,515

Deaths

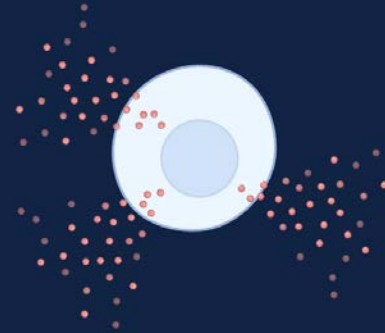
E protein is critical for inflammatory response



Localizes to
ERGIC



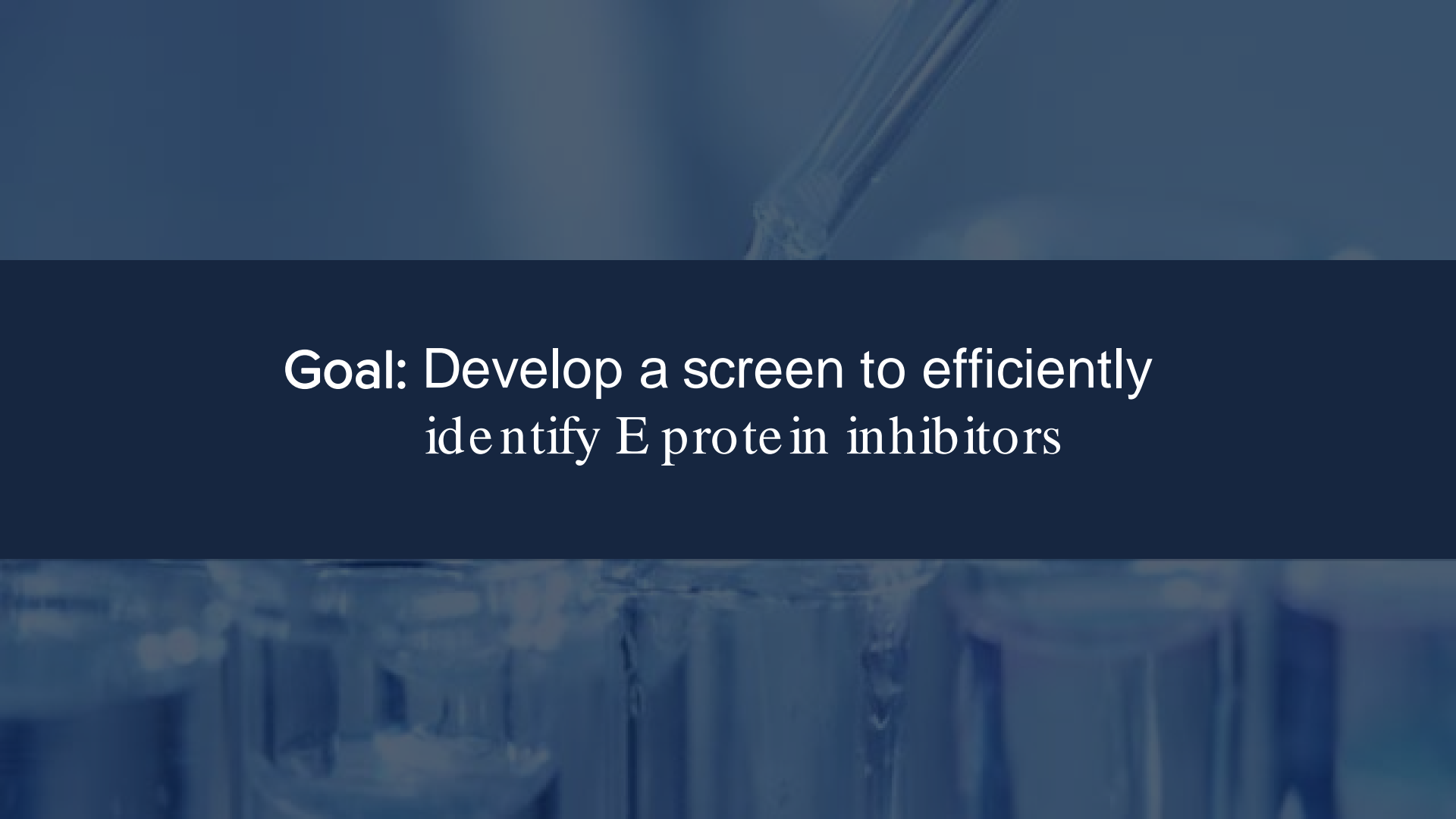
Disrupts Ca^{2+}
signaling



Activates
inflammatory
cytokines

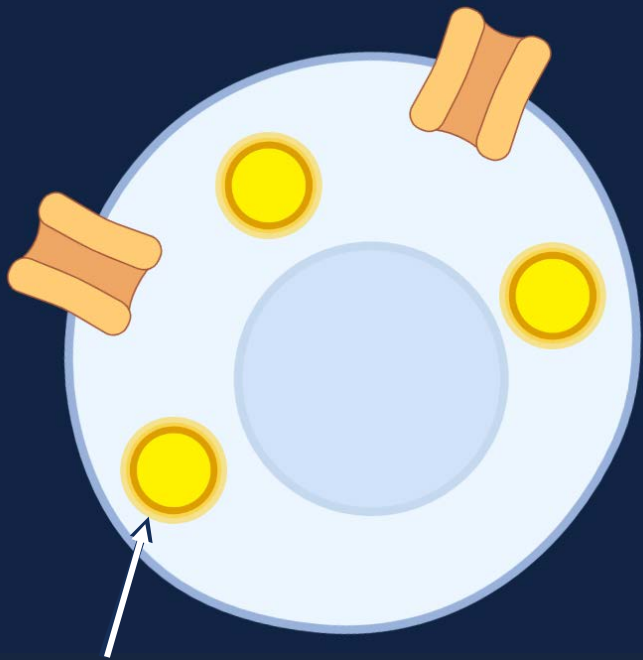


Acute
respiratory
distress

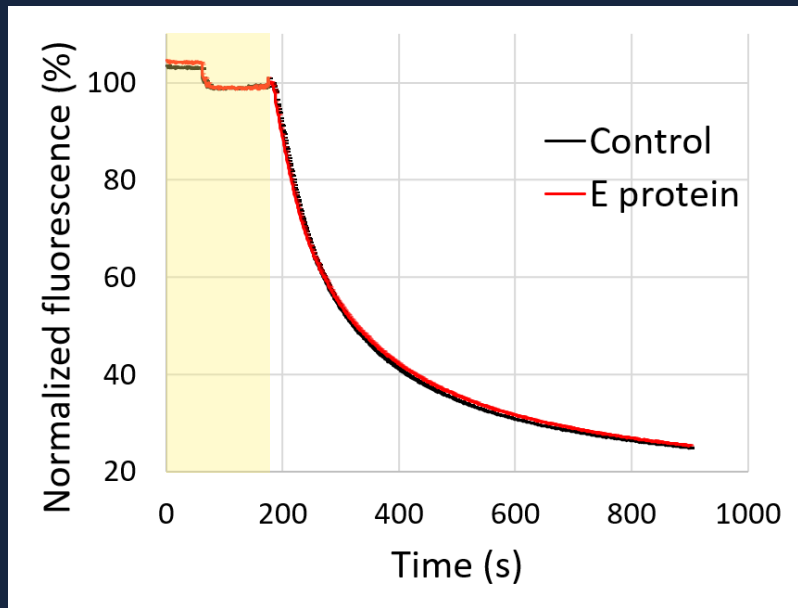


Goal: Develop a screen to efficiently
identify E protein inhibitors

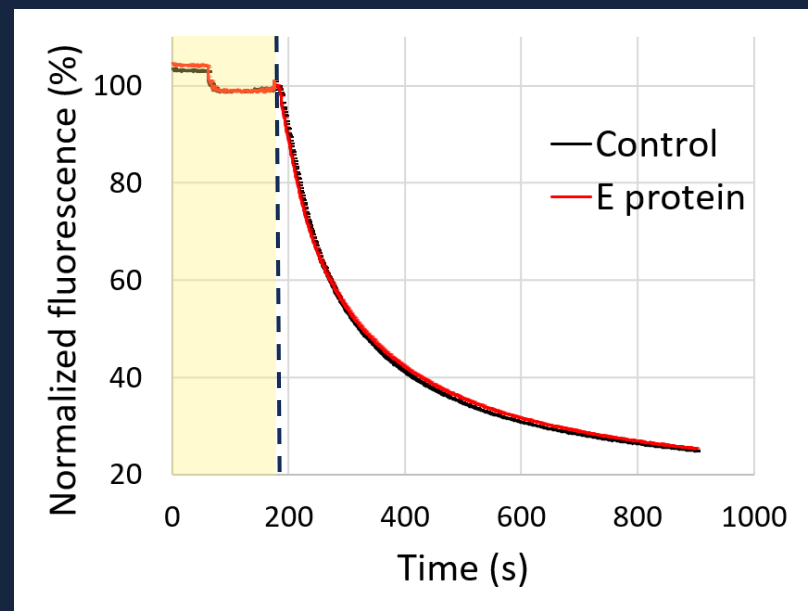
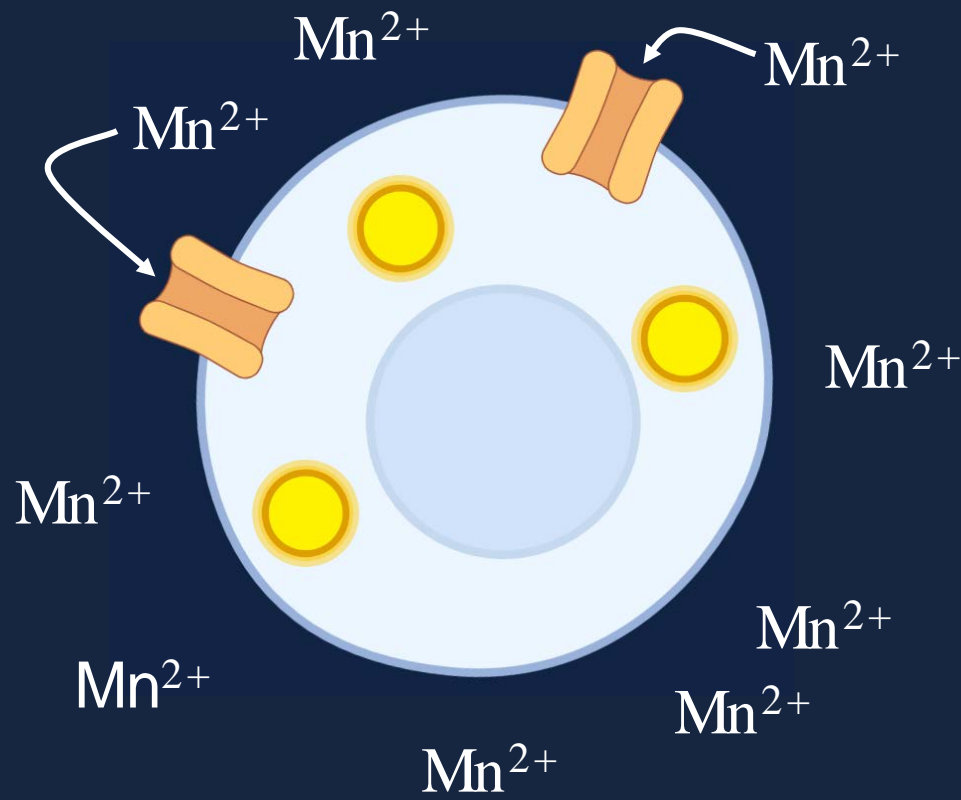
Screen Design



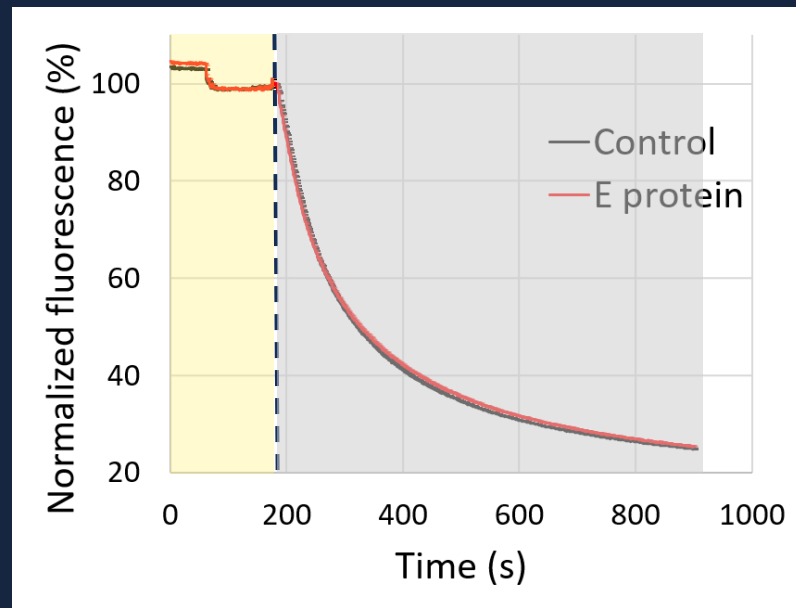
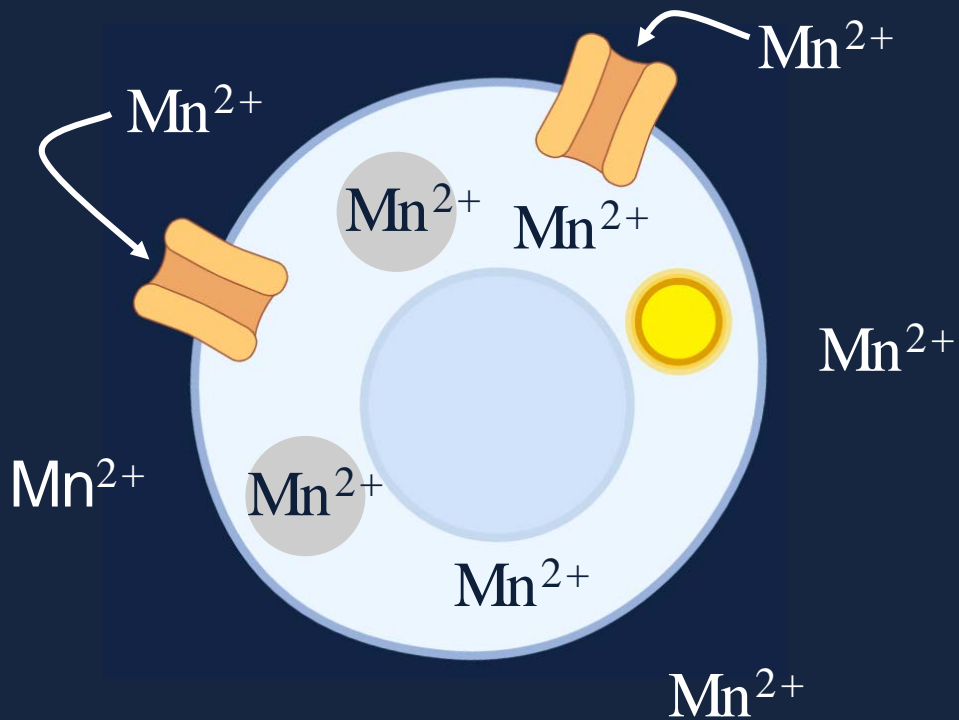
Fluorescent dye (Fura-2)



Screen Design

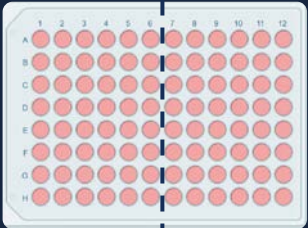


Screen Design



Screen Implementation

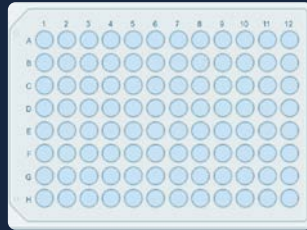
HEK 293 cells



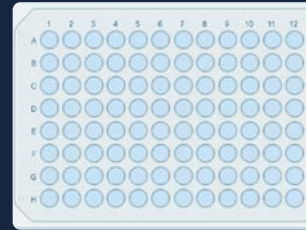
Control | E protein

Screen Implementation

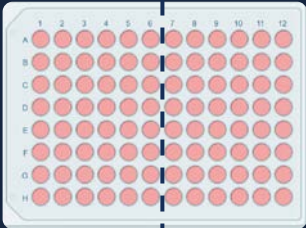
Compound plate



Mn²⁺ plate



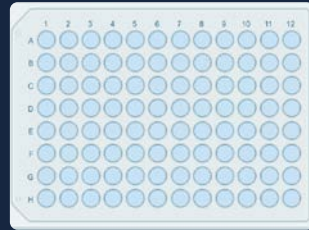
HEK 293 cells



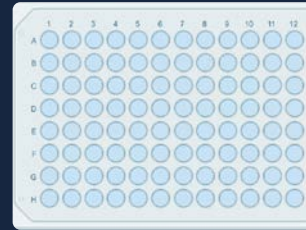
Control | E protein

Screen Implementation

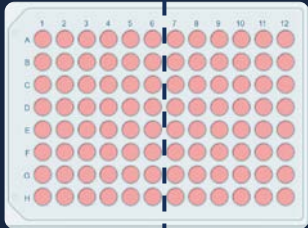
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HEK 293 cells



Control | E protein

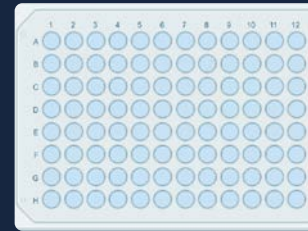
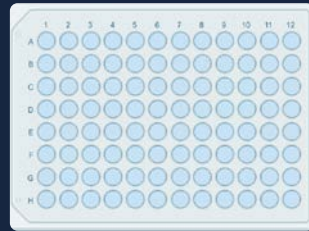
FDSS



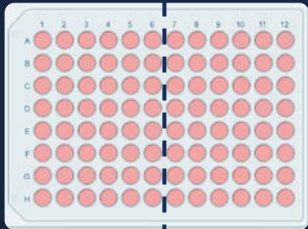
Screen Implementation

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Mn²⁺ plate



HEK 293 cells

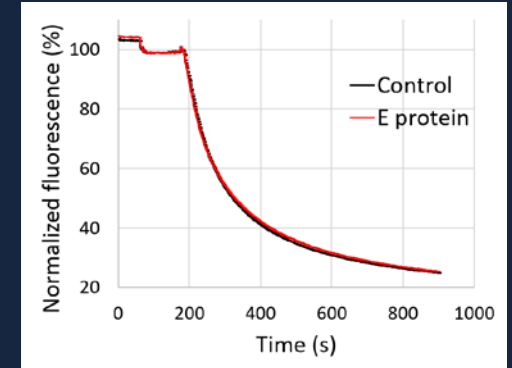


Control | E protein

FDSS

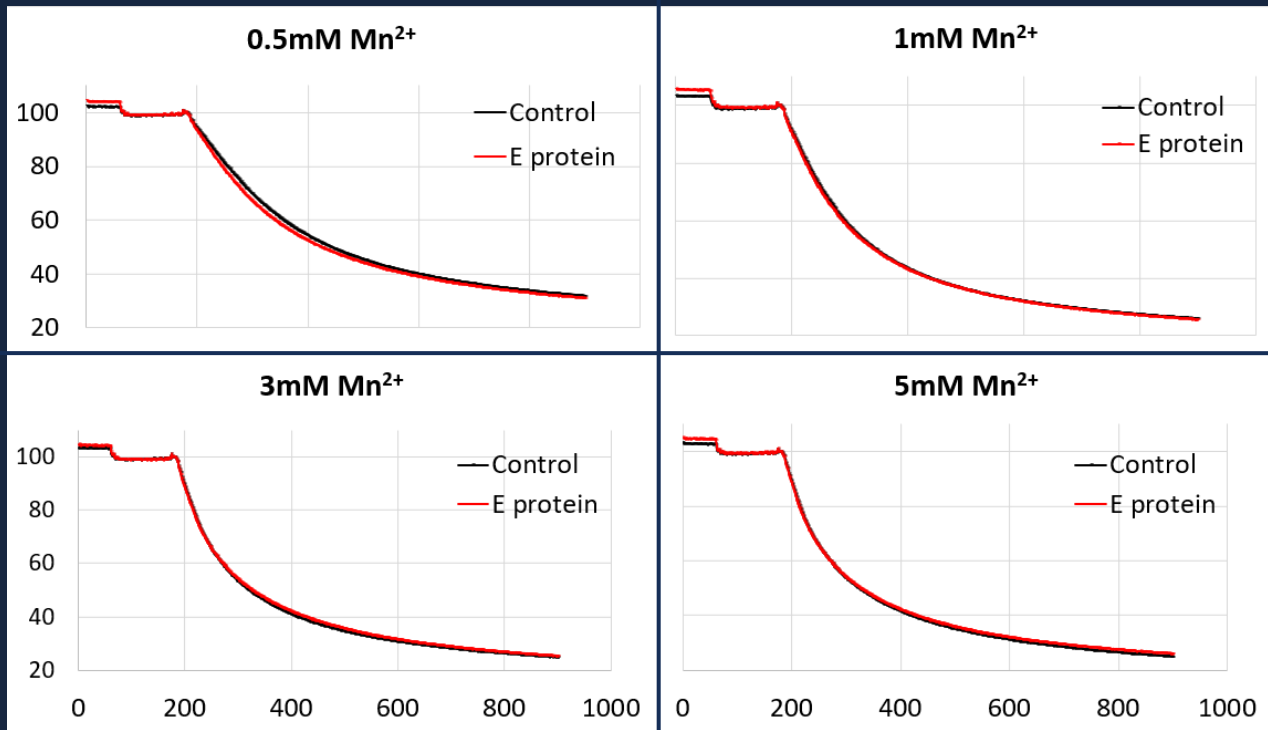


Data

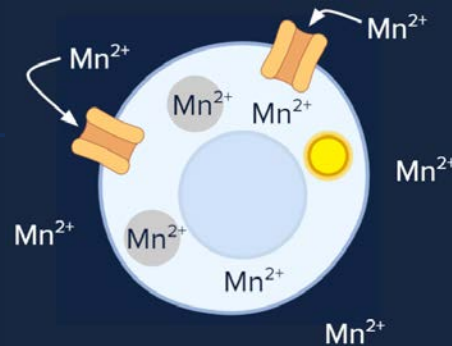


Mn²⁺ concentration does not affect E protein activity

Normalized fluorescence (%)

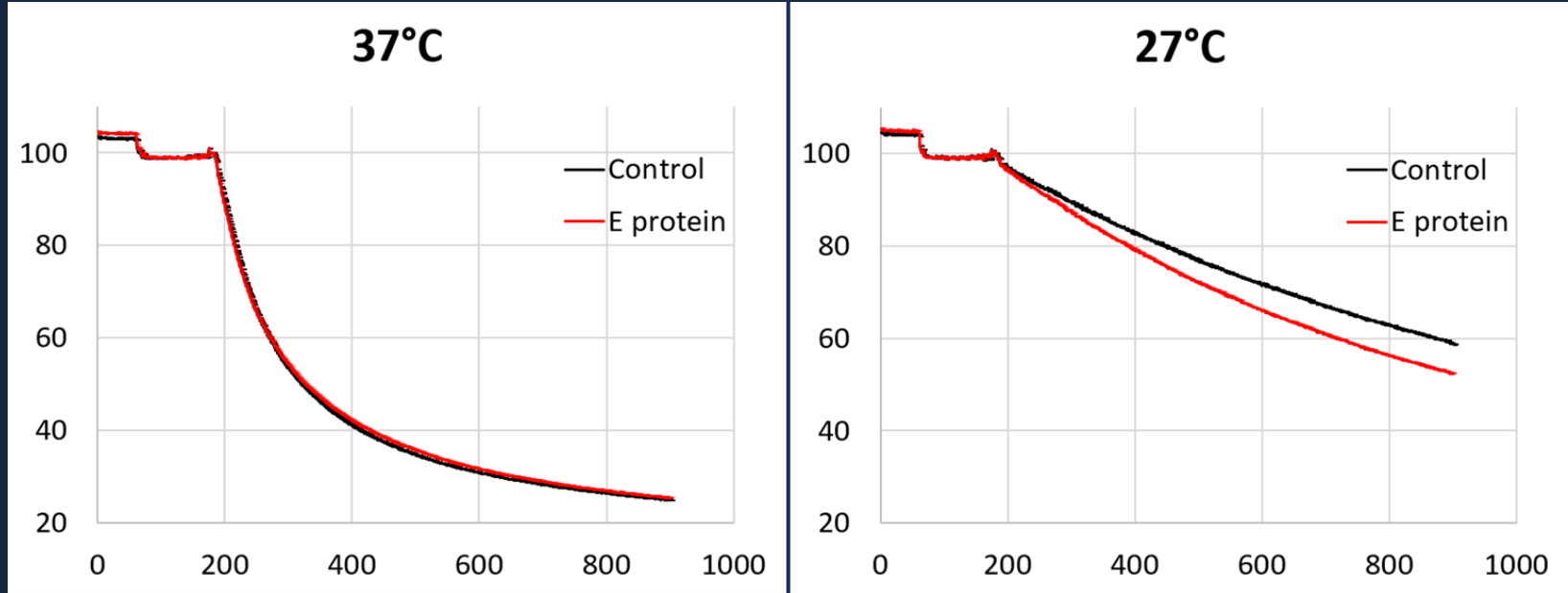


Time (s)



Reducing temperature increases E protein activity

Normalized fluorescence (%)



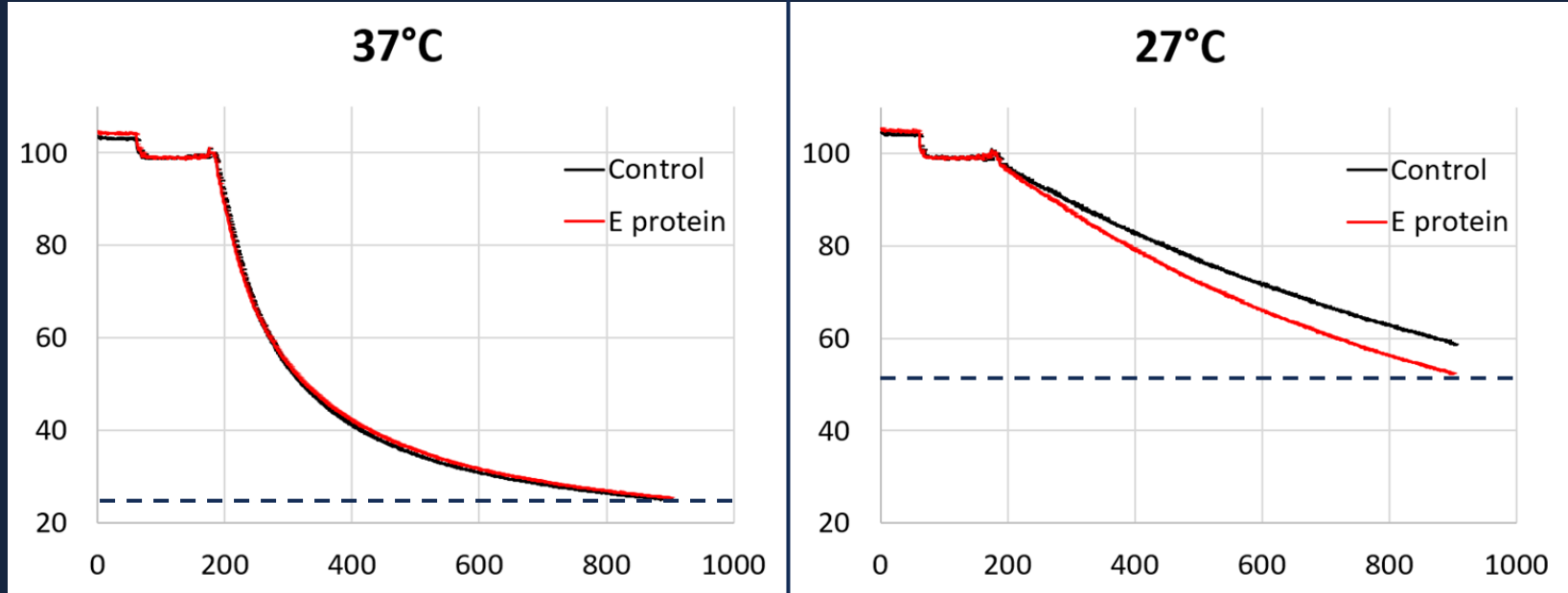
No significant difference

Time (s)

6.7% difference
($p < 0.0001$)

Reducing temperature increases E protein activity

Normalized fluorescence (%)



No significant
difference

Time (s)

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Summary: Incubation at 27°C enhances E protein activity in HEK293 cell plasma membranes

Conclusions

1. E protein forms a functional ion channel in a laboratory cell line

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2. Channel activity can be observed in a high throughput fluorescence-based system

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1. E protein forms a functional ion channel in a laboratory cell line
2. Channel activity can be observed in a high throughput fluorescence-based system
3. E protein localization can be manipulated by varying cultivation temperature

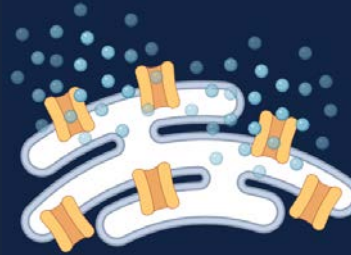
Future Directions



Genetically modify
E protein



Experiment with
varying pH



Investigate E protein
activity in intracellular
compartments



Test screen with
known inhibitors

Acknowledgements

- Research mentor: Dr. Brandon Johnson
- Queen's Summer Research Internship
- Grant funding: Hawai'i Community Foundation



Thank you!

Questions?