Understanding the Biology of the Freshwater Brain-eating Amoeba

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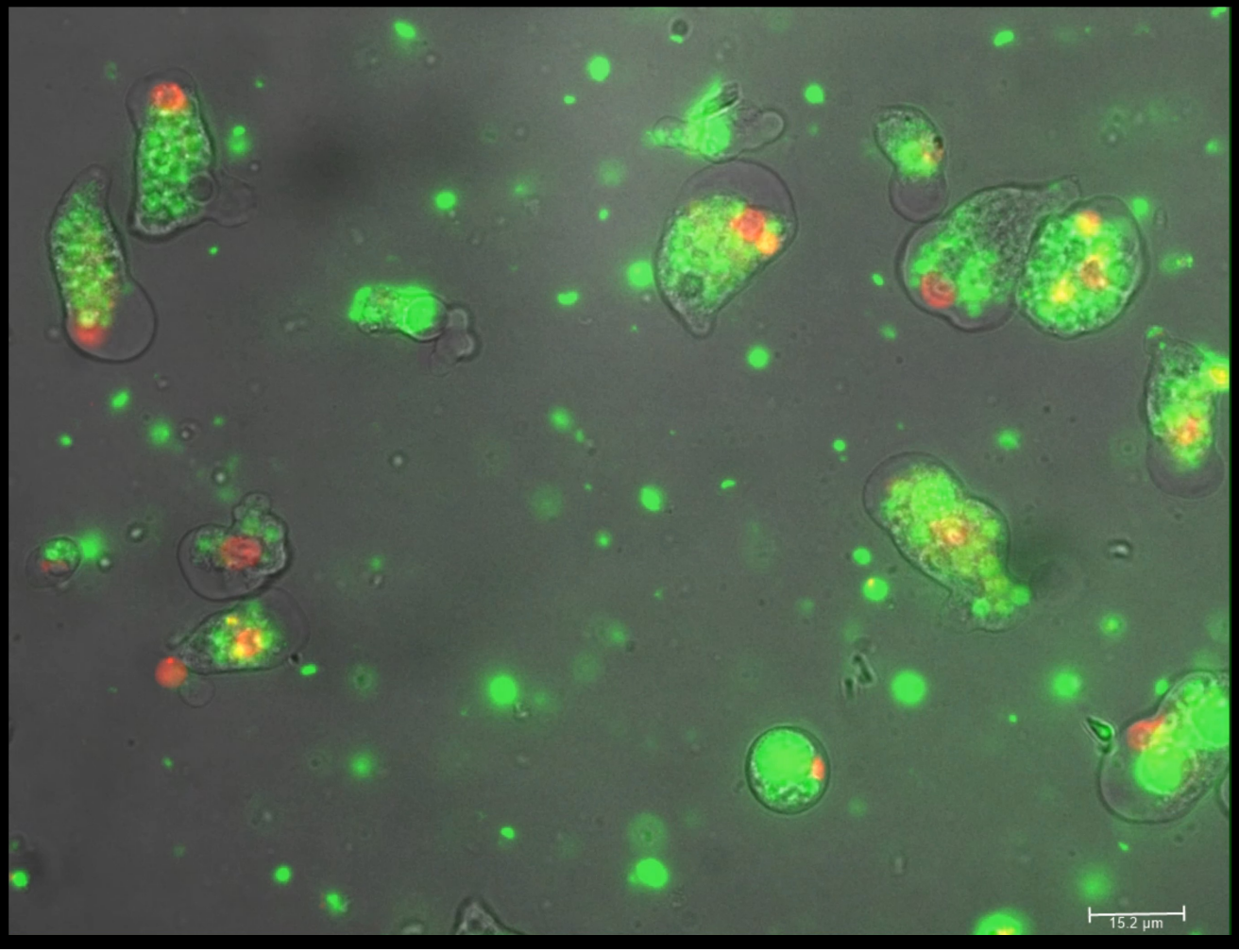
Naegleria

- “Brain-eating amoeba”
- Three stages of life cycle
- Genome has been sequenced

https://www.cdc.gov/parasites/naegleria/index.html

Naegleria gruberi

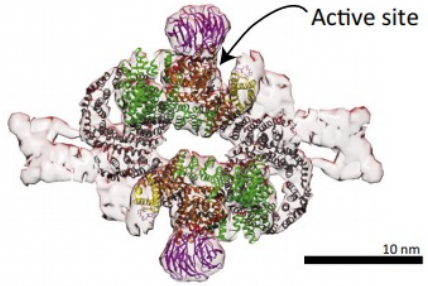
Nuclei
Vacuoles



TOR kinase

- Identified as the target of rapamycin
- Regulate cell cycle and actin polymerization
- Rapamycin
  - Antifungal agent
  - Immunosuppressant and chemotherapeutic

TOR complex

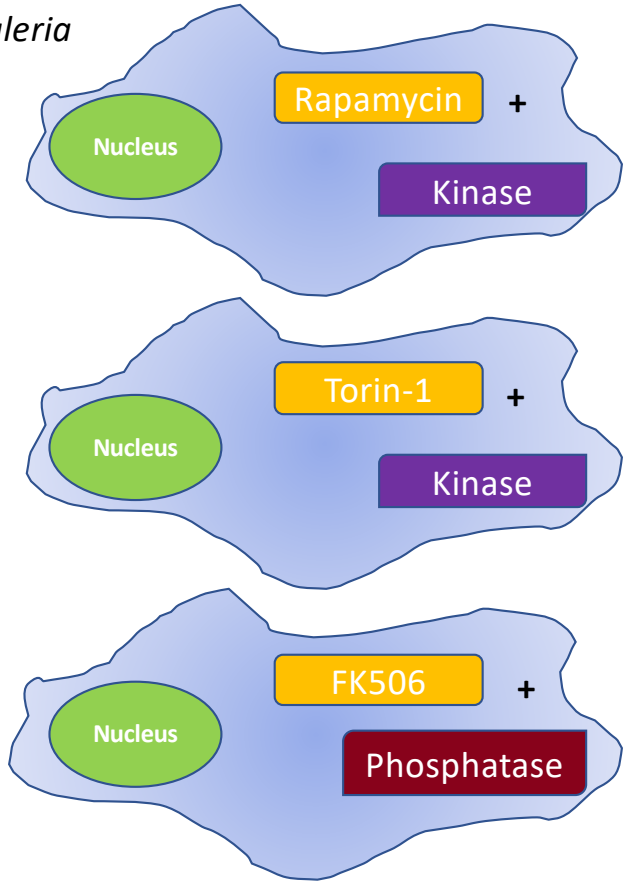


Hypothesis

When the TOR enzyme kinase is inhibited, growth and locomotion of the amoeba are also inhibited

Experiment: Drugs would inhibit TOR kinase and CaN phosphatase

Naegleria cells



= Inhibition of cell growth and locomotion

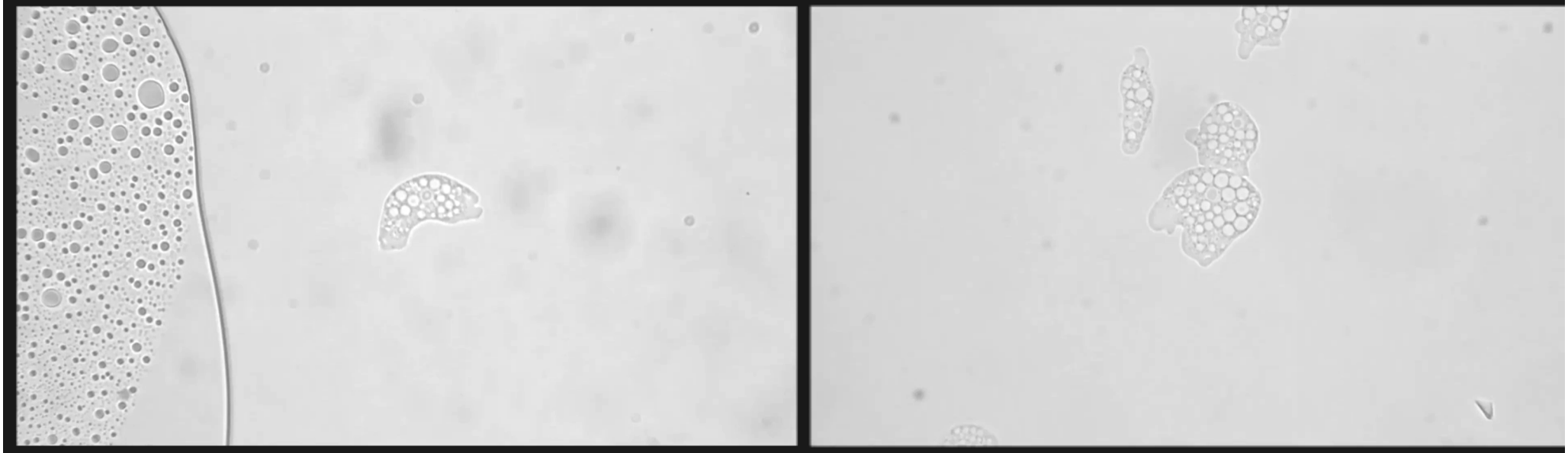
= Inhibition of cell growth and locomotion

= Inhibition of cell growth

Rapamycin does not inhibit amoeba's locomotion or growth

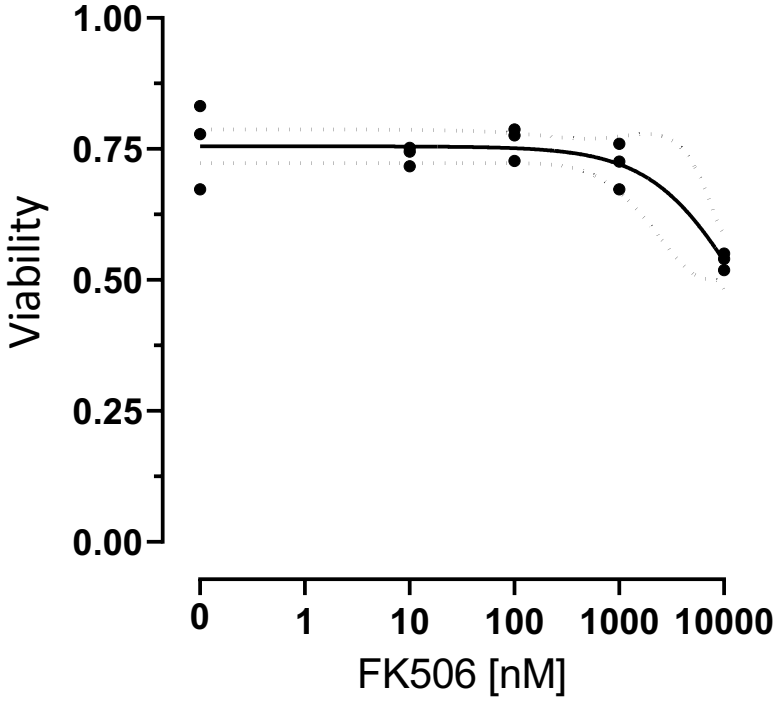
Control

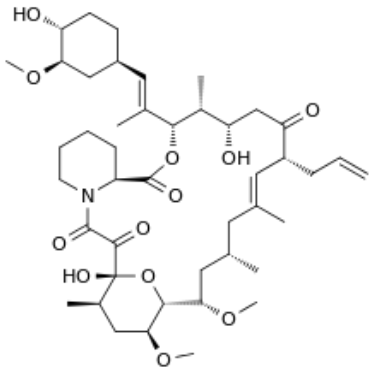
Rapamycin



48h post treatment

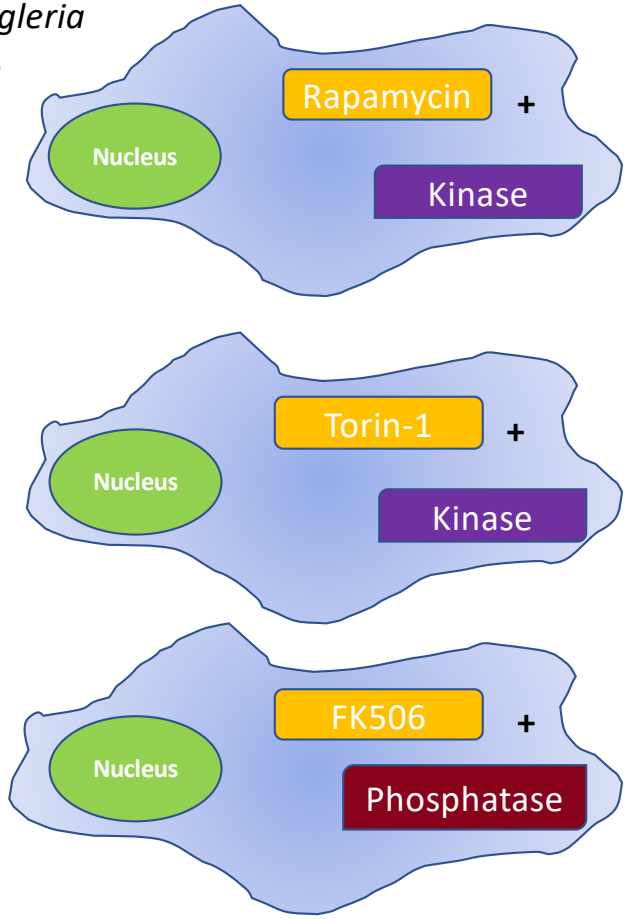
Naegleria is resistant to FK506





Rapamycin and FK506 do not inhibit TOR kinase

Naegleria cells



≠ Inhibition of cell growth and locomotion

= Inhibition of cell growth and locomotion

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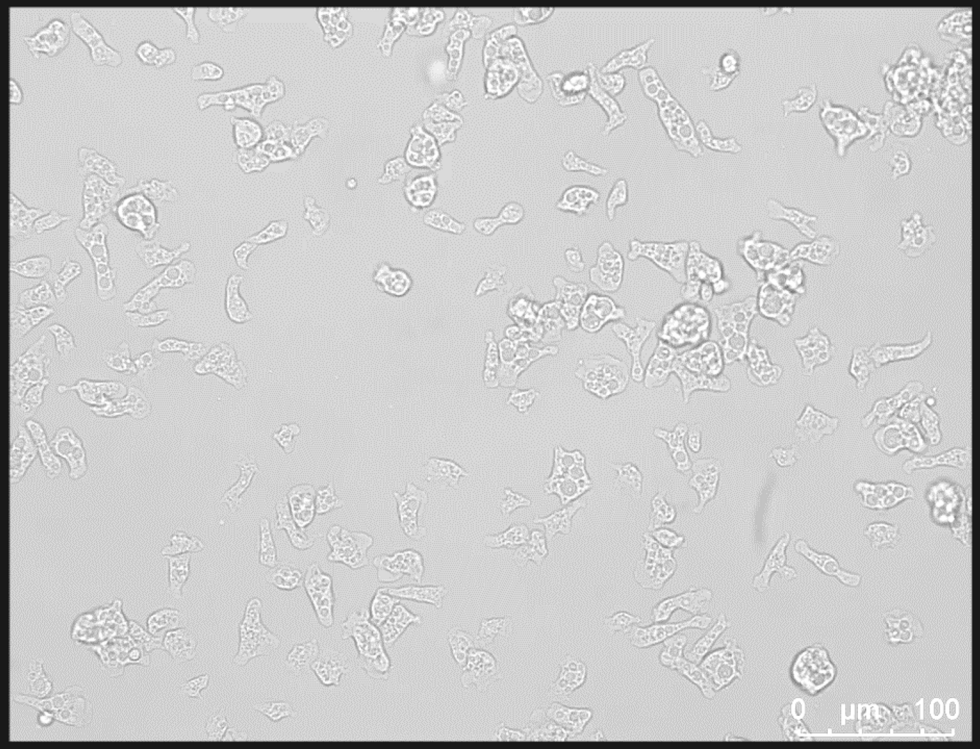
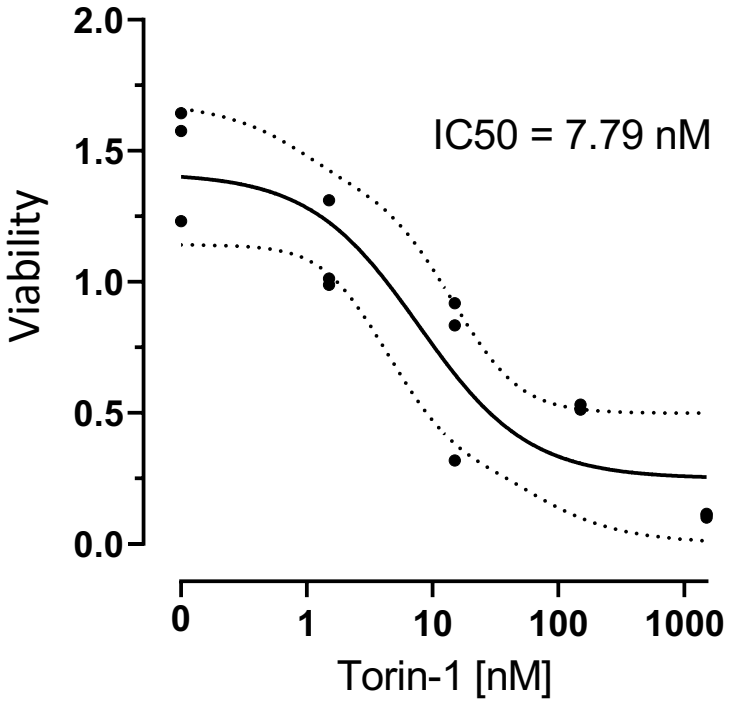
Torin-1 perturbs amoeba's morphology and locomotion

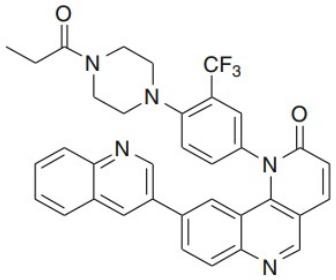
DMSO



Torin-1 (1.5uM)

Torin-1 suppresses viability in *Nagleria*



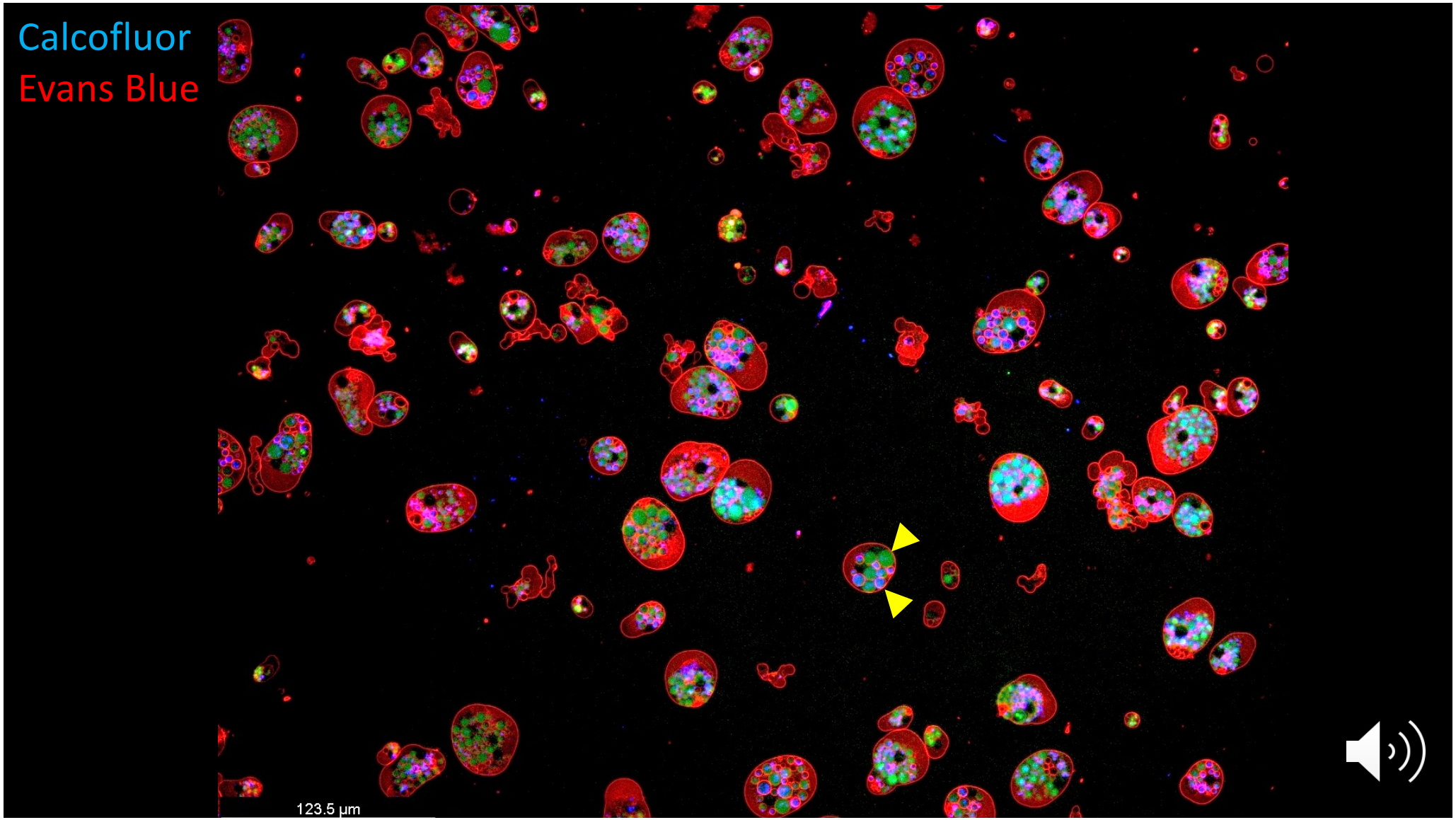


Summary

- TOR complex in the non-virulent strain, *Naegleria gruberi* was not sensitive to rapamycin or FK506
- Torin-1 decreased viability and induces morphological change in *N. gruberi* from trophozoite to cyst-like form

Future Directions

- Investigate the role of TOR kinase in encystation
- Study the relationship between autophagosome and encystment


Calcofluor
Evans Blue
123.5 µm

Acknowledgements

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References

- https://www.cdc.gov/parasites/naegleria/pathogen.html
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3236823/
- https://pubmed.ncbi.nlm.nih.gov/10702636/

Thank you!

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