Potential CFTR & BRCA2 Homologs Identified in *Naegleria*

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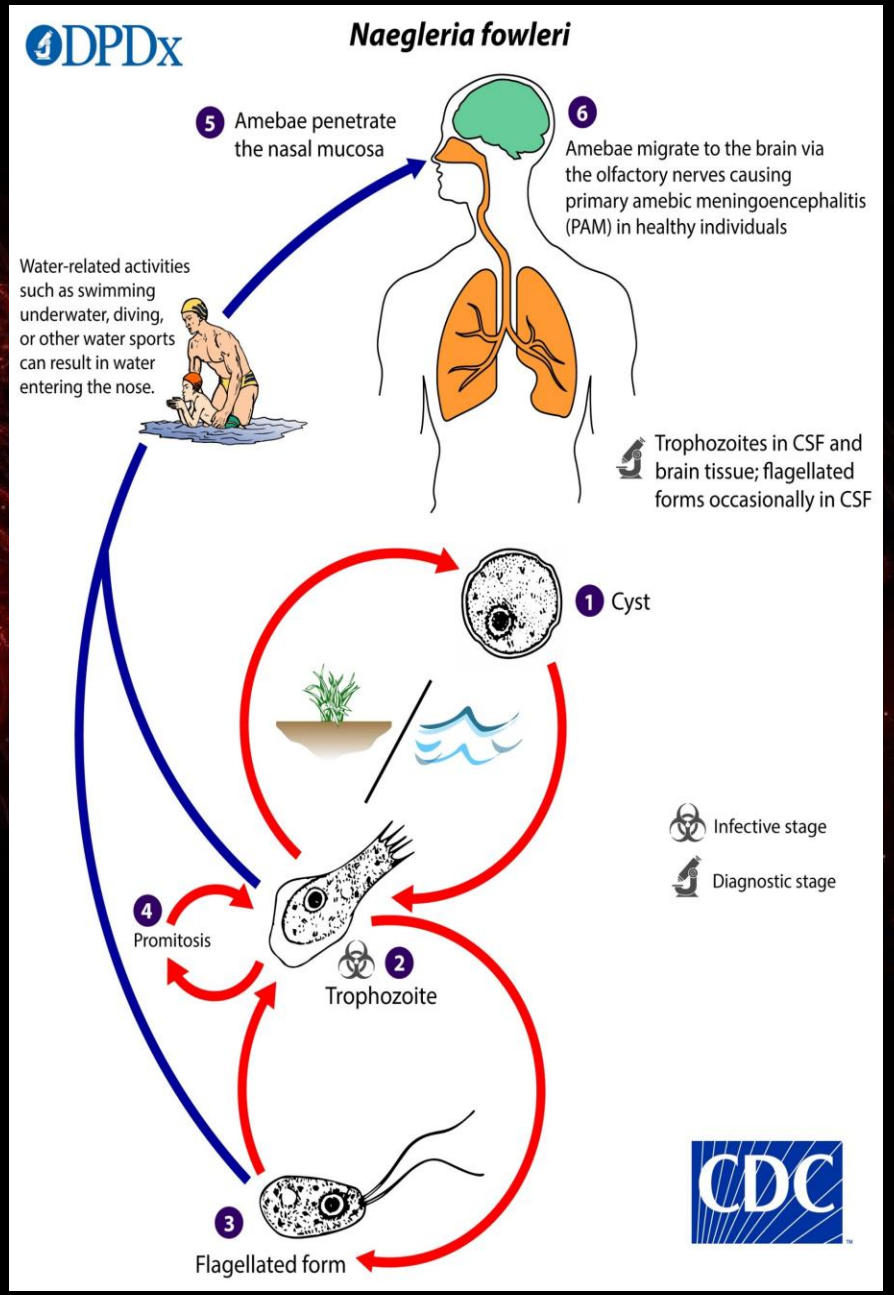
Introduction

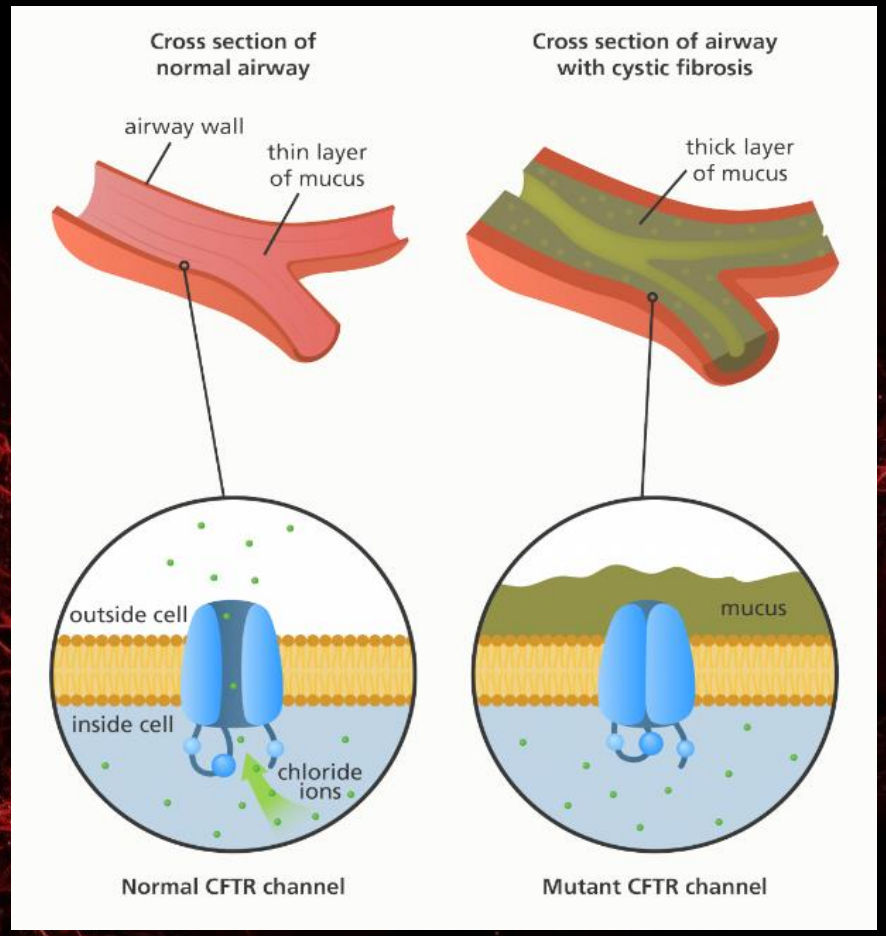
- When humans contract Primary Amebic Meningoencephalitis (PAM) from freshwater amoeba *Naegleria fowleri*, death is almost always imminent. In quest of foundational knowledge regarding potential drug targets, two human disease-causing proteins (BRCA2 and CFTR) were identified. Primers were generated and then used in conjunction with non-pathogenic amoeba for qPCR experiments which yielded specific amplification of target gene transcripts. These assays confirmed expression of the target genes and increase interest regarding function and potential avenues for advanced treatment.

Why Amoeba?

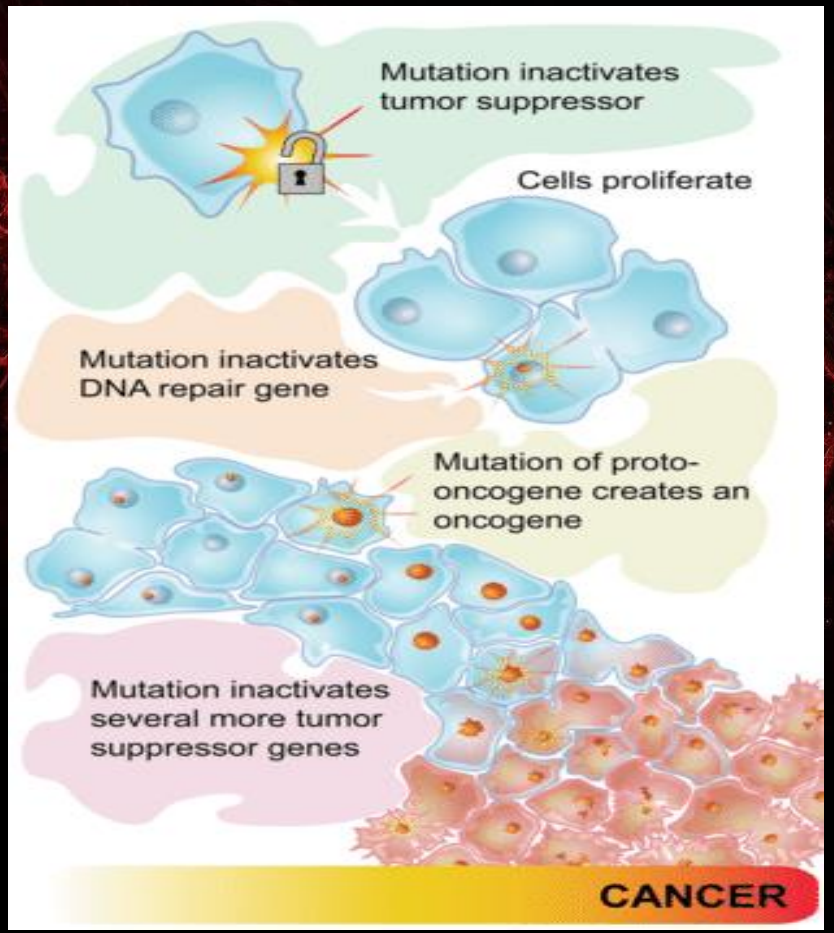
- Primary Amebic Meningoencephalitis (PAM)
- ~160 cases in United States since 1962
- 2.60% survival rate
- No established cure
- *Naegleria fowleri* vs. *Naegleria gruberi*



Genes of Interest

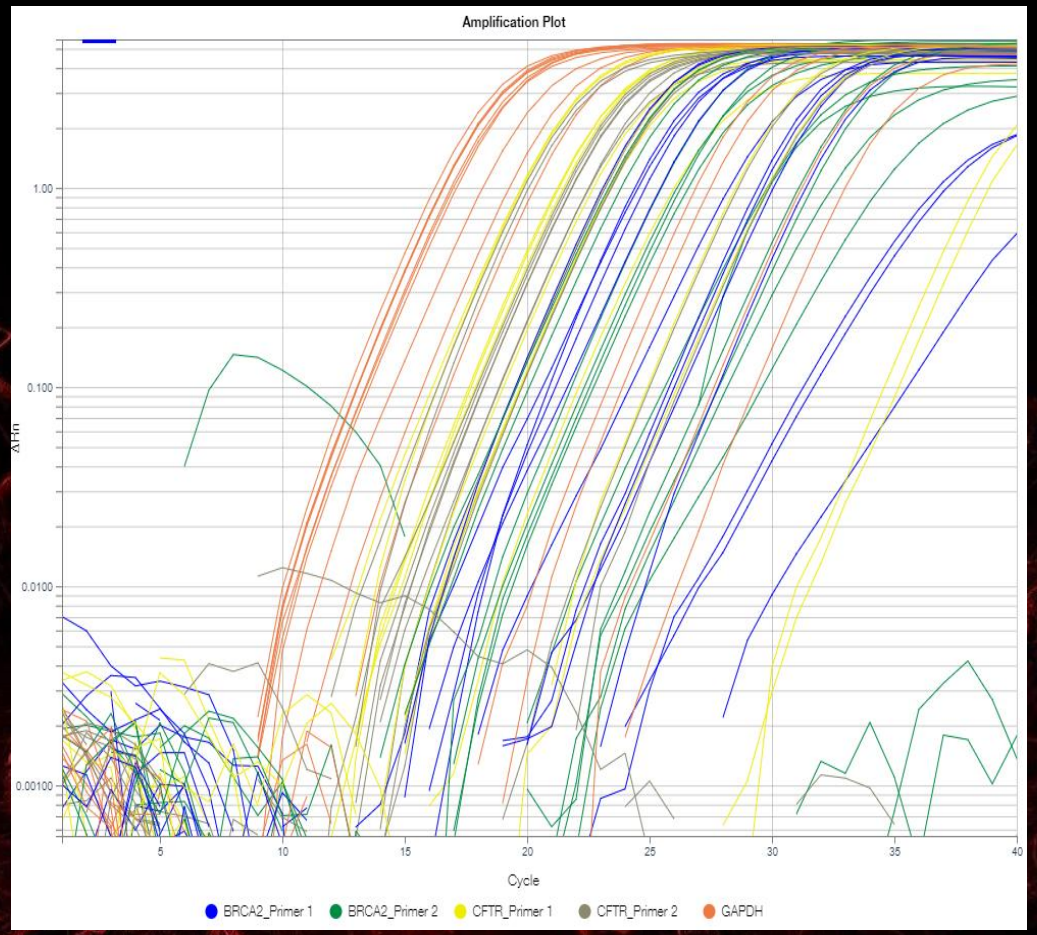


CFTR

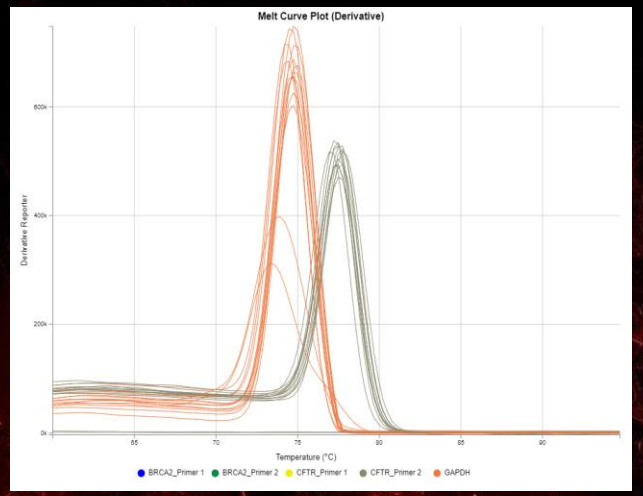


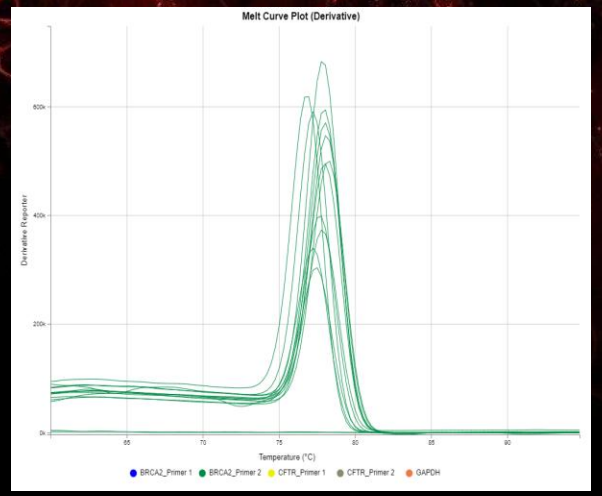
BRCA2

qPCR



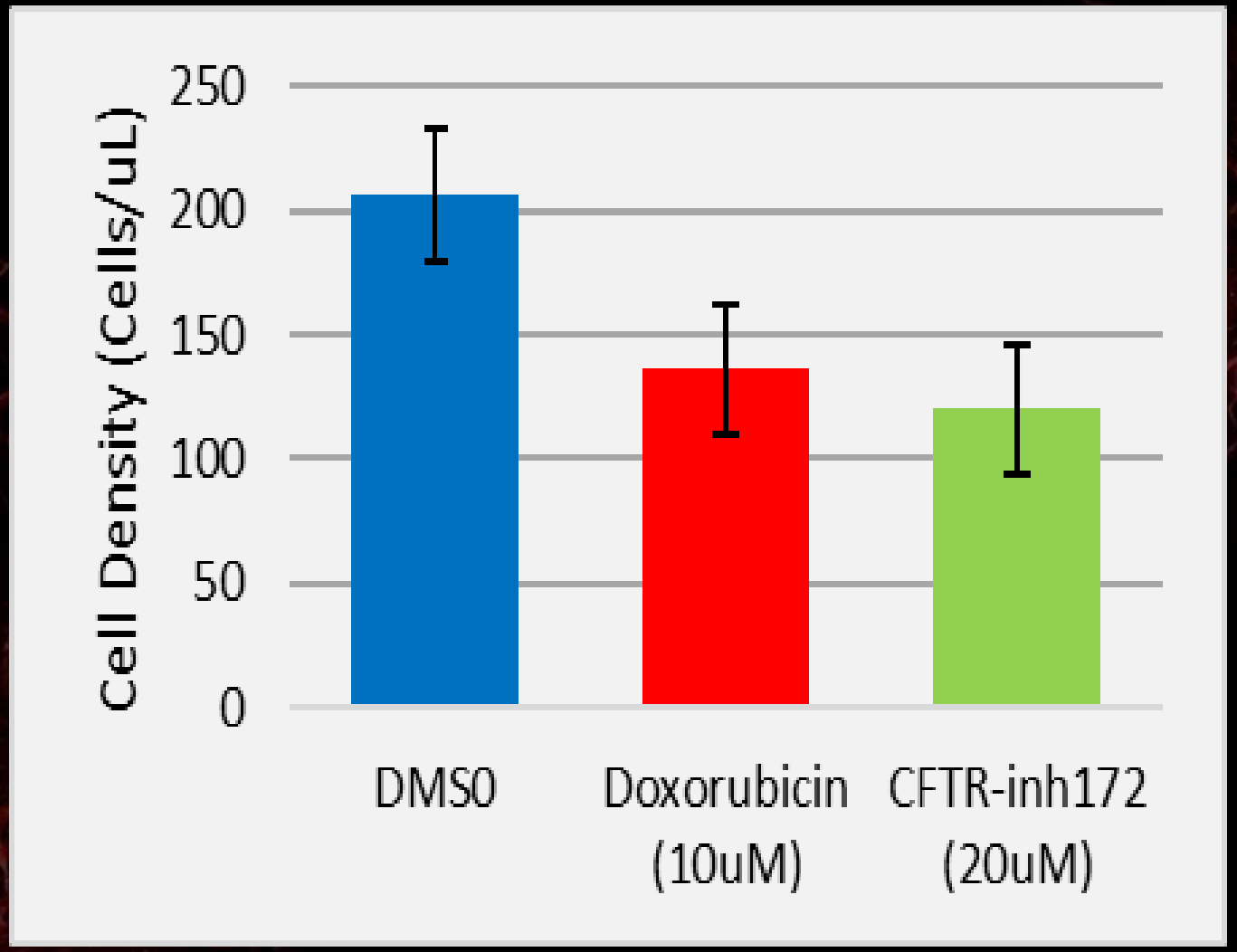
Amplification Plot



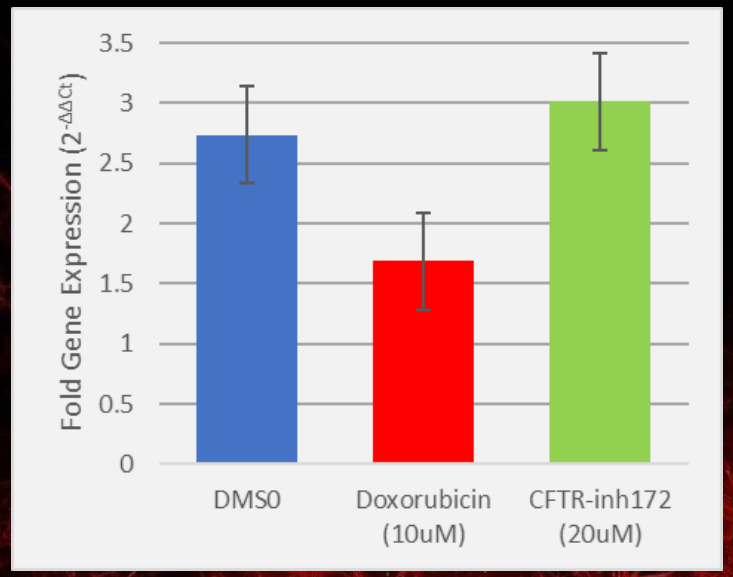


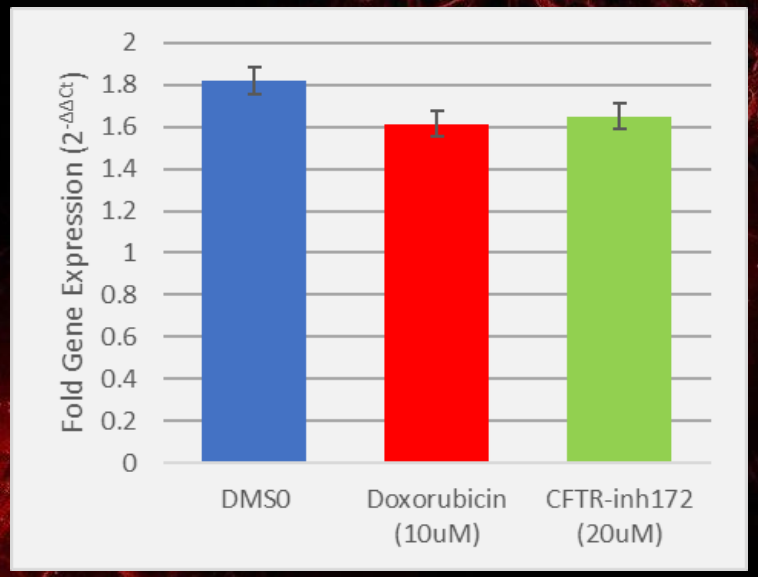
Melting Curves

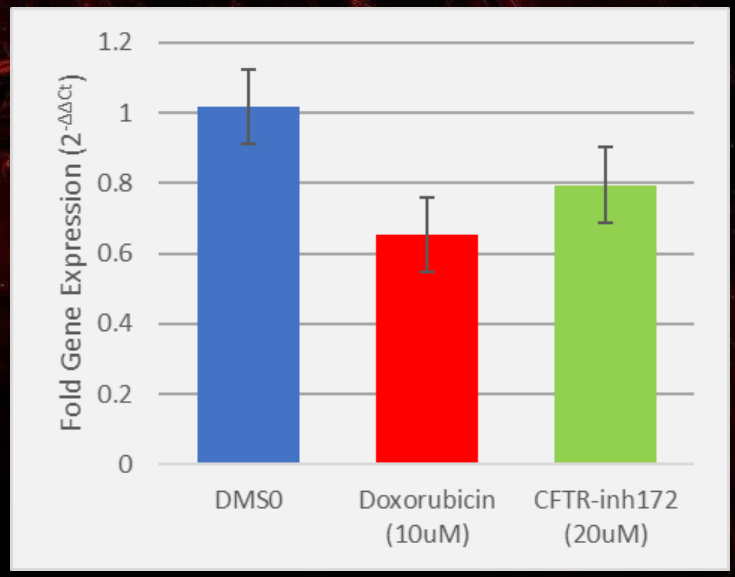
Drug Targets



Gene Expression



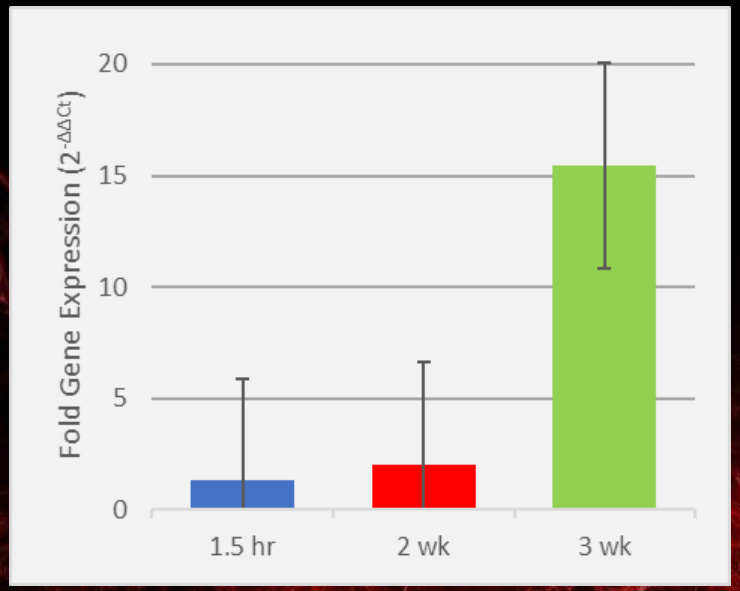


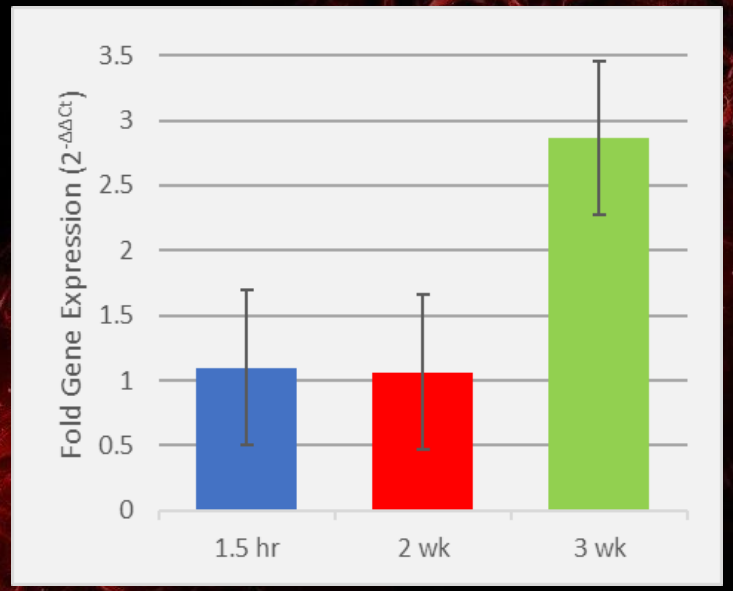


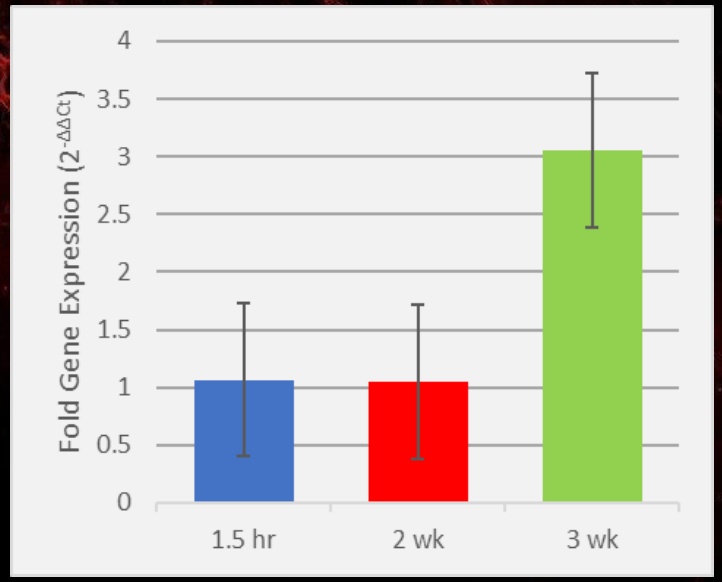
BRCA2-like
gene transcript

CFTR-like
gene transcript

Time Course







BRCA2-like
gene transcript

CFTR-like
gene transcript

Conclusions

- CFTR-like and BRCA2-like genes identified in *Naegleria* genomes
- Gene expressions confirmed
- qPCR primers generated

Conclusions

- Specific amplification of target gene transcripts
- Elevated gene expression in BRCA2-like and CFTR-like genes at Week 3
- Drug targets negatively affected *N. gruberi* growth at these concentrations

Future Directions

- Identify qPCR primers that will not be affected by a time course
- Investigate if BRCA2 pathway conservation in *Naegleria*
- Determine if Rad-51 is present in *Naegleria*
- Identify additional potential drug targets based on protein homology
- Verify if Doxorubicin targets the nucleus
- Determine if CFTR-inh172 binds to CFTR-like protein

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Resources:

https://www.cdc.gov/parasites/naegleria/pathogen.html https://www.yourgenome.org/facts/what-is-cystic-fibrosis/ https://www.ck12.org/book/ck-12-biology-advanced-concepts/section/8.25/

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