Using 4-D imaging of the zebrafish model to observe pharmacodynamics of a therapeutic drug on glioblastoma

Sophie Means[1], John Gamble[2], Leah Wehmas[3], and Julie Greenwood[2]

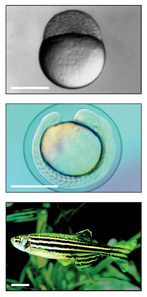
[1]Department of Integrated Biology [2]Department of Biochemistry and Biophysics [3] Department of Environmental and Molecular Toxicology

Glioblastoma Multiform

- Type of aggressive brain cancer
- Five year survival rate of 4.70%
- Not often detected until it's in the later stages when the symptoms appear
- Surgery is not an effective option due to invasion and proliferation of glioblastoma cells outside of the tumor mass before and after surgery

Why the Zebrafish Model?

- Transparent body
- Organism size
- Short assay period
- Little media required
- No adaptive immune system for 28 dpf
- Vertebrate anatomy and brain microenvironment

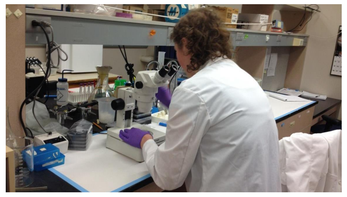


Experimental Outline

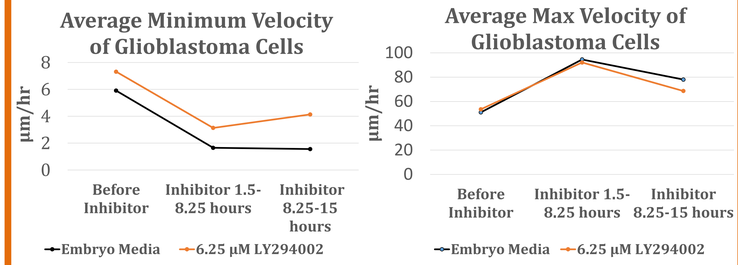
Hypothesis: treatment with 6.25µM LY294002 and 0.5% DMSO will reduce glioblastoma cell invasion in the brain microenvironment, as well as create a morphed cell shape.

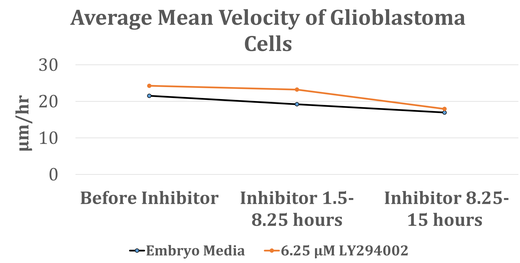
Procedure:

- Zebrafish are injected with glioblastoma cells.
- LY294002 is placed directly in the zebrafish water supply while imaging using the Zeiss 780 confocal microscope.
- The zebrafish are imaged overnight. A cell tracking software is used to measure the velocity and invasion of the glioblastoma cells in real-time.



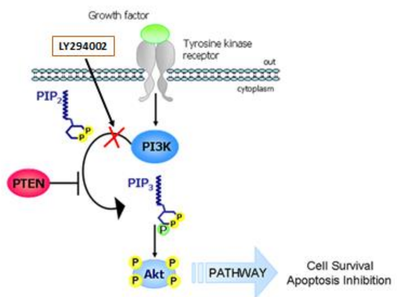
Results



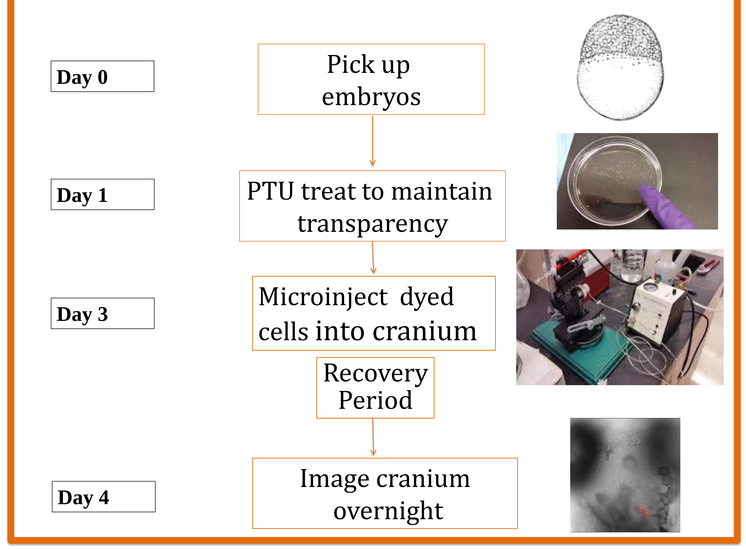


Therapeutic Inhibitor LY294002

- Phosphoinositide 3-kinase (PI3K) is involved in increased proliferation of glioblastoma cells.
- The compound LY294002 is thought to act as a potential therapeutic inhibitor, preventing PI3K from functioning.



Zebrafish Xenograft Procedure



Conclusion

- Glioblastoma cells treated and not treated with LY294002 move at a decreased velocity after fifteen hours.
- The compound LY294002 will be used in higher concentration or longer duration before imaging to get significant results in future experiments.
- A control with 0.5% DMSO in regular embryo media is necessary for future experiments.
- The zebrafish will be placed in the compound before imaging in future experiments to determine optimal time required for the compound to become effective.

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