Advantages and Applications of the Zebrafish Xenograft Model

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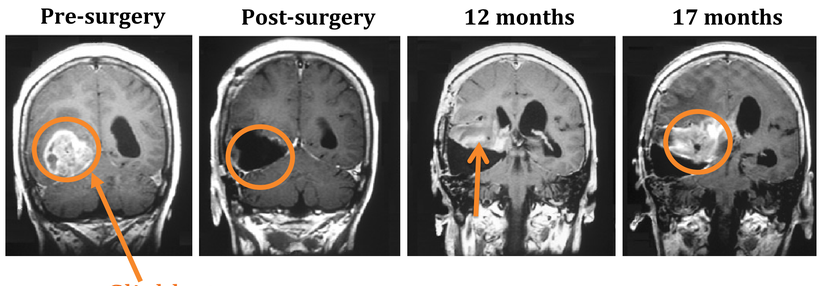
Glioblastoma Multiforme

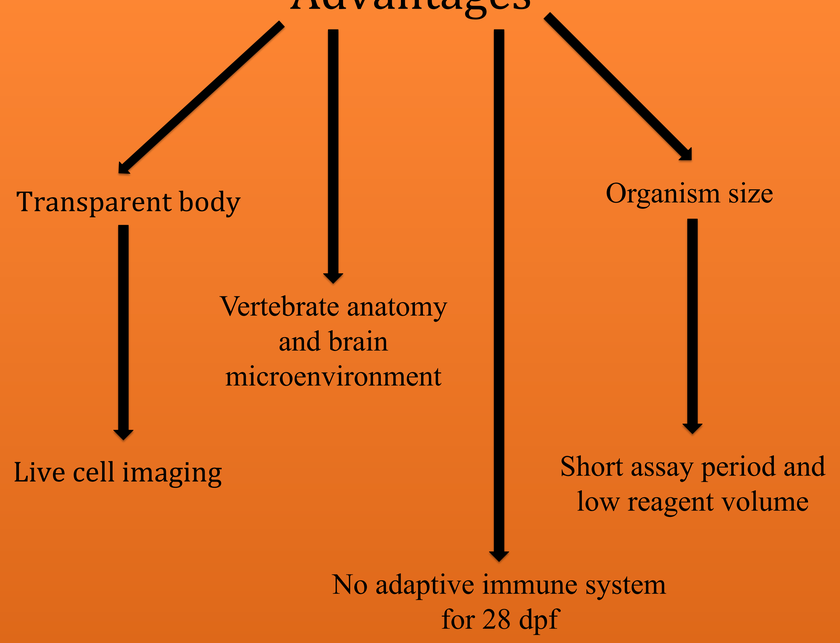
- Most common brain tumor in adults ages 45-70
  - 22,000 Americans diagnosed in 2010
  - Adjusted for inflation, economic costs amount to US$10.7 billion
- No effective long-term treatments
  - 5 year survival rate is less than 5%
- Takes the lives of individuals at their prime
  - The average age at which physicists do their Nobel Prize-winning work is 48

Gary Carter, MLB catcher (1954-2012)

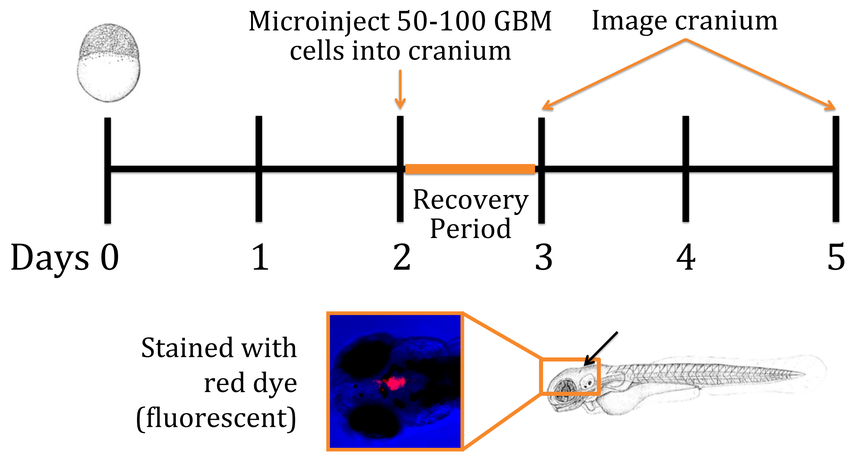
Ted Kennedy, US Senator (1932-2009)



Advantages



Basic Xenograft Procedure



Laminin α-5

Current Focus: John Gamble

- Laminins are a family of extracellular matrix glycoproteins
- Major noncollagenous constituent of basement membranes
- Implicated in cell adhesion, differentiation, migration, signaling, neurite outgrowth, and metastasis

Alterations to Procedure:

- Confocal Microscopy
- Live, real-time videos
- Use morpholino injections to knock down LAMA5

The Role of Calpain II in Glioblastoma Cell Invasion

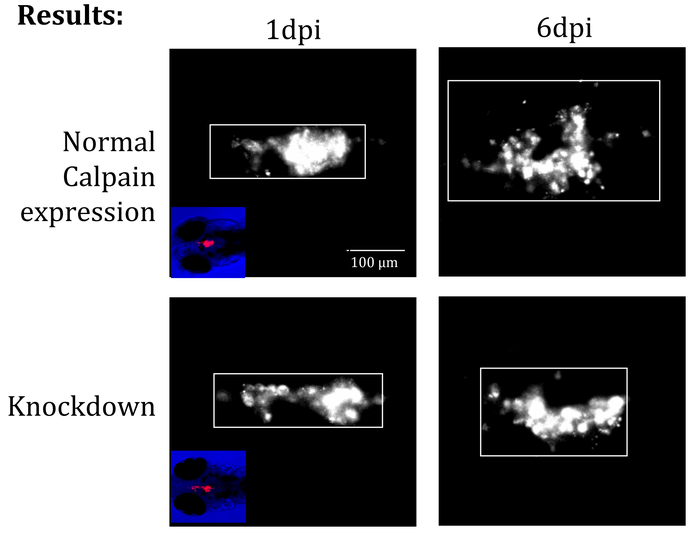
By: Sangeet Lal (2009)

Purpose: to determine if calpain II regulates glioblastoma invasion in a live brain

Alterations to Procedure:

- Cultured calpain II knockdown glioblastoma cells injected into cranium of a larvae 4 dpf
- Live cell imaging 1 dpi and 6 dpi

Results:



Conclusion: Calpain II is required for glioblastoma invasion

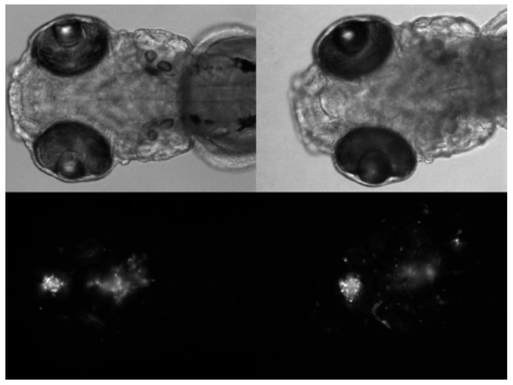
Screening Calpain II Inhibitors

By: Kayla Stalheim, Emily Cade, Leah Wehmas (2015)

- Screened two novel caplain II inhibitors using the xenograft model:
  - Synthetic
  - Developed by Dr. Isaac Donkor, University of Tennessee Health Science Center
  - Patent-pending

Alterations to Procedure:

- Injected embryos at 3 dpf
- Image and expose to inhibitors (through water supply) at 4 dpf
- Image again at 7 dpf



Zebrafish exposed to a 80 micomolar calpain II inhibitor show a qualitative reduction in cell invasion and migration.

Top images show embryos photographed using a brightfield camera one day (left) and four days (right) post injection.

Bottom images show the same embryos photographed under a fluorescent filter.

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