

Glioblastoma Treatment via Iron Oxide Nanoparticle Therapy

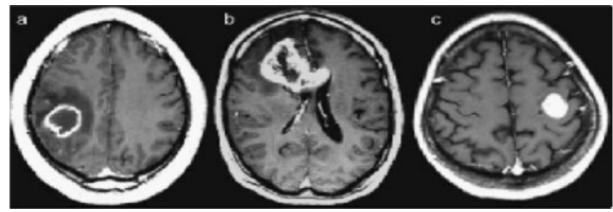
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Glioblastoma Background

- Glioblastoma (GBM) Aggressive cancer that originates from glial cells within the brain or spinal cord
- Highly resistant to therapy and the impediment of drug delivery by the blood-brain barrier (BBB) yields difficult treatment

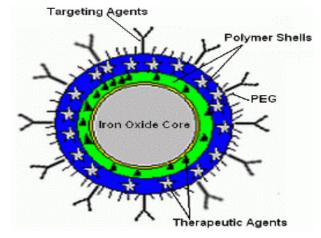


Glioblastoma Heterogeneity via MRI



Iron Oxide Nanoparticle Background and Utility

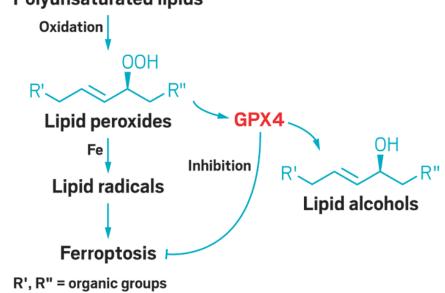
- Iron oxide core functionalized with biocompatible polymers
- Polymers allow attachment of various drugs and cellular targeting agents for targeted drug delivery
- Capable of targeting tumors
- Capable of crossing the blood-brain barrier
- Increase blood half life of the therapeutic delivered
- Biocompatible and non-toxic to humans





GPX4 Background

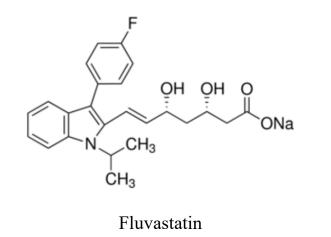
- GPX4 augments sarcoma cell resistance to ROS yielding resistance to radiation
 - We presume GBM cells will present the same reults
- Knocking down the GPX4 pathway induces ferroptosis
 - Enables enhanced effects of chemotherapeutics Polyunsaturated lipids

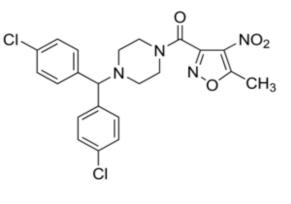




Materials and Methods

- Treated GBM6 and U87 cell lines (representative GBM cell lines) with inhibitors fluvastatin and ML210.
- 5 day incubation period
- Determined viability of GBM cells post-incubation with inhibitor via a microplate reader

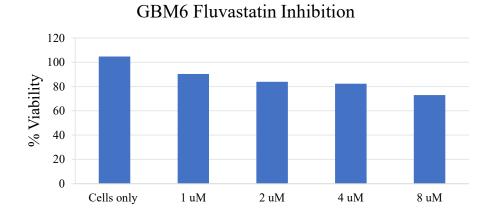




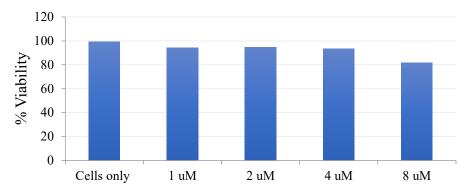
ML210



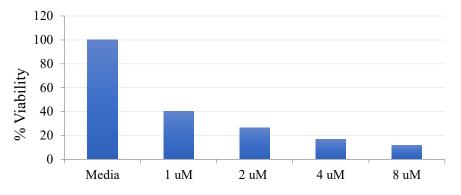
Preliminary Results



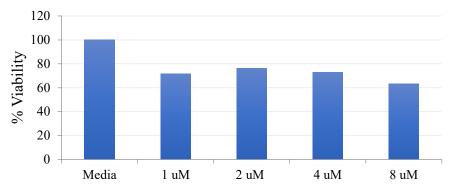
GBM6 ML210 Inhibition



U87 Fluvastatin Inhibition



U87 ML210 Inhibition

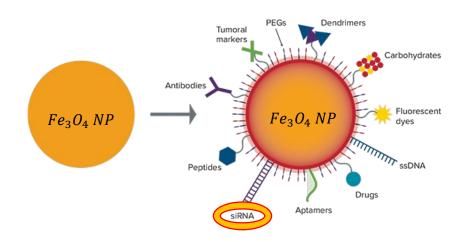


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Goals for Further Investigation

• Incorporate radiotherapy

- Functionalization of siRNA with nanoparticle
- Transition in to in vivo setting



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Acknowledgements

- Richard Ellenbogen, MD
- Mrs. Ellenbogen

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- Miqin Zhang, PhD
- Zach Stephen, PhD
- Hailey Loucks
- Mike Jeon
- Ellie Thorstad
- Neurosurgery colleagues
- Jana Pettit
- Jim Pridgeon
- Christine Mac Donald, PhD
- UW Neurological Surgery Donors, Faculty, Staff, and Residents

Grants

- NIH NINDS R25NS095377
- NIH/NCI RO1CA161953
- NCI T32CA138312



References

- Borman, Stu. "Treatment-Resistant Cancers Have Achilles Heel." *CEN RSS*, American Chemical Society, cen.acs.org/articles/95/i29/Treatment-resistant-cancers-Achillesheel.html.
- "Fluvastatin Sodium." *Sigma-Aldrich*, The Journal of Pharmacy and Pharmacology, www.sigmaaldrich.com/catalog/substance/fluvastatinsodium433459395755211?lang=en®ion=US.
- Hanif, F. et al. (2015). Glioblastoma Multifome: A Review of its Epidemiology and Pathogenesis through Clinical Presentation and Treatment [Abstract]. *Asian Pacific Journal of Cancer Prevention*, *18*(3), 9th ser.
- Hurst, Miranda N, and Robert K DeLong. "Spectral Signature Analysis of Surface Functionalized Nanoparticles." *Molecular Devices*, 16 Feb. 2012, www.moleculardevices.com/en/assets/app-note/br/spectral-signature-analysis-of-surface-functionalized-nanoparticles.
- "ML 210 SML0521." *Sigma-Aldrich*, The Journal of Pharmacy and Pharmacology, www.sigmaaldrich.com/catalog/product/sigma/sml0521?lang=en®ion=US.
- Viswanathan, V S, et al. "Dependency of a Therapy-Resistant State of Cancer Cells on a Lipid Peroxidase Pathway." *Advances in Pediatrics.*, U.S. National Library of Medicine, 27 July 2017, www.ncbi.nlm.nih.gov/pubmed/28678785.

