Nanoparticle Mediated GPX4 Knockdown to Combat Radio-resistance in Glioblastoma

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Glioblastoma

- Common and Aggressive Cancer
- Difficult to treat due to:
  - Mesenchymal Cell State (MSC)
  - Blood-Brain Barrier (BBB)

Glioblastoma Heterogeneity via MRI
GPX4 Induced Radio Resistance in MSC

- Therapy resistance dependent on protection from ferroptosis
- GPX4 and lipid peroxide dissipation

Polyunsaturated lipids

Oxidation

\[ \text{R'} \coon{\text{Fe}} \coon{\text{GPX4}} \coon{\text{Inhibition}} \coon{\text{R''}} \text{Lipid peroxides} \]

\[ \text{R'} \coon{\text{Fe}} \coon{\text{GPX4}} \coon{\text{Inhibition}} \coon{\text{R''}} \text{Lipid radicals} \]

\[ \text{R'} \coon{\text{Fe}} \coon{\text{GPX4}} \coon{\text{Inhibition}} \coon{\text{R''}} \text{Ferroptosis} \]

\[ \text{R'} \coon{\text{Fe}} \coon{\text{GPX4}} \coon{\text{Inhibition}} \coon{\text{R''}} \text{Lipid alcohols} \]

\[ \text{R'}, \text{R''} = \text{organic groups} \]
Nanoparticle for Crossing BBB

- Successfully cross the BBB
- Effective siRNA Loading
- Tumor Targeting
Methods

- Plated a U118 cell line and incubated in hypoxia
- 11 days of incubation
- Samples collected for GPX4 Expression analysis
Results

> qPCR shows a trend of GPX4 Upregulation
In Progress and Future Plans

> Nanoparticle mediated siRNA treatment
  – 1-11-day incubation with U118 cells

> Establish Comparative Radiation Survival Curves

> In vivo testing
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