Background

- Inflammatory breast cancer is rare, affecting 2-4% of all women with breast cancer, but makes up a disproportionately high number of breast cancer-related deaths at 10%(1,2,3).
- Previous work from our lab has shown that N-myc downstream regulated gene 1 (NDRG1) regulates cancer stem cells, tumor progression, and brain metastasis(4).
- From the same study, cancer cell lines with silenced NDRG1 expression generated a drastically reduced population of cancer stem cells than control (Fig. 1A and B)(4).
- Research to this point on effective methods of reduction of NDRG1 is lacking. However, examining the pathway of NDRG1, the direct upstream activator serum and glucocorticoid-regulated kinase 1 (SGK1) may represent a potential target for its inhibition (Fig. 1C).
- Our hypothesis is that inhibition of SGK1 will result in the regression of IBC tumors by reducing cancer stem cells and the expression of NDRG1 and phospho-NDRG1.

Methods

- IC50 Generation
  - SUM149 cells were treated with varying doses (ranging from 25 x 10^-5 nM to 25 μM) of GSK650394, an SGK1 inhibitor, over 72 hours.
  - Cell viability was measured by cell titer blue assay.
- Immunoblot Analysis
  - Referencing the IC50, a range of concentrations from 125 nM to 30 μM were chosen to treat cells for 1 hour.
  - Expression of pNDRG1, NDRG1, and SGK1 were quantified using immunoblot analysis.
- Flow Cytometry
  - Cells were tagged with PE mouse anti-human CD24 and FITC mouse anti-human CD44 and passed through a flow cytometer to measure the number of CD44 high/CD24 low population in control and GSK650394 treated groups.

Results

IC50 of SGK1 Inhibitor GSK650394 in SUM149 cells is 1.02 μM

GSK650394 treatments of 10 μM and 30 μM do not reduce cancer stem cell populations

Conclusions

- SGK1 inhibition resulted in reduction of NDRG1/pNDRG1 expression but did not significantly impact cancer stem cell populations.
- Further work is necessary to identify the optimal concentration and time interval of treatment for reducing cancer stem cell populations.
- Beyond identifying optimal dose and duration of drug treatment with GSK650394, this study could be moved in vivo into mouse models to examine how it functions in a biological context.

References

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3. Villodre et. al. Cancers, 2020
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