Pre-Clinical Animal Model for Ovarian Cancer Using Live Imaging System

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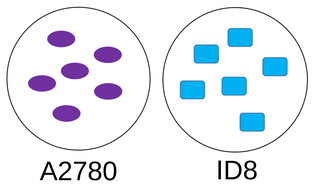
Introduction

Ovarian cancer is the fifth leading cause of cancer-related deaths among women and the deadliest of gynecologic cancers. Epithelial ovarian cancer (EOC), the most common type of ovarian cancer, is usually not detected until its advanced stages when the tumor has become widely metastatic.

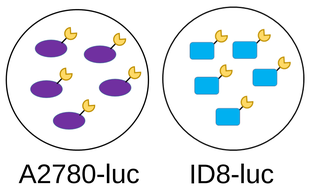
Current clinical methods are limited in their ability to diagnose ovarian cancer in its early stages. As a result, there is an urgent need to create a preclinical disease model that more closely mimics disease onset and progression to provide a more reliable testing tool for novel diagnostics and treatments. In particular, live imaging allows for real-time monitoring of orthotopic disease onset and progression, as well as the evaluation of treatment response following anticancer drug therapies without the need of having to sacrifice an animal to assess its tumor status. Consequentially, this will lead to a significant reduction of animals needed to conduct this research.

The goal of this experiment is to establish a more accurate and effective monitoring technique for an orthotopic ovarian cancer animal model using a live imaging system.

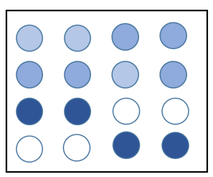
Methods



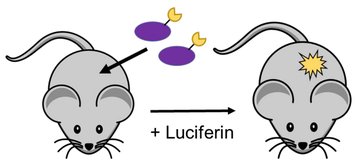
1) Cell Culture
- A2780 – Human EOC
- ID8 – Mouse EOC



2) Establish Cell Line
- MTT Assay
- Transfection - Luciferase
- Selection - Hygromycin B



3) Verify Luciferase Expression
- Luciferase Assay
- Protein Assay



4) In Vivo Live Imaging
- Inoculate mice with A2780-luc
- Monitor weight and abdominal circumference
- Assess tumor development and progression using IVIS live imaging system

Results

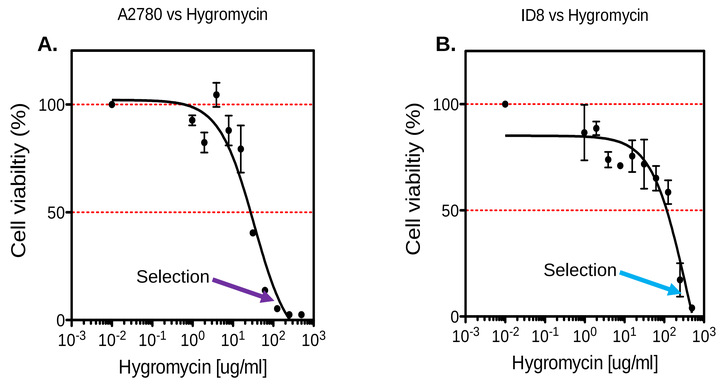


Figure 1. Methyl Thiazol Tetrazolium (MTT) Assay results showing cell response to various concentrations of Hygromycin B. A) A2780 and B) ID8 cells were selected at a concentration tolerating 10% cell viability (Inhibitory Concentration IC90).

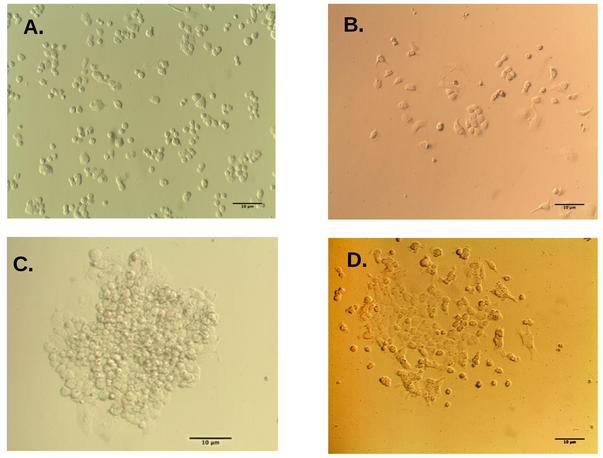


Figure 2. A) A2780 and B) ID8 cells prior to transfection. C) A2780-luc and D) ID8-luc cells after being transfected with luciferase. A2780 cells form "grape-like" clusters, while ID8 cells have a "cobblestone" morphology. Similar morphology between original and transfected cells suggest that we would expect similar drug responses when testing potential treatments.

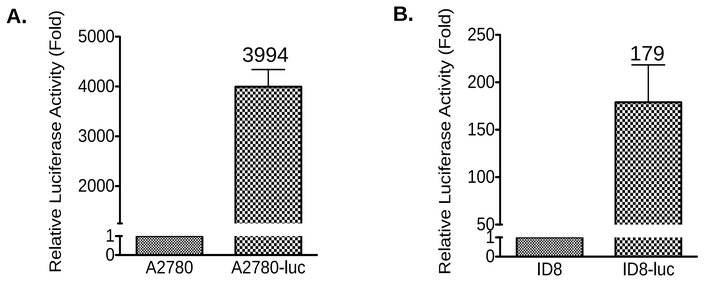


Figure 3. Results from Luciferase Assay, normalized to inherent luciferase activity, show that A) A2780-luc had almost 4000X more luciferase activity than untransfected A2780 cells. B) ID8-luc cells had around 180X more luciferase activity than original ID8 cells.

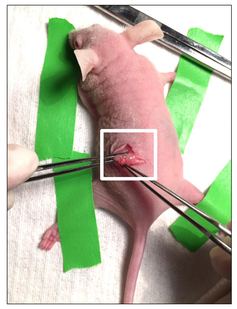


Figure 4. Dorsal view of 6-8 week old, female nude mouse showing incision used for accessing ovaries to orthotopically inoculate with A2780-luc cells (left ovarian bursa).

Conclusion

We were able to successfully establish a stable cell line of A2780-luc and ID8-luc.

The morphology of the original and transfected ovarian cancer cells are very similar, indicating it will be possible to evaluate drug response analogous in both cell lines.

The development of a live imaging animal model for orthotopic ovarian cancers will serve as a useful tool for studying mechanisms responsible in early disease and better understanding therapeutic response to various anticancer drug treatments. We expect our imaging results to show a proportionate relationship between tumor growth and the amount of luciferase activity detected.

Live imaging is advantageous because it allows researchers to monitor orthotopic tumor formation, progression, and treatment response without the need to sacrifice the animal. Utilizing this imaging method allows for more effective, continuous monitoring of ovarian cancer. It can also decrease the time and cost to test various anticancer treatment strategies in addition to studying underlying mechanisms.

References

Cho, S. (2013). *Anticancer Research 33*, 1317-1324.
Roby, K. F. (2013). *Carcinogenesis Vol. 21 No. 4*, 585-591.

Acknowledgements

I would like to express my sincere gratitude to the Janát-Amsbury Laboratory for supporting this research. This work was funded by Rosemary Gray and the ACCESS Program for Women in Science and Mathematics, 1R43CA177146-01A1, and the Department of Obstetrics and Gynecology at the University of Utah.