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Downregulation of MYC and KRAS modulates Ovarian Cancer Cell growth

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BACKGROUND

- Ovarian Cancer is the fifth leading mortality among women[3]
- Ovarian cancer health disparities exist for African American and Hispanic/Latin women[3]
- MYC is a proto-oncogene mandating tumor cell fate[4]
- Mutated KRAS oncogene induce constant cell proliferation and survival[2]
- Address the gap in knowledge about KRAS and MYC proteins' affect on cancer[6]

QUESTION

- Will decreasing MYC and KRAS proteins affect ovarian cancer cell growth?

METHODS

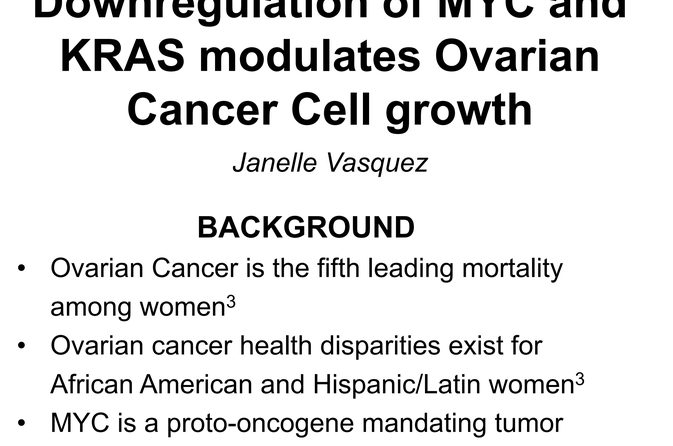

Figure 1. Methods to quantitively measure the affect of oncogene expression in ovarian cancer cells. First, ovarian cancer cells were received from Asian-American women in the United States. Those cells were transfected with the TET-ON/siRNA system[7]. Cells were selected for the positive transfection and then tested by qPCR. The qPCR methodology as shown above was used for both 2D and 3D models which showed the possible Doxycycline drug concentrations that affect the expression of the oncogenes. A cell viability test was done using the methodology shown above for both 2D and 3D models in order to see a significant correlation at the IC50 range.

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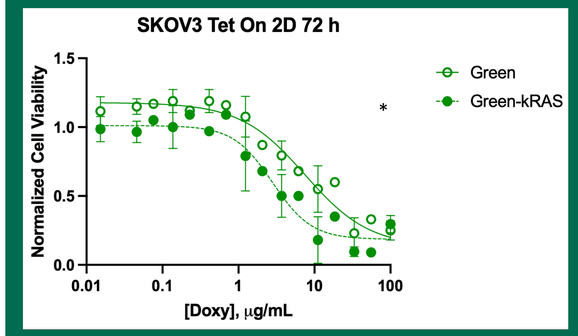
Decreasing KRAS expression decreases cancer cell survivorship

A.



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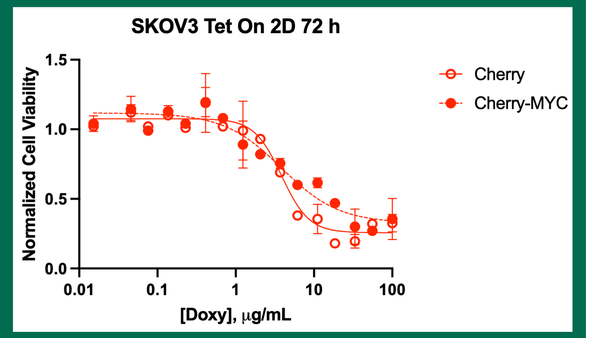

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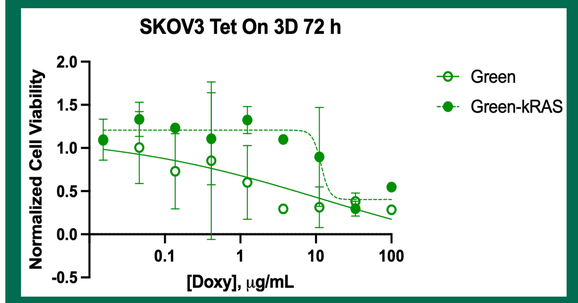

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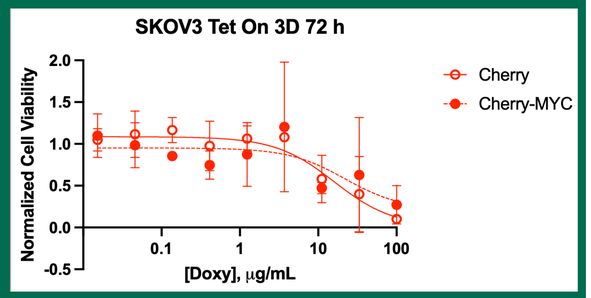
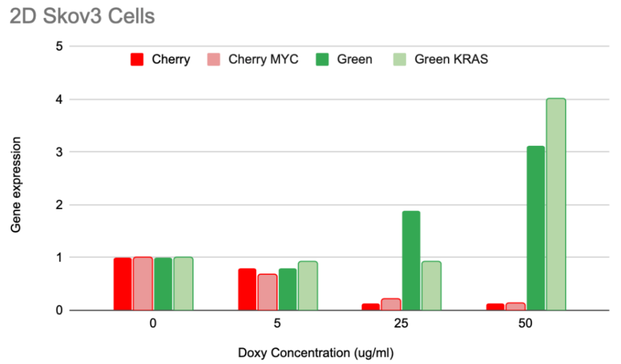


Figure 3. Doxycycline kill curves for 2D and 3D Skov3 cell lines. **A.** has an IC50 of 7.5 for the control and 2.8 for the knockdown, with a p value < 0.05, showing a significant correlation between decreasing KRAS oncogene to cell survivorship. Therefore, it is concluded that knocking down KRAS modulates the cancer cell growth which is also shown in the qPCR data at 25ug/ml. **B.** has an IC50 of 3.7 for control and 4.8 for knockdown, with a p value > 0.05, showing no significant correlation. **C.** has an IC50 of 0.7 for controls and 2.8 for knockdowns, with a p value > 0.05, showing no significant correlation. **D.** has an IC50 of 16.0 for control and 22.1 for knockdown, with a p value > 0.05, showing no significant correlation. C. and D. are inconsistent with the qPCR data as it shows a downregulation of KRAS and MYC at 25ug/ml for 3D cell lines.

Acknowledgments:

Thank you to Tracy Brooks, PhD, for providing mentorship and all the materials as the principal investigator. Additionally, I would like to thank Alexandra Psaras who started this project and guided me through it.

RESULTS



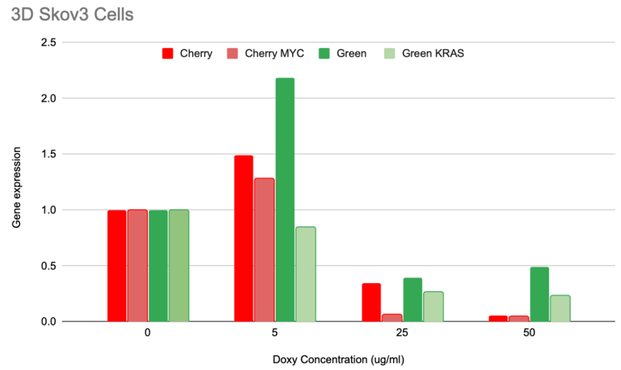


Figure 2. A. Gene expression of 2D Skov3 cancer cells. B. Gene expression of 3D Skov3 cancer cells. All 4 lines were tested for a 72h drug treatment at different Doxycycline concentration (ug/ml). 25ug/ml shows a constant decrease for all cell lines in the 3D model and 2D model. There are a few discrepancies which the expression is higher than the control (0ug/ml).

CONCLUSION

- 25 microgram/mL of Doxycycline decreased the target oncogene expression
- Knocking down KRAS modulated the cancer cell growth in a 2D, but not 3D, cancer cell model
- Inconsistency with experiments for 3D
- Cancer patients following certain criteria can benefit from the TET-ON/siRNA system gene therapy to improve chemotherapy outcomes

FUTURE WORKS

- The interaction between this system with common chemotherapy treatments

REFERENCES: