BACKGROUND

- Human Papillomavirus (HPV) causes over 694,000 new cancer cases annually and is a leading cause of cancer in women in developing countries.
- HPV positive models express viral oncoproteins E6 and E7 that bind and degrade tumor suppressor proteins p53 and Rb respectively, leading to abnormal cell growth and division, reduced cell differentiation and an increased risk of cancer development.
- Although HPV-positive tumors are molecularly distinct from HPV negative tumors, their treatments are identical.
- Standard treatments for HPV-driven cancers includes radiotherapy and chemotherapy that have chronic side effects and are not effective in 20% of HPV+ cancers.
- Therefore, there is an urgent need for therapies that are less toxic and more effective.
- Previously the Johnson lab conducted a high-throughput drug screen (HTDS) evaluating 864 unique compounds. In that HTDS, Aurora kinase inhibitors were more effective in HPV+ than in HPV- human cancer cells.

HYPOTHESIS

Aurora Kinase Inhibition in HPV+ cells will disrupt cell cycle process by delaying mitoses, lead to apoptosis and induce immune cells to target such cells.

METHOD

Since syngeneic mouse models are needed for understanding tumor micro-environment and ICD, murine cell lines, C3.43 and TC-1 cells lines were treated for 24 and 48 hrs with a concentration of 300 nM of Alisertib with vehicle(DMSO) control.

RESULTS

1. Aurora kinase A inhibition leads to apoptosis in murine HPV+ cancer cell lines.

![Figure 1](image)

2. Aurora kinase A inhibition results in Immunogenic cell death in murine HPV+ cancer cell lines.

![Figure 2](image)

3. Inhibition of the ATP-binding cassette (ABC) transporters increases alisertib-induced aurora inhibition and apoptosis in TC-1.

![Figure 3](image)

REFERENCES

- Sinha, Pragya, "Preclinical evaluation of immunomodulatory effects of Aurora kinase inhibition in HPV+ cancers." (2023). The University of Texas MD Anderson Cancer Center UTHSC Graduate School of Biomedical Sciences Dissertations and Theses (Open Access). 1281.

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