

# Studying the Effects of Senescence in Breast Cancer Cells Induced by Cotherapy with Poly (Adp-ribose) Polymerase Inhibitors and Radiation Aided by Senolytics Drugs

## INTRODUCTION

**Breast cancer** is considered the primary lethal female cancer in Saudi Arabia. According to multiple reports, senescent cells have been found to contribute to the recovery and regrowth of the treated tumour cells, which might have been led to cancer relapse. **Resistance** to chemotherapeutic agents is a central problem in cancer treatment. Tumors often respond to initial treatment but can develop resistance to **chemotherapeutic agents / radiation** throughout the course of treatment by altering tumor molecular and cellular behaviors. Studies have previously shown that **PARP inhibitors (PARPI)** can significantly delay tumour development in BRCA1-deficient mice. Also, **senolytics such as Venetoclax and Navitoclax** are drugs that have shown efficacy against senescent cells in the field of aging.

## OBJECTIVES

The overall aim of our project is to evaluate the ability of co-treatment of radiation and PARPI aided by senolytics to selectively eradicate breast cancer cells to induce into senescence eventually leading the cells to apoptosis.

## METHODS

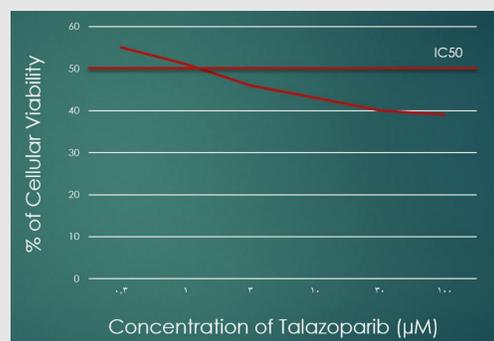
- MTT Cell viability** assay will be used to screen for an optimal dose of PARPI and senolytics combination in two breast cancer cell lines: MDA-MB231, and 4T1
- SA-β-galactosidase and C12-FDG staining** will be used to confirm Senescence in the treatment groups
- Flow cytometry-based Annexin V/7AAD apoptosis assay** to evaluate cellular death
- Reverse transcription-polymerase chain reaction (PCR)** to investigate Genes of senescence
- Western immunoblotting** to evaluate protein expression of senescence genes

## RESULTS

### MTT (colorimetric Assay)



**IC50 TLZ = 1.2 μM**



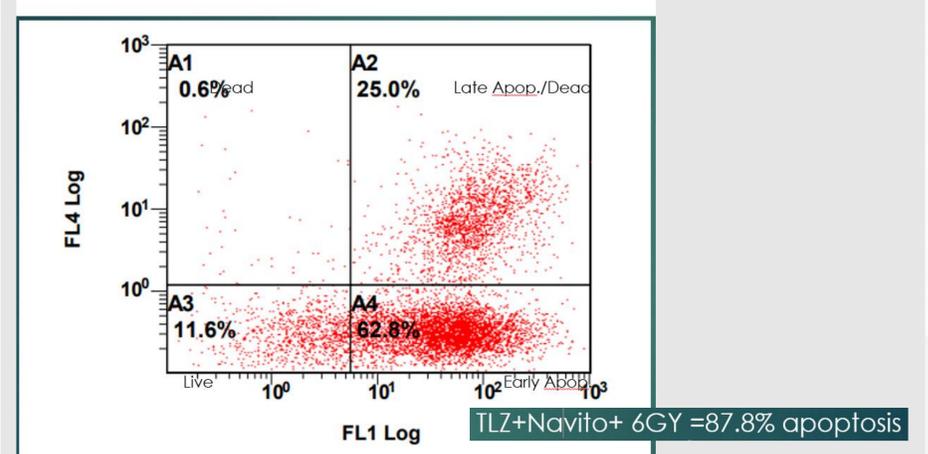
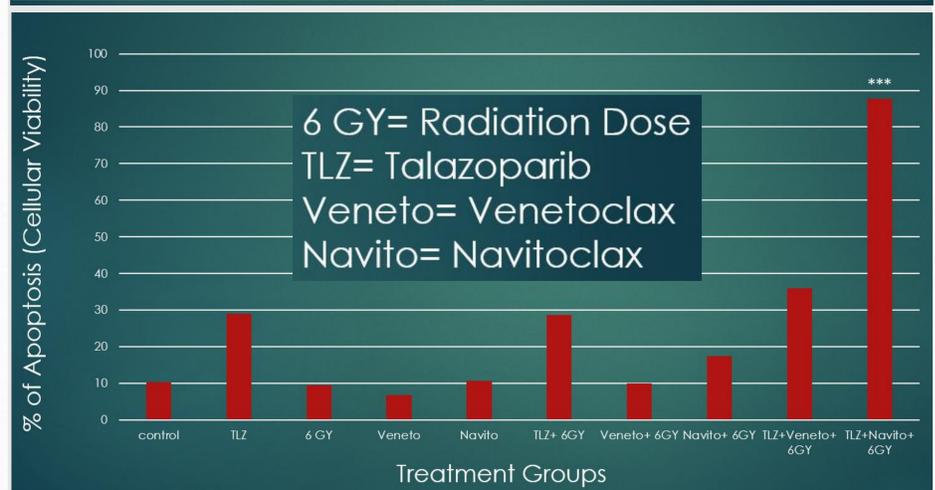
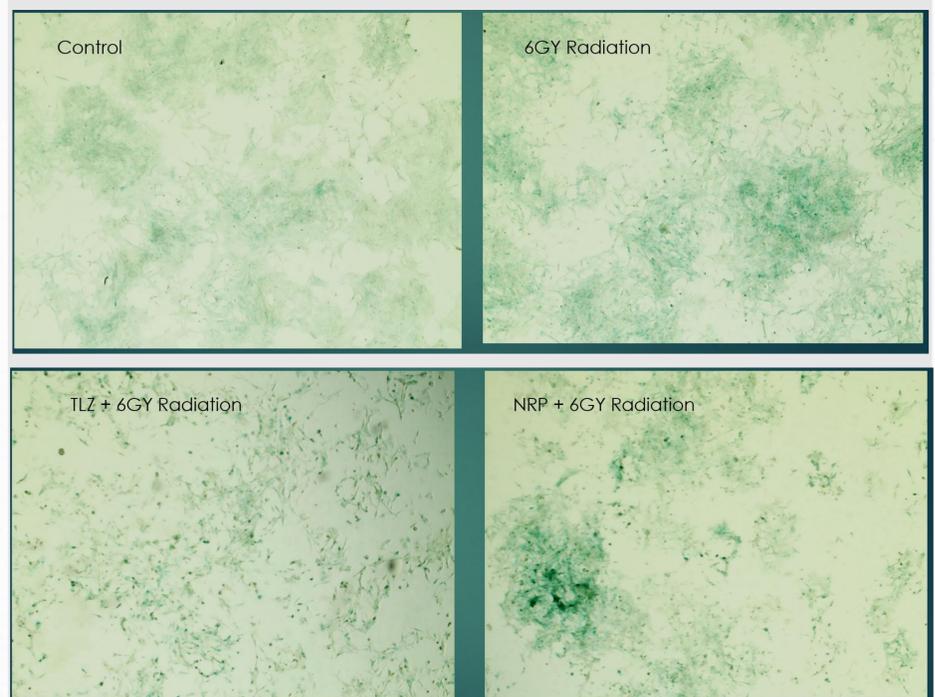
## Researchers

Abrar Softah – PhD Candidate  
Dr. Ali Alhoshani

Dr. Moureq AlOtaibi  
Dr. Homood AsSobeai

## RESULTS

### 4T1 B-Gal Second Experiment Results after Optimization Radiation Dose to 6GY



## DISCUSSION & CONCLUSION

Radiation and the PARPI Talazoparib aided by the senolytic Navitoclax synergistically has proven to provide a low dose therapy protocol with low risk of toxicity for the optimum treatment compared to the conventional breast cancer treatment used currently.