Drug repurposing approach for developing novel therapy for castration resistant prostate cancer

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Androgen receptor (AR) is an important therapeutic target in metastatic prostate cancer treatment.

The initial reprieve from androgen deprivation therapy (ADT) subsequently leads to castration-resistant prostate cancer (CRPC).

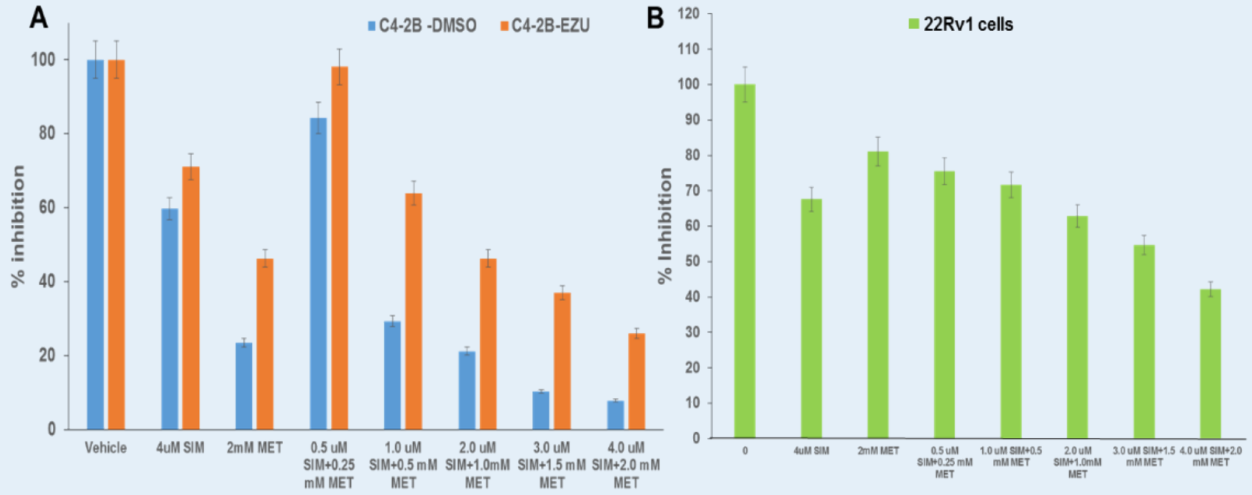
Enzalutamide (ENZU) exhibits survival advantage in CRPC patients, but ~30% develop resistance due to reactivated AR and Warburg effect

Effective low-cost therapeutic alternative with fewer side effects would increase survival, benefitting patient's quality-of-life.

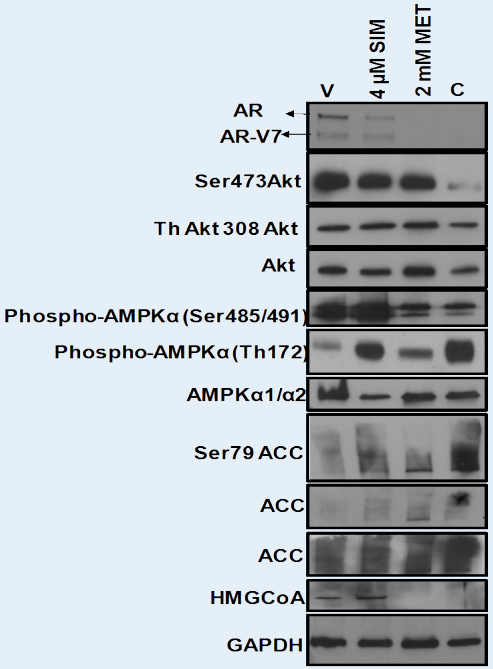
Our earlier studies revealed: synergistic combination of simvastatin (SIM), and metformin (MET), inhibits CRPC growth, with minimal effect on normal prostate epithelial cells.

Here we investigate whether combination of SIM and MET could be effective in the treatment of ENZU-resistant prostate cancer cells.

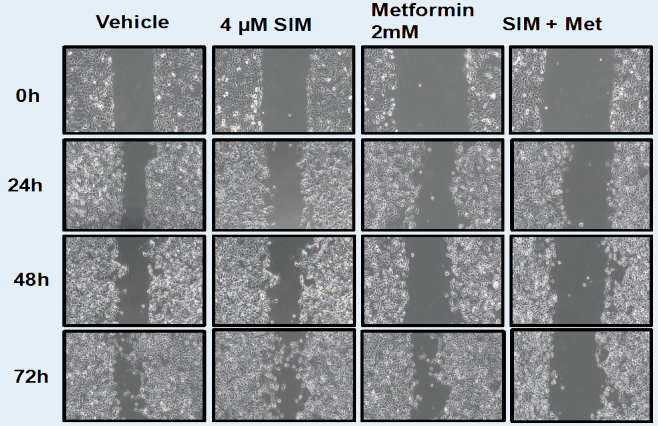
Combination SIM and MET inhibit cell proliferation

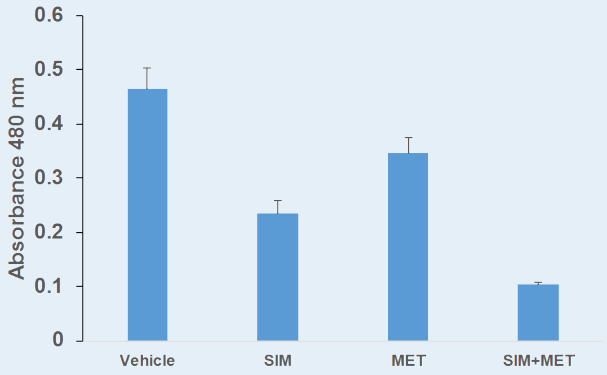


Combination SIM and MET ameliorates metabolic aberrations of CRPC cells



Combination SIM and MET inhibits cell migration & Invasion in CRPC cells





Combination SIM and MET causes cell cycle arrest in the G0-G1 phase in CRPC cells

22Rv1 cells	Control	SIM (4μM)	MET (2mM)	SIM+MET
G0-G1 phase	44.95%	70.90%	47.61%	75.64%
G2-M	18.81%	11.05%	21.42%	8.80%
S	36.42%	18.05%	30.97%	15.56%

Combined action of SIM and MET may be an effective regimen for treatment of ENZU-resistant tumors. This opens new therapeutic modality for castration-resistant prostate cancer patients.